NEW RESEARCH

NEW RESEARCH ABSTRACTS

AMERICAN PSYCHIATRIC ASSOCIATION

2002 ANNUAL MEETING

ABSTRACTS

Philadelphia, PA ■ May 18-23, 2002

NR1 Monday, May 20, 9:00 a.m.-10:30 a.m.

Mental Health of Detained Asylum Seekers

Allen S. Keller, M.D., *NYU School of Medicine, 125 Montclair Avenue, Montclair, NJ 07042*; Douglas Ford, J.D., Chris Meserve, M.D., Chau N. Trinh, Hawthorne Smith, Kathleen M. Allden, M.D., Barry Rosenfeld, Ph.D.

Summary:

Background: Asylum seekers arriving in the United States without documentation are likely to be held in detention by the Immigration and Naturalization Services for months or years pending adjudication of their asylum claims. Concerns have been raised that the experience of detention is further traumatizing these individuals. No studies, however, have been conducted to formally evaluate their mental health.

Methods: A longitudinal study of 46 asylum seekers detained in the New York City area was conducted. The Hopkins Symptoms Checklist 25 and the Harvard Trauma Questionnaire were used to evaluate symptoms of anxiety, depression and PTSD. At follow-up, 26 and 20 were detained and released, respectively.

Results: 75% of participants reported a history of torture in their native country. At baseline, 74% of detainees suffered from anxiety, 83% depression and 47% PTSD. At follow-up, detained individuals were significantly more likely to suffer from higher psychological morbidity than those who were released: anxiety (92% vs. 35%), depression (96% vs. 35%), and PTSD (61% vs. 10%) ($p < .001$).

Conclusion: Detained asylum seekers have high levels of anxiety, depression and PTSD. Distress levels decreased markedly among those who were released from custody but increased among those who remained in custody. Detention appears to be a contributing factor to this psychological distress.

NR2 Monday, May 20, 9:00 a.m.-10:30 a.m.

Utility of Mood Disorder Questionnaire and Bipolar Spectrum Diagnostic Scale

Christopher J. Miller, *Department of Psychiatry, Cambridge Hospital, 1492 Cambridge Street, Cambridge, MA 02139*; S. Nassir Ghaemi, M.D., Jeffry Klugman, M.D., Douglas A. Berv, M.D., Ronald W. Pies, M.D.

Summary:

Objective: To assess the sensitivity and/or specificity of two self-report questionnaires for bipolar disorder, the Mood Disorder Questionnaire (MDQ) and the Bipolar Spectrum Diagnostic Scale (BSDS), a newly designed scale.

Methods: 1) The MDQ was administered to 37 consecutive patients with bipolar illness, 16 also received the Scale to Assess Unawareness of Mental Disorder (SUMD) to measure insight.

2) The BSDS was administered to 73 consecutive patients with bipolar illness and 20 consecutive patients with unipolar major depressive disorder. Created by Ronald Pies, it consists of a description that captures subtle features of bipolar illness, to which patients may assent on a sentence-by-sentence basis.

All scales were compared to clinicians' DSM-IV based diagnoses.

Results: 1) Sensitivity of the MDQ was 58%, higher in bipolar I (69%) than bipolar II/NOS (30%, $p = 0.06$). 2 patients with impaired insight had false negative screens.

2) Sensitivity of the BSDS was 81%, equal in bipolar I and bipolar II subjects (77% each). The BSDS identified 85% of unipolar depressed patients as not having bipolar spectrum illness (specificity of bipolar versus unipolar illness was highly significant, $p < 0.0001$).

Conclusions: The MDQ was more sensitive for bipolar I than bipolar spectrum illness and less sensitive in uninsightful bipolar spectrum subjects. In contrast, the BSDS was highly sensitive and specific for bipolar spectrum illness.

NR3 Monday, May 20, 9:00 a.m.-10:30 a.m.

Risperidone Versus Olanzapine in Bipolar Disorder: A 16-Month Outcome

Klara J. Rosenquist, B.S., *Department of Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139*; S. Nassir Ghaemi, M.D., Jacob J Katzow, M.D., Frederick K. Goodwin, M.D.

Summary:

Objective: To compare long-term effectiveness and safety of risperidone versus olanzapine as adjunctive maintenance treatments of bipolar disorder.

Methods: Retrospective chart review of naturalistic treatment in 30 outpatients with bipolar or schizoaffective disorder (Type I = 16, Type II = 2, NOS = 5, and Schizoaffective bipolar subtype = 7) who received risperidone (RIS) or olanzapine (OLN) for at least 3 months, added to at least lithium or valproic acid for depression (n = 7), rapid cycling (n = 10), manic or mixed states (n = 8) and other indications (n = 8).

Results: Risperidone (2.0 mg/d) and olanzapine (8.8 mg/d) were used for a mean of 1.25 years. Medication was continued longer with risperidone (1.7 years) than olanzapine (0.8 years, $p = 0.07$). Mild or better efficacy was similar in both groups (71% for RIS and 73% for OLN). Moderate/marked response trended toward significance with risperidone (4/15, 27% vs. 0/14 with OLN, $p = 0.10$). Weight gain occurred more frequently with olanzapine (60%, mean 10.7 lbs., vs. 13%, $p = 0.02$) and led to drop-outs. EPS was similar and tardive dyskinesia did not occur.

Conclusions: Both agents produced similar mild or better efficacy, but risperidone produced greater moderate/marked benefit. Side effects were similar except for more weight gain with olanzapine. Risperidone-treated patients continued treatment longer.

NR4 Monday, May 20, 9:00 a.m.-10:30 a.m.

Antidepressant Wear Off and Outcomes in Bipolar Versus Unipolar Depression

James Y. Ko, Department of Psychiatry, *Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139*; S. Nassir Ghaemi, M.D., Nicholas J. Kontos, M.D., Claudia F. Baldassano, M.D., Frederick K. Goodwin, M.D.

Summary:

Objective: To determine if patients with bipolar disorder and unipolar major depressive disorder differed in frequency of antidepressant wear-off phenomenon, antidepressant-induced acute mania, depressive relapse after antidepressant discontinuation, and other clinical features.

Methods: We systematically assessed history of antidepressant outcomes in 40 patients with DSM-IV diagnoses of bipolar disorder (I = 26, II = 10, NOS = 4) and 38 unipolar major depressive disorder patients.

Results: Antidepressant wear-off was noted in 23/40 (58%) bipolar patients, compared with 7/38 (18%) unipolar patients ($p < 0.0001$). Fluoxetine was most associated, and paroxetine least associated with wear-off among antidepressants; TCAs and SSRIs as classes did not differ. Antidepressant-induced mania was present in 21/40 (53%) bipolar patients, and 0/38 unipolar patients ($p < 0.00001$). SSRIs and TCAs had similar acute switch rates (17–24%). Depressive relapse after antidepressant discontinuation was more frequent in unipolar (7/12, 58%) than in bipolar disorder (6/36, 17%; $p = 0.009$). Treatment resistance to therapeutic trials was more common in bipolar (20/40, 50%) than unipolar

depression (12/38, 28%), but did not reach statistical significance (p = 0.11).

Conclusions: Patients with bipolar disorder were more likely to experience antidepressant wear-off, and antidepressant-induced mania, but less likely to experience relapse into depression after antidepressant discontinuation than a comparison group of patients with unipolar depression. Bipolar patients may be more likely to have a history of antidepressant nonresponse.

NR5 Monday, May 20, 9:00 a.m.-10:30 a.m.

Marital Rates, Gender, and Age of Onset Among Brazilian Patients with OCD

Luana M. Miller, *Department of Psychology, SUNY at Buffalo, 266 Highland Parkway, #6, Buffalo, NY 14223*; Joanne Davila, Ph.D., Michelle T. Pato, M.D., Euripedes C. Miguel, Ph.D.

Summary:

Objective: Investigated associations between age of onset, gender, and marital status among Brazilian OCD patients to examine whether decreased marital rates are most evident among early onset males cross-culturally.

Method: A naturalistic epidemiological study of the marital status of 124 OCD patients seen in a Brazilian OCD specialty program. Data included gender, OCD age of onset (when OC symptoms started), and marital status.

Results: Among participants who were 18 years or older at intake (n = 106), 64% were never married, 32% were married/cohabiting, and 4% were divorced/separated. This is consistent with results from US and European studies, which indicated that between 60%–70% of OCD patients remain unmarried. In addition, male OCD patients were more than twice as likely to remain unmarried compared to females, and patients who were never married had a significantly earlier age of onset compared to married/cohabiting patients. Males were found to have an earlier age of onset (m = 12.91 years, sd = ±8.5) than females (m = 14.75, sd = ±10.9). Additional data on association between OCD symptom severity and romantic dysfunction will also be presented.

Conclusions: As expected, decreased marital rates among males and early onset patients appear constant across cultures. Our results suggest that OCD may cause interference with the development of romantic relationships and marriage, particularly among men and people with an early age of onset.

NR6 Monday, May 20, 9:00 a.m.-10:30 a.m.

Individual Religious Activity and Frequency of Suicide Attempts

Bogdan P. Sasaran, M.D., *University Hospital, SUNY Stony Broob T10 Room 020, Stony Brook, NY 11794*; Shereen A. Morse, M.D., Shereen A. Morse, M.D., Margaret Relja, M.D., Robert Southard

Summary:

Introduction: Although there have been many reports about the role of religion in psychiatry and particularly in suicide, these issues remain vague and often overlooked during emergency evaluations. Religion seems to be a protective factor, however, intensity of religiosity in suicidal patients needs further research.

Method: We reviewed the charts of 36 suicidal, non-psychotic patients that were evaluated in our emergency services. A case-control study (N = 28) was done to correlate the number of suicide attempts with religious activity.

Results: The patients that exhibited suicide attempts (SA), (77.7%), were divided in: group A (n = 14) with single SA, and group B (n = 14) with multiple SA. Being male and non-religious was associated with increased numbers of attempts (OR 6.2), even when the groups were mixed with suicidal patients with no attempts (n = 8), (OR 2.5). Passive religiosity was associated with an increased risk of having multiple SA (OR 2.6) when compared to active religiosity.

Conclusion: Sustained religious activity in non-psychotic, suicidal patients was associated with decreased number of suicide attempts. Non-religious males are at increased risk to present with multiple suicide attempts. These new and preliminary data will be used in our ongoing research and suggest that an interdisciplinary approach should be considered.

NR7 Monday, May 20, 9:00 a.m.-10:30 a.m.

Religious/Spiritual Coping and Outcome in Hospitalized Adolescents

Francis F. Hayden II, M.D., *Department of Psychiatry, NYU School of Medicine, 550 First Avenue, NB2156, New York, NY 10016*; Raul R. Silva, M.D.

Summary:

Objective: There are few studies that examine the relationship between mental health and religiosity. This study was designed to explore the relationship between adolescent religious and spiritual beliefs and outcome.

Method: 15 consecutive patients admitted to the adolescent psychiatric inpatient unit were screened. Diagnoses were based on DSM-IV. Measures: 1) Brief Multidimensional Measure of Religiousness/Spirituality 2) The Addressing of Spiritual Religious Issues scale 3) Relevance of SRI scale. *Outcome measures:* Length of stay (LOS), the Children's Global Assessment Scale (CGAS). Statistical analyses proceeded from descriptive statistics to a series of multiple regression analyses (MRA).

Results: Subjects' ages ranged from 12–17 years (mean = 14.6 ± 1.78), 9 were female. Ethnic distribution: African American, 28.6%, Hispanic, 14.2%, Asian, and 7.1% Caucasian. DSM-IV diagnoses: Depressive Disorders 42.9% (N = 6), Psychotic Disorders 35.7% (N = 5), and Disruptive Behavior Disorders 21.4% (N = 3). Mean admission CGAS: 28 ± 8.0, Mean change in CGAS: 24 ± 8.1, Mean LOS: 56 days ± 59.9.

Three factors correlated with changes in functioning. Daily spiritual experiences (p = .014, B = –0.795), and negative spiritual and religious coping (p < .0001, B = –0.902) were inversely related to change in CGAS. While positive religious coping was correlated with improvement in CGAS (p = 0.01, B = 0.750).

Only relevance of religious and spiritual issues to the present illness was significantly correlated (p = .001, 2 = .799) with LOS.

Conclusions: Greater levels of religious and spiritual coping are associated with improved outcome in psychiatrically hospitalized adolescents. Future studies should assess if these findings are generalizable to less severely ill adolescents.

NR8 Monday, May 20, 9:00 a.m.-10:30 a.m.

Decisional Capacity of Severely Depressed Individuals Requiring ECT

Maria I. Lapid, M.D., *Department of Psychiatry, Mayo Clinic, 200 First Street SW, Rochester, MN 55905*; Teresa A. Rummans, M.D., Kristine L. Poole, M.D., Keith G. Rasmussen, M.D., V. Shane Pankratz, Ph.D., Kemuel L. Philbrick, M.D., Paul S. Appelbaum, M.D.

Summary:

Objective: The decisional capacity of depressed individuals frequently comes into question. We aimed to determine the decisional capacity to consent to treatment in severely depressed individuals requiring electroconvulsive therapy (ECT), and assessed whether or not educational interventions improve their ability to provide informed consent.

Methods: Forty subjects with major depression requiring ECT were recruited. Decisional capacity was assessed using the MacArthur Competence Assessment Tool for Treatment (MacCAT-T), which was administered before a standardized education (videotape). Subsequently subjects were blindly randomized to either receive further education or not. The MacCAT-T was re-administered following these educational interventions.

Results: At baseline, there was no difference in the decisional capacity between the experimental and control group. Following the educational interventions, there was improvement in all areas of decisional capacity (understanding $p < 0.001$, reasoning $p < 0.001$, appreciation $p = 0.031$, choice $p = 0.006$), however, the standard group performed as well as the experimental group. Psychotic individuals scored lower than the nonpsychotic group on the initial appreciation scale ($p = 0.014$), and on the final reasoning ($p = 0.020$) and appreciation ($p = 0.005$) scales.

Conclusion: Our findings demonstrate that severely depressed individuals have decisional capacity to give informed consent. Education improves the decisional capacity of this population. There is an endpoint beyond which additional educational intervention does not result in further improvement in decisional capacity.

NR9 Monday, May 20, 9:00 a.m.-10:30 a.m.

Reduced Platelet 5-HT Content in Aggressive Personality-Disordered Subjects

Joseph S. Goveas, M.D., *University of Chicago, 5841 South Maryland Avenue, MC3077, Chicago, IL 60637*; Emil F. Coccaro, M.D., John G. Csernansky, M.D.

Summary:

Objective: The objective of this study was to test the hypothesis that platelet 5-HT content is correlated with measures of impulsive aggression in healthy human subjects.

Methods: Platelet 5-HT content (ng/mg protein) was measured in Personality Disordered (PD) and normal control (NC) subjects. Aggression and impulsivity was assessed by Life History of Aggression (LHA), Barratt Impulsiveness Scale (BIS-11) and by Integrated Research Criteria for Intermittent Explosive Disorder (IED-IR).

Results: LHA Aggression, but not BIS-11 Impulsivity, scores correlated with platelet 5-HT content in all subjects ($r = -.27$, $n = 88$, $p = .012$) and in PD subjects alone ($r = -0.34$; $n = 63$, $p = .007$). PD subjects with IED-IR had lower platelet 5-HT content compared with Non-IED-IR PD subjects (941 ± 135 vs. 1431 ± 115, $t_{74} = 2.63$, $p = .01$). These findings were not accounted for by differences in age or gender.

Conclusions: This study demonstrates an association between reduced platelet 5-HT content and aggression in personality-disordered subjects both dimensionally and categorically as in patients with IED. Similar to other studies of platelet 5-HT markers, these data suggest that platelet 5-HT content may also reflect central 5-HT alterations and may be used as a biological marker in appropriate patient samples.

NR10 Monday, May 20, 9:00 a.m.-10:30 a.m.

Beyond Blue: The National Depression Consumer Empowerment Initiative

Bernard G. McNair, R.N., *Beyond Blue, 91 Milton Street, Ashfield NSW 2131, Australia*

Summary:

Introduction: beyondblue: the National Depression Initiative was established in Australia in November 2000. One of beyondblue's key goals is to increase community awareness of depression and destigmatise the illness and examine new approaches to treatment. To achieve these goals, beyondblue has actively engaged in a number of community based activities.

Hypothesis: beyondblue hypothesises that by increasing community awareness of depression and collaborating with consumers and the community at large, that the stigma of depression can be lessened. Further, direct contact with consumers will enable specific treatment needs/expectations to be identified and integrated into treatment practices.

Methods: A series of community meetings (2000 participants - N = 2000) and focus groups (60 participants - N = 60), have been conducted and data has been collected.

Results: After one year beyondblue has a 22% recognition in the Australian community. The information from focus groups has offered clear indications of what consumers expect/want from care providers.

Conclusion: beyondblue has, in short time, made positive impact upon stigma in the Australian Community. The data collected from focus groups is enabling beyondblue to design new treatment approaches for general practioners and other primary care settings.

Discussion: This paper will discuss in depth the findings of the focus groups, and discuss initiatives with which beyondblue is involved in the areas of destigmatisation and consumer empowerment.

NR11 Monday, May 20, 9:00 a.m.-10:30 a.m.

Stereotactic Surgery for OCD: A Systematic Review

Antonio C. Lopes, M.D., *Federal University Sao Paulo, AV Ministro Oswaldo Aranha 150A.11, Sao Bernardo Campo 09626-000, Brazil*; Jose A. Del Porto, M.D.

Summary:

Objective: we aimed to develop a systematic review to investigate whether stereotactic neurosurgery offers benefits for the treatment of obsessive-compulsive disorder (OCD).

Methods: we identified all studies about surgery for OCD in various databases (MEDLINE, EMBASE, LILACS, PsycLit, OC Database, Cochrane Library, Biological Abstracts). Studies were categorized among randomized controlled trials (RCT), prospective (PS) or retrospective studies (RS). Case reports were excluded. We evaluated their methodological quality, intention to treat analysis, inclusion/exclusion criteria, description of pre-surgical therapies, evidence of refractoriness, cognitive/personality changes, neuroimaging techniques, long-term follow-up, ethical aspects, symptom/global changes and adverse events/complications.

Results: thirty studies were identified among four techniques: anterior cingulotomy (ACI), anterior capsulotomy (ACA), subcaudate tractotomy (ST) and limbic leucotomy (LL). We found 2 RCTs only, 25 PS and 3 RS. Global postoperative improvements ranged from 27–56% (ACI), 56–100% (ACA), 33–67% (ST) and 41–69% (LL) of patients. There were isolated convulsions, headaches, delirium, urinary retentions and intracerebral hemorrhages. Behavioral/personality changes were rarely observed. Mortality involved primarily suicide. Inclusion, exclusion, refractoriness criteria and comorbidity were not usually described.

Conclusions: there is still no evidence whether surgery for OCD offers a real benefit. More RCTs must be conducted.

NR12 Monday, May 20, 9:00 a.m.-10:30 a.m.

Pathological Gambling and its Relationship to the Impulsive-Compulsive Spectrum

Hermano Tavares, Ph.D., *Department of Psychiatry, University of Calgary, Addiction Center, 1403 29th Street, NW, Calgary, AB T2N 2T9, Canada*; Valentim Gentil, M.D.

Summary:

Background: Pathological Gambling (PG) is referred as compulsive sometimes as impulsive. Recently, PG was included on an Impulsive-Compulsive spectrum (ICS) of OCD-related disorders. In the ICS, disorders are placed along a unidimensional axis, ranging from a compulsive pole to an impulsive pole.

Objectives: (1) to investigate the relationship between PG and OCD by comparing Axis I and II features; (2) to investigate the correlation between Impulsivity and Compulsivity.

Methods: 40 gamblers, 40 OCD patients, and 40 normal control volunteers matched by gender, age, and educational level answered the *Schedules for Clinical Assessment in Neuropsychiatry,* the *Temperament Personality Questionnaire,* and the *Barratt Impulsiveness Scale* version 11.

Results: PG presented a higher association to substance dependencies, while OCD presented a higher association to somatoform disorders. Gamblers scored higher than OCD and controls on impulsivity, as for compulsivity OCD scored highest, but PG still scored higher than controls. Impulsivity and Compulsivity measures were independent for all samples.

Conclusions: PG's associations with substance dependence suggest that mixed impulsivity and compulsivity traits of personality could be a factor associated to addictive behaviors. Impulsivity and Compulsivity seem independent constructs, therefore authors propose another representation for the ICS on a bidimensional graphic with 2 orthogonal axis.

Support: The State of Sao Paulo Research Funding Agency, Brazil

NR13 Monday, May 20, 9:00 a.m.-10:30 a.m.

Alcohol Abuse Increases Suicidality and Psychosis in Mania

Alexander H. Fan, M.D., *Department of Psychiatry, UCLA, 300 Medical Plaza #1544, Los Angeles, CA 90095*; Mark A. Frye, M.D., Susan J. Masseling, M.S., Michael J. Gitlin, M.D., Sun Hwang, Ph.D., Lori L. Altshuler, M.D.

Summary:

Previous studies have indicated that a past history of alcohol abuse complicates the recovery from a manic episode. This retrospective study assessed the effect of recent alcohol abuse on treatment response for mania. Treatment response was evaluated by the hospital length of stay with a blind CGI of very much improved and much improved. Medical records of 40 manic patients (ages 18–45) hospitalized at UCLA Neuropsychiatric Institute from 1988–1992 were reviewed. Clinical and demographic information was harvested from medical records. AMA discharges were excluded as they were viewed as potential confounds for attenuating hospital length of stay. 10 of 40 (25%) patients met DSM-IV criteria for alcohol abuse or alcohol abuse in early remission. Preliminary analysis revealed that 6 of 10 alcoholic manics endorsed suicidality on hospital admission compared to 3 of 30 non-alcoholic manics ($p < 0.001$, $t = 3.74$, $df = 38$). The data also revealed that 9 of 10 alcoholic manics had psychotic symptoms on hospital admission compared to 14 of 30 non-alcoholic manics ($p < 0.016$, $t = 2.53$, $df = 38$). However, there was no statistical difference in length of hospital stay of alcoholic manics (mean 18.2 days) compared to non-alcoholic manics (mean 17.2 days). This data suggests that alcohol abuse increases the risk of psychosis and suicidal ideation in manic patients.

NR14 Monday, May 20, 9:00 a.m.-10:30 a.m.

Ages of Onset of Psychiatric Disorders in a Sample of Children of Bipolar Parents

Aude L. Henin, Ph.D., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, Suite 580, Boston, MA 02114*; Gary S. Sachs, M.D., Stephanie L. McMurrich, B.A., Louisa D. Grandin, B.A., Robert O. Knauz, Ph.D., Kenneth Park, Ph.D., Andrew A. Nierenberg, M.D.

Summary:

Objective: Children of bipolar patients are at increased risk for developing a wide range of psychiatric disorders, many of which appear before any mood disorders. The purpose of this study was to examine the ages of onset of psychiatric disorders in children of bipolar parents and to compare the relative ages of onset between these children and their parents.

Methods: We conducted structured diagnostic interviews of 55 children of 33 patients with bipolar disorder. Children under 18 were assessed using the KSADS-E. Children 18 and above and parents were assessed using the SCID and childhood disorder modules from the KSADS.

Results: The sequence of disorder onset for children and their parents was similar, characterized by sleep difficulties, elimination disorders, and disruptive disorders in early childhood, followed by anxiety disorders, mood disorders, and psychotic symptoms, and in early adulthood, the onset of substance use disorders. However, children had significantly lower ages of onset for anxiety disorders, depression, mania/hypomania, and psychosis, (e.g. mean ages of onset for depression were 10.1 and 19.6 for children and parents, respectively and 14.2 for mania/hypomania for children, compared to 23.7 for their parents).

Conclusion: The children of bipolar parents have an earlier onset of psychopathology compared to their parents.

NR15 Monday, May 20, 9:00 a.m.-10:30 a.m.

Comparison of African Americans and Caucasians Entering the Systematic Treatment Enhancement Program for Bipolar Disorder

Marketa M. Wills, M.D., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, Suite 580, Boston, MA 02114*; William B. Lawson, M.D., Jacqueline Ogutha, B.A., Leslie J. Yan, B.A., Jacki Flowers, B.A., Andrew A. Nierenberg, M.D., Gary S. Sachs

Summary:

Objective: The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) is a large multi-center NIMH study that assesses, and treats, patients for bipolar disorder in clinical practice settings rather than typical research programs. Clinical trials typically accession samples with few African-Americans, raising questions of the generalizability of these studies to African-Americans seeking treatment. This report compares characteristics of African-Americans entering STEP-BD to Caucasians.

Methods: STEP-BD collects demographic and clinical data using a battery of standardized evaluation procedures on study entry. At every visit subjects are assigned one of eight operationally defined clinical states based on the DSM criteria for acute episodes, subsyndromal states (continued symptomatic or roughening), and euthymic (recovering, recovered).

Results: Preliminary analysis found no statistically significant differences. Trends indicate the sample of African-Americans had a higher proportion of females (80.0% vs. 58.4%, Mantel-Haneszel chi-square, $p < 0.062$), a lower proportion entered euthymic (33.3% vs. 52.3%, Fisher's Exact $p < 0.056$), but nearly identical proportions of Bipolar I and BP II subtypes as that observed in the Caucasian sample.

Conclusion: African-Americans comprise only about 5% of the first 500 STEP-BD subjects. A larger sample is required to determine if apparent differences result from accession bias or represent true differences attributable to race.

NR16 Monday, May 20, 9:00 a.m.-10:30 a.m.

Stigmatizing Attitudes More Related to Psychotic Versus Depressive Behaviors

Matthew Schumacher, B.A., *Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94305-5723*; Patrick Corrigan, Psy.D., Terence A. Ketter, M.D.

Summary:

Background: Researchers distinguish between overt (i.e. gender, ethnicity) and potentially covert (i.e. religion, sexual orientation) stigma. The former arise from obvious, the latter from more subtle markers. A member of the latter group, mental illness stigma can yield public perceptions of dangerousness and threat, and need for social avoidance. Markers eliciting stigmatizing attitudes (STIGMATT) remain to be examined.

Method: 117 community participants rated narratives describing men exhibiting psychotic behaviors ("speaking incoherently and loudly, head and eyes moving as if looking for someone") versus depressive behaviors ("sad, moving slowly, not talking"); and having dirty versus clean appearances. Subjects rated perceived dangerousness, threat, and desire to avoid on Likert scales. Impact of psychotic versus depressive behaviors and dirty versus clean appearances on STIGMATT were compared.

Results: Psychotic, compared to depressive, behaviors elicited robustly (64–87%) higher perceived dangerousness, threat and social avoidance. In contrast, dirty compared to clean appearances tended to elicit only modest (5–15%) STIGMATT Increases.

Conclusion: Psychotic, compared to depressive, behaviors elicited markedly greater STIGMATT, which represent important targets for stigma-reduction. Assessment of protocols to reduce STIGMATT related to psychotic behaviors is warranted, including community interventions (i.e. educational programs to modify community perceptions) and clinical strategies (i.e. behavioral/ pharmacological treatments to attenuate patients' psychotic behaviors).

This study was completed, in part, to fulfill the first author's requirements for his Master's Degree at the University of Chicago. Efforts of the second author were supported by NIMH.

NR17 Monday, May 20, 9:00 a.m.-10:30 a.m.

Comorbidity of Panic Disorder with Depression and Other Anxiety Disorders

Patrick Ying, M.D., *NYU School of Medicine, 538 First Avenue, #7D, New York, NY 10016*; Eric D. Peselow, M.D., Gonzalo Laje, M.D., Mary Paizis, M.D. Mary T. Guardino, B.A.

Summary:

Objective: The purpose of this paper is to evaluate the comorbidity of panic disorder with other anxiety disorders, (OCD, social & specific phobias, generalized anxiety disorder) & depression in order to assess frequency of comorbid diagnosis

Method: Over the past 8 years, at the Freedom from Fear Clinic in Staten Island N.Y. (an outpatient anxiety disorder clinic associated with Columbia University) we have evaluated 213 patients who were diagnosed with panic disorder using a modified symptom check list adapted from the SCID during the acute stage of the illness. In addition using the modified SCID, at this same point, we also determined whether the patients met DSM-IV criteria for GAD, agoraphobia, social & specific phobia, OCD and depression.

Results: Overall only 63 of the 213 patients (29.6%) of the sample met criteria for a single diagnosis (one of the four other anxiety disorders or depression). 142 of the 213 patients met criteria for panic with agoraphobia (66.7%). Comorbidity of panic was as follows:

Panic with depression.....122/213 (57.3%)
Panic with social phobia.....62/213 (29.1%)
Panic with specific phobia.....28/213 (13.1%)
Panic with OCD.....79/213 (37.1%)
Panic with GAD.....129/213 (60.6%)

Conclusion: Overall the diagnosis of panic disorder was associated with a high rate of comorbidity. The greater the number of anxiety diagnoses the poorer the response to treatment of the panic disorder. Implications of these findings will be discussed

NR18 Monday, May 20, 09:00 a.m.-10:30 a.m.

Effects of Sex Hormone Changes on Women with Trichotillomania

Marc M. Solomon, B.A., *Clinical Science Laboratory, National Institute on Mental Health, 1820 Chicago Avenue, #4036, Evanston, IL 60201*; Marla A. Wax, M.A., Mark J. Smith, M.D.

Summary:

Introduction: Symptom aggravation or improvement during hormonal change can offer valuable information about a disorder's pathophysiology. Trichotillomania (TTM) has often been included in the Obsessive-Compulsive Disorder (OCD) Spectrum, although it lacks many OCD characteristics such as an equal sex ratio. We hypothesized that if TTM belongs to this spectrum, when sex hormonal levels change the effects on symptoms should be similar in TTM and OCD.

Method: Individuals with self-identified TTM completed a self-reported questionnaire on effects of hormonal conditions on TTM symptoms including ovulation, premenstrual phase, menarche, perimenopause, pregnancy, oral contraceptives, hormone replacement therapy, and selective estrogen response modifiers (SERMs) and were compared to a group of OCD patients rating effects of these same conditions on OCD symptoms. For each condition, subjects could respond 'not applicable,' 'no effect,' 'improved symptoms' or 'aggravated symptoms'. Improvement rates were calculated as the difference in percentage of improved minus worsened subjects, and rates >30% indicated a favorable result.

Results: For TTM results were favorable (in descending order) for pregnancy and SERMs, whereas none were for OCD. Premenstrual period, menarche, ovulation, perimenopause and menarche all aggravated TTM symptoms whereas only premenstrual phase aggravated OCD symptoms.

Conclusion: This suggests greater sensitivity to both positive and negative effects of female sex hormones in TTM.

NR19 Monday, May 20, 09:00 a.m.-10:30 a.m.

Thyroid Function in Early-Onset Versus Late-Onset 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., Richard J. Fonte, M.D.

Summary:

Introduction: Little data is available for comparison of thyroid function in early versus late onset depression.

Method: A retrospective chart review was conducted for all 946 patients admitted to a geriatric psychiatry unit over a two year period. Admission thyroid function tests were reviewed for 65 patients with late onset depression and 61 patients with early onset depression. Late onset depression was defined as first onset of depression after the age of 60. Early onset was defined as first onset of depression before the age of 60. 9 out of 61 early onset patients were bipolar depression and 7 out of 67 late onset patients were bipolar depression. All patients' TSH(thyroid stimulating hormone) and EFT (estimated free thyroxine) were analyzed with t test and chi square for significance.

Results: Early onset: 7% with TSH less than 1, 25% with greater than 3 but less than 5, 7% with greater than 5 and 6]% with normal level between 1–3. Late onset: 7% with TSH less than 1, 15% with TSH less than 5 but greater than 3, 9% greater than 5 and 69% with TSH 1–3. Females predominate in both early and late onset depression: 78% and 86% respectively. 70% of patients with late onset bipolar depression has TSH of less than 1. No significant difference ($p = 0.4$) in TSH and EFT levels in early vs late onset depression.

Conclusion: There is no significant difference in thyroid function between early and late-onset depression. Females predominate in both early and late onset depression. There is a preponderance of low TSH levels in patients with late onset bipolar depression which require further investigation.

NR20 Monday, May 20, 9:00 a.m.-10:30 a.m.

Nutrition and Insulin Use in Individual with Insulin-Dependent Diabetes

Teresa E. Hermida, M.D., *Department of Psychiatry, Cleveland Clinic, 5912 Haverford Dr, Cleveland, OH 44124-2710*; Donald Malone, M.D., Sethu Reddy, M.D.

Summary:

Objective: Insulin dependent diabetic females are at increased risk for developing eating disorder symptoms (1, 2). The aim of our research was to determine the prevalence of eating disorder symptoms and the level of nutritional knowledge in an outpatient population of insulin dependent diabetics at a tertiary care facility.

Method: Participants were 278 adults and adolescents aged 12–90 years coming for follow-up appointments at an outpatient specialty clinic. We collected demographic information, diabetes history, current height, weight and desired weight, nutritional knowledge, and current nutritional habits via a questionnaire.

Results: Insulin reduction and/or omission for the purpose of weight control occurred in 12.2% of the sample. While the majority of insulin reducers were female, 9.8% of the males had engaged in this behavior, 50% of whom were aged 51 and older. None of the adolescent females acknowledged such behavior. Of the insulin reducers, 55% of the females and 57% of the males reported 1 or more concurrent behavior of disordered eating and/or excessive exercise. There was found to be no correlation between educational level and level of nutritional knowledge.

Conclusions: This data reveals that disordered eating in the insulin dependent population is not restricted to the young female population.

NR21 Monday, May 20, 9:00 a.m.-10:30 a.m.

Vagus Nerve Stimulation Shows Benefits in Treatment-Resistant Depression for up to Two Years

James M. Martinez, M.D., *Department of Psychiatry, Baylor, 6655 Travis Road Suites 560, Houston, TX 77030*; Mark S. George, M.D., A. John Rush, M.D., Harold A. Sackeim, Ph.D., Lauren B. Marangell, M.D.

Summary:

Background: Vagus Nerve Stimulation (VNS) has shown promising antidepressant effects in an open, acute phase pilot study of adults in a treatment-resistant major depressive episode (Rush et al, 2000, Sackeim et al, 2001). This naturalistic follow-up study was conducted to determine whether the initial promising effects were sustained up to a two-year period, and whether changes in function would be observed.

Methods: Sixty adult outpatients with chronic or recurrent depression in a treatment-resistant, non-psychotic major depressive episode received up to two years of VNS Therapy™ following the 3-month acute study. Changes in psychotropic medications and VNS stimulus parameters were allowed during the long-term study. A priori definitions were used to define response [greater than or equal to 50% reduction in baseline Hamilton Rating Scale for Depression (HRSD28) total score] and remission [(HRSD28 less than or equal to 10)].

Results: Following acute study exit and after one year of VNS Therapy™ response rates increased from 31% to 45% ($p = 0.08$) and remission rates showed statistically significant improvements from 15% to 27% ($p = .04$). In the first cohort of 30 patients, improvements in depressive symptoms were sustained in acute study responders after 2 years of VNS Therapy™, and significant improvements ($HRSD_{528}$ reduction = 26%) were observed in acute study non-responders.

Conclusions: In this cohort of 60 patients with chronic or recurrent treatment-resistant depression, long-term (up to 2 years) VNS Therapy™ was associated with statistically significant improvement in depressive symptoms and sustained or enhanced functional status in this naturalistic follow-up study.

NR22 Monday, May 20, 9:00 a.m.-10:30 a.m.

Comparing Two Measures of Eating Restraint in Bulimic Women Treated with Cognitive-Behavior Therapy

Debra L. Safer, M.D., *Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94305-5722*; W. Stewart Agras, M.D., Susan Bryson, M.S.

Summary:

Objective: To examine in detail changes in dietary restraint patterns obtained from two different measures in a large sample of women with bulimia nervosa (BN) who completed 18 weeks of Cognitive Behavioral Therapy (CBT).

Method: 194 women with BN were offered manualized CBT. Of these, 134 completed treatment and pre and post-treatment dietary restraint assessments from the Eating Disorders Examination (EDE) and Three-Factor Eating Questionnaire (TFEQ). The TFEQ Cognitive Restraint scale was further analyzed into its Flexible and Rigid Control subscales.

Results: There was a statistically significant post-CBT reduction in the EDE Restraint subscale ($p < 0.001$) but not in the overall TFEQ Cognitive Restraint score. There was a significant reduction in the TFEQ Rigid Control ($p = 0.006$) but not Flexible Control. Item by item analysis of the Rigid Control subscale revealed the greatest effect from a decreased preoccupation with small weight gains.

Conclusions: Reduced dietary restraint, a prominent mediator of post-treatment improvement in BN, can be meaningfully assessed by self report measures. Significant decreases in the restraint measures in the EDE, but not in the TFEQ in relation to treatment outcome suggest that these scales capture different aspects of the dietary restraint concept. Implications of these differences in terms of the mechanism and outcome of CBT are presented.

NR23 Monday, May 20, 9:00 a.m.-10:30 a.m.

Gender and Medical Temporal Volumes in Normal and Depressed Subjects

Vasundhara Kalasapudi, M.D., *76-22 265th Street, New Hyde Park, NY 11040*; Elisse Kramer-Ginsberg, Ph.D., Manzar Ashtari, Ph.D., Blaine S. Greenwald, M.D., Jian Hu, M.D., Houwei Wu, M.D., Mahendra C. Patel, M.D.

Summary:

Objective: Age, gender, and presence of depression have been implicated in brain medial temporal lobe structure volumes, however a limited number of studies have reported inconsistent re-

sults. As such, the purpose of this study was to compare hippocampal and amygdala volumes in female versus male older normal and depressed subjects.

Methods: Elderly normal control (n = 46; 28 women, 18 men) and DSM-IIIR unipolar depressed (n = 42; 30 women, 12 men) subjects participated in an MRI study (Siemens Magnetom 1.0T). Brain images were obtained in the coronal plane and input onto a SUN workstation for volumetric analysis. Utilizing established anatomic guidelines for structure delineation, volumetric measurements were completed by the same operator under blinded conditions using a menu-driven, semi-automated computer mensuration system with patients and controls in random order. For this study, measurements included left and right posterior hippocampus and anterior hippocampus-amygdala complex.

Results: Prior analysis reported no differences between depressed vs. control subjects, and total (depressed + control) female vs. male subjects when height was covaried employing analysis of covariance (ANCOVA). In the present study, ANCOVA adjusting for age and height revealed no differences between women and men in medial temporal structure volumes in normal controls, however in the depressed group, left (p = .031), right (p = .014), and total (p = .012) anterior hippocampus-amygdala complex were significantly smaller in women as compared to men.

Conclusions: In elderly subjects, presence of depression was associated with significant gender-based differences in a medial temporal brain region implicated in memory, emotion and learning. These data suggest (a) the importance of gender as a variable in brain investigations of neuropsychiatric illness; and (b) the need for further studies that also include concomitant neuroendocrine variables.

NR24 Monday, May 20, 9:00 a.m.-10:30 a.m.

Menstrually Related Somatic Changes in Women with Bipolar Disorder

Figen Karadag, M.D., *Mood Disorder Unit, Bakirkoy State Hospital, Cemil Topuzlu C 103/6 Caddebostan, Kadikoy, IS 81060, Turkey*; Fisun Akdeniz, M.D., Evrim Erten, M.D., Sebnem Pirildar, M.D., Basak Yucel, M.D., Aslihan Polat, M.D.

Summary:

Objective: The aim is to compare the spectrum of premenstrual complaints and the rate of premenstrual syndrome among women with bipolar disorder and healthy controls.

Method: The bipolar women on mood stabilizers and controls with no history of medical/mental disorder with regular menstrual cycles were investigated in the study. The exclusion criteria were OC use, any current antipsychotic, anxiolytic, and antidepressant drug use. The subjects filled the Premenstrual Assessment Form (PAF) in the first visit and Daily Records of Severity of Problems (DRSP) prospectively for two months. To evaluate ovulation, the blood obtained for assessing serum progesteron levels. HAMD-17 and YMS were applied during the 19 to 22 days of the current menstrual cycle.

Results: 84 patients and 35 controls completed the study. One patient and one control had diagnoses of PMDD, 10 bipolar women and 12 of the controls had diagnoses of PMS. Controls complained more about premenstrual mood, behavioral changes than patients retrospectively (p = .01 for depressive, p = .001 for hostility, p = .005 for impulsivity subgroups) and prospectively (p = .03 for the premenstrual phase total score, p = .02 for depressive and anger subgroups).

Conclusion: Controls had experienced more mood (depressive and anger) fluctuations during two menstrual cycles. We may suggest that taking mood stabilizing agents may protect bipolar women against premenstrual complaints.

NR25 Monday, May 20, 9:00 a.m.-10:30 a.m.

Ziprasidone-Induced Manila: A Case Series and Review of the Mechanism

Deborah R. Kim, M.D., *Department of Psychiatry, University of Pennsylvania, 3535 Market Street, 2nd Floor, Philadelphia, PA 19104*; Christos A. Ballas, M.D., John Oreardon, M.D., Claudia F. Baldassano, M.D., Moira A. Rynn, M.D., Louis Littman

Summary:

Objective: To report the occurrence of mania induced by ziprasidone, an atypical antipsychotic recently approved by the Food and Drug Administration for the treatment of psychosis, in patients with bipolar disorder.

Method: We report four cases, as a restrospective case review, of ziprasidone-induced mania and to our knowledge these are the first reported for this drug.

Results: In each of the four cases presented, the patients had a manic switch after the addition of ziprasidone to their pharmacologic treatment. The ziprasidone was discontinued or reduced in all cases resulting in a resolution of manic symptoms.

Conclusion: As ziprasidone has substantial serotonergic action, we hypothesize it may be more likely to cause a manic switch than the other atypical antipsychotics. With increasing use of ziprasidone in bipolar disorder this question will become clearer. In addition, if ziprasidone proves to have significant antidepressant effects, it may prove useful in the treatment of affective disorders. We advocate future studies to evaluate ziprasidone's possible antidepressant efficacy and caution clinicians that induction into mania or hypomania is possible with this agent.

NR26 Monday, May 20, 9:00 a.m.-10:30 a.m.

Lifetime Rates of Alcoholism with Anxiety, Depression, or Comorbid Depression

David G. Gratzer, M.D., *Clarke Site, Centre for Addiction, 250 College Street, Toronto, ON M5T 1R8, Canada*; Robert D. Levitan, M.D., Tess Sheldon, M.S.C., Tony Toneatto, Ph.D., Neil A. Rector, Ph.D., Paula N. Goering, Ph.D.

Summary:

Background: It is well established that alcohol abuse/dependence is strongly associated with both major depression and anxiety disorders over the lifespan. Little research has examined the possible confounding effects of co-morbid depression and anxiety in understanding these relationships.

Methods: The sample consisted of 7195 individuals in Ontario, age 15–64, interviewed using the CIDI. Bipolar disorder was excluded. We compared rates of alcohol abuse/dependence in four groups consisting of normal controls, individuals with major depression but no anxiety disorders, individuals with one or more anxiety disorders without depression, and individuals with co-morbid major depression and anxiety. Age of onset of alcoholism in the four study groups was also compared.

Results: In both genders, there were significantly higher rates of alcoholism in all three psychiatric groups relative to controls. In females only, there was also a significantly higher rate of alcoholism in the depressed/anxious group than in the pure anxious group. The age of onset of alcoholism was the same across all four study groups.

Conclusions: While the rate of alcoholism in pure anxiety disorders and pure depression is similar, in females with anxiety disorders, co-morbid depression significantly increases the lifetime risk of alcoholism. Regarding age of onset data, depression and anxiety do not appear to influence the age of onset of alcoholism. Furthermore, no single temporal pattern of onset was identified in individuals with all three disorders.

NR27 Monday, May 20, 9:00 a.m.-10:30 a.m.

Cognitive Information Processing Basis of Dating Abuse

Brooke T. Myers, M.A., *Department of Psychology, fordham University, 440 East Fordham Road, Bronx, NY 10458*; David P. Bernstein, Ph.D., Brent Bounds, M.A., Margaret McClure, M.A.

Summary:

Objective: Young (1999) hypothesized that Early Maladaptive Schemes (EMS's), biased forms of information processing about self and others that originate in childhood, may explain why couples remain in abusive relationships. To test this hypothesis, we presented 21 male and 46 female students with vignettes describing mistreatment of female students by their male dating partners (e.g., verbal or physical abuse).

Methods: Twenty-one vignettes were developed for the study. Participants were asked whether the victimized female in each scenario should stay or leave the relationship and responded on a 4 point Likert scale. Internal consistency of 20 of the "stay or leave" scores was high (alpha=.84). EMS's were assessed by Young's Early Maladaptive Schema Questionnaire and childhood trauma by the Childhood Trauma Questionnaire.

Results: Females were significantly more likely than males to indicate that the female should leave the relationship ($p < 01$). Multiple regression analysis revealed that EMS's and childhood trauma were significantly related to "stay or leave" total scores, and that several of these effects were moderated by gender.

Conclusions: Findings suggest that male and female college students view the mistreatment of female partners differently, and that EMS's and childhood trauma appear to impact these perceptions. Hypothetical dating scenarios appear to be a fruitful means of investigating the cognitive processing basis of dating mistreatment.

NR28 Monday, May 20, 9:00 a.m.-10:30 a.m.

Depression, Seizures, and Quality of Life in Refractory Epilepsy

Lynn A. Flint, B.A., *Department of Neurology, New York University, 550 First Avenue, New York, NY 10016*; Laura S. Boylan, M.D., Stacey C. Jackson, R.N., Daniel L. Labovitz, M.D., Orin Devinsky, M.D.

Summary:

Objective: To analyze the impact of seizure-related variables and depression on quality of life (QOL) in patients with severe epilepsy.

Methods: Data on duration of epilepsy, seizure frequency, number of anticonvulsants (ACD) taken, depression (BDI) and QOL (QOLIE-31) were prospectively collected from patients admitted to an inpatient video-unit.

Results: 62 adults (35 women, mean age 41+/–SD 14 years) were studied. Thirty-one (53%) patients had abnormal BDI scores (22+/–9). Subjects had high seizure burden with mean seizure frequency 38+/–89 per month, duration of seizure disorder 17+/–11 years, and number of ACDs 2+/–1. In univariate analysis, only BDI predicted QOL (beta=–1.17, $p < 0.0001$). Multivariate analysis revealed no confounding by seizure-related variables.

Conclusions: Patients with severe epilepsy have high rates of depression and depression may have a greater impact on QOL than seizure-related factors. Although previous studies reported correlations between seizure frequency and QOL in epilepsy, these studies considered patients with milder illnesses and excluded those with psychiatric comorbidity. Studies in patients with ALS and Parkinson's disease have also reported that QOL is related primarily to psychological factors rather than motor disability. These findings highlight the importance of identification and treatment of depression in people with epilepsy.

(Funding Sources: National Alliance for Research on Schizophrenia and Affective Disorders (LSB), Stanley Foundation (LAF))

NR29 Monday, May 20, 9:00 a.m.-10:30 a.m.

Appetite Changes After September 11th

Svetlana L. Savchenko, M.D., *Psychopharmacology Consultation Service, Saint Elizabeth's Hospital, 2700 MLK Jr. Ave. SE, Smith Center 5th Fl, Washington, DC 20032*; Alvaro Guzman, M.D., Lourdes Castineira, M.D., John W. Stiller, M.D., Joan D. Steil, R.N., Manjula Borge, M.D., Teodor T. Postolache, M.D.

Summary:

Introduction: The psychological trauma of the September 11 disaster extends beyond those who were directly affected. Mood and sleep changes following major disasters have been described, but to our knowledge, there are no published reports on disaster related appetite changes. Previous studies suggest that stress induces changes in eating behavior but the reports on the direction of these changes have been inconsistent (1,2). During an ongoing longitudinal study on seasonal changes in mood and appetite, we happened to capture subjects' responses approximately one month prior, two weeks after and six weeks after September 11. We expected to find a decrease in mood and changes in appetite from before to after September 11.

Methods: A preliminary analysis was performed on 25 foreign nursing students studying in Washington, DC aged 32.8± 6.9 years, with 2(8%) males and 23(92%) females. Subjects had consented to participate in a study on seasonality of mood, approved by the IRB of DC-DMH. Visual analogue scales for mood and appetite were completed in August, end-of-September and October. Data were analyzed using a Friedman ANOVA with post-hoc Wilcoxon tests.

Results: Mood changes were not significant. Appetite changed significantly ($F = 8.61$, $N = 22$, $P = 0.013$), with end-of-September rating significantly lower than both the August rating ($Z = 2.64$, $N = 20$, $p = 0.008$) and October rating ($Z = 1.99$, $N = 18$, $p = 0.047$). Appetite did not differ between August and October.

Conclusion: It is unlikely that the decrease in appetite is due to photoperiodic changes, as, in September, they would be expected to increase rather than decrease appetite. In conclusion, the events of September 11 may have been associated with a transient decrease in appetite in foreign students. Additional data will be analyzed and implications of our findings will be discussed.

NR30 Monday, May 20, 9:00 a.m.-10:30 a.m.

Peritraumatic Memory with Traumatic Injury

Delia Cimpean, M.D., *Dartmouth Medical School, One Medical Center Drive, Lebanon, NH 03756*; Thomas A. Mellman, M.D., Kara Comins, B.S., Victoria Roatta, Psy.D., Karin F. Esposito, M.D.

Summary:

Acquisition of traumatic memory is important in the development of PTSD. Traumatic injury is a common antecedent of PTSD. A variety of factors that accompany traumatic injury may influence memory acquisition.

An objective of our ongoing research is to characterize and determine influences of recall of life-threatening events that produced injuries.

The subjects to date are 21 men and 9 women, mean age-34, admitted to a level I trauma center for injuries related to life-threatening experiences. They were awake and alert when res-

cued and did not have clinical or radiological evidence of brain injury.

Assessment during hospitalization included systematic query of recall of events-from immediately preceding, through the rescue phase of the traumatic incident.

Five of 30 subjects (17%) recalled peritraumatic events without significant gaps while recall was virtually absent in 3 (10%). Two thirds had gaps in their recall of the incident, half of patients had gaps for the forewarning and/or rescue phases. Three patients with limited recall "remembered" events that were not consistent with known facts.

Exposure to acceleration/deceleration forces and presence of bruises or lacerations on the face or scalp were significantly associated with, but did not account for all of the variance in recall. Initial PTSD symptoms were present in 14 (47%) of subjects who represented the full range of degrees of recall.

Determinants of peritraumatic recall and its relationship to PTSD warrants further investigation.

NR31 Monday, May 20, 9:00 a.m.-10:30 a.m.

Clinical Correlates of Premorbid Adjustment in Bipolar Disorder

Carrie L. Ernst, M.D., *Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139*; Joseph F. Goldberg, M.D.

Summary:

Background: Impaired psychosocial functioning has been well-documented in bipolar disorder, although little research has focused on specific outcome dimensions most impacted by poor premorbid adjustment. We retrospectively examined childhood and adolescent adaptation by standardized measures relative to components of outcome in an adult bipolar cohort.

Method: 56 DSM-IV bipolar I and II patients from the Cornell Bipolar Disorders Research Clinic (mean ± SD age = 40.8 ± 12.8 years; mean ± SD lifetime illness duration = 19.1 ± 11.4 years) completed standardized semistructured interviews to assess psychopathology, work performance, global outcome and premorbid social adjustment. Lifetime episodes were rated by the Life Chart Method.

Results: Poor premorbid adolescent adjustment was associated with a heightened risk for lifetime suicide attempts (OR = 0:807, 95% CI = 0.675–0.964) and adult alcohol abuse or dependence (OR = 0.870, 95% CI = 0.763 = 0.992). No significant correlations were found between premorbid adjustment and adult global functioning, work performance, or social adjustment.

Conclusions: Poor premorbid adjustment in bipolar patients may increase the potential to develop substance misuse comorbidities and heighten lifetime suicide risk. However, broader prognostic links between premorbid adjustment and functional outcome may be less robust.

NR32 Monday, May 20, 9:00 a.m.-10:30 a.m.

A Comparison of Self-Ratings and Observer Ratings in Bipolar Patients

Christine J. Truman, M.D., *New York Presbyterian Hospital, 525 East 68th Street, Box 140, New York, NY 10021*; Emily E. McNally, B.A., Joseph F. Goldberg, M.D.

Summary:

Objectives: While the Beck Depression Inventory (BDI) is widely used as a clinical and research tool in evaluating depressive symptoms, no similar scale exists for self-assessment of manic symptoms. The commonly cited concern that manic patients are lacking in insight into their illness and therefore are unable to accurately report their mood or symptoms is largely based on clinical opinion, rather than empiric research. The purpose of this study is to determine the reliability and validity of 3 self-rating mania assessment scales as compared to observer-ratings using the YMRS in all phases of mood episodes in patients with bipolar disorder.

Method: Self-report and observer-rated symptom measures were given to successive bipolar outpatients and inpatients. Assessments included the Altman Self-Report Manic Scale (ASRM), the Self-Report Manic Inventory (SRMI), the Internal State Scale (ISS), the BDI, the YMRS, and the Hamilton Depression Rating Scale-17 (HDRS-17).

Results: Preliminary results (n = 10) show a significant association between the ASRM and the YMRS (r = .82, p = .004) not found between the YMRS and either the SRMI or the ISS. Correlations were diminished among more severely ill manic patients. In contrast, higher correlations between the BDI and the HDRS-17 were observed among more symptomatic depressed patients (r = .90, p = .29) than less depressed patients.

Conclusions: Self-ratings of both manic and depressive symptoms have clear potential as clinical and research tools.

NR33 Monday, May 20, 9:00 a.m.-10:30 a.m.

Wireless Mood Telemetry: The Validity and Reliability of VMQ/VADIS

David M. Kreindler, M.D., *Department of Psychiatry, Sunnybrook Hospital, 2075 Bayview Avenue RM FG-35, Toronto, ON M6G 3L6, Canada*; Anthony J. Levitt, M.D., Charles J. Lumsden, Ph.D., Nicholas Woolridge, M.S.C.

Summary:

Introduction: To improve the state-of-the-art in longitudinal mood symptom self-report, we developed VMQ/VADIS, a 19-item questionnaire based on the visual analogue scale (VAS) with items drawn from the DSM-IV symptoms of mania and depression. VMQ/VADIS is administered on a handheld computer (HHC) to enhance subject compliance, reduce order and orientation bias, and simplify data collection. The HHC's display screen requires a smaller VAS size and digital display on the validity and reliability of the VMQ as compared to the standard VAS.

Method: Twenty-eight naive subjects used both 4cm and 10cm VAS's to indicate when six specified dates occur within the year. Thirty-nine naive subjects then repeated the same task using a 10cm paper VAS and a 4cm HHC-based VAS. To assess test-retest reliability twenty-nine subjects completed the VMQ/VADIS ten minutes apart. Finally, we studied transposition error rates by examining subjects' longitudinal ratings of day length over six months.

Results: VMQ/VADIS has comparable accuracy and validity of the conventional VAS; it also demonstrates excellent test-retest reliability. Transposition errors occurred in 0.4% of reports.

Conclusion: VMQ/VADIS is a valid and reliable tool for longitudinal mood data collection.

NR34 Monday, May 20, 9:00 a.m.-10:30 a.m.

PTSD in HIV-Positive Incarcerated Women

Catherine F. Lewis, M.D., *Department of Psychiatry, University of Connecticut, 263 Farmington Avenue, Farmington, CT 06030-2103*

Summary:

Introduction/Hypothesis: In Connecticut, 10% of female prisoners who agree to be tested are HIV positive. These women have sustained multiple traumas in their lives. The majority is African American or Hispanic. Diagnoses of Post-Traumatic-Stress Disorder can be difficult in this population. We hypothesize that the Clinician Administered PTSD Scale (CAPS) will diagnose a number of women with PTSD.

Methods: Eighty-four women were interviewed using structured instruments including the CAPS. Demographic data were gathered. The CAPS was scored for both current and lifetime PTSD.

Results: The sample consisted of 46 African American, 22 white, and 16 Hispanic women with a mean age of 38 (sd = 5.8 years). None of the women reported a diagnosis of PTSD in the past. Fifty-one had been sexually abused, 17 attacked with a weapon, and 62 witnessed violence in the home. Data from the CAPS showed 70% of the women had lifetime PTSD and 24% had current PTSD.

Conclusions/Discussion: This study demonstrates that a high percent of incarcerated women with HIV suffer from both current and lifetime PTSD. The correct diagnosis of PTSD is important in optimizing treatment programs and utilization for incarcerated women with HIV. Structured interviews may play an important role for this fragile population.

NR35 Monday, May 20, 9:00 a.m.-10:30 a.m.

The Impact of Religious Practice and Coping on Geriatric Depression Recovery

Kwang-Soo A. Park, M.D., *Duke University Medical Center, DUMC 3903, Durham, NC 27710*; Hayden B. Bosworth, Ph.D., Douglas R. McQuoid, Ph.D., David C. Steffens, M.D.

Summary:

Objective: To examine the impact of religious practice, positive or negative religious coping (i.e., appraisals of a higher spiritual force as a partner, support, strength and guidance vs. appraisal of the illness as punishment or abandonment) on recovery among a sample of initially clinically depressed elders.

Method: Incident and prevalent unipolar depression cases (n = 121, age range 58–83, mean age 69, 67% female and 90% Caucasian) were enrolled in the Duke MHCRC for the Study of Depression in Late Life. Patients were treated naturalistically using a medication algorithm for at least 12 weeks. Depression recovery was defined as a score of 6 or below on the Montgomery-Asberg Depression Rating Scale (MADRS). Patients completed self reports on both measures of religious practice and religious coping at subsequent follow-ups. A simple t-test was used to compare the groups.

Results: At the 12-week follow-up, among 116 patients who remained in the study, 50% of the sample was in remission based upon MADRS scores. Recovered patients, compared with symptomatic depressed patients, reported significantly more frequent public and private religious practices ($p < 0.055$), greater positive religious coping ($p < 0.005$) and less negative religious coping ($p < 0.01$).

Conclusion: Religious practice and religious coping are potential areas of clinical intervention.

NR36 Monday, May 20, 09:00 a.m.-10:30 a.m.

Risperidone Tolerability in Children

Hong Chen, M.D., *Department of Psychiatry, Hershey Medical Center, 32 University Manor E, Hershey, PA 17033*; Christopher A. Petersen, M.D.

Summary:

Introduction: Little published data is available to determine the tolerability of Risperidone in children in an acute setting.

Method: In this prospective pilot study, hospitalized children (n = 10) with age range of 7 to 10 year, were administered Risperidone gradually to 0.04 mg/kg/day as clinically indicated and only if tolerated. Side effect rating scales were completed at baseline, within 24 hours of first dose to assess acute change, at 0.04mg/kg/day if possible to assess effects of therapeutic dosage, and prior to discharge. The average study period is 10 days.

Results: Among 10 hospitalized children with newly started on Risperidone, three (30%) developed mild degree of loss of appetite with one also had diarrhea, one (10%) developed mild rigidity, drooling, slurred speech within 24 hours of first dose, one(10%) had mild sedation. In terms of short term weight change by discharge, three (30%) children gained average weight of 0.9 kg, one (10%) lost 0.7 kg. Nine children were discharged on Risperidone without remaining problems of loss of appetite, diarrhea and sedation except weight change, and one child had to discontinue and switch to another neuroleptics.

Conclusion: The study demonstrated unexpected high rate of side effect but with short duration and mild severity in children who take Risperidone. More studies regarding long term sequelea of weight change, and presence of EPS symptoms in children on Risperidone are needed in future research.

NR37 Monday, May 20, 9:00 a.m.-10:30 a.m.

Weight Gain in Patients with Panic Disorder Treated with Paroxetine

Gustavo D. Kinrys, M.D., *Department of Psychiatry, Mayo Foundation, 200 First Street, SW, Rochester, MN 55905*; Naomi M. Simon, M.D., John J. Worthington III, M.D., Michael W. Otto, Ph.D., Fany S. Toshkov, B.A., Frank J. Farach, B.A., Mark H. Pollack, M.D.

Summary:

Background: Antidepressant-associated weight gain may lead to poor medication compliance and weight-related health risks. Some reports suggest greater weight gain with paroxetine than other SSRIs. In this study we examine changes in weight associated with paroxetine therapy (as monotherapy or combined with clonazepam) in patients with panic disorder in a 12-week randomized controlled trial.

Methods: Weight at baseline and study endpoint (week 12 or last visit) was obtained for 51 patients (37 female; mean age 36.9 ± 11.4). Consistent with convention, significant weight gain was defined as >7% increase.

Results: 4% (2/51) of patients in the last visit carried forward (LVCF) analysis (mean duration of treatment 9.3 ± 4.2 weeks) and 3% of completers gained significant (>7%) weight. Mean weight change from baseline to endpoint visit was -0.367 ± 6.9 lbs. (LVCF) and -1.9 ± 6.0 lbs. (completer). Mean dose of paroxetine was 38 ± 5 mg/d. Changes in body mass index (BMI) and in weight were not significant within or across treatment group (with or without clonazepam) or sex.

Conclusion: Paroxetine therapy was not associated with significant weight gain in panic patients during this 12-week study. Results from this analysis should be interpreted in the context of the relatively brief duration of the trial. However, our data raise the possibility that risk of weight gain may be disorder-specific.

NR38 Monday, May 20, 9:00 a.m.-10:30 a.m.

Meteorological Factors Associated with Suicide

Eberhard A. Deisenhammer, M.D., *University of Innsbruck, Anichstrasse 35, Innsbruck A-6020, Austria*; Georq Kemmler, Ph.D., Peter Parson, Ph.D.

Summary:

Background: Suicidal behavior has been related to a variety of risk factors. These include genetic vulnerability and biological markers as well as demographic, psychosocial and environmental variables. A number of studies from several countries suggested an association of various meteorological and climatic factors with rates of attempted or completed suicide.

Method: This study presents data from Tyrol, Austria. Official suicide data from 1995 to 2000 were related to a number of

meteorological variables at the same day and at the preceding days. Weather data were assessed at 8 weather stations throughout the region run by the Austrian Central Institute of Meteorology and Geodynamics.

Results: 752 suicides were comitted during the period under investigation. No statistically significant association with the frequency of suicides was found for most of the weather variables assessed including atmospheric pressure, precipitation, cloudiness, and velocity of wind. There was, however, a positive correlation for mean, highest and lowest temperature as well as for thunderstorms on the same day and on the preceding day and a negative correlation for humidity.

Conclusion: Meteorological conditions seem to have a modifying effect on the proneness for suicide.

NR39 Monday, May 20, 9:00 a.m.-10:30 a.m.

How Accurate Are Depressed Patients in Reporting Their Antidepressant Treatment?

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

Summary:

Background: It is currently unknown how accurate patients are in describing and characterizing their antidepressant treatment history.

Methods: Seventy-three patients from an outpatient psychiatric practice were interviewed by an independent evaluator who was blind to each patient's treatment history. Information was obtained regarding which antidepressant and augmentation regimens patients had undergone, antidepressant doses, duration of trials, and the nature of response to each trial. The results of these interviews were then compared with patients' actual treatment history as elicited from an independent chart review.

Results: Patients recalled 85 of the 104 (81.7%) monotherapy trials they had undergone in the past 5 years, but only recalled 12 of 46 (26.1%) augmentation trials ($p < .001$). The more time that had passed since the trial occurred, the less likely it was to be recalled. Patients were found to be very reliable in distinguishing between those trials that were of adequate dose and duration and those that were not, and were quite reliable in depicting the quality of response to past trials. The presence of current depressive symptomatology did not adversely affect patients' ability to recall past trials or accurately describe their response to past regimens.

Conclusion: Patient report appears to be a satisfactory method for obtaining information regarding trial adequacy and response. Augmentation trials and the occurrence of tachyphylaxis, however, were not reliably reported.

NR40 Monday, May 20, 9:00 a.m.-10:30 a.m.

The Rating for Depression as Assessed by Clinicians, Patients, and Informants

Gonzalo Laje, M.D., *Department of Psychiatry, NYU School of Medicine, 75 West End Avenue, New York, NY 10023*; Eric D. Peselow, M.D., Jamie A. Luff, M.D., Patrick Ying, M.D., Mary Paizis, M.D., Ronald R. Fieve, M.D., Mary T. Guardino, B.A.

Summary:

Objective: Patients treated in outpatient settings, are often seen for 15–45 minutes q1–4 weeks. Thus we can not be sure if their observed behavior during this brief time period represents the way they are during the rest of the week-month. Thus observations by an informant & the patient self report are important and together they might be needed to give a better picture of the patients' symptoms.

Method: Data was obtained by having the patient, informant & interviewer fill out the Hamilton depression scale, CGI, MADRS (Montgomery-Asberg Scale) and Beck with the informant reporting on what they observed or felt the patient's pathology was. To date, we have evaluated 63 depressed outpatients by evaluating data obtained from the patient and his/her spouse/live-in companion and comparing it with the observations of the clinician to see how well the 3 assessors (clinician, informant & patient) agree on the pathology. The patients from the clinician's point of view met DSM-III criteria for major depression & had a minimum score of 18 on the Hamilton depression scale.

Results:

Mean scale score	Patient Rating	Clinician Rating	Informant Rating	Probability
Hamilton	28.87	26.17	23.78	p<.0001
MADRS	28.04	25.84	22.40	p<.0001
Beck	29.63	25.22	22.92	p<.0001
CGI	4.88	4.37	3.98	p<.0001

[4]For all scales above patient>iclinician>informant

Conclusion: The study shows significant differences in how the patient, clinician & informant view the patients' pathology. Data following clinical recovery will also be presented.

NR41 Monday, May 20, 9:00 a.m.-10:30 a.m.

Retrospective Assessment of ADHD Features in Nonsyndromal Bipolar Patients

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

Summary:

Objectives: Unresolved controversies persist regarding possible links between bipolar disorder and features of attention deficit disorder (ADD). The present study utilized a previously validated psychometric retrospective screen for childhood attention deficit disorder (ADD) in nonsyndromal bipolar outpatients.

Methods: Thirty DSM-IV bipolar outpatients (80% bipolar I; 20% bipolar II; mean ± SD age = 43.5 ± 15.1; mean ± SD Young Mania Rating Scale score = 7.7 ± 9.7; mean ± SD 31-item Hamilton depression score = 14.0 ± 14.4) completed the 61-item Wender Utah Rating Scale (WURS) for adults to identify childhood behaviors consistent with ADD.

Results: Three subjects (10.0%) carried previous diagnoses of childhood ADD. Eight subjects (26.7%) screened above threshold for WURS criteria consistent with childhood ADD, although only 1 of 3 with previously-diagnosed childhood ADD met WURS criteria. Seven of the 8 WURS screen-positive subjects (87.5%) were previously undiagnosed with ADD. Screen-positive subjects were significantly more likely than screen-negative subjects to have comorbid cocaine ($p = .034$) or marijuana ($p = .034$) abuse or dependence. Current severity of manic symptoms was, as a univariate variable, significantly associated with WURS scores, but became nonsignificant ($p = .152$) when controlled for by multiple regression in the presence of cocaine abuse ($p = .028$).

Conclusions: Childhood ADD features may be detectable in at least one quarter of adult bipolar outpatients, and as such may be underrecognized. While subthreshold manic features could influence the retrospective recall of childhood ADD features, previous cocaine abuse may be more robustly associated with features otherwise indicative of childhood ADD in adult bipolar patients.

NR42 Monday, May 20, 9:00 a.m.-10:30 a.m.

Life Events 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 examined the impact of life events on patients with mitral valve prolapse (MVP).

Methods: Patients with standard echocardiographically confirmed MVP were consecutively recruited. A total of 35 MVP patients were interviewed to make clinical diagnoses according to DSM-IV criteria. Their mean age was 32.2 ± 12.1, 14 (40%) male, 18 (51.4%) married, and education years 11.9 ± 3.7.

Results: Of the 35 MVP patients, 27 (77.1%) had DSM-IV psychiatric disorders. Eighty percent (n = 28) of the MVP patients reported experiencing at least one life event, of which, 85.7% (n = 24) considered that the life event contributed to the onset of their illnesses. In face of the life events, anxiety (67.9%, n = 19) is the most common emotional reaction, then anger (53.6%) and depression (35.7%). Although the life events were mostly resolved (64.3%) thereafter, the symptoms of illnesses still persisted. Moreover, the occurrence of life events was highly associated with the presence of DSM-IV psychiatric disorders (Fisher's Exact Test, p = .003).

Conclusions: The high prevalence of life events and their impact on patients with MVP highlights the importance of psychiatric consultation for them. Efforts may focus on increasing the capacity of patients' stress coping, especially at the beginning of a life event.

NR43 Monday, May 20, 9:00 a.m.-10:30 a.m.

A Taxometric Analysis of Aggression: Implications for Intermittent Explosive Disorder

Michael S. McCloskey, Ph.D., *Department of Psychiatry, University of Chicago, 5841 South Maryland Avenue MC3077, Chicago, IL 60637*; Emil F. Coccaro, M.D., John Ruscio, Ph.D., Mitchell E. Berman, Ph.D.

Summary:

Objective: To determine if the boundary between normal and pathological (i.e. Intermittent Explosive Disorder: IED) aggression is dimensional or categorical (taxonic) in nature.

Method: A Taxometric analysis was performed on data from 311 community volunteers who completed the Buss Durkee Hostility Inventory (BDHI), Affect Lability Scale (ALS), and a full diagnostic assessment. Twenty-seven participants (9%) were identified as having IED during their lifetime. This was used to estimate the base rate of pathological aggression in the sample. Two mathematically distinct taxometric procedures were used, MAMBAC (Meehl & Yonce, 1994) and MAXEIG (Waller & Meehl, 1998). The direct (physical) aggression, verbal aggression, irritability, and hostility subscales of the BDHI, and the anger lability scale of the ALS were used as "indicator" variables based on their theoretical association to IED, and their psychometric acceptability for the proposed analyses.

Results: Nineteen of the 20 MAMBAC curves, and four of the five MAXEIG curves ascended and peaked to the far right, suggesting a taxonic solution with a low base rate.

Conclusions: IED may represent a distinct category of aggressiveness, which may necessitate interventions different from those used to deal with milder forms of aggression.

NR44 Monday, May 20, 9:00 a.m.-10:30 a.m.

Clinical Correlates of Migraine in Bipolar Patients

Jennifer R. Cooper, *Department of Psychiatry, New York Presbyterian Hospital, 525 East 68th Street, New York, NY 10021*; Joseph F. Goldberg, M.D.

Summary:

Objective: An increased risk of migraine in patients with bipolar disorder has been previously suggested, particularly in patients with an earlier onset of the disorder and a history of suicide attempt. We have examined the data obtained at our site as a part of a multicenter prospective study of patients with bipolar disorder for evidence that there is an earlier age of onset and an increased risk for psychosis and suicide attempt in subjects with comorbid migraine compared to those without migraine.

Methods: To date, 45 bipolar patients have undergone standardized interviews to assess psychopathology, lifetime suicide attempts, and medical comorbidity, including migraine history. Corollaries to migraine were examined by descriptive statistics.

Results: Bipolar patients with migraine had a younger age of onset as compared to those without migraine. Additionally, histories of psychosis and suicide attempt were more prevalent among bipolar patients with migraine than among those without migraine.

Conclusions: The presence of migraine in bipolar patients may indicate an illness subtype with more extensive overall psychopathology.

NR45 Monday, May 20, 9:00 a.m.-10:30 a.m.

Autoimmunity to Neuronal Proteins in the Pathogenesis of Autism

Martin M. Evers, B.S., *Department of Psychiatry, Mount Sinai, One Gustave Levy Place, Box 1230, New York, NY 10029*; Eric Hollander, M.D.

Summary:

Objective: Autism shares numerous general features with autoimmune disorders. We investigated whether autistic individuals, or a subset thereof, display elevated levels of autoantibodies to neuronal heat shock protein 90 (hsp90). Such an association would join a body of literature suggestive of an immune pathogenesis for some autism cases.

Method: Enzyme-linked immunosorbent (ELISA) assays were used to assess levels of serum autoantibody to hsp90 in 21 autistic individuals, 35 subjects with an autoimmune disorder, and 61 controls. All individuals were under standard clinical care at an academic medical center. Study groups did not differ significantly in age, race or gender.

Results: Autistic patients had significantly elevated levels of autoantibodies to hsp90 compared to both controls (p = 0.023) and those with autoimmune disorders (p = 0.001). Antibody levels were especially elevated in a subset of autistic patients.

Conclusions: These findings join other studies that have detected elevated levels of antineuronal antibodies in autistic subjects, suggesting that an autoimmune pathogenesis may account for some subset of autistic patients. Identification of a distinct group with this pathophysiology may ultimately lead to improved clinical care through immunomodulatory therapies, and an improved understanding of the course of illness in these individuals.

NR46 Monday, May 20, 9:00 a.m.-10:30 a.m.

Disability in Major Depressive Disorder: Vantaa Depression Study

Heikki K. Rytsala, M.D., *Department of MHAR, NPHI, Mannerheimintie 166, Helsinki 00300, Finland*; Tarja K. Melartin, M.D., Ulla S. Leskela, M.A., T. Petteri Sokero, M.D., Paula S. Lestela-Mielonen, M.A., Erkki T. Isometsa, M.D.

Summary:

Objective: Major Depressive Disorder (MDD) is the most important mental disorder causing functional and work disability. We investigated risk factors for disability among patients with MDD.

Method: In the Vantaa Depression Study, in- and outpatients (N = 269) with MDD in Vantaa city, Finland, were examined. Axis I and II disorders were assessed via semi-structured SCAN 2.0 and SCID-II interviews. Objective psychosocial disability was rated

with the Social and Occupational Functioning Assessment Scale (SOFAS), and subjective with Social Adjustment Scale-Self Report (SAS-SR). Work status was also recorded.

Results: The dominant factor predicting objective disability in the SOFAS was severity of depression ($p < 0.0001$), but older age ($p = 0.01$), widow(er)hood ($p = 0.02$), lower education level ($p = 0.02$) and having a personality disorder ($p = 0.006$) also contributed. Severity and total duration of depression, phobic disorders, alcoholism, and personality disorders all predicted high subjective disability in the SAS-SR. More of the working females (50%) than males (25%) were currently on sick-leave ($p = 0.007$). The most important risk factor for sick-leave was severity of depression.

Conclusions: Severity of depression is the most important single factor causing functional and work disability, but comorbid mental disorders and other characteristics also contribute.

NR47 Monday, May 20, 9:00 a.m.-10:30 a.m.

Body Dysmorphic Disorder in Patients with Anorexia Nervosa

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

Summary:

Background: The rate of body dysmorphic disorder (BDD) in patients with anorexia nervosa (AN) is unknown. We hypothesized that BDD would be underdiagnosed in patients with AN and that comorbidity with BDD would result in greater overall dysfunction.

Method: 41 patients with DSM-IV AN completed the Body Dysmorphic Disorder Questionnaire. A follow-up interview was conducted using a reliable clinician-administered semi-structured diagnostic instrument for DSM-IV BDD. Delusionality about appearance was assessed using a validated semistructured interview. Comorbid DSM-IV diagnoses, number of hospitalizations and suicide attempts were obtained by means of a detailed diagnostic interview.

Results: Sixteen (39%) of the 41 anorectics were diagnosed with BDD independent of weight concerns. The anorectics with BDD had significantly lower overall functioning and higher levels of delusionality than the anorectics without BDD.

Discussion: These preliminary results suggest that BDD may be relatively common among anorectics. The presence of comorbid BDD may indicate a more severe form of illness and have subsequent treatment implications.

NR48 Monday, May 20, 9:00 a.m.-10:30 a.m.

An Open-Label Study of Naltrexone in the Treatment of Kleptomania

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

Summary:

Background: The present study was designed to test the short-term efficacy and safety of naltrexone in the treatment of kleptomania.

Method: 10 subjects (7 women, 3 men) who fulfilled DSM-IV criteria for kleptomania, and were free from other Axis I diagnoses by SCID screening, participated in a twelve-week naltrexone open label trial. Kleptomania symptom change was assessed with the Clinical Global Impression and the Kleptomania Symptom Assessment Scale. Functioning was assessed with the Sheehan Disability Scale and the Global Assessment of Functioning scale. Side effects were monitored weekly and liver function tests every two weeks.

Results: Naltrexone reduced urges to steal and stealing behavior. Subjects showed significant improvement over the treatment period in all measures compared to baseline. Seven subjects (70.0%) were very much improved and 2 (20.0%) were much improved at study end. Subjects also reported overall significant improvement in social and occupational functioning. Men responded to naltrexone as well as women. The average naltrexone dose required for effective symptom control was 145 mg/day.

Conclusions: The present findings provide evidence that naltrexone may be effective in the treatment of kleptomania. The present report is preliminary. Further studies are needed to confirm these findings.

NR49 Monday, May 20, 9:00 a.m.-10:30 a.m.

Assessing Trauma Histories, PTSD, and Subthreshold PTSD Syndromes in Psychiatric

C. Laurel Franklin, Ph.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Thomas Sheeran, Ph.D., Mark Zimmerman, M.D.

Summary:

Objectives: This study addressed four questions: (1) What is the prevalence of PTSD and subthreshold PTSD in this sample? (2) How well does the SCID screening question detect a trauma history, PTSD, and subthreshold PTSD? (3) Does using a trauma list, rather than the screening question, improve detection of PTSD or subthreshold PTSD? (4) Is there an optimal termination point for assessing subthreshold PTSD with the SCID?

Method: The Structured Clinical Interview for DSM-IV (SCID) was used with 1300 psychiatric outpatients.

Results: Three hundred seventy nine (29%) participants met lifetime criteria for PTSD or subthreshold PTSD. Although using a trauma list increased the number of participants reporting a trauma history, our results suggest that the SCID screening question captures almost all individuals who go on to meet diagnostic criteria for a PTSD or subthreshold PTSD. When assessing for subthreshold PTSD, the evaluation can be terminated upon failure to meet criterion B.

Conclusions: Implications are discussed in light of the current PTSD literature.

NR50 Monday, May 20, 9:00 a.m.-10:30 a.m.

Outpatients PTSD and Comorbid Personality Disorders

C. Laurel Franklin, Ph.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Mark Zimmerman, M.D.

Summary:

Objective: Previous studies have examined the occurrence of personality disorders (PD) in individuals with PTSD; however, they have been limited by the use of participants preselected for other diagnoses or the use of homogeneous groups. The present study examined the occurrence of PD comorbidity in a sample of psychiatric outpatients meeting criteria for current PTSD ($n = 99$).

Method: A semi-structured interview was used to assess the 10 PDs defined in the Diagnostic and Statistical Manual (DSM-IV; American Psychiatric Association, 1994) main manual. Two PDs defined in the DSM-IV appendix and one defined in an earlier edition of the DSM (DSM-III-R) appendix were also assessed.

Results: Most participants had at least one PD, the most frequent being borderline (65%) and depressive PD (65%). Differences in frequencies of PDs across participants' demographic and clinical characteristics (e.g., gender, age of onset, index trauma, principal diagnosis) also were analyzed.

Conclusions: Most patients diagnosed with PTSD have multiple comorbid Axis II disorders. The frequent co-occurrence of PDs and PTSD suggests that Axis II disorders need to be routinely assessed in all individuals with PTSD. Failing to assess PDs or ignoring the impact of these disorders on treatment may hinder treatment effects.

NR51 Monday, May 20, 9:00 a.m.-10:30 a.m.

Psychiatric Diagnoses in Patients of an Urban County Domestic Violence Center

Robert C. Stone, *Department of Psychiatry, University of Texas at Southwestern, 5323 Harry Hines Boulevard, Dallas, TX 75390-9070*; Laura Adams, M.S., Trevor Mills, M.D., Donald Smith, Ph.D., Sharon Walker, Ph.D., Lisa Vinuesa, M.S.

Summary:

Hypothesis/Introduction: Medical and psychiatric care are often unavailable to victims of domestic violence (DV). The Violence Intervention and Prevention (VIP). Center at Parkland Hospital in Dallas, Texas is the first medically-oriented DV treatment center in the U.S. and is chartered to provide comprehensive medical and psychiatric services to all victims of violence in Dallas county. Referrals for psychiatric evaluation and treatment are now common from all of the county's DV shelters. Easily apparent was the significant level of psychiatric morbidity experienced by this subpopulation of DV victims.

Methods: Retrospective chart review of the first 75 psychiatric evaluations performed at the VIP Center. Evaluation was completed using the Mini International Neuropsychiatric Interview in Spanish or English administered by a psychiatrist or psychology intern under supervision.

Results: The most common diagnostic criteria met by this population includes MDD and PTSD (64% each); Bipolar I (20%); OCD, Panic DO, Eating DO, Substance Abuse (10% each). 7% met criteria for a psychotic disorder.

Conclusions/Discussions: This study indicates that some percentage of the female DV population at large suffers from one or more major psychiatric disorders. An epidemiological study is warranted.

NR52 Monday, May 20, 9:00 a.m.-10:30 a.m.

Comorbid Disorders in 350 Patients with OCDE

Damiaan Denys, M.D., *Department of Psychiatry, UMC, Heidelberglaan 100, P O Box 85500, Utrecht 3508 GA, Netherlands*; Harold Van Megen, M.D., Herman Westenberg, Ph.D.

Summary:

Background: Several authors have emphasized the co-occurrence of obsessive-compulsive symptoms and other psychiatric disorders. Few have looked at broad-spectrum comorbidity in a well-defined sample of patients with obsessive-compulsive disorder (OCD)

Aims: In this study, we examined the cross-sectional prevalence of comorbid DSM-IV axis I and axis II disorders in a clinically defined population with primary OCD.

Methods: 50 outpatients with OCD were interviewed at admittance at the University Medical Center in Utrecht. Patients were evaluated for demographic, clinical characteristics and comorbid pathology.

Results: 46% of patients met criteria for a current comorbid axis I disorder. Mood disorders (27%) were most prevalent, followed by anxiety disorders (12%) and substance related disorders (4.3%). 36% of patients met criteria for a current personality disorder (PD), of which obsessive-compulsive PD (9%) was most prevalent, followed by dependent PD (7.4%) and PD not otherwise specified (7%). Associated comorbidity did not affect clinical severity of OCD, but was related to higher levels of depression and anxiety.

Conclusions: Although the pattern of comorbid diagnoses in this study is in agreement with previous reports, prevalence rates are largely comparable to those found in the general population. OCD appears to be a very distinctive and independent psychiatric disorder.

NR53 Monday, May 20, 9:00 a.m.-10:30 a.m.

Double-Blind Comparison of Paroxetine and Venlafaxine in OCD

Damiaan Denys, M.D., *Department of Psychiatry, UMC, Heidelberglaan 100, P O Box 85500, Utrecht 3508 GA, Netherlands*; Nic Van Der Wee, M.D., Harold Van Megen, M.D., Herman Westenberg, Ph.D.

Summary:

Objective: To compare efficacy and tolerability of venlafaxine, a serotomin-norepinephrine reuptake inhibitor (SNRI) with paroxetine, a selective serotonin reuptake inhibitor (SSRI) in patients with obsessive compulsive disorder (OCD)

Method: 150 patients with primary OCD according to DSM-IV criteria were randomly assigned in a 12 week, double-blind trial to receive dosages titrated upward to 300 mg/day of venlafaxine (n = 74) or 60 mg/day of paroxetine (n = 76). Primary efficacy was assessed by change from baseline on the Yale-Brown obsessive-compulsive scale (Y-BOCS). A responder was defined by a decrease of $\geq$ 25% on the Y-BOCS. Other assessments included the Hamilton depression rating scale (HDRS) and Hamilton anxiety rating scale (HAS).

Results: An intent-to-treat, last-observation-carried-forward analysis demonstrated a mean decrease on the Y-BOCS of 30% $\pm$ 29.5% in the venlafaxine group and of 30% $\pm$ 26% in the paroxetine group. In both treatment groups a responder rate of 60% was found. The incidence of adverse events for venlafaxine were somnolence, dry mouth, sweating, constipation and for paroxetine dry mouth, sweating and abnormal ejaculation.

Conclusion: These results show that venlafaxine was equally effective to paroxetine in treating patients with OCD. To date, this is the first randomized, double-blind study that found venlafaxine to be efficacious in OCD treatment.

NR54 Monday, May 20, 9:00 a.m.-10:30 a.m.

Symptom Structures in OCD

Damiaan Denys, M.D., *Department of Psychiatry, UMC, Heidelberglaan 100, PO Box 85500, Utrecht 3508 GA, Netherlands*; Femke De Geus, Harold Van Megen, M.D., Herman Westenberg, Ph.D.

Summary:

Background: Obsessive-compulsive disorder (OCD) is a broad concept encompassing a rich variety of heterogeneous symptoms. The identification of homogenous subgroups may elucidate specific pathogenetic mechanisms and enhance the ability to treat successfully OCD patients.

Objective: To identify subgroups based on homogenous structures in OCD.

Methods: 150 patients with primary OCD according to DSM-IV criteria were interviewed at the University Medical Center Utrecht. On admission, a clinician rated scale (Yale-Brown Obsessive Compulsive Scale (Y-BOCS) Symptom Checklist) as well as a self-report questionnaire (Padua Inventory revisited) was simultaneously administrated. A principal component analysis with varimax rotation was performed on category and item level on the Y-BOCS CL and on the PI-R. Pearson correlations were used to

compare total sores and scores of obsessive/compulsive subscales on Y-BOCS and PI-R.

Results: Analysis on item level identified in both scales four common and consistent factors: "contamination and cleaning", "symmetry and precision", "aggressive and sexual obsessions", and "high risk assessment and checking". The Y-BOCS correlated well with the PI-R on severity scores. Patients with "contamination and cleaning" had a significantly later onset of disease than other subgroups.

Conclusion: Our data provide evidence for distinct subgroups within the uniform, nosological entity of obsessive-compulsive disorder.

NR55 Monday, May 20, 01:00 p.m.-2:30 p.m.

Mitochondrial Enzymes in Schizophrenia

Jicheng Tang, M.D., *Department of Psychiatry, New York Presbyterian Hospital, 21 Bloomingdale Road, White Plains, NY 10605*; Vahram Haroutunian, Ph.D., Hui Xu, M.D., Kenneth L. Davis, M.D., Thomas E. Smith, M.D., John P. Blass, M.D., Gary E. Gibson, Ph.D.

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 disease controls (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 post-mortem interval (10:10) gave similar conclusions. A cognitive dementia rating was poorly correlated (r, p value) with activities of KGDHC (0.02, 0.9) or PDHC (–0.27, 0.1). 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.

References:

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2. Gibson GE, Park LCH, Sheu KR, Blass JP, Calingasan NY: The α-ketoglutarate dehydrogenase complex in neurodegeneration: Neurochemistry International 2000; 36:97–112.

NR56 Monday, May 20, 01:00 p.m.-02:30 p.m.

Psychosis in Siblings with Schizophrenia and Patients with Bipolar Disorder

Urban Osby, M.D., *Department of Neuroscience, Karolinska Institute, Karolinska Hospital S4, Stockholm SE-17176, Sweden*; Lena Brandt, B.S.C., Lars Terenius

Educational Objectives:

At the conclusion of this session, the participant should be able to differentiate the risk for psychotic disorders in full and half siblings to probands with schizophrenia and bipolar disorder.

Summary:

Objective: The familial risks in schizophrenia and bipolar disorder are larger than any other risk factors, but there are no population-based studies where the familial risks for both disorders were investigated simultaneously.

Methods: All inpatients in Sweden with a diagnosis of schizophrenia or bipolar disorder from 1973 to 1995 were identified from the Swedish patient register. All siblings were identified by the second-generation register, and their inpatient diagnoses from the patient register. Standardized incidence ratios (SIR) for full and half siblings were calculated in 5-year age and calendar time classess.

Results: In 23,223 full and 8,369 half siblings to 13,870 schizophrenia probands, SIR for schizophrenia was 7.4 for full and 4.4 for half siblings, and for bipolar disorder 3.6 for full and 2.8 for half siblings. In 8,846 full and 2,758 half siblings to 5,400 bipolar probands. SIR for bipolar disorder was 12.8 for full and 8.1 for half siblings, and for schizophrenia 4.4 and 2.2, respectively.

Conclusion: The diagnosis-specific increased risks for siblings in both schizophrenia and bipolar disorder indicate different specific risk genes, while not diagnosis-specific risks indicate shared risk genes.

References:

1. Berrettini WH: Are schizophrenic and bipolar disorders related? A review of family and molecular studies. Biol Psychiatry 8:531–8, 2000.
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NR57 Monday, May 20, 01:00 p.m.-02:30 p.m.

White Matter Integrity in First-Episode Psychoses: A Voxel-Based Morphometric Approach

Konasale M.R. Prasad, M.D., *Western Psychiatric Institute, 3811 O'Hara Street, Pittsburgh, PA 15213*; Vaibhav A. Diwadkar, Ph.D., Sarah D. Sahni, Kar L. Hoffman, Antonio Hardan, M.D., Michael D. DeBellis, M.D., Matcheri S. Keshavan, M.D.

Educational Objectives:

At the end of the presentation, the participant should be able to understand the disconnection syndrome hypothesis of psychoses, neurodevelopment origins of psychoses and examine the evidence.

Summary:

Introduction: White matter abnormalities, such as smaller bilateral white matter volumes specifically in the splenium of corpus callosum, temperoparietal and frontal lobes have been shown in schizophrenia (1, 2). We assessed white matter microstructure in patients with first episode psychoses using voxel-based morphometry.

Methods: T1 weighted SPGR images of 28 patients diagnosed with first-episode psychoses (mean age, 27.1 years, 19 males) and 23 matched healthy controls (mean age 29.6 years, 12 males) were analyzed. The images were spatially normalized into stereotactic space using SPM 99. White matter maps were extracted for each subject using probabilistic classification. These maps were subsequently smoothed by convolving with a Gaussian smoothing kernel (12×12×12 FWHM). The white matter maps of patients were compared to controls and voxels showing hypoden-

sity of tissue were identified using a preset threshold (p=0.001). Age and gender were used as covariates.

Results: Regions of significant white matter hypodensity were observed in the right subgyral and left middle frontal gyral white matter in first-episode psychotics.

Discussion: White matter abnormalities together with grey matter changes in first-episode psychoses indicate that these abnormalities are present at the onset of psychoses and, perhaps, are not the consequence of psychoses. The presence of white matter abnormalities supports the hypothesis that illnesses like schizophrenia could be characterized as disconnection syndromes. Furthermore, hypodensity in subgyral and frontal white matter may perhaps be indicative of more specific disconnection of the prefrontal cortex with the medial temporal and other subcortical structures. Thus, there is distinct possibility that cortico-subcortical disconnection underlies the etiology of psychotic disorders.

References:

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2. Lim KO, Hedehus M, Moseley M, de Crispigny A, Sullivan EV, Pfofferbaum A. Compromised white matter tract integrity in schizophrenia inferred from diffusion tensor imaging. Arch Gen Psychiatry. 56:367–374, 1999.

NR58 Monday, May 20, 01:00 p.m.-02:30 p.m.

MRI Assessment of Gray and White Matter Distribution in Poor and Good Outcome Schizophrenia

Serge A. Mitelman, M.D., *Department of Psychiatry, Mount Sinai, One Gustave Levy Place, Box 1505, New York, NY 10029*; Lina S. Shihabuddin, M.D., Adam M. Brickman, B.A., Erin A. Hazlett, Ph.D., Kenneth L. Davis, M.D., Monte S. Buchsbaum, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize cortical Brodmann's area differences in good and poor outcome schizophrenia.

Summary:

Background: Reduced cortical gray matter volumes is a frequent finding in schizophrenia. However, previous studies often been limited because analyses have been restricted to specific brain regions. We performed a detailed analysis of gray volume of separate Brodmann's areas in a large group of good and poor outcome schizophrenia patients and normal controls.

Method: T1-weighted MR images were obtained on thirty-seven patients with schizophrenia, subdivided into poor-outcome (n = 13) and good-outcome (n = 24) subgroups and thirty-seven normal volunteers. Poor-outcome patients were defined as having unremitting symptomatology and dependency on others for life necessities for at least 5 continuous years. Detailed volumetric analysis of gray matter distribution across the selected Brodmann's areas of the frontal, temporal, and occipital lobes was done.

Results: Schizophrenia patients had significantly reduced cortical gray matter volume, especially in the left temporal lobe, compared to normal controls. When good- and poor-outcome patients were compared, poor-outcome patients had significantly reduced gray matter volume in the temporal and occipital lobes, while no differences were found in the total frontal lobe volumes. Poor-outcome patients showed a significant reduction in cortical gray matter in the primary auditory regions, Brodmann's area 31 in the cingulate gyrus, and unimodal association and primary sensory cell-type regions. Gray matter volumes were larger in poor outcome group in the proisocortex, polymodal association and motor-premotor cortical cell-type regions.

Conclusions: Poor-outcome in patients with schizophrenia may be associated with more posterior gray matter deficits.

References:

1. Shenton RE, Dickey, CC, Frumin, M, McCarley, RW, A review of MRI findings in schizophrenia. Schizophrenia Research, 49, 1–52, 2001.
2. Roy, M, Merette, C, Maziade, M. Subtyping schizophrenia according to outcome or severisty: a search for homogenous subgroups. Schizophrenia Bulletin, 27, 115–138, 2001.

NR59 Monday, May 20, 1:00 p.m.-2:30 p.m.

Hyperintensities in Depressed Elderly: Predictors of Dementia

Warachal E. Faison, M.D., *MUSC, 5900 Core Road, Suite 203, N. Charleston, SC 29406*; James R. MacFall, Ph.D., Martha E. Payne, M.P.H., David C. Steffens, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the clinical, cognitive, and imaging variables in depressed elderly that are predictors of development of later dementia.

Summary:

Introduction: Previous studies have reported that elderly depressed patients have more white and gray matter hyperintensities than nondepressed elderly controls. Few studies have studied cognitive outcomes of geriatric depression.

Methods: 180 nondemented depressed elderly patients were enrolled in the Duke Clinical Research Center. They were compared on several clinical and demographic risk factors. All subjects had a baseline MRI brain scan and we used volumetric analytic techniques to determine total volumes of cerebrum, white matter and subcortical gray matter lesions. They were followed up to 5 years with quarterly clinical evaluations and annual neuropsychological testing. We examined predictors of later dementia using survival analysis.

Results: Analysis of maximum likelihood estimates revealed that total white matter lesions, years of education, age, MMSE, and e4 were all significant predictors of later dementia. In contrast, in two separate analyses that included gray matter lesions, e4 and years of education were not significant predictors. In survival analyses, baseline MMSE ($p < 0.0027$), baseline age ($p < 0.0034$), total white matter lesion volume ($p < 0.0046$), and gray matter lesion volume ($p < 0.0153$) were associated with later dementia.

Conclusion: Both gray matter and white matter hyperintensities are related to development of dementia in depressed elderly.

References:

1. Steffens DC, Krishnan KR: Structural neuroimaging and mood disorders: recent findings, implications for classification, and future directions. Biol Psychiatry 1998;43:705–712
2. Garde E, Mortensen EL, Krabbe K, et al: Relation between age-related decline in intelligence and cerebral white-matter hyperintensities in healthy octogenarians: a longitudinal study. Lancet 2000;356:628–634

NR60 Monday, May 20, 1:00 p.m.-2:30 p.m.

Defining Familial Alcoholism: A Comparative Study

Bjorn Ebdrup, B.M.D., *Department of Psychiatry, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160*; Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.A.,

Joachim Knop, M.D., Per Jensen, M.D., William F. Gabrielli, Jr., M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to identify nine different methods of defining familial alcoholism, their correlations with each other, and their predictive validity in a 30-year follow-up of Danish men at high and low risk for alcoholism.

Summary:

Objective: Longitudinal data originating from Denmark in the late 1950's were used to compare the validity of nine definitions of familial alcoholism in predicting drinking outcomes and other related features at age thirty.

Method: This sample of 241 men who completed the 30-year follow-up examination was drawn from a cohort of 9,182 births that was extensively studied perinatally and one year later. From this cohort, when approximately age 19, a sample of high risk sons of alcoholics (n = 156) was selected and compared to a matched sample of low risk sons of non-alcoholics (n = 79) as determined from archival information contained in the Danish National Psychiatric Register and local alcoholism clinics. At age 19–20 and at 30 years, these subjects were systematically evaluated with a variety of procedures that included a series of comprehensive, structured interviews. Nine methods of defining familial alcoholism were extracted from these data: six were based on the family history method (i.e., subjects' reports at age 30) and ranged from very simple to very complex; two were based upon archival information only; one was based upon a combination of both archival and family history methods. The 16 pre-selected validity measures obtained at age 30 included DSM-III-R diagnoses, lifetime alcoholism severity and sequelae, psychiatric comorbidity among the subjects and their families, and levels of psychosocial functioning.

Results: All nine methods were significantly correlated with each other, although the family history methods only modestly correlated with the archival methods. All nine methods predicted a minimum of three validity measures; however, the archival methods were much less efficient in doing so than the family history methods which typically predicted fourteen or more of the sixteen 30-year outcomes.

Conclusion: The most efficient method of defining familial alcoholism, predicting all sixteen validity measures, was the easily derived *tri-level method* consisting of the following three categories based on the subjects' reports: 1) *No* first or second degree alcoholic relative; 2) only *one* 1st or 2nd degree alcoholic relative; 3) *two or more* 1st or 2nd degree alcoholic relatives.

References:

1. Stoltenberg SF, Mudd SA, Blow FC, Hill EM (1998). Evaluating Measures of Family History of Alcoholism: Density vs. Dichotomy. Addiction 93(10), 1511–1520.

2. Alterman AI (1988). Patterns of Familial Alcoholism, Alcoholism Severity and Psychopathology. Journal of Nervous and Mental Disease, 176 (3), 167–175.

NR61 Monday, May 20, 1:00 p.m.-2:30 p.m.

Perceived Discrimination and Psychiatric Service Utilization

Denise De Guzman, M.D., *Department of Psychiatry, University of Maryland, 701 West Pratt Street, 4th Floor, Baltimore, MD 21201*; Mark Salzer, Ph.D., Anthony L. Rostain, M.D., Trevor Hadley, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that there is a relationship between perception of racial discrimination and psychiatric service utilization.

Summary:

Objective: To assess the relationship between mental health service utilization and perception of racial discrimination in patients participating in a consumer-operated service program (COSP) for co-occurring mental health and substance abuse disorders.

Introduction: It is well known that there are tremendous disparities in access, quality, and availability of mental health services to minorities. In spite of this, few studies have examined the relationship between perception of racial discrimination and mental health service utilization. Those that do address the perceived discrimination-mental health link have not specifically targeted mental health patients. Recently, there has been renewed attention to the key role of culture, race, and ethnicity in providing effective psychiatric treatment. This study provides a unique opportunity to examine the relationship between race and perceived discrimination with service utilization in patients with co-occurring disorders.

Methods: 288 patients participating in an inner-city, COSP for co-occurring disorders comprised the sample. Data on mental health service utilization, perception of racial discrimination, and demographics were obtained from baseline interviews. Chi-square and univariate analyses of variance were utilized for between-group comparisons.

Results: 79% of African-Americans and 75% of Non-African descent patients perceived experiencing racial discrimination, overall. However, a larger number of African Americans perceived discrimination specifically in traditional mental health services than Non-African Americans (75% vs. 25%). Similar rates of perceived discrimination were found with regard to COSP's between African-Americans and Non-African Americans. Almost twice the rate of psychiatric emergency room services utilization was found among patients with no perception of discrimination (p=0.05). Other differences were also found.

Conclusions: High percentages of African-American patients perceive discrimination in traditional mental health services. There is a striking difference in psychiatric emergency service utilization in patients that perceive discrimination. Psychiatrists and other mental health clinicians should be aware of the relationship between perception of discrimination and mental health service utilization. Further research is necessary to fully elucidate the relationship between discrimination and other types of psychiatric service utilization.

References:

1. U.S. Department of Health and Human Services: Mental Health: Culture, Race, and Ethnicity. A Supplement to Mental Health: A Report of the Surgeon General. Rockville, MD: David Satcher, M.D., August 26, 2001.

2. Klein, Amelia A., Cnaan, R., and Whitecraft, J. (1998). Significance of Peer Social Support With Dually Diagnosed Clients: Findings from a Pilot Study. Research on Social Work Practice, 8(5), 529–551.

NR62 Monday, May 20, 1:00 p.m.-2:30 p.m.

Ethnic Differences in Antipsychotic Use Following Bipolar Disorder Onset

David E. Fleck, Ph.D., *Department of Psychiatry, University of Cincinnati, 231 Albert Sabin Way, Cincinnati, OH 45267-0559*; Wendi L. Hendricks, M.S.W., Melissa P. Del Bello, M.D., Stephan M. Strakowski, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize potential discrepancies between African-American and Caucasian patients with respect to antipsychotic medication treatment and compliance during the early course of bipolar disorder.

Summary:

Objective: Antipsychotic medications are commonly prescribed as maintenance pharmacotherapy for patients with bipolar disorder. However, double-blind, placebo-controlled studies have yet to demonstrate a significant prophylactic effect of maintenance antipsychotic use in bipolar disorder and may place the patient at risk for neuroleptic-induced tardive dyskinesia. African-American patients may be at increased risk because excess antipsychotic prescription appears to be common in this population, although this issue has not been longitudinally studied in bipolar disorder.

Method: Fifty-eight DSM-IV bipolar patients, manic or mixed, were recruited at the time they were admitted for a first psychiatric hospitalization and then received longitudinal follow-up for up to two years. Comparisons were made between African-American and Caucasian patients in medications prescribed and medication compliance after controlling for differences in clinical course.

Results: The African-American and Caucasian patient groups were similar demographically. After controlling for differences in clinical course, African-Americans were significantly more likely than Caucasians to receive antipsychotics for a greater percentage of follow-up time, receive antipsychotics during periods without psychotic symptoms, and receive conventional antipsychotics. African-Americans also demonstrated poorer treatment adherence, although that did not explain the differences in antipsychotic prescription.

Conclusion: Even when demographically similar to Caucasian patients, African-Americans with bipolar disorder may be more likely to receive maintenance antipsychotic treatment. The specific reasons for this are not clear, suggesting studies are warranted that examine clinicians' rationale for differentially prescribing antipsychotics for African American and Caucasian patients during the early course of bipolar disorder.

References:

1. Fleck DE, Hendricks WL, DelBello MP, Strakowski SM: Differential prescription of maintenance antipsychotics to African-American and Caucasian patients with new-onset bipolar disorder. J Clin Psychiatry under review.
2. U.S. Department of Health and Human Services. Mental Health: Culture, Race, and Ethnicity—A Supplement to Mental Health: A Report of the Surgeon General. Rockville, MD, U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Mental Health Services, 2001.

NR63 Monday, May 20, 1:00 p.m.-2:30 p.m.

Prophylaxis of Panic Disorder: Medication Versus no Medication

Mary Paizis, M.D., *Department of Psychiatry, NYU School of Medicine, 564 First Avenue, #17T, New York, NY 10016*; Jamie A. Luff, M.D., Eric D. Peselow, M.D., Gonzalo Laje, M.D., Patrick Ying, M.D., Mary T. Guardino, B.A.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the long term stability of panic patients who continue on medication vs. those who are withdrawn from medication.

Summary:

Objective: An important questions in clinical psychiatry for patients who show response to treatment for any psychiatric disorder, is when to take them off medication. With respect to panic disorder, we evaluated the course of 30 patients who recovered from their panic attacks & remained stable on medication for 3 years and then were subsequently withdrawn from the medication. This group was compared with a group of 152 patients who remained stable for 3 years & continued on medication.

Method: The above sample was drawn from patients who were treated at the Freedom from Fear Clinic in Staten Island NY. The evaluation was carried out within the context of clinical care as the patients withdrawn from medication chose to do so on their wishes along with the consent of the treating psychiatrist. Thus this was a non-random design.

Results: The group withdrawn from medication actually were more stable than the group that remained on medication in that the former group had lower anticipatory anxiety, phobic avoidance & functional impairment vs the group that continued on medication. Overall the probability of remaining free of a subsequent panic attack for the 2 groups was as follows.

	Group withdrawn from meds	Group remaining on medication	P value
at 1 year	67.2%	84.1%	<.0001
at 2 years	32.1%	79.4%	0001
at 3 years	16.8%	73.8%	<.0001
% relapsing	22/30 (73.3%)	40/152 (26.3%)	<.0001

Conclusion: Despite a prior 3 year stability discontinuation of medication led to significant relapse.

References:

1. Rickols R, Schweizer E, Weiss S, et al: Maintenance drug treatment for panic disorder. Arch Gen Psychiatry 50:61–68, 1993
2. Mavissakalian M, Perel JM: Protective effects of imipramine maintenance treatment in panic disorder with agoraphobia. Am J Psychiatry 149: 1053–1058, 1992

NR64 Monday, May 20, 1:00 p.m.-2:30 p.m.

Pituitary Volume in Pediatric Maltreatment: Related PTSD

Lisa A. Thomas, M.D., *Department of Psychiatry, WPIC Room 392, 3811 O'Hara Street, Pittsburgh, PA 15213*; Michael D. DeBellis, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the effects of childhood maltreatment on the hypothalamic-pituitary-adrenal axis.

Summary:

Objective: Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis has been reported in adult PTSD, maltreated children, and pediatric maltreatment-related posttraumatic stress disorder (PTSD). These findings may be associated with greater levels of corticotrophin releasing hormone (CRH) or factor in distressed individuals.

Method: Magnetic resonance imaging was used to measure pituitary volumes in 61 medication naive maltreated subjects with PTSD (31 males, 30 females) (mean age 11.7±2.6 years) and 121 non-traumatized healthy comparison subjects (62 males, 59 females; 11.7±2.5 years) who were similar in age, sex, height, weight, and handedness.

Results: Overall, no differences were seen between PTSD subjects (0.91±0.26 cm3) and controls (0.90±0.21 cm3)(F=1.23, df= 1,178, p ;eq0.27) in pituitary volumes. There were significant increases in pituitary volume with age in the PTSD (r=.60, df=59,

p < .0001) and control ((r=.40, df=119, p < .0001) groups. However, there was a significant age-by-group effect for PTSD subjects to have greater increases in pituitary volume with age than controls (F=6.47, df=1,178, p=.01). Age of onset of abuse significantly correlated with pituitary volume (r=.40, df=59, p < .002).

Conclusions: These findings may suggest developmental alterations in pituitary volume in maltreatment-related pediatric PTSD. This finding may be associated with stress-related increases in CRH.

References:

1. De Bellis MD, Baum A, Birmaher B, Keshavan M, Eccard CH, Boring AM, Jenkins FJ, Ryan ND: AE. Bennett Research Award. Developmental Traumatology: Part I: Biological Stress Systems. Biological Psychiatry 45:1259–1270, 1999.
2. De Bellis, MD, Chrousos, GP, Dorn, LD, Burke, L, Helmers, K, Kling, MA, Trickett, PK, Putnam, FW: Hypothalamic-pituitary-adrenal axis dysregulation in sexually abused girls. Journal of Clinical Endocrinology and Metabolism 78:249–255, 1994.

NR65 Monday, May 20, 01:00 p.m.-02:30 p.m.

Association of a Glutamate Receptor Gene with OCD

Paul D. Arnold, M.D., *Neurogenetics, Cenre for Addiction and Mental Health, 250 College Street, Toronto, ON M5T 1R8, Canada;* Margaret A. Richter, M.D., Emanuela Mundo, M.D., Joanna McBride, M.A., James L. Kennedy, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the possible role of a glutamate receptor gene in the pathogenesis of OCD; and Understand how the interaction between genotype and age of onset may predict OCD.

Summary:

Neuroimaging studies indicate a possible role for glutamate in the pathogenesis of obsessive-compulsive disorder (OCD), which may be particularly important for individuals with early onset of symptoms. The effects of glutamate may be mediated by interaction of N-methyl-D-aspartate (NMDA) receptors with serotonin function in cortico-striatal circuits.

Objective: We set out to investigate the possible association of a glutamate receptor gene with transmission of OCD in affected families.

Method: We genotyped the BstYI polymorphism of the NMDAR2B receptor subunit gene (called GRIN2B for glutamate receptor, ionotropic, NMDA 2B), in 179 nuclear families of adult OCD probands. We tested for association with obsessive-compulsive disorder using the Family Based Association Test (FBAT). Secondary analyses were performed in affected subjects using two-way ANOVA for the effects of GRIN2B genotype and age of onset on symptom severity as measured by the YBOCS.

Results: The FBAT analysis revealed a significant association of Grin2B with transmission of OCD (p=0.003). Furthermore, we found that the interaction of GRIN2B genotype and early (prepubertal) onset predicted symptom severity (p=.045) in affected subjects. Neither factor alone predicted YBOCS score.

Conclusions: These findings provide preliminary evidence for GRIN2B as a susceptibility gene for OCD, which may be particularly important in individuals with early onset.

References:

1. Rosenberg DR, MacMaster FP, Keshavan MS, Fitzgerald KD, Stewart CM, Moore GJ: Decrease in caudate, glutamatergic concentrations in pediatric obsessive-compulsive disorder patients taking paroxetine. J Am Acad Child Adolesc Psychiatry 39(9):1096–1103, 2000.
2. Billett EA, Richter MA, Kennedy JL: Genetics of OCD. In Obsessive Compulsive Disorder: Theory, Research, and Treatment, edited by Swinson RP, Antony MM, Rachman J, Richter MA, New York, Guilford Press, pp 181–208, 1998.

NR66 Monday, May 20, 1:00 p.m.-2:30 p.m.

Psychiatric Patients, Vulnerability After the September 11th Terrorist Attacks

C. Laurel Franklin, Ph.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905;* Diane D. Young, Ph.D., Mark Zimmerman, M.D.

Educational Objectives:

At the conclusion of this presentation participants should be able to describe the impact that the events of Sept. 11th had on the medical community in general and psychiatric patients in particular.

Summary:

Objective: Since the terrorist attacks of September 11th, there has been much speculation about their impact on the population at large, and the vulnerability of psychiatric patients to psychological distress (e.g., increase in levels of anxiety and depression) in particular (Doyle, Butterworth, Clothier, & Mellman, 2001). The goal of this project was to understand the impact of national terrorist attacks on psychiatric and general medical outpatients (*N*=308)

Method: Two to three weeks following the events of September 11th, a group of psychiatric and medical (*N* = 308) patients were given questionnaires assessing background information and psychiatric symptoms, including the Posttraumatic Diagnostic Scale (PDS; Foa et al., 1997)

Results: Twenty seven percent of our sample had significantly distressing PTSD symptoms. Psychiatric patients (33%) were significantly more likely than medical patients (13%) to report distressing traumatic stress symptoms on the PDS, despite no differences in how the groups learned about the attacks or personal involvement with the victims of the attacks. Psychiatric patients also were more likely to report wanting to speak to their treatment provider about the attacks. Lastly, patients meeting the cutoff for PTSD on the PDS were more likely to schedule an appointment to speak with their treatment provider about their reactions

Conclusion: These findings suggest that psychiatric patients are at increased risk for experiencing distressing and impairing symptoms following national terrorist attacks.

References:

1. Doyle B, Butterworth R, Clothier J, Meliman T: America's state of mind: Confronting PTSD, depression, and anxiety in the wake of terrorism. Medical Crossfire 2001, 2, 2–15.
2. Schuster MA, Stein BD, Jaycox LH, Collins RL, Marshall GN, Elliott MN, Zhou AJ, Kanouse DE, Morrison JL, Berry SH: A national survey of stress reactions after the September 11th, 2001, terrorist attacks. The New England Journal of Medicine, 245, 1507–1512, 2001.

NR67 Monday, May 20, 1:00 p.m.-2:30 p.m.

Attitudes of Physicians Toward Gifts from the Pharmaceutical Industry

Saurabh Kaushik, M.D., *Department of Psychiatry, Brookdale Hospital, 7 Hegeman Avenue, # 9H, Brooklyn, NY 11212;* Parinda Parikh, M.D., Vasundhara Kalasapudi, M.D., Amarsingh M. Ghorpade, M.D., Sheldon S. Berman, M.D.

Educational Objectives:

At the conclusion of the presentation, participants should be able to recognize the influence of Pharmaceutical companies and

their drug representatives. After the presentation, Clinicians including Residents and Medical students should be able to formulate some guidelines regarding their working relationship with the drug companies.

Summary:

Objective: To survey physicians' attitudes towards gifts and incentives offered to them by pharmaceutical companies.

Methods: A cross sectional study was conducted using a self-report questionnaire, given to Attending Physicians and Physicians-in-Training (Residents and Fellows) in 8 clinical departments at a community-teaching hospital. Data was analyzed by ANOVA, Post-hoc test: Bonferroni and Tukey, chi-square, and logistic regression using SPSS version 10.0.

Results: Response rate was 80.7% (n = 187). Most physicians (80.8%) said pharmaceutical Companies and their representatives (PR) sponsored freebies had no influence on their prescribing patterns, 86.1% reported not receiving any formal guidelines regarding interactions with PRs, and 93.4% were not aware of websites catering to indigent patients. Physicians-in-Training favored (a) accepting textbooks as compared to faculty (Mean Likert's Scale Value (MLSV) 4.19 vs. 3.58 respectively), (b) having nationally reputed Grand Rounds Speakers (MLSV 4.11 vs. 3.74), and (c) outings for personal enjoyment (MLSV 3.36 vs. 2.56), which were sponsored by PRs. Significant interdepartmental variations were noted in (a) frequency of interactions with PRs ($p < 0.05$), (b) receiving promotional items ($p < 0.001$), (c) opinions regarding accuracy of medication information provided by PRs ($p < 0.001$), (d) views about maintaining the same degree of contact with PRs regardless of gifts ($p < 0.001$) and (e) the necessity of guidelines ($p < 0.01$). More male physicians (81.3% vs. 18.8% females) reported receiving financial support from Pharmaceutical companies for attending national meetings. Physicians in general agreed to participate with the goal of reducing medication price by refusing freebies, with female physicians more strongly agreeing as compared to male physicians who were either neutral or agreed ($p < .05$).

Conclusions: Despite minimal awareness about ethical guidelines regarding gifts and websites that help support indigent patients' medication, physicians at our hospital reported that PR sponsored gifts do not influence their prescribing patterns. Our preliminary study did not indicate a potential for pharmaceutical company influence. We propose to correlate actual physician prescribing pattern and relationship to PRs' visits. Of more immediate concern is the lack of physician knowledge and understanding of ethical issues pertaining to gifts. More immediate attention must be paid to medical students and residents' education.

NR68 Monday, May 20, 3:00 p.m.-5:00 p.m.

The Effect of Valproic Acid on Leptin Biology

Diane C. Bird, B.Sc., *Department of Psychiatry, Dalhousie University, 5909 Jubilee Road, Lane Building, Room 4083, Halifax, NS B3H 2E2, Canada;* Mark W. Nachtigal, Ph.D.

Summary:

Objective: Valproic acid (VPA) has significant effects on energy balance and can induce weight gain, through an unknown mechanism. We examined *in vitro* and *in vivo* whether VPA modulates the production or secretion of leptin, an adipocyte-derived hormone that signals to the brain to modulate energy balance.

Method: Adipose cells (3T3-L1) were treated with VPA (0-10 mM) for 6–48 hours and leptin protein and RNA were measured. In addition, rats were treated for 30 days perorally (3x daily) with VPA (n = 8), divalproex sodium (DS) (n = 6) or saline (n = 8) and serum leptin levels were measured.

Results: Radioimmunoassay results showed a significant reduction in leptin accumulation in the media following 6 hours of treatment with VPA. Rats treated with VPA and DS had a trend for decreased leptin serum levels, when compared to controls. Northern blot analysis demonstrated leptin RNA levels in 3T3-L1 cells treated with VPA were not different from untreated 3T3-L1 cells.

Conclusions: VPA treatment is associated with a dose-dependent decrease in leptin secretion without a change in leptin RNA levels, suggesting VPA has posttranslational effects on leptin biology. Both *in vitro* and *in vivo* results suggest that VPA can reduce circulating leptin levels and thus may contribute to the modulation of patient weight.

NR69 Monday, May 20, 3:00 p.m.-5:00 p.m.

Prolactin Levels and Erectile Function with Risperidone Treatment

John J. Spollen III, M.D., *Department of Psychiatry, Little Rock VAMC, 2200 Fort Roots Drive 116 F2, North Little Rock, AR 72114;* R. Greg Wooten, M.D., George Bartzokis, M.D.

Summary:

The use of antipsychotic medications has been associated with erectile dysfunction which has been shown to be positively correlated with prolactin levels but not neuroleptic dose (Burke et al, 1994). Several studies have shown risperidone is associated with more sexual side effects than olanzapine (Tran et al, 1997), which is most likely secondary to prolactin. Measuring nocturnal penile tumescence is superior for detecting the impact of medications on erectile function, and also reduces the large variance involved in patient-report measures.

Methods: Scrum measurements of prolactin, total testosterone, free and weakly bound testosterone (FWB), and risperidone were performed on 16 patients. Erectile function assessments, using the RigiScan, an instrument which measures nocturnal penile tumescence and rigidity, were performed on two nights.

Results: Consistent with previous reports, the correlation between total risperidone level and prolactin was high ($r=.92$, $df=12$, $p < .0001$), but risperidone did not appear to affect either testosterone ($r=.29$, $df=5$, $p=.51$) or FWB ($r=.11$, $df=10$, $p=.72$). Contrary to expectations, prolactin levels from the second night were positively correlated with erectile function ($r=.68$, $df=9$, $p=.022$). These results are tentative given the small sample.

Conclusions: Using objective measures, we were unable to confirm a detrimental association between prolactin levels and male erectile function.

NR70 Monday, May 20, 3:00 p.m.-5:00 p.m.

The Prevalence of Abnormal Plasma Lipids in the Chronic Mentally Ill

Anthony M. Tobia, M.D., *930 Chestnut Ridge Rd, Morgantown, WV 26505;* Carol A. Brooks, R.N.C., Albert W. Jekelis, Ph.D., Sondra Soskel, R.N., Elizabeth Vreeland, APN, Robert G. Stern, M.D.

Summary:

Objective: This study assessed the prevalence of abnormal lipid levels among patients attending a partial hospitalization program serving the severely mentally ill. Abnormalities were dichotomized as requiring treatment versus no treatment necessary. Furthermore the study tested for the possible association between prescribed antipsychotics and dyslipidemia.

Method: A cross-sectional chart review (n = 156) was conducted to extract basic demographics, diagnosis, lipid levels (total cholesterol, low-density lipoproteins, high-density lipoproteins and triglycerides) and medications prescribed at a university-based partial hospitalization program. Abnormal lipid levels were assessed as requiring treatment according to published guidelines.

Results: Complete data was available for 106 patients, of which 62.9% had treatment-requiring dyslipidemia. Treatment indications were met for abnormalities in total cholesterol (33.3%), low-density lipoproteins (2.9%), high-density lipoproteins (2.9%), and multiple abnormalities (23.8%). 12 patients with isolated hypertriglyceridemia did not reach indications for treatment. Some correlations were found between prescribed antipsychotics and dyslipidemia.

Conclusions: The high prevalence of dyslipidemia (62.9%) found in this study by far exceeds the prevalence rates previously reported. Future studies are needed to assess the extent to which our findings apply to partial hospitalization patients elsewhere. These studies should also explore the contribution of other factors to the high prevalence of dyslipidemia found in this population.

NR71 Monday, May 20, 3:00 p.m.-5:00 p.m.

Quetiapine Counteracts Decrease of Brain-Derived Neurotrophic-Factor Expression Induced by Immobilization Stress

Xin-Min Li, M.D., *Department of Neuropsychiatry, University of Saskatchewan, 103 Wiggins Road/A14 Med Res Bldg, Saskatoon, SK S7N 5E4, Canada*; Haiyun Xu, Ph.D., Hong Qing, M.D., Wenfu Lu, M.D., David L. Keegan, M.D., Steven Richardson, M.D.

Summary:

Objective: To examine the effect of quetiapine on the decrease of brain-derived neurotrophic factor (BDNF) expression, induced by chronic immobilization stress, in the hippocampus of the rat.

Methods: Rats were divided into 3 groups of 10. Rats in the first group (Nou) were controls and were handled daily for 3 weeks but received neither solution injection nor immobilization. The second group (Veh/S) was pretreated with 0.8% glacial acetic acid and subjected to immobilization stress for 2 hours. The third group (Q/S) was subjected to the same manipulations with pretreatment with injection quetiapine in the same volume of vehicle. Immunoreactivities in hippocampal pyramidal cells and dentate granule cells were detected by immunohistochemical staining, and levels of BDNF protein in the rat hippocampi were assessed by Western Blot.

Results: BDNF immunoreactivities in hippocampal pyramidal cells and dentate granule cells of Veh/S rats were markedly lower than Non and Q/S rats. Levels of BDNF protein in hippocampi of Veb/S rats was also lower.

Conclusions: Quetiapine pretreatment counteracts the decrease of BDNF expression induced by chronic immobilization stress. Chronic administration of quetiapine may be neuroprotective to hippocampal neurons in schizophrenia, and this effect may be related to its antipsychotic effect in patients with schizophrenia.

NR72 Monday, May 20, 3:00 p.m.-5:00 p.m.

Intellectual Change After the Onset of Illness in Schizophrenic Patients

Hey-Won Moon, M.S., *INHA University Hospital, 2-GA Shinheungdong Ehung Gu, Incheon 400-211, Korea*; Chul-Eung Kim, M.D., Jung-Sub Lee, M.D., In-Soon Han, M.S., Jae-Nam Bae, M.D., Min-Hee Kang, M.D.

Summary:

Objective: This study aimed to compare the intelligence of schizophrenia with that of other psychiatric disorders and evaluate the characteristics of intellectual decline after the onset of schizophrenia.

Methods: The study groups comprised 91 patients who performed intelligence test(Korean Wechsler Adult Intelligence Scale : K-WAIS) from January 1999 to December 2000 : 43 with schizophrenia, 15 with mood disorder, and 33 with other psychiatric diagnoses(neurotic patients) according to the DSM-IV criteria. These 3 diagnostic groups were compared each other by current and premorbid intelligence. The schizophrenia were classified into 3 groups based on intellectual decline patterns and examined their characteristics.

Results: Compared to the neurotic patients, schizophrenic patients showed a significantly lower mean value for performance IQ(PIQ). 58% of patients with schizophrenia maintained average premorbid intellectual level. Those who displayed IQ decline of 10 points or greater than the premorbid level have significantly younger age at onset of illness. The age of onset in patients with schizophrenia was negatively correlated with IQ decline.

Conclusion: There were common deficits of PIQ in schizophrenic patients especially in executive function and psychomotor speed but all of these patients did not demonstrate the same pattern or degree of intellectual impairment. These findings suggest different pathogenesis and courses of illness according to characteristics of intelligence.

NR73 Monday, May 20, 3:00 p.m.-5:00 p.m.

Adherence to Medication in Early Psychosis

Eliana L. Coldham, B.S.C., *Department of Psychiatry, University of Calgary, Early Psychosis Program, Calgary, AB T2N 2T9, Canada*; Jean M. Addington, Ph.D., Donald E. Addington, M.D.

Summary:

Objective: The aim was to examine the rates of adherence to antipsychotic medication in patients experiencing a first episode of psychosis and to determine the correlates of adherence in this group.

Method: Subjects were the first 200 consecutive admissions to an Early Psychosis Program. Adherence was determined on a three point scale. Positive, negative and depressive symptoms, medication side effects and substance use were examined longitudinally.

Results: In their first year in the program 42% were non-adherent, 19% were inadequately adherent, and 39% were adherent. Non-adherent patients demonstrated more positive symptoms, more relapses, more alcohol and cannabis use, reduced insight, and poorer quality of life. They were younger, had an earlier age of onset and were less likely to have a family member involved in treatment.

Conclusion: Results for this 1st episode group are similar to those reported in the literature despite the use of strategies designed to enhance compliance. Correlates are more often the consequence of non-adherence. Non-compliance has to be anticipated and relationships maintained with both patients and families in order to intervene as soon as possible in order to minimize the consequence of non-compliance.

NR74 Monday, May 20, 3:00 p.m.-5:00 p.m.

Adolescent Functioning in Early Psychosis: A One-Year Follow-Up

Alissa H. Pencer, M.Sc., *University of Calgary, 2500 University Drive, NW, Calgary, AB T2N 1N4, Canada*; Jean M. Addington, Ph.D., Brian L. Brooks, M.Sc., Lori Hogg, M.D., Donald E. Addington, M.D.

Summary:

Objectives: To examine adolescents' level of functioning initially and 1 year after admission to an Early Psychosis Program, determine if there was improvement over this time, and compare their level of functioning to adults at 1 year.

Method: Positive and negative symptoms, depression, suicide attempts, hospital admissions, substance use, cognitive functioning, and quality of life were assessed in 45 adolescents and 45 adults at initial presentation and 1 year follow-up.

Results: In the adolescents, there was significant improvement on positive symptoms ($p < 0.001$) but not negative symptoms. There was also significant improvement in depressive symptoms ($p < 0.05$), alcohol use ($p < 0.05$), cannabis use ($p < .001$), hallucinogen use ($p < .01$), and quality of life ($p < 0.001$). There was no significant improvement in cognitive functioning. At 1 year follow-up, adolescents did not differ from adults on any of the above measures.

Conclusions: The results of this study demonstrate that adolescents with psychosis are as ill as adults after 1 year of optimal treatment, even though they present earlier for treatment. Results also suggest that adolescents experiencing their first psychotic episode, admitted to an Early Psychosis Program, do improve in a number of areas after 1 year. These findings emphasize the need for early intervention in adolescents with psychosis.

NR75 Monday, May 20, 3:00 p.m.-5:00 p.m.

Impact of Premorbid Functioning on Two-Year Outcome in First-Episode Psychosis

Sarah B. Vanmastrigt, B.A., *Early Psychosis Program, University of Calgary, 1403 29th Street, NW, Calgary, AB T2N 2T9, Canada*; Jean M. Addington, Ph.D., Donald E. Addington, M.D.

Summary:

Objectives: To determine in a first episode sample if premorbid functioning predicts outcome one and two years after optimal treatment in a comprehensive First Episode Program.

Method: Sample was 149 individuals, mean age 24 years, who were being treated in an early psychosis program. The majority had a diagnosis of schizophrenia or schizophreniform. Premorbid functioning at each development stage (childhood, early and late adolescence, adulthood) was assessed on admission using the Cannon-Spoor. Positive and negative symptoms, level of substance use, quality of life, relapse rates and a wide range of neurocognitive functioning were assessed one year ($n = 149$) and two years ($n = 84$) after admission to the program.

Results: At each developmental stage poor premorbid functioning was associated with negative symptoms at one year ($p < 0.01$); relapse rates at one year ($p < 0.05$); poor verbal fluency; and both residual positive symptoms and poor quality of life one and two years after admission ($p < 0.01$). There were no associations with substance use.

Conclusions: First episode subjects who have poor premorbid functioning prior to the onset of the illness are more likely to have a poorer quality of life and more residual symptoms even after early optimal care.

NR76 Monday, May 20, 3:00 p.m.-5:00 p.m.

Cognition in Early Psychosis

Brian L. Brooks, M.Sc., *University of Calgary, 2500 University Drive, NW, Calgary, AB T2N 1N4, Canada*; Jean M. Addington, Ph.D., Alissa H. Pencer, M.Sc., Donald E. Addington, M.D.

Summary:

Objectives: To examine the extent of cognitive impairment in a large sample of individuals presenting with a first episode of psychosis and to determine whether there are differences in cognition among the different schizophrenia spectrum diagnoses.

Method: Cognition was assessed in the first 300 subjects who completed a cognitive assessment from 358 consecutive admissions to an Early Psychosis Program. The cognitive battery included immediate and delayed visual and verbal memory, verbal fluency, motor speed, executive functioning, abstractive reasoning, attention and early information processing. Symptoms were assessed with the PANSS.

Results: In this first episode sample there was a wide range of cognitive impairment. Regardless of diagnosis the majority of subjects demonstrated impairment on verbal and visual memory. Approximately 60% demonstrated impaired information processing, attention and verbal fluency. Only 20% demonstrated impairment on the WCST (executive functioning) suggesting this may be a measure of disability in this first episode group.

Conclusions: This large sample allows us to examine differences in cognition among different diagnoses of first episode psychosis. Individuals with a first episode of psychosis regardless of diagnosis demonstrate a range of cognitive impairment. However since subjects demonstrate a range of impairments this may have implications for later functional outcome.

NR77 Monday, May 20, 3:00 p.m.-5:00 p.m.

HIV Infection in an Acute Psychiatric Ward in South Africa

Dinesh Singh, M.D., *University of Natal, 5 Chez Nous 22 Ridge Road Berea, Durban 4001, South Africa*; Margaret G. Nair, M.D., Urvashi Vasant, M.D.

Summary:

Objective: KwaZulu-Natal, South Africa is the epicentre of the HIV pandemic. Patients have no access to antiretroviral agents thus we see the unaltered progression of the disease. The study aimed to determine the seroprevalence and psychiatric manifestations of HIV in a heterosexual population.

Method: All patients admitted to the psychiatric ward in a general hospital in Durban; South Africa from 1 July 2001 to 28 December 2001 were tested for HIV-1 using the anonymous linked method. Demographic and clinical data were later matched with the HIV status of the patient.

Results: Sixty patients were HIV positive and 146 were HIV negative. The average age between the two groups was similar - 30.1 years. Comorbid substance abuse occurred in 30% of the positives and 41% of the negatives. Cannabis was the commonest substance abused. 54 (90%) of the HIV positive patients were psychotic on admission. 36 (60%) were first episode psychosis. Depression or mania occurred in 40% of the HIV positive patients. SPECT findings for 6 HIV positive patients were abnormal despite a normal CT scan.

Conclusion: There is a high seroprevalence of HIV in psychiatric patients. Psychosis may be a neuropsychiatric manifestation of HIV.

NR78 Monday, May 20, 3:00 p.m.-5:00 p.m.

Quitting and Relapse Among Non-Treatment-Seeking Marijuana Smokers

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

Summary:

Marijuana is the most widely used illicit substance. This study examines self-reported reasons for quitting and relapse among a convenience sample of 83 non-treatment-seeking marijuana smokers who had made at least one "serious" quit attempt: 49 participating in a UCLA lung health study and 34 in non-treatment studies at the NIDA IRP. Subjects were largely white (69%) males (88%), with an average age of 38.9 years (SD = 10.8), who had used marijuana for 21.8 (9.69) years, using 2.47 (3.6) joints/day

and making 4.4 (12.6) "serious" lifetime quit attempts. A Principal Components Analysis of 23 possible reasons for quitting identified 7 factors that accounted for 73% of the variance: "Social pressure (32%)", "Health Concerns" (10%), "Personal consequences" (8%), "Self Image" (7%), "Self efficacy" (6%), "Prove not addicted" (5%), and "Personal resources" (5%). "Legal problems related to marijuana use" loaded equally across factors, and was endorsed by only 20% of subjects. No factor was significantly associated with greater quit duration. "Missed the high" (10%), "Boredom" (10%), and "Peer pressure" (6.7%) were the most frequently cited reasons for relapse. These data suggest that marijuana quitting is more associated with social pressure than with legal concerns, whereas relapse is associated with desiring the hedonic effects of marijuana as well as social pressure.

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

NR79 Monday, May 20, 3:00 p.m.-5:00 p.m.

Substance Abuse in Schizophrenia: A Singapore Perspective

Swapna K. Verma, M.D., *Department of Epidemiology, Woodbridge Hospital Center, 10 Buangkok View, Singapore 539747, Singapore*; Mythily Subramaniam, M.D., Siow A. Chong, M.B.

Summary:

Objective: Most of the information on the prevalence and patterns of substance abuse in patients with schizophrenia has been from studies conducted in Western countries and data from Asian countries is conspicuously lacking. This study was undertaken with the aim to identify the prevalence and patterns of substance abuse among patients with first-episode schizophrenia in the city-state of Singapore.

Method: Patients with first-episode schizophrenia or schizophreniform disorder who were seen in one calendar year in the Institute of Mental Health and its affiliated clinics were included in the study. Diagnosis was confirmed using DSM IV classification criteria. Information about socio-demographic data, episodes of violence, self-harm, and forensic records was noted.

Results: In a sample of 272 patients, 201 (73.6%) were abstainers, 43 (15.8%) had "mild" substance use and 28 (10.3%) had "heavy" use patterns. Alcohol was the most frequently substance abused. The substance users were more likely to be males and had significantly increased history of forensic record than the abstainers.

Conclusion: To our knowledge, this is the first study that examines the co-morbidity of substance abuse in schizophrenia in an Asian population. Our findings once again highlight the fact that patients with schizophrenia are at a higher risk for substance abuse than the general population.

NR80 Monday, May 20, 3:00 p.m.-5:00 p.m.

Gender and Self-Efficacy as Predictors of Nonabstinence Versus Heavy Drinking

Carlos A. Hernandez-Avila, M.D., *Department of Psychiatry, University of Connecticut Health Center, 263 Farmington Avenue, Farmington, CT 06030*; Ola Blomqvist, M.D., Anjum S. Ashraf, M.D., Joseph Burleson, M.D., Henry R. Kranzler, M.D.

Summary:

Objective: Consistent with social learning theory, measures of self-efficacy have been shown to predict relapse among alcoholics. The aim of the present study was to determine whether different dimensions of self-efficacy and their interaction with gender predict different kinds of alcoholic relapse.

Methods: An initial analysis (n = 140) and a replication analysis (n = 181) were conducted using data from alcohol-dependent patients [79% male, mean age = 41.2 (SD = 8.8) yr] who had participated in one of three 12-week, placebo-controlled trials of medication combined with coping skills treatment. The 39-item Situational Confidence Questionnaire (SCQ) was used to measure respondents' confidence in their ability to resist drinking in a variety of imaginary situations. Hierarchical logistic regression was used to examine the predictive value of the three second-order factors of the SCQ (Negative Affect [NA], Positive Affect [PA] and Urges and Testing [UT]) and their interaction with gender, with the criterion measures being a return to Any Drinking (i.e., non-abstinence) and relapse to Heavy Drinking.

Results: In both analyses, men with higher SCQ-PA scores were more likely to be abstinent. In contrast, the only SCQ factor that predicted Heavy Drinking (in both men and women) was the SCQ-UT score.

Conclusions: Different dimensions of self-efficacy appear to predict abstinence compared with relapse to heavy drinking, and these appear to interact differentially with gender. This finding supports the clinical distinction that is drawn between these two definitions of relapse and raises the question of whether different treatment approaches may be indicated in alcoholic men and women to promote abstinence vs. preventing heavy drinking.

NR81 Monday, May 20, 3:00 p.m.-5:00 p.m.

A Medical/Neurological Link to BDD

Vilma Gabbay, M.D., *300 West 110th Street #19F, New York, NY 10026*; Gregory M. Asnis, M.D., Jacqueline Bello, M.D., Mary A. O'Dowd, M.D.

Summary:

Introduction: The etiology and pathophysiology of Body Dysmorphic Disorder (BDD) has not been delineated. We propose a link between neurological dysfunction and BDD and present neuroimaging studies in support of this link.

Method: Charts of patients treated in our clinic with severe BDD during the year 2001 were reviewed. Histories, laboratory data and neuroimaging studies were reviewed to identify possible triggering factors.

Results: 8 cases of severe BDD were identified, all males, aged 17–22. In all three cases, a medical illness had occurred prior to the development of BDD (A:Bell's palsy without sequelae, B:Ulcerative Colitis, C:Encephalitis). Extensive and sequential neuroimaging studies obtained for patient C showed a new and progressive atrophy in the left frontal and temporal lobes.

Conclusions: BDD's preferential response to selective serotonin reuptake inhibitors suggests a serotonin dysfunction (1). We hypothesize that this neurochemical dysfunction was triggered by the inflammatory process in our cases, since it has been suggested that some cytokines suppress serotonin synthesis (2). Case C provides neuroimaging evidence of a possible link to a specific neuroanatomical pathology and suggests frontal and/or temporal lobe dysfunction as an etiology for this disorder. Future research including neuroimaging studies with larger sample of BDD patients are suggested.

NR82 Monday, May 20, 3:00 p.m.-5:00 p.m.

The Influence of a National Tragedy on Local Detoxification Patterns

Diana F. Melazzo, D.O., *Department of Psychiatry, MIHS, 570 West Brown Road, Mesa, AZ 85201*

Summary:

Introduction: Different stressors have been found to cause a multitude of effects with regard to substance abuse. The purpose

of this paper is to investigate the influence of the 9/11 attack on patterns of admission to an intercity detoxification center.

Methods: Data was collected from an inter-city community detoxification center for this study. 16,383 charts were included in this retrospective study over 3 years. A profile analysis incremented by week was used to assess differences in patterns of admission pre and one month post 9/11/01. Independent analysis of the primary drug used (alcohol, heroine or cocaine) was examined by three separate analyses. Gender difference and interaction between gender difference and pattern of response were also analyzed.

Results: The number of admissions did not significantly increase in the month after the event. There were no gender differences noted. These findings are counterintuitive to the expectation that a national tragedy would increase number of admissions. Interestingly, the ratio of admissions for alcohol abuse compared to other drugs was increased. This trend may represent a unique reaction in alcohol abusers. This study suggests that following a stressor of this magnitude community outreach should be directed at both genders equally with emphasis placed on alcohol abuse treatment.

NR83 Monday, May 20, 3:00 p.m.-5:00 p.m.

Body Image in Patients with BDD

Tracy Kuniega-Pietrzak, M.D., *Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI 02906*; Jason Siniscalchi, M.S., Katharine A. Phillips, M.D.

Summary:

Objective: We studied body image in body dysmorphic disorder (BDD) because this central aspect of BDD has received little investigation.

Method: 97 subjects (32 males and 65 females) with DSM-IV BDD completed a reliable, valid, and widely used self-report measure of body image, the Multi-Dimensional Body Self Relations Questionnaire (MBSRQ). This scale and its subscales assess 2 dimensions (Evaluation and Orientation) of 3 domains of body image (Appearance, Health/Illness, and Fitness). It also includes a subscale to evaluate satisfaction with discrete body features. MBSRQ scores were compared to population norms. BDD severity was assessed with the BDD-YBOCS, and delusionality regarding the perceived appearance flaws was assessed with the Brown Assessment of Beliefs Scale.

Results: BDD subjects scored significantly lower than population norms on Appearance Evaluation (feelings of attractiveness), and men scored significantly higher than these norms on Appearance Orientation (extent of investment in appearance). Both men and women scored significantly lower than norms on the Body-Areas Satisfaction subscale (less satisfaction with appearance of discrete body features). In the domain of Health/Illness, BDD subjects scored significantly lower than norms on Health Evaluation (i.e., they feel less physically healthy), and women scored significantly lower on Health Orientation (i.e., less investment in a healthy lifestyle). On Illness Orientation (extent of reactivity to being ill), women but not men scored lower than norms, and in the Fitness domain women scored lower on Fitness Evaluation (feelings of being physically fit). Greater BDD severity and greater delusionality were significantly correlated with several MBSRQ subscales, including poorer Appearance Evaluation and lower Body-Areas Satisfaction scores.

Conclusion: Body image is severely and negatively affected in BDD, especially in more delusional and severely ill patients.

NR84 Monday, May 20, 3:00 p.m.-5:00 p.m.

Validity of Dual Diagnosis in a Residential Substance Abuse Treatment Center

Christopher M. Stewart, M.D., *University of Louisville, 2205 Wrocklage Avenue, Louisville, KY 40205*; Rif S. El-Mallakh, M.D.

Summary:

This quality control interview study was performed at a residential treatment facility for patients with known substance abuse, with all participants having alcohol abuse in common as well as a history of bipolar disorder. Participants were voluntarily administered the Structured Clinical Interview for DSM-IV. Criteria for participation include either a history of being treated for bipolar disorder by a psychiatrist or current treatment of bipolar disorder as an outpatient. The study remains an ongoing project, and 30 interviews have been conducted to date. Anyone at the facility who meets criteria is asked to participate, with no reward or payment for volunteering except the knowledge of their own interview results during an exit interview once the data from the SCID has been reviewed. Only 6 out of the 30 participants have met criteria for bipolar I disorder as defined by the SCID.

Reviews of literature revealed some interview studies exploring comorbidity of axis I disorders (especially alcohol abuse) with bipolar disorder but did not address the issue from a quality control standpoint. This study is demonstrating that patients with substance abuse are frequently misdiagnosed by psychiatrists using the SCID as the standard. Considering that the DSM IV criteria are not ideal for determining dual diagnosis, it is noteworthy that even these criteria are not being met in these participants who were receiving treatment for bipolar disorder. Further studies need to be done with this population, and this study continues to have a growing number of participants.

NR85 Monday, May 20, 3:00 p.m.-5:00 p.m.

NMR Spectroscopy in Mild Cognitive Impairment and Alzheimer's Disease

Adriana P. Hermida, M.D., *Department of Psychiatry, University of Chicago, 1030 North State Street #2FC, Chicago, IL 60610*; Maria T. Caserta, M.D., Leon J. Wise, B.S.

Summary:

Introduction: Patients with Alzheimer's Disease(AD) have abnormalities with NMR Spectroscopy(NMRS): increased myoinositol(MI) and a decrease in N-acetylaspartate(NAA).

Objective: To test the applicability of proton NMRS in mildly cognitively impaired(MCI) individuals and mild probable AD(-MPRAD) in vulnerable brain areas such as hippocampus, temporal lobe, and cingulate gyrus.

Method: A complete neurological, neuropsychological evaluation and MRI were obtained in 6 MPRAD and 6 MCI subjects and 16 normal controls. Single voxel proton data was acquired in three different regions: Right hippocampus/temporal lobe(RH/TL), Left hippocampus/temporal lobe(LH/TL) and posterior cingulate gyrus. The NMRS data was expressed as ratios of NAA, Choline(CHO) and MI to creatine.

Results: Significant decrease in NAA was found in the RH/TL area in subjects with MPRAD($p < 0.03$) and MCI($p < 0.003$) compared to controls. CHO ratios in the RH/TL were decreased in MPRAD($p < 0.04$) but not in the other groups. MI levels were not affected in any groups.

Conclusions: The findings suggests early neuronal loss/integrity as measured by NAA ratio beginning at RH/TL in MPRAD and MCI subjects. CHO ratios were only affected in MPRAD subjects suggesting membrane degradation at later stage of neuropathology. MI ratios were not affected in this population.

NR86 Monday, May 20, 3:00 p.m.-5:00 p.m.

Decreased Prefrontal Cortical Gamma-Aminobutyric Acid in Bipolar Disorder Patients Compared with Healthy Controls

Po W. Wang, M.D., *Department of Psychiatry, Stanford University, 401 Quarry Road, Room 2124, Stanford, CA 94305*; Nathan F. Dieckmann, B.A., Olga V. Becker, M.D., Napapon Sailasuta, Ph.D., Elfar Adalsteinsson, Ph.D., Daniel Spielman, Ph.D., Terence A. Ketter, M.D.

Summary:

Background: GABA, the primary inhibitory neurotransmitter in human brain, is implicated in the pathophysiology of mood disorders. Magnetic resonance spectroscopy allows non-invasive cerebral GABA assessment. Euthymic bipolar patients, primarily on GABAergic medications, have increased occipital cortical GABA, compared to healthy controls (Wang, 2001); depressed bipolar patients have near normal levels (Mason, 2000).

Methods: A modified GABA-edited PRESS (double spin echo) sequence [TE 68msec, TR 1500msec, 512 averages; scan time 26minutes], on a 3-Tesia General Electric Signa scanner, was used to measure cerebral GABA, in a 12.5 cm^3 midline medial prefrontal cortical voxel, in nine euthymic, bipolar disorder patients, primarily on GABAergic medications, and six age- and gender-matched, medication-free healthy controls.

Results: Spectra consistently yielded the 3.0ppm GABA gamma-CH2 peak, 3.7ppm glutamate/glutamine peak, 2.3ppm GABA/glutamate/glutamine peaks, and 2.0ppm residual NAA peak. Patients, compared to controls, tended to have 50% increased medial prefrontal cortical GABA (GABA/Cr ratio ±SD = 0.266±0.109 versus 0.179±0.177).

Conclusions: Prefrontal GABA levels can be measured, despite the technical challenges. These preliminary, prefrontal GABA findings are consistent with our prior studies of occipital GABA and with the notion that medication-free depressed bipolar patients have near normal cerebral GABA, which rises with effective treatment. Prospective, within subject studies are warranted.

NR87 Monday, May 20, 3:00 p.m.-5:00 p.m.

Cognitive Processing of Nonconscious Stimuli: An fMRI Study

Rajendra D. Badgaiyan, M.D., *Department of Psychiatry, Harvard University Medical School, 33 Kirkland Street, Cambridge, MA 02138*

Summary:

The question whether a nonconscious stimulus can elicit a well-processed cognitive response is under scrutiny for over a hundred years. Experimental protocols have been devised to show effects both, in favor and against the argument. Since behavioral studies have failed to reach to a conclusion, in this experiment a neuroimaging method was used. After a series of pictures (3 sec/picture) had been studied, the studied and nonstudied pictures were presented subliminally (16 msec) and subjects were asked to make a forced-choice decision whether a picture was studied earlier. They correctly recalled 65% of studied pictures. Behavioral data confirmed that subliminal cues elicited retrieval of studied pictures. To examine whether these cues elicited a well-processed cognitive response, the pattern of cortical activity was examined using fMRI technique. Retrieval of studied pictures was associated with increased activation in the left middle frontal gyrus, right superior frontal gyrus, and right hippocampus. Nonstudied pictures activated left middle frontal gyrus. Since, similar patterns of activation have been observed in the experiments that have used conscious cues, results indicate that cognitive processing elicited by a subliminal stimulus is similar to that elicited by conscious stimuli. It therefore appears that nonconscious stimuli elicit a well-processed cognitive response.

NR88 Monday, May 20, 3:00 p.m.-5:00 p.m.

Divalproex Sodium: Oral Loading During Combination Drug Therapy in Children

Candace R. Good, M.D., *Department of Psychiatry, Penn State College of Medicine, 479 Rockwood Drive, Elizabethtown, PA 17022*; Christopher A. Petersen, M.D., Valentins F. Krecko, M.D.

Summary:

Objective: To identify factors (i.e., drug preparation or combinations) that may alter doseage requirements during rapid titration of divalproex sodium.

Method: A retrospective chart review revealed that divalproex was initiated in 45 inpatients (mean age 9 yrs.) over a 1 yr. period. Initiation dose approximated 15 mg/kg/day. Trough blood levels were obtained on day 5 following initiation/dose adjustment.

Results: Initial drug levels were 37–121 ug/ml. Dose titration occurred in 20/45 patients. Divalproex was used most frequently with an atypical antipsychotic (29/45 patients, 13 patients also received a stimulant). A smaller number received monotherapy, concurrent stimulant and/or antidepressant. No significant differences in discharge dose or drug level were apparent by age, sex, or drug combination. Patients administered the divalproex sprinkles formulation (n = 6) required significantly higher doses to achieve comparable blood levels.

Conclusions: Therapeutic levels of divalproex sodium can be achieved quickly following an initial 15 mg/kg oral load. Combination drug therapy does not appear to precipitate toxicity at clinically effective doses. Divalproex formulation may alter doseage requirements acutely.

NR89 Monday, May 20, 3:00 p.m.-5:00 p.m.

Aggressive Youth on Divalproex: Effectiveness as Reviewed in Medical Record

Carl A. Fleisher, *Fegan 8, Children's Hospital, 300 Longwood Avenue, Boston, MA 02115*; Joseph M. Gonzalez-Heydrich, M.D., Sergio R. Korndorfer, M.D., Darcy Raches, B.A., Enrico Mezzacappa, M.D.

Summary:

Objective: To examine divalproex effectiveness in aggressive youth treated in a practice setting.

Methods: Medical records were searched for aggressive patients <18 yrs treated with divalproex from 11/98 to 4/01. Diagnoses, histories, and prospectively entered clinical global impressions (CGIs) were extracted.

Results: 48 youth were identified: 77% male; age 12.6 ± 4.0 years; daily dose divalproex 815 ± 440 mg; 75% had psychiatric and 29.2% had medical co-morbidities. Seven patients had abnormal EEGs; six of the seven had seizures. Previous medication trials averaged 2.3 ± 2.1/patient. At end visit, 14.6% of patients were receiving divalproex monotherapy; 66.6% were receiving concomitant antidepressants, atypical neuroleptics, or mood stabilizers; 48% were on stimulants/alpha-adrenergics. At last visit, mean CGI-Improvement score was 2.4 ± 1.2, mean CGI-Severity 3.8 ± 1.2, and 56% of subjects were much or very improved. Using multivariate analysis, CGI-Improvement scores were not explained by valproic acid plasma level, age, concomitant atypical neuroleptics, initial CGI-Severity or Clinical Global Assessment of Function (CGAF). Adverse effects were none or slight in 85%.

Conclusions: Divalproex use was associated with significant global improvement and few adverse effects in this unselected sample of aggressive youths; however, most patients required

concomitant treatment with other psychotropic agents. Prospective, controlled studies of combined pharmacotherapy with divalproex are needed.

NR90 Monday, May 20, 3:00 p.m.-5:00 p.m.

Methylphenidate Increases Plasma Neurosteroid Levels in Boys with ADHD

Allon Nechuad, M.D., *Department of Biological Psychiatry, Felsenstein Resident Center, Beilinson Campus, Petah-Tikva 49100, Israel*; Baruch Spivak, M.D., Rachel Maayan, PH.D., Roni Yoran-Hegesh, M.D., Rael Srous, M.D., Roberto Mester, M.D., Abraham Weizman, M.D.

Summary:

Objective: Dehydroepiandrosterone (DHEA) and Dehydroepiandrosterone-sulfate (DHEAS) are neurosteroids, which may have favorable effects on cognition, aggressive behavior and mood through various neural pathways. We examined whether methylphenidate treatment may alter circulatory levels of these neuromodulators in boys suffering from attention deficit hyperactivity disorder (ADHD).

Methods: Fifteen outpatients boys (aged 11.5 ± 1.6 years) with "pure" ADHD, combined type, were examined for circulatory levels of DHEA, its precursor pregnenolone, DHEAS and cortisol before and after three months of methylphenidate treatment (mean dose 14.7 ± 4.4 mg/day). Subjects were evaluated with specific rating scales for inattention and impulsivity before and after methylphenidate treatment.

Results: Methylphenidate improved ADHD symptoms and significantly elevated DHEA and DHEAS circulatory levels (23% and 87%, respectively). No significant changes were noted in pregnenolone and cortisol levels.

Conclusions: Methylphenidate treatment is associated with a significant ($p < 0.05$) increase in DHEA and DHEAS circulatory levels in ADHD boys. The absence of cortisol elevation may exclude a methylphenidate induced general adrenal hyperactivity. Activity of DHEA/S at the GABAergic, glutamatergic, dopaminergic and noradrenergic systems may be relevant to the amelioration of ADHD symptoms.

NR91 Monday, May 20, 3:00 p.m.-5:00 p.m.

20-Month Outcomes with Risperidone Treatment in Children

Christopher Lam, M.D., *Department of Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139*; Klara J. Rosenquist, B.S., S. Nassir Ghaemi, M.D.

Summary:

Objective: To determine the naturalistic efficacy of risperidone treatment in children.

Methods: Retrospective chart review of 35 children (27 males, 8 females, mean age 12.1 years) treated with risperidone. Response was assessed with the Clinical Global Impression Scale for Improvement (CGI-I). The most common diagnosis was pervasive developmental disorder (n = 15, 33%), followed by affective disorders (n = 9, 20% 3 unipolar, 6 bipolar). 91% received concurrent antidepressants or mood stabilizers. 27/35 (77%) did not have psychotic features. Mean risperidone dose was 2.0 mg, with a mean duration of 1.8 years.

Results: 31% bad mild improvement and 48% moderate to marked improvement. Dose, age, gender, presence of psychosis, and family history of psychiatric illness did not predict response. However, pervasive developmental disorder did tend to be predictive of response to risperidone (10/15, 67% with pervasive developmental disorder responded vs. 7/20 with other diagnoses, $p = 0.09$). 20/35 (57%) had no side effects. The most common side effects were weight gain (8/35, 23%), sedation (7/35, 20%) and amenorhea (3/35, 9%). 25/35 (71%) continued risperidone treatment, while 7/35 (20%) dropped out due to lack of efficacy and 3/35 (9%) stopped due to side effects.

Conclusions: Risperidone appeared effective and tolerable in nearly 2-year outcome in children and adolescents with varied, mainly non-psychotic neuropsychiatric conditions, particularly pervasive developmental disorder.

NR92 Monday, May 20, 3:00 p.m.-5:00 p.m.

Divalproex in Children with Bipolar Disorder: A 16-Month Outcome

Supported by Abbott Laboratories

Charles A. Henry, M.D., *Department of Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139*; Linda S. Zamvil, M.D., Christopher Lam, M.D., Klara J. Rosenquist, B.S., S. Nassir Ghaemi, M.D.

Summary:

Objective: To assess the effectiveness and safety of divalproex in children and adolescents.

Methods: This is a partial dataset based on a retrospective chart review of children and adolescents treated with divalproex. All patients met DSM-IV criteria for bipolar disorder and were treated on an outpatient basis (current n = 15, mean age 13.5 years, 10 males and 5 females). Mean dose of divalproex was 966 mg/day (mean blood level 79.4) with 1.4 year duration of treatment. Response was based on moderate to marked response on Clinical Global Impression-Improvement (CGI-I) ratings.

Results: To date in the data analysis, 8/15 (53%) patients have responded. The most common indications for treatment were mixed episode (n = 6), disruptive behavior (n = 4), pure mania (n = 3) or depression (n = 2). 6/15 (40%) discontinued divalproex, most due to side effects (n = 5, mostly weight gain). 7/15 (47%) experienced no side effects, while 4/15 (27%) experienced weight gain, which was the most common side effect.

Conclusions: Divalproex was well-tolerated and effective in the long term, 1.4 year treatment of bipolar disorder in children and adolescents. A final data analysis from the complete sample will be presented.

NR93 Monday, May 20, 3:00 p.m.-5:00 p.m.

Citalopram in Children with Autism-Spectrum Disorders: A Case Series

Jennifer L. Couturier, M.D., *Department of Psychiatry, University of Western, 1012-560 Proudfoot Lane, London, ON N6H 5C9, Canada*; R. Nicolson, M.D.

Summary:

Objective: Although selective serotonin reuptake inhibitors (SSRI's) have been used to treat symptoms of aggression and anxiety in children and adolescents with autism spectrum disorders (ASD's), their adverse effects often limit their use in pediatric populations. The purpose of this study was to examine the assess the benefits and adverse effects of citalopram in a group of children and adolescents with ASD's.

Methods: Seventeen patients with ASD's were treated with citalopram for at least two months. Target behaviours included aggression, anxiety, and stereotyped behaviour. Outcome was based upon a consensus between clinician and parents, using the Improvement Item of the Clinical Global Impressions Scale (CGI) as a guide.

Results: Ten (59%) children judged to be responders based upon a rating of much or very much improved in target behaviour. Citalopram was generally well tolerated, although adverse effects included insomnia and agitation.

Conclusions: The results of this case study suggest that citalopram has beneficial effects on some interfering behaviours associated with ASD's. Further controlled trials are warranted.

NR94 Monday, May 20, 3:00 p.m.-5:00 p.m.

Cerebellar Volume in Adolescent-Onset Alcohol Use Disorders

Anandhi Narasimhan, M.D., *Department of Psychiatry, WPIC Room 392, 3811 O'Hara Street, Pittsburgh, PA 15213*; Michael D. DeBellis, M.D., Matcheri S. Keshavan, M.D., Duncan B. Clark, M.D., Paul H. Soloff, M.D.

Summary:

Objective: Studies focusing on brain injury associated with ethanol use and the cerebellum have been done primarily in adults. Alcohol use disorders (AUD, defined as DSM-IV alcohol dependence or abuse) are prevalent and serious problems among adolescents. As childhood cerebellar volumes are uniquely influenced by shared environment, we compared cerebellar volumes of adolescents and young adults with adolescent onset AUD to those of matched comparison subjects.

Methods: Magnetic resonance imaging was used to measure cerebellar volumes in 12 subjects (5 males, 7 females) with an AUD (mean age 17.6 ± 2.6 years) and 24 comparison subjects (10 males, 14 females; 17.3 ± 2.6 years) matched on age, sex, and handedness.

Results: Overall no differences were seen between AUD subjects (144.5 ± 14.0 cm3) and controls (143.1 ± 8.6 cm3). However, there was a suggestion of a significant sex-by-group effect for males with an adolescent onset AUD to have smaller cerebellar volumes than control males ($F = 3.13$, $df = 1,31$, $p < .09$).

Conclusions: Unlike previous findings which suggested that the male and female adolescent hippocampus may be particularly susceptible to the adverse effects of alcohol, these findings may suggest sex differences for males with an adolescent onset AUD to have smaller cerebellar volumes than control males. Further studies are warranted.

NR95 Monday, May 20, 3:00 p.m.-5:00 p.m.

Psychiatric Morbidity in End-stage Renal Disease Patients: A Comparative Study

Laxmi N. Vadlamani, M.D., *Addenbrooke's Hospital, 62A, Barton House, Adrian Way, Cambridge CB2 2SB, United Kingdom*; Anand Bhojarajv, M.D., Krishnamurth Kartikeya, M.D.

Summary:

Objectives: The purpose of the study was to assess the psychiatric morbidity, quality of life and correlation between biochemical and psychological parameters in End Stage Renal Disease (ESRD) patients.

Method: 4 groups were studied-patients with Chronic Renal Failure, on Hemodialysis; post transplant and control group. 20 patients in each group were randomly selected after consenting for the study. All relevant data was collected. Patients were assessed for severity of renal disease by ESRD-SI (Craven et al., 1991), for psychiatric morbidity by SCID-III R. T-test was employed for comparing variables between two different groups and 1-way ANOVA for comparing all groups. Bivariate Correlational Analysis was used for correlation between biochemical and psychological parameters.

Results: 40% in CRF group and 35% in Hemodialysis group had psychiatric illness. Patients with high ESRD-SI scores had poor quality of life.

Conclusion: 1. There is higher psychiatric morbidity in ESRD patients when compared to controls. 2. Higher values of renal biochemical parameter higher the scores on psychiatric scales, hence higher psychiatric morbidities.

NR96 Monday, May 20, 3:00 p.m.-5:00 p.m.

Psychotropic Prescription Practices in Child Psychiatric Inpatients

Manoj S. Lekhwani, M.D., *Department of Psychiatry, MCP Hahnemann University, 3200 Henry Avenue, Philadelphia, PA 19129*; Chand C. Nair, M.D., Ilia Nikhinson, M.D., Paul J. Ambrosini, M.D.

Summary:

Objective: The study examined prescribing patterns of psychotropic medications among child psychiatric inpatients at a university-based hospital.

Method: Charts of 257 patients admitted between 1998–2001 were reviewed for demographic variables, diagnoses, and medications prescribed.

Results: The cohort was 79% male and 68.5% African-American. The mean age was 7.2 years. 56% of patients were on one medication on admission, which increased to 80.5% on discharge. 86% of patients had a 'Behavior Disorder' diagnosis on both admission and discharge. A diagnosis of Mood disorder was seen in 32% of patients on admission and 28% of patients on discharge. 36.2% of patients were on stimulants on admission and on discharge this percentage increased to 58%. Other medication prescribed at discharge in the rank order of its frequency was antidepressant (15.5%), atypical antipsychotic (12%), and alpha2-agonist (8.9%). On admission these percentages were 8.9%, 9.3%, and 10.9% respectively. Logistic regression was used to look at the predictors of pharmacotherapy.

Conclusions: The variables which significantly predicted being on one medication at discharge were length of stay and the diagnostic subcategory of 'behavior disorder'. Length of stay was the only variable predictive of polypharmacy at the time of discharge.

NR97 Monday, May 20, 3:00 p.m.-5:00 p.m.

Efficacy and Safety of Nefazodone in Adolescents with MDD

Moira A. Rynn, M.D., *Department of Psychiatry, University of Pennsylvania, 3535 Market Street, Suite 670, Philadelphia, PA 19104*; Robert L. Findling, M.D., Graham J. Emslie, M.D., Ronald N. Marcus, M.D., Lori A. Fernandes, M.D., M. Frances D'Amico, M.S., Sterling A. Hardy, M.S.

Summary:

Objective: To determine the efficacy and safety of nefazodone vs. placebo in adolescents with Major Depressive Disorder (MDD).

Methods: After a 2–4 week baseline phase, 195 adolescents (aged 12-17) meeting DSM-IV criteria for MDD with a Childhood Depression Rating Scale-Revised (CDRS-R) score ≥ 45 were randomized to receive 8 weeks of nefazodone ($n = 99$) or placebo ($n = 96$) at 15 sites. Adolescents randomized to nefazodone initially received 100 mg daily in equally divided doses BID and were titrated by 100 mg/week to targeted total daily doses of 300–400 mg based on clinical response and tolerability. Efficacy and safety were evaluated weekly. The primary efficacy measure was the nefazodone to placebo comparison in mean CDRS-R score from baseline to week 8 (LOCF).

Results: A longitudinal analysis which compares the change in CDRS-R over the 8 weeks was significant in favor of nefazodone ($p = 0.03$). There was a significant difference in the CDRS-R score favoring nefazodone at Week 7 (−26.7 vs. −21.3, $p = 0.006$) and a 4.0 point improvement in CDRS-R score at week 8 which narrowly missed statistical significance (−26.5 vs. −22.5, $p = 0.055$). The nefazodone group was superior to placebo at week 8 on CGI

response rate (62% vs. 42%, p = 0.005), CGI Improvement (2.3 vs. 2.8, p = 0.012), CGI Severity. (–1.7 vs. –1.3, p = 0.022), HAM-D (–10.0 vs. –8.2, p = 0.023) and CGAS (17.2 vs. 13.0, p = 0.020). Nefazodone was well tolerated with a rate of discontinuation for AEs equal to placebo (3.0%).

Conclusions: In this study nefazodone was shown to be safe and effective in the acute treatment of adolescents with MDD.

NR98 Monday, May 20, 3:00 p.m.-5:00 p.m.

Social Function in Patients with Mitral Valve Prolapse

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

Summary:

Objective: This study compared the social function of patients with mitral valve prolapse (MVP) before and after the onset of symptoms.

Methods: Patients were diagnosed for MVP by cardiologists with standard echocardiography. A total of 35 MVP patients were then consecutively recruited and interviewed by a psychiatrist according to DSM-IV criteria. The social function was evaluated by a Likert-type scale, including three dimensions as working performance, interpersonal relationship and leisure-time arrangement. Their mean age was 32.2 ± 12.1, education years 11.9 ± 3.7, 60% female and 51.4% married.

Results: Of the 35 MVP patients, 27 (77.1%) had DSM-IV psychiatric disorders. The social function was significantly impaired after the onset of symptoms associated with MVP (paired t = 4.2 to 6.2, p = .000). In addition, MVP patients with, compared to those without, psychiatric disorders had more social function impairment in above three dimensions (t = 2.8 to 3.8, p = .008 to .001).

Conclusions: The social function of patients with MVP was commonly impaired after the onset of the symptoms, especially among those having comorbid psychiatric disorders. Psychiatric treatment may be beneficial for their working performance, interpersonal relationship and leisure time arrangement.

NR99 Monday, May 20, 3:00 p.m.-5:00 p.m.

Psychiatric Comorbidities Among Patients with Hepatitis-C Infection

Muhamad A. Rifai, M.D., *University of Virginia, VAMC, 1970 Roanoke Boulevard 116A7, Salem, VA 24153*; James K. Moles, M.D., Corinne J. Belsky, M.D., Joseph Doumit, M.D., Sonia P. Yovtcheva, M.D., Brian J. Van Der Linden, M.D.

Summary:

It is estimated that 1.8% of the US populations is chronically infected with the hepatitis C virus (HCV). The veteran population is at increased risk for HCV infection, and although they only represents 9% of the total US population, veterans account for 15–20% of the total infected US population. We assessed the prevalence of psychiatric disorders among hepatitis C positive HCV+ patients at a Veterans Affairs Medical Center in Salem, Virginia. Medical records of 400 randomly selected HCV+ patiens were reviewed for past and present DSM-IV based psychiatric disorders. A similar group of HCV negative veterans were utilized as a control. Each Psychiatric diagnosis was independently confirmed (by 2 reviewers) with DSM-IV criteria recorded in the chart. Only the diagnoses which could be independently confirmed were selected for analysis. The pervalence rates of psychiatric disorders in the HCV+ patients versus HCV negative patients are as follows: Mood disorders 38% vs. 17%, personality disorders 30% vs. 7%, Post-Traumatic Stress Disorder 19% vs. 13% and Psychotic disorders 17% vs. 4%. Alcohol abuse/dependence disorders were found in 86% of HCV+ patiens vs. 23% of HCV negative patients. Patients with psychiatric illnesses engage in behaviors that puts them at a high risk for HCV infection. Our data indicate that the prevalence rates of psychiatric diagnoses are significantly higher in veterans with HCV+ status when compared with the general veterans population, and the general US population.

NR100 Monday, May 20, 3:00 p.m.-5:00 p.m.

Plasma Levels of Citalopram in Depressed Patients with Hepatitis-C

Ondria C. Gleason, M.D., *Department of Psychiatry, University of Oklahoma, 2808 South Sheridan, Tulsa, OK 74129*; William R. Yates, M.D., Michelle A. Philipsen, B.A., M. Daniel Isbell, B.S., Bruce G. Pollock, M.D.

Summary:

Introduction: Hepatitis C affects an estimated 4 million Americans and 100 million people worldwide. Rates of depression in patients with hepatitis C are higher than that seen in the general population; and safe and effective management of depression is important. Liver disease can affect the metabolism and clearance of drugs resulting in alterations in plasma concentrations.

Methods: 15 subjects with hepatitis C and major depression completed an 8-week trial of citalopram. Plasma levels of citalopram were measured at weeks 4 and 8 and compared to previously reported levels in subjects without hepatitis C.

Results: Mean levels were lower than expected (53.0 +/– 35.2 ng/ml at week 4 and 55.1 +/– 31.7 ng/ml at week 8). Four subjects were receiving interferon during the study. There was a trend toward lower plasma levels in those subjects receiving interferon (35.4 +/– 18.9 ng/ml versus 62.2 +/– 34.9 ng/ml) although a statistically significant difference was not observed (p = 0.0533).

Conclusion: These results suggest that citalopram is safe and well tolerated in adults with concurrent hepatitis C and major depression. Concurrent treatment with interferon may lower plasma citalopram levels.

NR101 Monday, May 20, 3:00 p.m.-5:00 p.m.

Epidemiology and Predictors of PRN Psychotropic Medication Use in a State Hospital

Shanna L. Palmer, M.D., *Department of Psychiatry, University of Arkansas Medical Science, 4301 W Markham, Slot 589, Little Rock, AR 72205-7199*; Richard R. Owen, Jr., M.D., Purushottam Thapa, M.D., Andrea Huntley, M.P.H., James A. Clardy, M.D., Laurence H. Miller, M.D.

Summary:

Objectives: To describe the epidemiology and identify predictors of PRN ("as needed") psychotropic medication use in a state hospital.

Methods: Medical records of 223 new admissions between July 15, 1999 and October 15, 1999 were reviewed from 3 acute adult psychiatric units of the Arkansas State Hospital, Little Rock. Detailed data were collected on demographic and clinical characteristics, scheduled and unscheduled medications from the MAR. Logistic regression analysis was used to identify predictor variables associated with PRN medication use.

Results: The number of PRN psychotropic medications administered in the study period was 1812 (mean 8.1). Haloperidol and chlorpromazine (37.8%) and lorazepam (35.4%) were the most frequently used medications. 47.8% of the PRN medications were given during the first week of admission. PRN medications were more likely to be given in the evening shift, 3PM-11PM (46% vs 33.2% and 20.5% in the 7am-3pm and Midnight-7AM shifts, respectively [p < 0.0001]. Independent predictors of PRN medication (0 vs >10) use were Global Assessment of Functioning (GAF) score <30 on admission (Odds ratio[OR] 3.0, 95% CI 1.1–8.6, p

0.03), 1st psychiatric hospitalization >5 years (OR 6.0, 95% CI 1.7–24.4, p 0.007), transferred from another psychiatric institution (OR 0.2, 95% CI 0.06–0.9, p 0.03), and presence of anxiety symptoms on admission (OR 0.2, 95% CI 0.03–0.7, p 0.02).

Conclusions: Identification of factors (such as first week of admission, evening shifts, and GAF<30) associated with PRN psychotropic medication use can help in the development of intervention strategies.

NR102 Monday, May 20, 3:00 p.m.-5:00 p.m.

p53 Gene Polymorphisms in Patients with Schizophrenia and Lung Cancer

Jin-Kyung Park, M.D., *Kyunghee University Hospital, 1 Hoegi-Dong Dongdaemun-Ku, Seoul 130-702, Korea*; Tae M. Kim, M.D., Do-Hyung Kim, Ji-Young Song, M.D., Doh-Joon Yoon, M.D.

Summary:

Objective: Incidence studies show that patients of schizophrenia possess a lower risk of developing cancer compared to the general population. The mechanism underlying the apparent tumor resistance in schizophrenia patients may be of etiological significance to schizophrenia itself. One mechanism which plays a central role in both tumorigenesis and neurodevelopment is apoptosis, p53, a gene involved in tumor suppression & neuronal apoptosis, could be seen as a candidate susceptibility gene of schizophrenia.

Methods: Two p53 restriction site polymorphisms(BstUI and MspI SNPs in exon 4 and intron 6, respectively) were studied in 187 controls, 191 schizophrenia patients, and 42 lung cancer patients by PCR and RFLP.

Results: There was no difference between schizophrenia patients and controls in terms of the distribution of the BstUI and MspI restriction site variations in the p53 gene. However, a significantly higher proportion of the lung cancer patients studied were MspI heterozygotes than in the schizophrenia patients and the controls.

Conclusions: The results of this study suggest that the MspI restriction site polymorphism of the p53 gene may be an indicator of susceptibility to lung cancer; however not to be the case for schizophrenia. Further studies of other genetic factors regulating apoptosis should be conducted.

NR103 Monday, May 20, 3:00 p.m.-5:00 p.m.

Impact of the September 11th Attacks on Geriatric Mental Health Needs

Lucy Y. Wang, Penn State, *161 University Manor East, Hershey, PA 17033*; Paul A. Kettl, M.D., Edward Bixler, Ph.D., William P. Milchak, M.S.W., Charles P. Gilbert, A.C.S.W.

Summary:

Objective: This study assessed the degree to which mental health professionals caring for the geriatric population in central Pennsylvania saw additional need for services after the tragedies of September 11th.

Method: Anonymous surveys were distributed to attendees of conferences sponsored by the Central Pennsylvania Psychiatric Institute 4–6 weeks after September 11th. 209 surveys were returned (response rate of 49.5%), primarily by nursing home nurses, social workers, and psychologists practicing in central Pennsylvania. The surveys asked participants about changes they observed in their practices, and how prepared they were to handle these changes.

Results: 10.0% of respondents reported increased referrals due to the tragedies. An average of 0.6 new clients per provider were seen following September 11th. Larger percentages saw increased acuity in current clients (67.9% of psychologists and 44.1% of social workers). 51.6% felt that their agency could handle increased numbers of clients. The largest need was for training on how to handle such events in the future, with 50.5% of all respondents requesting more education.

Conclusions: The tragedies of September 11th had a small but measurable effect on geriatric mental health needs in central Pennsylvania. An increase in acuity in patients occurred along with a small number of increased referrals. Mental health training remains an important need for health care professionals caring for the geriatric population.

NR104 Monday, May 20, 3:00 p.m.-5:00 p.m.

Capacity Assessment and Advance Directive Counseling for Alzheimer's Patients

Alan D. Schlechter, *Department of Psychiatry, Mount Sinai School of Medicine, 1 Gustave-Levy Place Box 1230, New York, NY 10029*; Adriana K. DiMatteo, M.A., Margaret Sewell, Ph.D.

Summary:

Objective: To assess Alzheimer's patients' capacity and preferences and effectiveness of counselling.

Method: Twenty subjects were recruited from an Alzheimer's Disease Research Center. Consented patients were administered the MacArthur Competence Assessment Tool, Mini-Mental Status Exam (MMSE), and a family interview.

Results: Mean age was 77 (60% female; 90% Caucasian). Mean MMSE was 22. Capacity decreased as decisions became complex ($F=19.22$, $p<.0001$). Using the basic legal standard—ability to evidence a logical choice—to define capacity, 85% had capacity to choose a health care proxy, and 4% had capacity to relate preferences for CPR and lubefeeding. The majority (86%) declined aggressive care. In 40% of the cases, caregivers failed to predict their family member's wishes. Seventy percent of subjects had advance directives, but only 25% had given a copy to their doctor. Following the interview, the modification in, or creation of advance directives were made in 80% of the cases.

Conclusion: A high percentage of mild stage Alzheimer's patients have capacity to discuss end-of-life care. Advance directive counseling is feasible and effective, as most participants made or changed their advanced directives following the family interview.

NR105 Monday, May 20, 3:00 p.m.-5:00 p.m.

Pathological Gambling, Gender, and Risk-Taking Behavior in a Brazilian Setting

Silvia S. Martins, M.D., *Department of Psychiatry, University of Sao Paulo, Rua Ovidio Peres Campos, S/N, Sao Paulo, SP 05403-010, Brazil*; Hermano Tavares, Ph.D., Valentim Gentil, M.D., Daniela S. Lobo, M.D., Ana Maria Galleti, M.D.

Summary:

Objective: To compare risk-taking behaviors such as sexual risk behaviors, suicide attempts and illegal behaviors in male and female pathological gamblers (PG).

Method: Seventy five female gamblers and 75 male gamblers admitted from April 1998 to December 2001 to an outpatient treatment program at University of Sao Paulo Medical School, selected by SOGS and DSM IV criteria. Subjects answered a socio-demographic questionnaire, a psychiatric diagnosis questionnaire (SCAN), the Barrat Impulsivity Scale (BIS) and the Temperament and Character Inventory (TCI). Genders were compared regarding sexual risk behaviors, suicide attempts and illegal behaviors with control for demographic differences, psychiatric comorbidity and personality factors.

Results: Men were slightly younger than women (p:0.059), women were more single than men (p: 0.037). No difference in job status, education, racial/ethnic background and religion. Men

and women did not differ regarding illegal acts related to gambling. Women attempted suicide more than men (p:0.012), which is related to females having more neurotic (p:0.001) and depressive (p:0.000) symptoms. Men had more sexual risk behavior than women (p:0.001).

Conclusion: Female and male gamblers differ in aspects of their risk taking behavior, suggesting that impulsivity in PGs may show itself differently in each gender, reinforcing the necessity of specific treatment for each gender.

NR106 Monday, May 20, 3:00 p.m.-5:00 p.m.

Block Versus Longitudinal Training in Consultation-Liaison Psychiatry

Bellelizabeth Foster, *Dartmouth Medical School, One Medical Center Drive, Lebanon, NH 03756*; Bradley V. Watts, M.D., Ronald L. Green, M.D., Candi Monson, Ph.D.

Summary:

Objective: To assess the level of psychiatry resident satisfaction following a curriculum change in the Consultation/Liaison, (C/L), rotation comparing the educational effectiveness of the two models.

Methods: A 6 item Likert scale based questionnaire was utilized to survey psychiatry residents, (n = 27), who served on the C/L service under a longitudinal model. The C/L service was then changed to a traditional C/L block model and after six months, the Likert scale questionnaire was readministered to psychiatry residents who had worked under the new model (n = 17). Scores from the C/L subsection of the Psychiatry Resident in Training Examination. PRITE, were compared for the longitudinal and block groups to determine if there was a change in knowledge.

Results: Residents were more satisfied with the block rotation model than the longitudinal model in two areas: overall satisfaction, 3.8 verses 2.69 (p=001), and education value, 4.00 verses 2.56 (p=.0001). Comparisons between the two models, among the remaining variables, showed no significant differences. Residents who received training in the block model scored significantly higher on the PRITE compared to those trained in longitudinal model, 41.93% verses 67.25%.

Conclusion: Psychiatry residents showed improvement in C/L knowledge and greater satisfaction overall with block model.

NR107 Monday, May 20, 3:00 p.m.-05:00 p.m.

Nutritional Assessment of Mentally Ill Persons Living in the Community

Refaat Hegazi, M.D., *Department of Gastoenterol, UPMC Presbyterian, 200 Lothrop Street, Pittsburgh, PA 15213*; Kenneth S. Thompson, M.D.

Summary:

Objective: To survey the nutritional status of mentally ill persons living in community settings.

Method: This case control study included 43 severe mentally ill persons with a history of hospital admissions now living in a variety of community housing programs and 43 age and sex matched control subjects living in Allegheny County, PA. A questionnaire, 24-hour dietary recall and measurement of weight and height were conducted.

Results: Body mass index (Kg/m^2) was >25 in 79% and >30 in 49% of cases, while it was >25 in 51% and >30 in 21% of the controls. ($p < 0.05$) On the contrary, the average daily caloric intake was significantly lower among cases than controls (1815.65 ± 667.27 Kcal vs 2534.36 ± 769.63 Kcal) ($p < 0.05$). Persons on antidepressants were more obese than those on anti-psychotics. The average daily intake of study subjects for calcium, magnesium, phosphorus, vitamins D, K and E and not vitamin B were significantly lower than those of the control subjects ($p < 0.05$).

Conclusion: Mentally ill people living in community settings are more obese and frequently have nutritionally inadequate diets than the controls. Medications and lifestyle appear to contribute to these findings. Nutritional consultation and support are badly needed for this population.

NR108 Monday, May 20, 3:00 p.m.-05:00 p.m.

Health Care Practices and Risk-Taking Behaviors Among Psychiatric Inpatients

Maribel Abbate, M.D., *Department of Psychiatry, SUNY at Buffalo, 462 Grider Street, Buffalo, NY 14215*; Ramandeep Kaur, M.D., Paula Del Regno, M.D., Antoinette M. Valenti, B.A.

Summary:

Medical illness is more common among psychiatric patients than the general population and it frequently goes unrecognized or untreated (Goldman, 1999). A significant number of deaths in this population have been attributed to cardiovascular and cerebrovascular diseases, endocrine disorders and neoplasms (Hafner and Bickel, 1989). Studies of outpatients with schizophrenia suggest that these patients practiced fewer health promoting behaviors, and more than 50% had physical conditions requiring medical management (Holmberg and Kane, 1999). This study sought to determine health and wellness practices and risk-taking behaviors in acute psychiatric inpatients. Factors such as exercise, diet, living arrangements, socioeconomic status and preventive health care practices were determined and examined in relation to age, gender and psychiatric diagnosis. Data was collected from 155 consecutively admitted patients who were asked to complete a survey; 60% were caucasian, 32% African American, 4% Hispanic, and 4% other. Males constituted 56% of the group while 44% were females. Relating to preventive health care practices, 63% of patients reported to have a primary care physician, 64% had been tested for HIV, and 43% reported going to the dentist regularly. Wellness questions revealed that 57% of patients drink alcohol, 81% do not follow a particular diet and 44% eat "fast foods" more than twice a week; however 68% reported they exercised on a regular basis. In terms of risk taking behaviors 45% of patients have been physically injured in the past two years, 78% have ridden in a car without a seatbelt, 28% frequently drive above the speed limit, 37% have driven while intoxicated, and 47% have had sex with someone they just met. Patients with psychotic disorders were noted to have less preventive care in general than the rest of the group and patients with a primary substance disorder were less likely to engage in wellness practices. Overall, patients with substance disorders and adjustment disorders were more likely to engage in risk taking behaviors than patients with psychotic or mood disorders.

NR109 Monday, May 20, 3:00 p.m.-05:00 p.m.

Risk of Occult Gastrointestinal Bleeding with SSRIs

Zafar A. Rasheed, M.D., *Psychopharmacology, St. Elizabeths Hospital, 2700 MLK Avenue, SE, Smith Ctr 5th Floor, Washington, DC 20032*; Walter Fava, R.Ph., Alvaro Guzman, M.D., Richard Zebrak, M.D., Minh-Chao Nguyen, M.D., Lourdes Castineira, M.D., Teodor T. Postolache, M.D.

Summary:

Introduction: Serotonin is a mediator in regulating the haemostatic response to vascular injury (1). Several case reports suggested increased bleeding risk and one case-control study reported increased macroscopic gastrointestinal bleeding with SSRIs (2). We hypothesized that patients taking SSRIs would have a higher proportion of *occult* GI bleeding as compared to

patients taking non-serotoninergic antidepressants. In this pilot work, we intended to evaluate the proportion of individuals with occult GI bleeding among patients taking SSRIs.

Methods: The protocol was approved by the IRB of DC-DMH. Subjects were patients from DC-DMH, 14 females (42.42%) and 19 males (57.58). Patient's age was 47.58±8. Subjects were on fluoxetine (14), sertraline (9), paroxetine (7), and citalopram (3) for at least four weeks. Patients gave three stool samples for supersensitive guaiac testing. Patients with gastrointestinal disorders or receiving anticoagulants or chemotherapy were excluded. To study a more vulnerable population, we did not exclude patients with diabetes and hypertension or receiving aspirin, NSAIDS, valproate, and atypical anti-psychotics.

Results: To date, out of 33 patients, only one tested positive (3.03%).

Conclusion: These pilot data suggest *occult GI bleeding,* even in more vulnerable patients, is not a highly prevalent phenomenon and studying it would require larger samples.

NR110 Monday, May 20, 3:00 p.m.-05:00 p.m.

Risperidone Augmentation in Rapid-Cycling Bipolar Disorder

Cristinel M. Coconcea, M.D., *Department of Psychiatry, CWRU University Hospitals, 150 Southwood Road, Akron, OH 44313*; Melvin D. Shelton III, M.D., Pedro L. Delgado, M.D., Joseph R. Calabrese, M.D., Lana Amawi-Sultan, M.S.S.A.

Summary:

Objective: To evaluate risperidone as augmentation strategy in the treatment of rapid cycling bipolar patients.

Method: During the initial stabilization phase of a controlled study comparing valproate and lithium in rapid cycling bipolar patients, open-label risperidone was administered. From a total of 357 patients in the study, 25 received risperidone (between 0.25–9 mg per day), in addition to valporate and/or lithium, for an average of 7.4 weeks (0.1–23). The study included weekly psychiatric evaluation and administration of: Beck Depression Inventory (BDI), Hamilton-D (HAM-D), Young Mania Rating Scale (YMRS), and Global Assessment of Functioning (GAF).

Results: At the end of the open-label risperidone augmentation, preliminary data showed improvement from baseline in 77.7% (7/9) patients on BDI, 73.3% (11/15) on HAM-D, 57.1% (8/14) on YMRS, and 71.4% (10/14) on GAF. An increase in symptomatology was noted in 11.1% (1/9) patients on BDI, 13.3% (2/15) on HAM-D, 28.5% (4/14) on YMRS, and 7.1% (1/14) on GAF. No changes: 11.1% (1/9) on BDI, 13.3% (2/15) on HAM-D, 14.2% (2/14) on YMRS, and 21.4% (3/14) on GAF.

Conclusions: Risperidone may be an effective augmentation strategy for rapid cycling bipolar illness. More studies are needed in order to determine its safety and efficacy.

NR111 Monday, May 20, 3:00 p.m.-05:00 p.m.

Divalproex Sodium in Conduct Disorder: Response Rates and Aggression

Lisa M. Remsing, M.D., *Child Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94303-5719*; Kiki D. Chang, M.D., Melissa A. Silverman, B.A., Kirti Saxena, M.D., Hans Steiner, M.D.

Summary:

Objective: To examine response rates to DVP of affective aggression versus predatory aggression in adolescents with severe comorbid conduct disorder in a randomized, controlled, and double-blinded clinical trial.

Methods: 58 ethnically diverse males (mean age: 16) were exposed to a seven-week trial of DVP. Assessments at baseline and weekly thereafter included: CGI ratings and standardized personality assessment (Weinberger Adjustment Inventory) among others.

Results: Analysis of Variance and Chi Square associations showed expected significant differences. Youths with personality characteristics indicative of impulsive/reactive aggression were significantly more likely to be rated as responders to therapeutic levels of DVP at the exit from the study by a blinded research clinician. In contrast, therapeutic levels of DVP in youths with prominent features of premeditated aggression did not lead to improvement nor did sub-therapeutic levels of medication.

Conclusion: This study lends further support to the idea that anti-kindling agents are effective therapeutic agents for specific subtypes of aggression in Conduct Disorder.

NR112 Monday, May 20, 3:00 p.m.-05:00 p.m.

Uses of Atypical Antipsychotic Medicine for Nonschizophrenic Disorders

Graciana Lapetina, M.D., *Dartmouth Medical School, One Medical Center Drive, Lebanon, NH 03756*; Bradley V. Watts, M.D.

Summary:

Objective: Antipsychotic medications are increasingly being used in the treatment of nonschizophrenic disorders, including post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD) and dementia. As yet, there are no studies proving the efficacy of these newer antipsychotic medications for the treatment of nonschizophrenic disorders. The purpose of this study is to determine the current uses of atypical antipsychotics in clinical practice.

Methods: A chart review was performed on all 433 patients admitted to the psychiatric unit of the White River Junction VA Medical Center in the year 2000. The authors noted the psychiatric diagnosis for which the antipsychotic medication was prescribed.

Results: Over half (52%) of the inpatients were treated with antipsychotic medications. Of those, 29% were treated with typical antipsychotics, 28% with risperidone, 36% with olanzapine, 12% with quetiapine and 2% with clozapine. Other than schizophrenia, the primary psychiatric diagnoses treated with atypical antipsychotics were: bipolar disorder, PTSD, and borderline personality disorder.

Conclusions: The results show that physicians are routinely prescribing atypical antipsychotics for the treatment of nonschizophrenic disorders. Given the high frequency with which atypical antipsychotics are being used for disorders such as PTSD and borderline personality disorder, further studies are necessary to determine the efficacy of these off-label uses.

NR113 Monday, May 20, 3:00 p.m.-5:00 p.m.

Emergency Room Use by Primary Care Patients with Psychiatric Disorders

Amarendra Das, M.D., *Columbia University, 1051 Riverside Drive, Unit 24, New York, NY 10032;* Marc J. Gameroff, Ph.D., Olueen Carrasquillo, M.D., Mark Olfson, M.D., Myrna M. Weissman, Ph.D.

Summary:

Objective: To characterize patterns of medical and psychiatric Emergency Room (ER) use by primary care patients with psychiatric disorders based on actual encounter data.

Methods: After a systematic sampling and psychiatric screening of adult patients to a hospital-based general medical practice, we examined the hospital's computerized encounter data to determine the number of ER visits made between 6 months before and 1 year after psychiatric screening. We compared the number of

medical and psychiatric ER visits based on screen status for panic, generalized anxiety, major depressive, alcohol use, and substance use disorders. All analyses were adjusted for sociodemographic variables.

Results: Of 986 patients, 450 made medical ER visits and 21 had psychiatric ER visits during the 18-month period. An increased number of medical ER visits was made by patients who have panic disorder ($M \pm SD$: 1.78 ± 4.53 vs. 1.16 ± 2.15, $P = 0.03$) and generalized anxiety disorder (1.67 ± 3.79 vs 1.13 ± 2.11, $P = 0.01$) versus those who do not. Panic disorder also has a positive association with number of psychiatric ER visits (0.14 ± 0.63 vs 0.02 ± 0.21, $P = 0.001$), as does alcohol use disorder (0.19 ± 0.88 vs 0.02 ± 0.15, $P < 0.001$) and substance use disorder (0.23 ± 0.99 vs 0.03 ± 0.23, $P < 0.001$).

Conclusions: Consistent with prior studies using self-reported data, our study of computerized encounter data shows that a subset of primary care patients with anxiety and substance use problems has increased ER utilization.

NR114 Monday, May 20, 3:00 p.m.-5:00 p.m.

International Medical Graduates: A Historical Descriptive Analysis

Dinu P. Gangure, M.D., *St. Luke's Hospital, 515 West 59th Street, New York, NY 10019*

Summary:

Objective: To comprehensively analyze the data available in the literature on International Medical Graduates (IMGs). The characteristics of the IMGs are presented from the perspective of their influence on healthcare services.

Methods: A comprehensive retrospective analysis of the data on IMGs was performed. We compared the IMGs in psychiatry with the IMGs in all specialties taken together. Nominal, normative and ordinal analyses were done, and the data are tabulated and presented in representative graphic format.

Results: IMGs were found to be more prone to pursue additional training after completion of the residency, to grow steeper in number in the last 15 years, and to more likely be geographically located in urban poverty areas, comparative with the US medical graduates. These conclusions are valid for IMGs in psychiatry, as well as for IMGs in all specialties taken together.

Conclusions: IMGs are a population that matches with many of the needs of the U.S. health care system. By being cognizant of the demographic backgrounds of our physicians, we could better design measures to improve the structure and function of the healthcare providers system. We are then closer to predict and control the influences of the healthcare providers system on the psychiatric services.

NR115 Monday, May 20, 3:00 p.m.-5:00 p.m.

To Whom Do Psychiatrists Offer Smoking Cessation Counseling?

Seth S. Himelhoch, M.D., *Johns Hopkins, 600 North Wolfe Street, Carnegie 285, Baltimore, MD 21287;* Gail Daumit

Summary:

Background: Individuals with mental illness have high rates of tobacco dependence. Smoking cessation counseling is an important first step in helping individuals quit smoking. However, little is known about the various factors that influence a psychiatrist's decision to offer smoking cessation counseling to their patients that smoke.

Methods: Using the National Ambulatory Medical Care Survey (1992–1996), we identified 1555 psychiatric office visits for patients aged sixteen and older who were current smokers with a psychiatric diagnosis. We performed bivariate and multivariate analyses to investigate the relation between smoking cessation counseling and patient and visit characteristics

Results: Psychiatrists offered cessation counseling at 13.3% of visits for patients who smoked. The adjusted relative odds of receiving smoking cessation counseling were approximately twice as high for visits for patients with the following characteristics compared to those without these characteristics: serious mental illness (OR [95% CI], 1.84, [1.26–2.71]), chronic medical condition (OR [95% CI], 1.92 [1.30–2.85]) age greater than 50 (OR [95% CI], 1.92 [1.17–3.12]) and metropolitan location ((OR [95% CI], 2.21, 95% CI [1.48–3.31]). For initial patient visits the adjusted relative odds for counseling were 2/3 higher than for follow-up visits, (OR [95% CI], 1.66 [1.0–2.76]). The model adjusted for above factors as well as gender, race, geographic location, insurance type, antipsychotic and antidepressant use and types of medical staff seen at the visit.

Conclusions: Psychiatrists are more likely to offer smoking cessation counseling to patients that are at higher risk for the medical consequences of smoking (e.g. older patients with chronic medical illness). However, psychiatrists missed many opportunities to offer smoking cessation counseling to their patients that smoke.

NR116 Monday, May 20, 3:00 p.m.-5:00 p.m.

Utilization of Health Care Services by Obstetric Patients with Psychiatric Disorders

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

Summary:

Objective: The purpose of this study was to investigate potential relationships between psychiatric symptoms during pregnancy and utilization of obstetric services.

Method: We retrospectively reviewed clinical course in 1188 pregnancy cases (1225 deliveries) among women seen through the obstetrics service at a tertiary care hospital. Data were obtained from the computerized electronic medical record.

Results: Among women with psychiatric symptoms, there was a nearly two-fold increase compared to women without psychiatric symptoms, in the mean number of phone calls/hospital visits to providers during pregnancy. Women who reported a current or past history of anxiety symptoms (generalized anxiety, PTSD, panic) exhibited a greater utilization of healthcare services (telephone calls and hospital visits) compared to women who reported other psychiatric symptoms (depression, substance abuse, eating disorder).

Conclusion: These findings demonstrate a greater utilization of healthcare resources by patients who experience psychiatric symptoms during pregnancy. The data may be useful in helping providers plan their services appropriately, for this high-risk population.

NR117 Monday, May 20, 3:00 p.m.-5:00 p.m.

Antidepressant Treatment in Patients with Schizophrenia

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

Summary:

Objective: Schizophrenic patients are often treated with antipsychotics and antidepressants. This study analysed the antidepressant prescriptions in schizophrenia.

Method: A sample of 400 schizophrenic patients according to DSM-III-R criteria was ascertained. Information about drug pre-

scriptions, age at ouset, course of symptoms and mood symptoms, was obtained. Studen's t test was used in the analysis of the data, with a level of significance of p = 0.05. SAS was used for all statistical analysis.

Results: Eighty-two schizophrenic patients (20.5%) received antidepressant (males: 69.5%; females: 30.5%). Antidepressants were always prescribed in combination with antipsychotics. In comparison with the total sample, the age at onset (16.5 years, DS 9.15) was significantly earlier (p < 0.05). Sixty-eight patients (83%) reported depressive symptomatology and 33 cases (40%) showed a high risk of self-harm (suicide attempts). A tendency to chronic course was observed in sixty-two patients (76%).

Conclusions: In this sample, males patients received more antidepressant prescriptions than females. Important depressive symptomatology was also observed. Both the course of illness and the early age at onset suggest that these patients present a poor prognosis schizophrenia.

NR118 Monday, May 20, 3:00 p.m.-5:00 p.m.

Familial Aggregation of Affective Disorders in Schizophrenic Probands

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

Summary:

Objective: It has been suggested that there is a familial relationship between schizophrenia and mood disorders. The objective of this study was to compare the risk for affective disorders in the first degree relatives of schizophrenia probands (FDRS) and in the general population (GP) of Santiago, Chile.

Method: Forty-four schizophrenic probands, according to the DSM-III-R criteria, were selected. The FDRS (n = 235) were interviewed using the Composite International Diagnostic Interview (CIDI) and the DSM-III-R Check-list. Test for proportions was used in the analysis of the data; with a level of significance of p = 0.05. SAS was used for all statistical analysis.

Results: Psychiatric morbidity was observed in 51.9% of FDRS and in 33.7% of GP. The difference was statistically significant (p < 0.05). The morbidity risk for affective disorders in FDRS (31.5%) was significantly higher than in GP (19.8%) (p < 0.05), both in males and females.

Conclusions: An increased familial risk for affective disorders was found in the FDRS. The results support a possible biological relationship between schizophrenia and mood disorders.

NR119 Monday, May 20, 3:00 p.m.-5:00 p.m.

Physiological Inattentiveness Correlates with Behavioral Inattentiveness

Thomas P. Tarshis, M.D., *Department of Psychiatry, Maricopa Medical Center, 2601 East Roosevelt, Phoenix, AZ 85008*; Jason M. Johnson, B.S., Kendall J. Vermilion, B.S., Drake D. Duane

Summary:

Hypothesis: Electroencephalographic (EEG) mid-latency auditory evoked potentials (N-100 and P-300) may provide a useful objective measure that correlates with subjective inattentiveness findings in Attention-Deficit/Hyperactivity Disorder (ADHD).

Methods: Subjects were obtained via a retrospective chart review of 91 children (age 7–12 years, mean 9.4 ± 1.4 years) who had initial neuropsychiatric evaluations between January of 1999 and September of 2001. Sixty-seven males (74%) and 24 females (26%) who had EEGs and parental DSM-IV rating scales for ADHD were used in the analysis. Each child had a clinical diagnosis of ADHD, with 52 (57%) inattentive type and 39 (43%) combined or hyperactive-impulsive type.

Results: The N-100 latency was significantly positively correlated with the DSM-IV inattentive rating scale (r = 0.29, p < 0.02). The P-300 latency, although borderline correlated with the N-100 measure (r = 0.20, p = .09) was not correlated with the DSM-IV inattentive rating scale. There was no difference in N-100 or P-300 latencies based on sex or sub-type of ADHD.

Conclusion: The N-100 latency was significantly correlated with subjective behavioral ratings for pre-adolescents with ADHD. The use of neurophysiologic testing should be further explored as an objective measure of dysfunction in children with ADHD.

NR120 Monday, May 20, 3:00 p.m.-5:00 p.m.

ADHD Subtypes and Degree of Executive Dysfunction

Thomas P. Tarshis, M.D., *Department of Psychiatry, Maricopa Medical Center, 2601 East Roosevelt, Phoenix, AZ 85008*; Jason M. Johnson, B.S., Kendall J. Vermilion, B.S., Drake D. Duane

Summary:

Introduction: Pre-adolescent children with Attention-Deficit/Hyperactivity Disorder (ADHD) were tested on measures to evaluate the degree of inattentiveness as measured by the Achenbach Child Behavior Checklist (CBCL) and executive functioning as measured by the Wisconsin Card Sorting Test (WCST).

Methods: Subjects included 91 children (age 7–12 years, mean 9.4 ± 1.4 years) who had initial neuropsychiatric evaluations between January of 1999 and September of 2001. There were 67 males (74%) and 24 females (26%). Each child had a clinical diagnosis of ADHD, with 52 (57%) inattentive type and 39 (43%) combined or hyperactive-impulsive type.

Results: There were no differences on any of the performance measures on the WCST based on ADHD subtype. Children with a score above 70 on the CBCL-Attention scale performed worse (25^{th} versus 38^{th} percentile, p = 0.02) on non-perseverative errors, but there was no difference in perseverative errors (42^{nd} vs 48^{th} percentile, p = NS) between the two groups. A positive correlation was found (r = 0.32, p < 0.01) with the number of trials needed to complete the first category of the WCST and the CBCL-Attention scale.

Conclusion: Executive dysfunction type did not differentiate between the two subtypes of ADHD. Regardless of ADHD subtype, the CBCL-Attention scale appears to correlate with executive functioning.

NR121 Monday, May 20, 3:00 p.m.-5:00 p.m.

Effects of the Antidepressant Duloxetine on Sexual Function

Michael J. Detke, M.D., *Eli Lilly and Company, Lilly Corporate Center DC 2206, Indianapolis, IN 46285*; Pierre V. Tran, M.D., David J. Goldstein, M.D., Craig Mallinckrodt, Ph.D., Mark A. Demitrack, M.D.

Summary:

Objective: To determine the effect of the antidepressant duloxetine, a potent and balanced inhibitor of serotonin and norepinephrine (Bymaster et al., 2001; Pitsikas, 2000), on indices of sexual function in depressed patients.

Method: Data were obtained from 4 double-blind placebo- and active comparator-controlled trials (duloxetine at 40–120 mg/d n = 444, placebo n = 293, paroxetine 154, and fluoxetine 67). Sexual function was evaluated by the Arizona Sexual Experience (ASEX) questionnaire and reported adverse events. Patients were treated for up to 9 weeks.

Results: Mean changes on the ASEX total score did not differ among groups. However, the treatment-by-gender interaction approached significance (p = .089). The treatment-by-gender interaction was not significant for mean response on questions 1, 2, 3, or 5. On question 4 (How easily can you reach an orgasm), treatment-by-gender interaction was highly significant (p = .004). Differences between groups for females did not approach significance, but for males, duloxetine and paroxetine had significantly greater (worsening) mean changes than placebo. For adverse events, duloxetine-treated patients reported decreased libido (4.9% vs. 1.4%), abnormal ejaculation (7.0% vs. 1.6%), and impotence (6.2% vs. 0.5%) significantly more often than placebo-treated patients but were not significantly different from fluoxetine or paroxetine.

Conclusion: No differences between treatment groups were detected in female sexual function. Duloxetine and paroxetine delayed orgasm in males; the magnitude of the effect was numerically greater for paroxetine.

NR122 Monday, May 20, 3:00 p.m.-5:00 p.m.

The Antidepressant Duloxetine Lacks Adverse Cardiovascular Effects

Michael J. Detke, M.D., *Eli Lilly and Company, Lilly Corporate Center DC 2206, Indianapolis, IN 46285*; Pierre V. Tran, M.D., David J. Goldstein, M.D., Craig Mallinckrodt, Ph.D., Mark A. Demitrack, M.D.

Summary:

Objective: To examine the cardiovascular effects of duloxetine, a potent and balanced dual reuptake inhibitor of serotonin and norepinephrine (Bymaster et al., 2001; Pitsikas, 2000), in depressed patients.

Method: Data from 7 double-blind placebo-controlled trials were pooled (duloxetine at 40–120 mg/d, n = 1032, placebo n = 723). Patients were treated for up to 12 weeks.

Results: Mean baseline to endpoint changes in supine systolic and diastolic blood pressure for duloxetine-treated patients were approximately 1.5 mm Hg, and did not increase markedly by dose. Incidence of treatment-emergent elevated blood pressures (diastolic ≥ 90 or systolic ≥ 140, and change from baseline ≥ 10) at endpoint for duloxetine-treated patients (doses pooled) were 6.9% and 4.4% for systolic and diastolic BP, respectively. Corresponding rates in the placebo group were 3.3% and 2.3%. There were no significant differences between duloxetine and placebo treatment groups in the incidence of sustained elevations (at least 3 consecutive visits) in diastolic (duloxetine: 0.3%; placebo: 0.2%), systolic (duloxetine: 0.5%; placebo: 0.2%), or either (duloxetine: 0.7%; placebo: 0.4%). Duloxetine reduced the mean baseline to endpoint corrected QT interval and the incidence of abnormal increases in QTc (change from baseline ≥30 msec) did not differ from placebo.

Conclusions: Duloxetine has no clinically meaningful cardiovascular effects.

NR123 Monday, May 20, 3:00 p.m.-5:00 p.m.

Duloxetine 60mg QD Is an Efficacious Depression Treatment

Michael J. Detke, M.D., *Eli Lilly and Company, Lilly Corporate Center DC 2206, Indianapolis, IN 46285*; Yili Lu, Ph.D., David J. Goldstein, M.D., Mark A. Demitrack, M.D.

Summary:

Objective: To examine the antidepressant efficacy of duloxetine, a potent and balanced dual reuptake inhibitor of serotonin (5-HT) and norepinephrine (NE) (Bymaster et al., 2001 Pitslkas, 2000), at a dose of 60 mg QD in patients with major depressive disorder (MDD).

Methods: In a multicenter study, adult patients (n = 245), meeting DSM-IV criteria for MDD, were randomly assigned to receive placebo or duloxetine 60 mg QD double-blind for a 9-week treatment period. The primary efficacy assessment was $HAMD_{17}$ total score. Physical symptoms were measured by somatic symptom inventory and visual analog scales for pain.

Results: Duloxetine was statistically significantly superior to placebo at weeks 2 through 9 of the study in the reduction of $HAMD_{17}$ total score and resulted in an odds ratio for remission of 2.6 relative to placebo. Duloxetine resulted in a significant reduction in severity of overall pain compared to placebo. Duloxetine was well tolerated.

Conclusions: These results indicate that duloxetine administered at 60 mg once daily is a safe and efficacious treatment for MDD. These results also indicate that duloxetine may be the treatment of choice for MDD patients with painful physical symptoms.

NR124 WITHDRAWN

NR125 Monday, May 20, 3:00 p.m.-5:00 p.m.

Use of Novel Antipsychotic Medications in Diabetes: A Retrospective Review

Benjamin P. Yu, M.D., *Department of Psychiatry, University of California, 101 The City Drive, Building 3, Orange, CA 92868*; Yun S. Chong, M.D., Tony Ortiz, B.S., Jeremy W. Shaw, Charles Tuan-Tu S. Nguyen, M.D., Gerald A. Maguire, M.D.

Summary:

Novel antipsychotic medications have been reported through isolated case reports to lead to glucose intolerance and possible induction of diabetes mellitus. However, new research has revealed that no one antipsychotic medication has an increased risk over any other. Also, little is known of the effects of these medications on individuals with known diabetes mellitus. Twenty-one subjects (aged 23 to 86, 14 female, seven male) with diabetes mellitus and comorbid psychotic disorders were reviewed in regard to the effects on fasting glucose levels associated with treatment with novel antipsychotic medications. In this retrospective analysis, patient charts were reviewed for fasting glucose levels and time course of antipsychotic medication. Ten subjects received olanzapine doses from 2.5mg to 30mg), nine subjects received risperidone (doses from 25mg to 8mg), and two subjects received quetiapine (doses from 25mg to 800mg) with a mean duration of therapy of 24.6 days. Analysis revealed no worsening of fasting blood glucose associated with any one agent. Of note ulanzapine was associated with a reduction of fasting blood glucose and favorable modification of diabetes medication treatment in four of the 10 cases analyzed.

NR126 Monday, May 20, 3:00 p.m.-5:00 p.m.

Prevalence of Executive Impairments Detected by a Consultation Service

Jason E. Schillerstrom, M.D., *Department of Psychiatry, UTHSCA, 7703 Floyd Curl Drive, San Antonio, TX 78229*; Donald R. Royall, M.D., Stephen L. Stern, M.D., Melissa Deuter, M.D., Robert Wyatt, M.D.

Summary:

Objective: Executive Control Function (ECF) is strongly associated with behavioral and functional disability in medical and psychiatric patients. However, ECF assessment has not been widely implemented by clinicians. The Mini-Mental State Exam (MMSE) and similar screening tests are insensitive to ECF. Thus, ECF impairments risk to be either ignored or misattributed to "depres-

sion" and/or 'normal aging." This study measures the prevalence of ECF impairment among medical/surgical inpatients using the Executive Interview (EXIT25) and an executive clock-drawing task (CLOX)

Methods: N = 28 consecutive inpatients referred for psychiatric consultation at a public teaching hospital were administered the EXIT25, CLOX, and MMSE. The percentage of patients failing each test was calculated.

Results: The EXIT25 and CLOX identified 40% more patients with cognitive impairment than the MMSE. 15 (54%) failed the EXIT25 at 15/50, 16 (57%) failed the CLOX at 10/15, and 9 (32%) failed the MMSE at 24/30. This assessment took <30 min, and was well tolerated by the patients.

Conclusions: ECF impairment is common among inpatients seen by a psychiatric consultation service. The MMSE is insensitive to ECF impairment and is an inadequate "global" measure of cognition. Routine assessment should facilitate the integration of ECF into psychiatric case management.

NR127 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Influence of Season and Latitude on a Community Bipolar Sample

Ayal Schaffer, M.D., *Department of Psychiatry, Sunnybrook and WCHSC, 2075 Bayview Avenue, Toronto, ON M4N 3M5, Canada*; Anthony J. Levitt, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to identify the prevalence of seasonal bipolar disorder, and recognize the degree of seasonality among bipolar subjects.

Summary:

Objective: To report on the prevalence of seasonal bipolar disorder (BD), seasonal effects on mood and behavior, and impact of latitude in a community sample of BD subjects.

Method: Random telephone survey of 1,605 participants evenly distributed across latitude in the Province of Ontario, Canada. Timing of mood episodes was determined for subjects diagnosed with BD. The Global Seasonality Score (GSS), derived from the Seasonal Pattern Assessment Questionnaire (SPAQ), was used to quantify the degree of seasonality among participants. Exact latitude was determined for each participant, enabling comparison of subject variables across different latitudes.

Results: Fourteen out of 62 (23%) bipolar subjects reported seasonal mania, seasonal depression, or both. The mean GSS among bipolar subjects (11.2, SD = 5.5) was significantly greater than the mean GSS among unipolar subjects (8.2, SD = 4.9) or healthy controls (5.2, SD = 4.0) ($p < 0.001$ for both). Latitude had no effect on the prevalence of BD or on GSS scores.

Conclusions: This community survey found that 23% of people with BD had a seasonal pattern of illness. In addition, bipolar subjects as a group had greater seasonal fluctuations in mood and behavior than unipolar subjects or healthy controls.

References:

1. Faedda GL, et al.: Seasonal mood disorders. Arch Gen Psychiatry 1993; 50:17–23.
2. Kasper S, et al.: Epidemiological findings of seasonal changes in mood and behavior. Arch Gen Psychiatry 1989; 46:823–833.

NR128 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

A Comparative Trial of Treatments for PTSD in Substance Dependence

Elisa G. Triffleman, M.D., *S3 Project, Public Health Institute, 1124 International Boulevard, Oakland, CA 94606*; Philip K. Wong, M.A., Celeste Monnette, M.S.W.

Summary:

PTSD among the addicted significantly worsens prognosis, including for treatment retention. There is a continuing need to identify suitable treatment interventions.

Methods: In this pilot study, a specialized treatment, Substance Dependence - PTSD Therapy (SDPT) was compared with Cognitive-Behavioral Coping Skills Therapy for substance dependence (CBCST) to ascertain outcome differences. *Inclusion criteria:* reading English at a 5th grade level; current partial and full lifetime PTSD; ≥1 day of substance use/past month; opiate-agonist-maintained. *Exclusion criteria:* homelessness; concurrent psychosocial treatment; psychotic disorders, severe major depression.

Results: 36 subjects randomized; 34 attended ≥ 1 session. 56% female; 47% African-American, 35% white. At baseline: 77% had current PTSD; 65.7 ± 21.7 mean CAPS PTSD severity; 88% of urine tox. screens positive for stimulants or heroin. Outcomes: SDPT subjects attended more sessions (mean: 26.1 ± 10.1) than CBCST (mean 18.8 ± 10.7; log-rank = 7.83, p = .005), during more weeks (SDPT: 16.9 ± 5.7; CBCST: 13.0 ± 7.1; log-rank = 13.85, $p < .002$). 94% of SDPT subjects were very satisfied with treatment vs. 40% of CBCST subjects ($x^2 = 10.23$, $p < .005$). PTSD severity declined by 43% at 1.5-yr post-treatment follow-up ($F = 4.01$, $p = .05$). Reductions in ASI drug composite severity scores were present (F's = 1.89 – 3.05, p's < .02 – .05). PTSD severity was strongly associated with drug severity (F's = 6.34 – 12.06, p's < .0001 – .01) and time effects (F = 3.76 – 4.54, p's < .0001–.001)

Conclusions: SDPT retained subjects. Good outcomes observed across treatments. PTSD treatment components are compatible with substance abuse treatment.

NR129 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Sex Risk Behaviors for HIV in Alcoholics and Mixed Substance Abusers

Steven J. Schleifer, M.D., *Department of Psychiatry, New Jersey Medical School, 185 South Orange Avenue, Newark, NJ 07103*; Steven E. Keller, Ph.D., Sally J. Czaja, Ph.D.

Summary:

Sexual transmission of HIV in substance abusing populations remains of major concern, with injecting drug users (IDUs) receiving much attention. Others may be at risk due to interactions with the primary high risk populations.

Methods: In a study of behavioral and health risk factors in an inner city alcohol treatment program, we assessed 288 subjects: 97 exclusive alcoholics (SCID-DSM-III-R alcohol dependent), 127 alcoholics who abused other substances, 27 abusers of substances other than alcohol, 37 community nonabusers.

Results: Alcohol abusers were older and had more major depression (MD). Controlling age, gender, and MD, ANOVA revealed differences in numbers of sex partners (past 6 months) ($p < .04$). Alcoholics (1.3 ± 1.6) (mean ± s.d.) and nonabusers (1.1 ± 0.9) showed lower rates than mixed abusers (2.0 ± 2.9) and nonalcohol abusers (2.1 ± 1.8). These effects persisted when controlling for IDU history. Lifetime MD was also associated with current partners (1.9 ± 2.7 vs 1.3 ± 1.1) ($p < 0.05$). Participants' knowledge of their partner(s)' IDU history also differed ($p < .02$): nonalcohol abusers had higher rates of positive/unknown partner IDU history (44%) vs alcohol (29%), mixed (28%), and nonabusers (11%).

Conclusion: Abuse of other substances, but not alcohol, and MD are behavioral risk factors for HIV transmission in this population.

NR130 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Citalopram in Patients with Parkinson's Disease and Major Depression

Supported by Forest Laboratories, Inc.

Matthew A. Menza, M.D., *Department of Psychiatry, RWJ Medical School, 675 Hoes Lane, Room D207A, Piscataway, NJ 00854*; Humberto Marin, M.D., Kenneth R. Kaufman, M.D.

Summary:

Objective: Parkinson's disease (PD) is the second most common neurodegenerative disorder among the elderly and is frequently accompanied by depression. Depression is found in approximately 40% of patients with PD, and yet, there are relatively few data on the use of antidepressants in these patients. This trial is a prospective, open label trial of the tolerability and efficacy of citalopram in well-characterized patients with idiopathic Parkinson's disease.

Methods: 10 patients with levodopa-responsive PD and major depression, without dementia, were given flexible dose citalopram, beginning at 10 mg/day, in an eight week, open-label study. Patients were seen at 2-week intervals. The primary outcome measure was the 24-item Hamilton Depression Rating Scale (HAM-D), and secondary outcomes included anxiety (HAM-A), PD symptoms (UPDRS), functional impairment (RDRS), and cognition (MMSE). All ratings were done during on periods.

Results: Of the 10 patients (6F, 4M), 8 completed the trial. Both early terminations (one worsening depression and one nausea) were included in the LOCF analysis. 8 of the 10 patients improved on the HAM-D and 5 of the 10 had a 50% or greater improvement in the HAM-D. Paired t-tests showed significant improvement for the whole group (pre-post) on the HAM-D, which went from 24.2 at baseline to 14.9 at endpoint (P = .009). Anxiety symptoms and functional impairment also improved significantly from baseline to endpoint (HAM-D, P = .03; RDRS, P = .015). Cognition and PD symptoms did not significantly change from baseline to endpoint. The drug was well tolerated.

Conclusion: Citalopram was well tolerated and efficacious in treating depression in this prospective, open-label trial of patients with PD and depression. Improvement was seen in measures of mood, anxiety and functional capacity. While these data need to be confirmed in a double-blind trial, they suggest that citalopram may be a useful treatment for patients with PD and depression.

NR131 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Can Prefrontal Transcranial Magnetic Stimulation Transiently Improve Working Memory?

Kaori Yamanaka, *Medical University of South Carolina, 67 President Street, Room 502N, Charleston, SC 29425*; Xingbao Li, M.D., Ziad H. Nahas, M.D., Daryle Bohning, Ph.D., Mark S. George, M.D.

Summary:

Objective: To extend previous studies in the literature (Boroojerdi, Topper et al) and test whether small does of prefrontal TMS can transiently improve working memory in healthy young adults.

Method: To date, 9 right-handed men (mean age:35,-5SD) have performed the modified Stenberg working memory task with TMS (or, on a different day, sham TMS) intermittently applied over the left prefrontal cortex using a probabilistic placement. TMS was applied at 100% motor threshold, 5Hz 10sec on, 30sec off *17* 2times = 1700 stimulation/subject/day. The Sternberg was done during TMS, as well as during off times between TMS blocks.

Results: Over the 40 minutes of intermittent TMS, reaction time improved 9.3(9.2SD)% from baseline on the real TMS day, compared with 2.4(16.2SD)% worsening with sham. Error rates were higher during TMS than in the epochs between stimulation.

Conclusions: These preliminary results are consistent with prior published findings and suggest that prefrontal TMS might have utility in temporarily boosting working memory or reaction time. Further work is needed to confirm this finding, to determine the optimum use parameters to maximize this effect, and to understand its translational mechanism.

NR132 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Longitudinal Wisconsin Card Sorting Performance in Schizophrenia

Gary Bryson, Psy.D., *A Healthcare System, 950 Campbell Avenue, Box 116B, West Haven, CT 06516*, Morris D. Bell, Ph.D.

Summary:

Objective: The objective of this research is to determine the stability of Wisconsin Card Sorting Test (WCST) performance over an extended (4–7 year) period for people with schizophrenia. Furthermore, we wished to contrast these stability results with a measure of general cognitive function (WAIS-R Digit Symbol (DSST) for the same people.

Method: Forty-six outpatients, with DSM-IIIR diagnosis of either schizophrenia or schizoaffective disorder were assessed using the WCST and DSST at two time points on average 4.3 years apart.

Results: Results indicate that most WSCT variables remained stable, however, there was significant improvement on WCST preservative error standardized score and on the DSST standard score 57% of those participants who improved on WCST PE also improved on DSST. These cognitive test changes were unrelated to type of psychotropic medication and only modestly related to symptom variables.

Conclusion: In an outpatient schizophrenia sample WCST performance is generally stable over 3 to 7 year time period, but WCST PE and DSST performance may improve even without direct intervention.

NR133 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

An Accurate Point-of-Care Test to Monitor White Blood Cell and Absolute Neutrophil Cell

William M. Glazer, M.D., *Mass General Hospital, Harvard Medical School, 100 Beach Plum Lane, P.O. Box 121, Menemsha, MA 02552*; Raymond F. Akers, M.D., Stanton L. Gerson, M.D.

Summary:

Background: This presentation will describe a unique, disposable device developed to determine instantly the white blood cell (WBC) and absolute neutrophil cell (ANC) count from a fingerstick blood sample. The patient's finger is lanced and the blood sample is placed on the device and the WBC and ANC are available within minutes. The test employs a "Particle ImmunoFiltration Assay" technology that utilizes antigen-antibody interactions (involving cell membrane targets) to cause a matrix that migates through a system of membranes and allows a semi-quantitative expression of the number of cells present.

Methods: **Study #1:** over 100 laboratory samples from patients with different hematological conditions are compared using the rapid test and the standard laboratory test currently employed in clinical settings. **Study #2** will report biometric properties of the test from a sample of patients maintained on clozapine (where WBC is required every two weeks).

Results: Preliminary findings from Stuy # indicate a high correlation between the two tests for WBC (R^2 = .9774, N = 102) and ANC (R^2 = .9751, N = 105). Test-retest correlations will also be reported.

Conclusion: This new test is highly accurate and will be of interest to clinicians monitoring WBC and ANC in patients receiving medications like clozapine and carbamazepine.

NR134 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Emotion Recognition and Cognition in Schizophrenia in Patients

Gabriele Sachs, M.D., *Department of Psychiatry, University of Vienna, Waehringer Guertel 18-20, Vienna 1090, Austria*; Dorothea Steger-Wuchse, Ph.D., Ilse Kryspin-Exner, Heinz Katschnig, M.D.

Summary:

Introduction: Previous investigations have found impaired recognition of facial affect in schizophrenia. Controversy exists as to whether this impairment represents a specific emotion recognition deficit or whether impaired processing of emotion is part of a general cognitive decline. We compared patients and healthy control subjects on computerized tasks of emotion in order to find out whether emotion processing deficits were correlated with neurocognitive performance.

Methods: Forty patients (25 male, 15 female, mean age ± SD:30.4 ± 8.1) with schizophrenia (DSM-IV, 18 first episode and 22 chronically ill patients) treated with atypical neuroleptics and 40 healthy volunteers, matched for age and gender, underwent a computerized neuropsychological test battery (CNP, Gur et al. 1992). A German version of the PENN Facial Discrimination-, Differentiation- and Memory Test was administered. Participants were tested neuropsychologically and were rated for positive and negative symptoms.

Results: Patients with schizophrenia performed worse than control subjects on all emotion tasks ($p < 0.01$). We found higher error rates for identification of emotion in happy ($p < 0.02$) and happy female faces ($p < 0.01$), for differentiation of sad versus happy faces ($p < 0.001$) and for facial memory ($p < 0.04$). Impairment in emotion recognition was similar in first-episode and chronically ill patients. Poorer performance in emotion discrimination and facial memory correlated with severity of negative symptoms, abstraction-flexibility ($p < 0.001$), verbal memory ($p < 0.01$), and language ($p < 0.001$).

Conclusions: The study did not reveal a specific deficit for emotion recognition in schizophrenia. These findings lend support to the concept that emotion recognition is associated in schizophrenia with key cognitive deficits. Similar emotion recognition impairment in first-episode and chronically ill patients suggests a trait deficit.

NR135 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Validation of the Delirium Rating Scale in a Structured Format in Critically Ill Patients

Maria del Carmen Flores-Miranda, M.D., *Instituto Nacional de Ciencias, Medicas y Nutricion Salvador Zubiran, Vasco de Quiroga 15, Mexico City 14000, Mexico*; Juan J. Calva Mercado, M.D., Guillermo Dominguez Cheritt, Gabriel Alejo Galarza, Judith Gonzalez-Sanchez, Maria de Angeles V. Martinez, Adrian Gonzalez Hernandez

Summary:

Objective: To validate the Delirium Rating Scale for use in critically ill patients receiving mechanical ventilation and sedative medication.

Method: We modified the Delirium Rating Scale to a structured approach in order to uniform the interview for non verbal patients.

Design: Cross sectional.

Setting: The adult intensive care unit from the Instituto Nacional de ciencias médicas y Nutrición Salvador Zubirán.

Participants: Forty-one patients including both ventilated and nonventilated patients who were also receiving sedative medication with a maximum Ramsay sedation score of four (41 independent paired evaluations).

Main Outcome Measure: The interrater agreement of the Delirium Rating Scale in a structured format in critically ill patients.

Results: The interrater agreement obtained with kappa statistics were: .83 for intubated patients; 1 for nonintubated patients; 1 for patients without sedative medication; .66 for patients receiving sedative medication with a Ramsay sedation score of 1 and 2; 1 for patients receiving sedative medication with a Ramsay sedation score of 3 and 4.

Conclusion: The Delirium Rating Scale in a structured format showed a high interrater agreement in mechanically ventilated patients and different levels of sedation. This may be useful in this challenging population

NR136 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Prevalence of Anxiety and Depression in the Aged Community

Sergio L. Blay, *UNIFESP, R Botucato 740, Sao Paulo, SP 04023-900, Brazil*; Sergio B. Andreoli, Ph.D., Fabio L. Gastal, Ph.D.

Summary:

Aim: The aim of this study was to assess the the prevalence of anxiety and depression morbidity in the elderly living in the community

Method: In a cross-sectional design, a representative sample of persons 60 years old and over persons (with a sample size of N = 7840) was examined to estimate the prevalence of anxiety and depression in the state in Brazil. All subjects were examined by means of a six-item validated reduced version of the OARS mental health screening questionnaire.

Results: 38% of the study subjects were identified as probable anxiety and depression cases. Prevalence estimates were calculated adjusting for differential performance according to previous validation study. True prevalence was 22%. Screening scores were higher within women, less educated, living in rural areas, and presenting an unmarried status.

Conclusion: Prevalence of anxiety and depression is high among the elderly living in Brazil. The higher prevalence among women, less educated, unmarried, and living in rural areas is similar to other findings in the literature.

NR137 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

RCT of Venlafaxine Versus Sertraline for Depressed Nursing Home Residents

Ira R. Katz, M.D., *Department of Geriatric Psychiatry, University of Pennsylvania, 3535 Market Street, Room 3001, Philadelphia, PA 19104*; David W. Oslin, M.D., Catherine J. Datto, M.D., Joel E. Streim, M.D., Tom Tenhave

Summary:

Introduction: In nursing homes, old age and potential drug-drug and drug-disease interactions may affect the relative safety and efficacy of antidepressant medications, and suggest the need for specific research.

Design and Subjects: Double-blind RCT of venlafaxine (to 150 mg/day) versus sertraline (to 100 mg/day) for 10 weeks in 52 elderly nursing home residents with major depression and, at most, mild-moderate dementia. Average age (SD) was 82 (10); MMSE was 22 (5) 44% were female.

Findings: 12 subjects were discontinued due to significant adverse events (SAE), 5 with other significant side effects (SE), and 2 withdrew consent (WC). With venlafaxine, time to termination

was lower for SAE (log rank statistic 5.28; p = .022), for SAE or SE (8.08; .005), or for SAE, SE or WC (10.04; .002). Hamilton scores (SD) at baseline were 20.2 (3.4) for sertraline and 20.3 (3.7) for venlafaxine; and 12.2 (5.1) and 15.7 (6.2) (F = 3.45; p = .069) at intention to treat endpoint; there were no differences in responses among completers. There were no differences in categorical responses in either analysis.

Summary: Venlafaxine was less tolerated and, possibly, less safe than sertraline in this frail elderly population without evidence for an increase in efficacy.

NR138 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Personality Predictors of Suicidal Ideation in Elderly Men and Women

Paul R. Duberstein, Ph.D., *Department of Psychiatry, University of Rochester, 300 Crittenden Boulevard, Rochester, NY 14642*; Paul T. Costa, Jr., Ph.D., Gerald M. Eggert, Ph.D., Robert R. McCrae, Ph.D., Jeffery H. Herbert, Ph.D.

Summary:

Objective: The aim of this study is to examine personality predictors of suicidal ideation among men and women aged 65 to 100 years who volunteered for a randomized controlled trial of primary and consumer-directed care for people with chronic illnesses.

Method: 1,162 residents of West Virginia, Ohio, and New York without dementia but at risk for hospitalization were assessed. Suicidal ideation was measured by the 4-item PaykelSSuicide Scale (PSS). Personality was assessed by the NEO Five-Factor Inventory. Hierarchical multiple regression was used to examine the incremental validity of personality factors net of (1) demographics (education, marital status, income and age) and (2) self-rated health, life dissatisfaction (LD), and number of physical illnesses.

Results: Younger age, higher income, and greater life dissatisfaction predicted male PSS scores. For women, number of physical illnesses and being unmarried were associated with high PSS scores. For both men and women, high Neuroticism, low Extraversion, low Agreeableness, and low Conscientiousness were independent predictors of suicidal ideation.

Conclusions: Four of the five personality dimensions predicted suicidal ideation for men and women. In addition to the known risk factors for suicide, assessment of these major personality dimensions in both men and women might aid psychiatrists' understanding of suicidal ideation.

NR139 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Long-Acting Risperidone for the Management of Elderly Patients Psychotic Disorders: A Favorable Benefit-Risk Ratio

Gahan J. Pandina, Ph.D., *Department of Psychiatry, UMDNJ-RWJMS/UBHC, 335 George Street, #3700, New Brunswick, NJ 08901*; Georges Sharabawi, M.D., Marielle Eerdekens, M.D., Young Zhu, Robert A. Lasser, M.D.

Summary:

Background: Atypical antipsychotics carry an improved benefit/risk ratio compared with conventionals. However, only short-acting drugs, necessitating daily dosing, have been available. A long-acting risperidone formulation (Risperdal Consta™) has been developed. This can be expected to offer a balanced benefit/risk ratio to elderly patients.

Methods: Elderly patients (mean age 71 years) with schizophrenia or schizoaffective disorders received 25, 50 and 75 mg of long-acting risperidone every 2 weeks for a period of up to 50 weeks.

Results: Data on efficacy were available for 41 patients receiving 25 or 50 mg of long-acting risperidone. Symptom improvements (reductions in PANSS total scores) were seen throughout the 50 weeks and at endpoint. Data on safety were available for 57 patients receiving 25, 50, or 75 mg of long-acting risperidone. Adverse events seen in >10% of patients were insomnia (in 10.5%), constipation (in 10.5%), and bronchitis (in 12.3%). The incidence of adverse events was not dose related. Changes in ECG and vital signs were not clinically relevant. Mean weight increased by 0.3 kg at endpoint.

Conclusion: This favorable therapeutic index suggests that long-acting risperidone can be successfully used over an extended period of time at these doses in this fragile patient population.

NR140 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Quetiapine in Treatment of Psychiatric Disturbances Associated Lewy Body Dementia

Andeius Baskys, M.D., *Department of Psychiatry, UCI, 5901 East 7th Street, Long Beach, CA 90822*; Paul Davis

Summary:

Objective: Approximately 20% of demented patients suffer from Lewy body dementia (LBD). One prominent characteristic of LBD is psychosis however no effective treatments have been identified. We studied effectiveness of the atypical antipsychotic quetiapine in the treatment of psychiatric disturbances associated with LBD.

Method: This is a single center, open label, 12-week dose titration study of individuals who meet clinical criteria for LBD (McKeith et al., 1996). Subjects were selected from the Long Beach VA Memory clinic. The screening visit included psychiatric, physical and neurological evaluations, MRI/CT, EKG, chest x-ray as well as comprehensive laboratory panel. The outcome measures were completed at baseline and interim visits (every three weeks for 12 weeks).

Results: Preliminary data indicate that treatment with quetiapine at an average dose of 25 mg/day for the first three weeks produced a 46.7 ± 5.5 (mean ± s.e.m) reduction in Neuropsychiatric Inventory (Cummings, 1994) scores. There was a 37.8% ± 8.8 (mean ± s.e.m) change from the baseline $p < .05$, t-test, n = 5 subjects) in delusions, hallucination, anxiety, and agitation subscales without a significant ($p > .05$) change in Simpson-Angus and AIMS scores.

Conclusions: These preliminary findings indicate that Quetiapine may be an effective and well-tolerated therapeutic agent for the treatment of psychosis associated with LBD.

NR141 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Personality Predictors of Depression in Young and Old Community Elders

Paul T. Costa, Jr., Ph.D., *Department of Gerontology, National Institute on Aging, 5600 Nathan Shock Drive ERC2C06, Baltimore, MD 21224*; Jeffrey H. Herbst, Ph.D., Robert R. McCrae, Ph.D., Paul R. Duberstein, Ph.D., Gerald M. Eggert, Ph.D.

Summary:

Objective: The aim of this study is to examine personality predictors of depressive symptoms among young-old (65 to 79 years) and old-old (80 to 100 years) participants who volunteered for a randomized controlled trial of primary and consumer-directed care for people with chronic illnesses.

Method: 1,162 residents of West Virginia, Ohio, and New York without dementia but at risk for hospitalization were assessed. Depression was measured by a DSM-IV based interview for MDE criteria. Personality was assessed by the NEO Five-Factor Inventory. Hierarchical multiple regression was used to examine the incremental validity of personality factors net of (1) demographics

(education, marital status, income and gender) and (2) self-rated health, life dissatisfaction (LD), and number of physical illnesses.

Results: Among the young-old, depressive symptoms were predicted by number of physical illnesses, LD, Neuroticism and low Agreeableness. Among the old-old, depressive symptoms were predicted by lower education, self-rated health, as well as LD, Neuroticism and low Agreeableness.

Conclusions: The personality dimensions of neuroticism and antagonism appear to be of importance in predicting depression in this population. Psychiatrists and other clinicians dealing with the growing number of older patients should consider routinely adding personality measures to clinical assessments.

NR142 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Anticholinergic Effect of Atypical Antipsychotics in Elderly Patients

John P. Docherty, M.D., *Department of Psychiatry, Comprehensive Neuroscience, 21 Bloomingdale Road, White Plains, NY 10605*; Judy Napolitano, R.N., Ramy A. Mahmoud, M.D., Rick A. Martinez, M.D., Robert A. Lasser, M.D., Gahan J. Pandina, Ph.D., Georges Gharabawi, M.D.

Summary:

Objective: Clinical trials data consistently supports the use of atypical antipsychotics in managing behavioral disorders in the elderly, but adverse effects can compromise patient safety and compliance. A large body of evidence exists associating anticholinergic burden with adverse consequences, particularly in the elderly. We hypothesize in an exploratory analysis that adverse affects may be diminished, and more favorable behavioral and cognitive outcome achieved, by using an atypical with a reduced anticholinergic load. We test our hypothesis in data from a controlled trial by evaluating the anticholinergic effects of two commonly used atypical antipsychotics in elderly patients with psychosis.

Method: In a double-blind, randomized, 8-week trial, 157 elderly patients with schizophrenia or schizoaffective disorder received risperidone 1 to 3 mg/day or olanzapine 5 to 15 mg/day. Anticholinergic effects were evaluated at baseline and week 8 using the Anticholinergic Symptom Scale (ACS).

Results: Both treatment groups improved from baseline to end point on the mean ACS total score and the vision subscore. Despite a lower baseline score, a numerically greater improvement was seen in the risperidone group on the mean ACS total score (risperidone, -1.2 ± 0.65; olanzapine, -0.6 ± 0.7; P = n.s.). The Urinary Function subscale appears to be a primary source of drug differences, improving significantly in the risperidone group (-0.4 ± 0.20, $P < .05$) while worsening in the olanzapine group (0.4 ± 0.32, P = NS.; $P = .006$, between groups).

Conclusions: The clinical consequences identified are consistent with known differences in cholinergic receptor affinity between risperidone and olanzapine. Further studies are needed to confirm the apparent advantageous effects of risperidone over olanzapine and to establish whether such effects are, in fact, mediated by anticholinergic load.

NR143 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

EEG Bispectral Index Correlates Dementia Severity in Alzheimer's Disease and VAD

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., Scott D. Greenwald, Ph.D., Melinda L. Morgan, Ph.D., Koren Hanson, M.A., Barbara Siegman

Summary:

Objective: We examined the usefulness of two-channel EEG monitoring using the Bispectral Index (BIS, Aspect Medical Systems) for assessment of patients with dementia. BIS is a quantitative EEG parameter based largely upon bispectral analysis. BIS values are correlated with brain metabolism during anesthesia ($r = -0.81$)[1] and preoperatively are lower in demented patients than normal elderly [2].

Methods: Awake, resting EEGs were recorded from elderly normal controls (CON, n = 18) and from patients with mild to moderate Alzheimer's Disease (AD, n = 11) or Multi-infarct Dementia (MID, n = 7), as previously reported. The average Bispectral Index (BIS-XP, 4.0U) was calculated for each subject using T3-Fp1 and F7-Fp1 channels. Mini-Mental State Exam (MMSE) scores estimated degree of impairment.

Results: BIS decreased with decreasing MMSE ($r = 0.46$ $p < 0.05$). Group MMSE and BIS showed statistically significant differences between controls and each demented group. Neither MMSE nor BIS showed differences between dementia groups.

Conclusions: BIS values decreased with increasing dementia, changes similar to those observed during light anesthesia. An easily-used, dual-channel instrument may be able to provide physiologic data comparable to multi-channel EEG for monitoring disease progression and treatment response to augment clinical assessments. Refinements to the BIS algorithm may provide an improved neurophysiologic index for diagnosis and/or monitoring treatment in dementia.

NR144 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Risperidone in the Treatment of Agitation and Psychosis of Dementia

Jeffrey Kirwan, M.B., *Department of Psychiatry, Princess Margaret Hospital Older Persons Hlth, Cashmere Road, Christchurch 8002, New Zealand*; Henry Brodaty, M.D., David Ames, John Snowdon, M.A., Michael Woodward, M.B., Roger Clarnette, M.B., Emma Lee, Ph.D.

Summary:

Objective: To evaluate the efficacy of risperidone in treating behavioral disturbances of dementia.

Method: After a seven-day placebo washout, 337 nursing home patients with dementia were randomly assigned to receive flexible-dose 0.5 to 2 mg/day oral risperidone solution or placebo for 12 weeks. Symptoms were evaluated at baseline and at weeks 4, 8, and 12 using the CMAI physical and verbal aggression subscales and the CGI.

Results: Sixty-seven percent of placebo patients and 73% of risperidone patients completed the trial. Mean dosage of risperidone was 0.95 mg/day. The change from baseline to end point on the aggression score of the CMAI was significantly different between groups; the risperidone group score decreased an average of 7.8 (SE = 1.00), whereas the placebo group score decreased by 2.8 (SE = 0.96) ($P < .001$). There also was a statistically significant difference favoring risperidone in the CGI change from baseline to end point ($P < .001$). Ninety-two percent and 94% of the placebo and risperidone patients, respectively, reported at least one adverse event.

Conclusions: Risperidone is effective in the management of agitation in patients with dementia.

NR145 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Simple and Reliable Prediction of Future Cognitive Decline in Nondemented People Memory Complaints

Nawab Qizilbash, M.D., *Department of Epidemiology, Glaxosmithkline, Third Avenue, Harlow CM19 SAW, United*

Kingdom; Karen Ritchie, Ph.D., Sylvaine Artero, Ph.D., Peter Lane, Ph.D.

Summary:

Objective: We conducted an analysis to identify psychometric tests that would reliably discriminate those people with memory problems who were destined to future cognitive decline from those who would remain stable.

Method: We analysed the Montpellier population-based longitudinal study, whose subjects were assessed in their homes by research staff. We identified, at baseline those people complaining about cognitive decline (mainly memory) but without dementia, who went on to decline further in the follow-up period. To identify variables that predicted future cognitive decline we used unconditional logistic regression.

Results: The Montpellier study provided records on 365 people followed for two years. Mean age at baseline was 73 years. A score of less than 4 in delayed recall of names produced good discrimination for identifying those individuals who declined further in the future. Sensitivity was 60%, with 82% specificity. The area under the Reciever Operating Characteristic curve was 0.623.

Conclusions: We have established that a simple test of memory recall is effective in identifying early in their disease, individuals without dementia who are destined to experience future cognitive decline.

NR146 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Validation of a Dementia-Behavior and Care-Burden Measure in Nursing Homes

Leah Kleinman, Ph.D., *Medtap International, 7101 Wisconsin Avenue, Bethesda, MD 20814*; Lori Frank, Ph.D., Gabrielle Ciesla, M.Sc., Henry Brodaty, M.D., Marcia Rupnow, Ph.D.

Summary:

Objective: The objective of this study was to evaluate the psychometric properties of the Modified Strain in Nursing Care Assessment Scale (M-NCAS), a 32-item scale for assessing nursing ratings of behaviors commonly displayed by dementia patients (agreement), and extent of job burden caused by those behaviors (coping). The items represent both negative (e.g., anxious, unpredictable, paranoid) and positive (e.g., compliant, calm) behaviors.

Method: Data were collected in a randomized double-blind clinical trial (n = 281) comparing risperidone to placebo in nursing home patients diagnosed with dementia (RIS-AUS-5 trial). Internal consistency reliability was assessed via Cronbach's alpha and validity was assessed through correlation to the BEHAVE-AD and the Cohen-Mansfield Agitation Inventory.

Results: The scale is internally consistent, with alphas of 0.74 for the agreement scale and 0.95 for the coping scale. The M-NCAS agreement and coping scales correlated most highly with the BEHAVE-AD aggressiveness and anxiety/phobia subscales ($r = 0.36$, $r = 0.35$; $r = 0.43$, $r = 0.35$ respectively; $p < 0.05$) and the CMAI verbal/non-aggression and aggression subscales ($r = 0.45$, $f = 0.32$; $r = 0.34$, $r = 0.31$, $p < 0.05$), indicating adequate construct validity.

Conclusions: The 32-item M-NCAS is an internally consistent and valid scale for evaluating nursing response to dementia-specific behaviors. It provides a detailed method of eliciting extent of burden associated with caring for dementia patients.

NR147 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Emotional and Neuroendrodrine Dysregulation in Fibromyalgia

Barbara L. Loevinger, M.D., *Department of Womens Health, University of Wisconsin, 6245 S Highlands Avenue, Madison, WI 53705-1114*; Carmen Alonso, Ph.D., Daniel Muller, M.D., Christopher Coe, Ph.D.

Summary:

Introduction: As fibromyalgia has become more prevalent, controversy has grown over the role of emotions in its pathogenesis. The objective of this study was to evaluate the balance of positive and negative emotion in relation to neuroendocrine/immune dimensions of fibromyalgia.

Methods: Sixty women with fibromyalgia (ACR criteria) were compared to healthy controls (n = 45) and rheumatoid arthritis controls (n = 20) recruited from the community. Assessments included SCID interviews, tender point examinations, urine and blood neuroendocrine and immune profiles, and self-report questionnaires measuring childhood trauma, affective states an fatigue.

Results: Women with fibromyalgia experienced significantly more childhood trauma, especially emotional abuse and neglect. They were less optimistic and manifested less positive affect. Initial analyses suggest higher rates of depression and PTSD. Fibromyalgia was associated with elevated norepinephrine levels and skewed norepinephrine/cortisol ratios. Early emotional neglect was strongly correlated with anxious arousal, anhedonic depression, pain and fatigue in fibromyalgia participants.

Discussion: Consistent with previous studies, these data suggest that fibromyalgia is associated with early trauma, psychiatric comorbidity and altered physiology. Emotional dysregulation may mediate some neuroendocrine changes and symptomatology. The role of early emotional trauma in the genesis of fibromyalgia will be discussed, with a focus on affect dysregulation, physiological set points, and symptoms.

NR148 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Response of Delusional and Nondelusional BDD to Fluoxetine Versus Placebo

Katharine A. Phillips, M.D., *Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI 02906*; Steven A. Rasmussen, M.D., Ralph S. Albertini, M.D., Jane L. Eisen, M.D.

Summary:

Background: Preliminary data suggest that BDD's delusional variant (a type of delusional disorder) may respond to SRIs, and that SRIs may improve insight in patients with BDD. However, this has not been investigated in a placebo-controlled trial.

Methods: 67 patients with DSM-IV BDD or its delusional variant were randomized into a 12-week placebo-controlled parallel-group study of fluoxetine. Subjects were evaluated with standard scales, including the BABS, a reliable and valid measure that assessed the delusionality (insight) of patients' beliefs that their appearance was abnormal.

Results: Fluoxetine was more reflective than placebo for BDD (response rate of 53% vs 18%, $p = .003$). There was no interaction between delusionality and improvement in BDD symptoms over time. Patients categorized as delusional at baseline (n = 27) were as likely as those who were nondelusional at baseline (n = 37) to have response of BDD symptoms to fluoxetine (50% vs 55%). However, delusional patients were less likely than nondelusional patients to have response of BDD symptoms to placebo (0% vs 35%, $p = .01$). In delusional patients, the response rate of BDD symptoms to fluoxetine was higher than to placebo (50% vs 0%, $p = .002$). This was not the case for nondelusional patients (55% vs 35%, $p = .23$), although power was limited. In the entire sample, delusionality was the only predictor of treatment response, with (as previously noted) delusional patients less likely than nondelusional patients to respond to placebo; BDD severity, BDD duration, gender, and the presence of a personality disorder, current OCD, or current major depression did not predict BDD response. Regard-

ing whether insight improved with treatment, BABS scores decreased significantly more in treatment responders than in nonresponders.

Conclusion: Fluoxetine was as effective for BDD symptoms in delusional as in nondelusional patients. The implications of these findings for other types of delusions requires investigation.

NR149 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Comorbidity in Body Dysmorphic Disorder

John J. Gunstad, M.S., *Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906*; Katharine A. Phillips, M.D.

Summary:

Objective: Comorbidity in body dysmorphic disorder (BDD) has received very little investigation. This study assessed rates of comorbid disorders in patients with BDD and clinical correlates of this comorbidity.

Methods: Comorbidity rates and patterns were examined based on data from the Structured Clinical Interview for DSM-III-R (SCID) for 175 patients with DSM-IV BDD who participated in a descriptive study of BDD's clinical features.

Results: Subjects had 1.7 ± .93 (range = 0 to 3) current comorbid disorders and 2.3 ± 1.5 (range = 0 to 7) lifetime comorbid disorders. 13% had no current comorbid disorders, 34% had 1, 31% had 2, and 22% had 3 or more. Mood disorders were most common (current rate = 69%, lifetime rate = 92%), followed by anxiety disorders (current rate = 56%, lifetime rate = 66%), substance use disorders (current rate = 13%, lifetime rate = 31%), and eating disorders (current rate = 4%, lifetime rate = 8%). Major depression was the most common current and lifetime comorbid condition (62% and 77%, respectively), followed by social phobia (31% and 37%) and OCD (25% and 30%). Increased rates of current comorbidity were associated with more BDD-related suicide attempts [$\chi^2(3) = 10.4$, $p = .015$], total suicide attempts [$\chi^2(3)) = 10.9$, $p = .013$], and psychiatric hospitalizations [$\chi^2(3) = 13.4$, $p = .004$]. Increased rates of lifetime comorbidity were associated with a greater likelihood of being unemployed [$\chi^2(3) = 8.8$, $p = .032$].

Conclusion: Comorbidity rates are high in BDD patients and associated with significant morbidity.

NR150 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Panic Attacks and Hyperventilation: A Test in Panic and Depressive Disorders

Isabella Nascimento, M.D., *Department of Psychiatry, Federal University Rio Janiero, Rua Prof Hermes Lima 364/103, Rio De Janeiro, RJ 22795-065, Brazil*; Antonio E. Nardi, M.D., Alexandre M. Valenca, M.D., Fabiana L. Lopes, M.D., Marco A. Mezzasalma, M.D., Walter Zin, M.D.

Summary:

Our aim was to determine whether panic disorder (PD) patients, major depressive patients without panic attacks (MD), and major depressive patients with panic attacks (MDP) respond similarly to hyperventilation challenge tests. We randomly selected 35 PD, 33 MDP, and 27 MD patients and also 30 normal volunteers with no family history of anxiety or mood disorder. The patients had not been treated with psychotropic drugs for at least one week. They were induced to hyperventilate (30 breaths/min) for 4 min, and anxiety was assessed before and after the test. A total of 16(45.7%) PD patients, 12 (36.4%) MDP patients, four (11.1%) MD patients, and two (6.7%) normal volunteers had a panic attack after hyperventilating. The PD and MDP patients were significantly more responsive to hyperventilation than the MD patients and the normal volunteers. The MD patients had a significantly lower heart-rate response to the test than all the other groups. There is growing evidence that PD patients are more sensitive to the vasoconstrictive effects on basilar arterial blood flow caused by hyperventilation-induced hypocapnia than are comparison subjects. Our data suggest that there is an association between PA and hyperreactivity to the test.

NR151 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Efficacy of Sertraline in Two Randomized, Placebo-Controlled, Double-Blind, Multicenter Trials for Social Phobia (Social Anxiety Disorder): Combined Results

Kathryn M. Connor, M.D., *Department of Psychiatry, Duke University, Box 3812 DUNC, Durham, NC 27710*; Jonathan R.T. Davidson, M.D., Henry Chung, M.D., Cathryn M. Clary, M.D., Ruoyong Yang, Ph.D.

Summary:

Background: The objective of the current study was to evaluate the efficacy and tolerability of sertraline for the treatment of moderate to severe social phobia (social anxiety disorder) in adults in the U.S. and in Canada.

Method: Efficacy and safety results of sertraline vs placebo were pooled across 2 randomized, double blind multicenter studies of sertraline vs placebo with flexible dosing of 50–200mg; one in the U.S. (12 wk) and one in Canada (20 wk). The similar flexible dosing schedules in the Canadian study (50 mg increases every 3 wk after a fixed dose of 50 mg in the initial 4 wk) and the U.S. study (25 mg for 1 wk, then 50 mg for 2 wk, and flexible dosing thereafter) allowed for examination of efficacy at the observable time points of wk 6 and 7 and wk 12 and 13, (US and Canadian, respectively). Primary outcomes were Brief Social Phobia Scale (BSPS) total score and the percentage of CGI-I responders. Least squared means and standard errors (SE) are provided from ANCOVA analysis adjusting for treatment, protocol, and baseline terms.

Results: 346 patients were randomized to sertraline (60% male, mean ± SD age, 35.3 ± 10.1 years, baseline BSPS, 47.7 ± 0.5 (SE); mean illness duration 17.2 years), and 273 patients were randomized to placebo (57% male, mean ± SD age, 35.2 ± 10.2 years, baseline BSPS, 47.4 ± 0.6 (SE); mean illness duration 19.1 years). Study subjects had moderate-severe illness as measured by a mean CGI-S score of 4.8 +/– 0.7. At weeks 12–13, the mean change in BSPS Total Score was –16.6 vs. –10.6 for sertraline vs. placebo, ($p < .001$) with a greater proportion of responders on sertraline (CGI-I ≤ 2: 53.4% vs. 27.7%; $p < 0.001$). At LOCF-endpoint, 49.3% of sertraline subjects were CGI-I responders compared to 26.4% of placebo treated subjects ($p < .001$) with a significant reduction in BSPS total score vs. placebo (mean change from baseline: –16.0 vs. –10.0; $p < 0.001$). Sertraline was significantly superior to placebo on all BSPS subscale measures (fear, avoidance, and physiologic) at LOCF endpoint. Sertraline was well-tolerated, with 9.3% attrition due to adverse events vs. 2.6% attrition on placebo.

Conclusion: The results of the current combined analysis confirms the efficacy of sertraline in the treatment of social phobia and its core symptoms, even in a large sample of patients with high level of severity.

NR152 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Comorbidity of Panic Disorder and Personality Disorder

Eric D. Peselow, M.D., *Department of Psychiatry, New York University School of Medicine, 32 Bassett Avenue, Brooklyn, NY 11234*; Gonzalo Laje, M.D., Patrick Ying, M.D., Jamie A. Luff, M.D., Mary Paizis, M.D., Mary T. Guardino, B.A.

Summary:

Objective: The purpose of this report is to evaluate frequency of DSM-IV personality disorders encounters in patients with panic disorder during active illness & following clinical recovery

Method: To date we have evaluated 213 patients from an anxiety disorder clinic affiliated with Columbia University with panic disorder who were diagnosed using a modified symptom check list adapted from the SCID during the acute stage of the illness & following clinical recovery (defined as being free from a full-blown panic attack for at least 1 month) 12–16 weeks later. To assess personality disorders the SIDP for DSM-IV was used both during the acute phase of the illness & upon clinical recovery. From the SIDP we were able to assess both dimensional personality traits & categorical diagnosis. In addition using the modified SCID, at baseline.

Results: At baseline, 134 of the 213 patients (64%) met criteria for at least one DSM-IV personality disorder with the two most frequent being avoidant (41.3%) & dependent (37.6%). However upon clinical recovery, only 81 of the 213 patients (38.0%) met criteria for at least one DSM-IV personality disorder. The frequency of meeting criteria for a DSM-IV personality disorder as well as the dimensional trait score with respect to the Cluster A & Cluster C traits decreased to a significant level when the panic attacks ceased. Panic patients with a greater comorbidity of other anxiety disorders tended to retain the personality diagnosis.

Conclusion: Assessment of Axis II pathology is confounded by active psychopathology but even during symptom free periods, there is high comorbidity between panic disorders and DSM-IV personality disorders.

NR153 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Possible Phenotypes in OCD

Juliana B. Diniz, M.D., *Department of Psychiatry, Psychiatric Institute, R Dr Ovidio Pires de Campos SN, Sao Paulo, SP 05403-010, Brazil*; Maria C. Rosario-Campos, M.D., Sergio A. Brotto, M.D., Mariana Curi, Priscila J. Chacon, Ana G. Hounie, M.D., Euripedes C. Miguel, Ph.D.

Summary:

Introduction: This study tries to determine which phenotypic characteristics emerge as different when subdividing OCD patients according to the age when their OC symptoms (OCS) started, presence of tics, and previous history of Rheumatic Fever (RF).

Methods: One hundred sixty-two outpatients (19 had previous RF) were interviewed with SCID, YBOCS, YGTSS, and USP Harvard repetitive behaviors interview.

Results: Younger mean age at onset was associated with comorbidity with tic disorders ($p < 0.001$), bipolar disorder ($p = 0.007$), presence of sensory phenomena (SP) preceding their compulsions ($p = 0.007$), and higher frequencies of hoarding ($p < 0.001$), repeating rituals ($p = 0.001$), mental rituals ($p = 0.001$), and tic-like compulsions ($p < 0.001$). Patients with comorbid tics presented an earlier age at onset of OC symptoms ($p < 0.001$), higher frequencies of hoarding ($p = 0.004$), intrusive sounds ($p = 0.007$), somatic obsessions ($p = 0.012$), repeating rituals ($p = 0.004$), counting ($p = 0.015$), and tic-like compulsions ($p = 0.001$). Previous history of RF did not predict any clinical differences in the data analyses. Correspondence analyses with these findings revealed an association with early age at onset, comorbidity with tics, presence of SP, and hoarding. Previous history of RF and presence of eating disorders were associated.

Conclusions: Age of onset OCS and co-morbidity with tics are important factors in sub-typing OCD and present overlapping features. RF may not be associated to any of these putative subgroups.

NR154 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Brief Behavioral Therapy for Avoidant Paruresis: Shy-Bladder Syndrome

Steven D. Soifer, Ph.D., *Department of Social Work, University of Maryland, 525 West Redwood Street, Baltimore, MD 21215*; Joseph A. Himle, Ph.D., Daniel Fischer, M.S.W.

Summary:

Objective: Is brief behavioral therapy in a weekend workshop format effective in treating paruresis?

Method: One hundred and one self selecting patients (89 male; 12 female) with avoidant paruresis or shy bladder syndrome, a form of social phobia that involves difficulty initiating urine in the presence of others, were treated in eight weekend workshops across the U.S. with behavioral exposure therapy. Exposure therapy was delivered in a three-day concentrated group workshop format. The primary intervention strategy involved repetitive exposure to progressively more challenging restroom situations. Psychoeducation and group support were also included in the workshop. Pre-test, post-test, and one-year follow up surveys were administered.

Results: Statistically significant improvement was observed from the beginning to the end of the group ($t = 5.138$; $p = .0001$). Improvement was maintained at one-year follow-up. Similar outcomes were observed for male versus female subjects. A detailed description of the treatment protocol will be included in poster.

Conclusions: Brief behavioral therapy delivered in a three-day concentrated group workshop format is effective for treating paruresis, and gains are maintained for at least one year following workshop.

NR155 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Nocturnal Panic Attacks: A Phenomenological Study

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., Isabella Nascimento, M.D., Alexandre M. Valenca, M.D., Marco A. Mezzasalma, M.D., Walter Zin, M.D.

Summary:

Background: Panic disorder (PD) patients has been linked to abnormalities in respiration. Our aim was to compare the nocturnal and daytime panic attacks symptoms.

Methods: We describe a cross-sectional retrospective study and a prospective-longitudinal follow-up of the 28 PD patients (DSM-IV). The sample was divided in: (1) nocturnal panic attacks (NPA), (2) daytime panic attacks (DPA), (3) nocturnal and daytime panic attacks (NDPA). Each subject was grouped in the prominent respiratory symptoms or nonrespiratory symptoms groups. The Panic Disorder Severity Scale (PDSS) was used.

Results: The final sample consisted of 61% NDPA ($n = 17$) and 39% DPA ($n = 11$). 46.5% of the NDPA presented prominent respiratory symptoms compared with 21.5% of the DPA. The NDPA group tended to present a higher score on the PDSS at the follow-up ($p = 0.086$): frequency (mean = 1.1 vs 0.5), distress (mean = 2.0 vs 0.5), and impairment in work (mean = 1.5 vs 0.8) and in social functioning (mean = 1.1 vs 0.5), for NDPA and DPA respectively.

Conclusion: It is suggested that the NDPA group exhibit a worst prognosis and it seems to be more correlated with the respiratory symptoms, leading to a direct relationship with the False Suffocation Alarm Theory.

NR156 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Predictive Factors of Treatment Response in OCD

Roseli G. Shavitt, M.D., *Department of Psychiatry, University of Sao Paulo, Rua Sergipe 290 AP102, Sao Paulo, SP 01243-000, Brazil*; Cristina Belotto, Maria C. Rosario-Campos, M.D., Mariana Curi, Euripedes C. Miguel, Ph.D.

Summary:

Introduction: About 40% of OCD patients do not respond to conventional treatments. Among the responders, full recovery is rare. The aim of this study was to investigate whether the response to pharmacological treatment in the short term could be associated to phenotypic variables, such as sensory phenomena (mental or physical sensations in the absence of obsessions), or peculiarities of the OCD subtypes, such as the early-onset and the tic-related OCD.

Method: 42 patients (23 men, age range 18–52 years) with a DSM-IV diagnosis of OCD were studied. All received clomipramine up to 250mg/day for 14 weeks. Assessments were made blindly through the Structured Clinical Interview for DSM-IV Diagnoses, USP-Harvard Interview for Repetitive Behaviors, Y-BOCS Checklist/Scale, and the Yale Global Tic Severity Scale. Response was considered in terms of percent reduction of the initial YBOCS scores.

Results: Multivariate analysis showed a positive correlation between treatment response and the presence of sensory phenomena ($p = 0.006$), and negative correlations with the presence of tricotillomania, skin-picking, and onicophagia ($p = 0.03$) and with the initial severity of symptoms ($p = 0.03$).

Conclusions: Sensory phenomena predicted a good response to pharmacologic treatment in the short term. Greater initial severity of symptoms and comorbidity with OCD spectrum disorders of the grooming type predicted a pooter outcome.

NR157 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Results from a Randomized, Double-Blind, Multicenter Trial of Sertraline in the Treatment of Moderate-to-Severe Social Phobia (Social Anxiety Disorders)

Michael D. Leibowitz, M.D., *176 Broadway, Apt. 3A, New York, NY 10038-2516*; Nicholas Demartinis, M.D., Karen L. Weihs, M.D., Henry Chung, M.D., Cathryn M. Clary, M.D.

Summary:

Background: Generalized social phobia is a prevalent and highly chronic, frequently disabling anxiety disorder with a lifetime prevalence of approximately 5%. The objective of the current study was to evaluate the efficacy and tolerability of sertraline for the treatment of social phobia in adults in the U.S.

Method: After a one-week, single-blind, placebo lead-in period, patients were randomized, to 12 weeks of double-blind treatment with flexible dose of sertraline (50–200 mg) vs. placebo. Primary efficacy outcomes were the Liebowitz Social Anxiety Scale (LSAS) total score and the responder rate based on the Clinical Global Impression-Improvement scale (CGI-I). Additional assessments included the Duke Brief Social Phobia Scale (BSPS), the Quality of Life, Enjoyment and Satisfaction Questionnaire (Q-LES-Q), the Sheehan Disability Inventory (SDI), and the Endicott Work Productivity Index.

Results: 211 patients were randomized to sertraline (60.2% male, mean ± SD age, 35.1 ± 10.6 years, baseline LSAS, 91.3 ± 15.9; mean illness duration 20.8 years), and 204 patients were randomized to placebo (58.8% male, mean ± SD age, 35.0 ± 10.6 years, baseline LSAS, 93.9 ± 16.0; mean illness duration 21.5 years). The study subjects had moderate-severe illness as measured by a mean CGI-S score of 4.8 +/– 0.7. At LOCF-endpoint, 47% of sertraline subjects were CGI-I responders compared to 26% of placebo treated subjects ($p < .001$) with a significant reduction in LSAS total score compared to placebo (mean change from baseline: –31.3 vs. –21.4; $p < 0.001$). At week 12, the mean change in LSAS Total Score was –35.0 vs. –24.2 for sertraline vs. placebo, $p < .001$ with a greater proportion of responders (CGI-I ≤ 2: 55.6% vs. 29.5%; $p < 0.001$). Sertraline was significantly superior to placebo on most secondary efficacy measures, including quality of life and functional measures. Sertraline was well-tolerated, with 7.6% attrition due to adverse events compared to a 2.9% attrition on placebo.

Conclusion: The results of the current study confirm the efficacy of sertraline in the treatment of generalized social phobia, even in a study sample with high levels of severity.

NR158 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Predictive Factor of PTSD in Victims 32 Months After Bomb Attack

Louis Jehel, *Department of Psychiatry, Hospital Tenon, 6 Rue De La Chine, Paris 75970, France*; S Paterniti, M.D., Aileen S. Brunet, M.D., C Duchet, Ph.D., Julien D. Guelfi, M.D.

Summary:

Objective: Identify factors that predict occurrence and severity of PTSD after a terrorism attack in a Paris subway.

Method: Sociodemographic characteristics, clinical data, and physical injuries were used to predict PTSD occurrence and severity in 35 victims, 32 months after a bombing attack. The Watson's PTSD Inventory (PTSD-I) and the Impact of Event Scale (IES) by Horowitz were used to evaluate occurrence and severity of PTSD, respectively.

Results: Thirty-nine percent of participants met PTSD criteria at six months and 25% had PTSD at 32 months. Women ($p = 0.07$), psychotropic drug users before the attack ($p = 0.01$), and subjects with PTSD at six months ($p = 0.003$) had a higher risk of PTSD occurrence at 32 months. PTSD-I score at six months was significantly and positively associated with IES scores at 32 months ($r = 0.55$, $p = 0.004$). In a linear regression model, physical injuries, employment status, and psychotropic drug use before the attack were independent predictors of severity of PTSD at 32 months.

Conclusions: PTSD prevalence observed in our study was similar to PTSD prevalence reported by North et al (1997). Our findings contribute to propose variables concerning people before a traumatism as recommended by Brewin et al (2000).

NR159 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Do Severe Gastrointestinal Symptoms Modify Venlafaxine Extended Release Efficacy in GAD?

R. Bruce Lydiard, M.D., *Department of Psychiatry, South East Health Consultants, 1 Poston Road, Suite 150, Charleston, SC 29407*; Bruno Pitrosky, Ph.D., David Hackett, M.S.C.

Summary:

Objective: Inhibitors of serotonin reuptake are associated with the occurrence of gastrointestinal (G-I) symptoms, such as nausea 1. Further, patients experiencing anxiety often report GI symptoms 2. The aim of this analysis was to evaluate the extent of the presence of GI symptoms in a clinical trial population of patients with Generalized Anxiety Disorder (GAD), and the impact of this upon the efficacy of the serotonin and norepinephrine reuptake inhibitor, venlafaxine extended-release (XR).

Method: Data from 5 double-blind, placebo-controlled, studies with venlafaxine XR were pooled (N = 1839). G-I symptom severity was defined according to item 11 of the HAM-A scale: scores = <2 defined patients as having no-to-moderate G-I symptom (82.4%), while scores >2 defined patients with severe GI symptom (17.6%).

The severe G-I symptom subgroup had a longer duration of anxiety episode and a higher overall anxiety severity, including psychic anxiety.

Conclusion: Venlafaxine XR was more effective than placebo in reducing the HAM-A total score, regardless of G-I symptom severity. In the severe G-I symptom subgroup, the emergence of adverse events or rates of discontinuation were not altered by venlafaxine XR when compared to placebo.

The results suggest that severe GI symptoms do not alter the efficacy of venlafaxine XR treatment in GAD.

NR160 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Psychoactive Properties of Tofisopam

Herbert W. Harris, M.D., *Vela Pharmaceuticals, 3131 Princeton Pike Bldg 4 #216, Lawrenceville, NJ 08648*; Robert Kucharik, Steve Leventer, Ph.D., Kevin Keim, Ph.D.

Summary:

Background: Tofisopam is an atypical 2,3-benzodiazepine that has demonstrated efficacy in a wide range of clinical settings, including anxiety, depression and perimenopausal symptoms. Despite this well-characterized clinical activity, the phamacologic mechanism of action of tofisopam remains unclear.

Methods: The *in vitro* receptor binding profile of tofisopam was examined. In addition, tofisopam was tested in a series of animal behavioral models, including the elevated plus-maze and the water-immersion stress test.

Results: Tofisopam was screened against approximately 60 receptors. The compound exhibited little or no affinity at any site tested, including the GABA/benzodiazepine receptor. In contrast with typical benzodiazepines, tofisopam showed no activity in the elevated plus-maze; in the water-immersion stress test, however, tofisopam produced consistent dose-dependent reduction in stress-induced ulcers.

Conclusion: Although tofisopam is a clinically effective anxiolytic agent with a chemical structure similar to the benzodiazepines, its binding profile is clearly distinct from any known typical 1,4- or 1,5-benzodiazepine receptor agonist. In addition, unlike typical benzodiazepines, tofisopam was inactive in a conventional animal model of anxiety, the elevated plus-maze. Tofisopam was active in the water-immersion stress test. This activity, consistent with an anxiolytic effect, suggests a mechanism of action that may involve stress pathways. These data indicate that tofisopam has a unique preclinical neurochemical and behavioral profile, one that is clearly distinct from classical benzodiazepines.

NR161 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Migraine in Patients with Panic Disorder

Hisanobu Kaiya, M.D., *Imon Nagoya Building, Panic Disorder Research Center, 1-16 Tsubakicho Nakamuraku, Nagoya 453-0015, Japan*; Gaku Yamanaka, M.D., Hideto Tsuchida, M.D., Shin Yasuda, M.D., Hiroaki Kumano, M.D., Yojiro Sakai, M.D.

Summary:

The subjects were 191 patients (mean age: total; 34.2 ±8.6, 92 male; 34.2 ± 8.6, 99 female; 34.1 ± 8.7) diagnosed as having panic disorder with or without agoraphobia according to DSM-III R criteria, whose intake was between August 1995 and January 1997 at Nagoya Mental Clinic. They answered a questionnaire about panic disorder and migraine. Seventy-eight patients (total: 40.8% male 36.9% female 44.0%) had reported to experience migraine. The patients who experienced migraine showed more symptoms of a first panic attack (7.1 ± 2.6 *vs* 6.0 ± 2.4, p = 0.01) and higher points on Sheehan's Anxiety Rating Scale (71.8 ± 25.9 *vs* 62.8 ± 26.6, p = 0.03) as compared with those patients who had no migraine. Otherwise, there were no statistical differences in clinical history between patients with or without migraine. The most frequent regions of headache were occipital and cervical (50.5%), hemicranial (35.4%) and whole or central (22.2%). The most often reported nature of headaches were pulsatory (46.5%), fastening (33.3%), and throbing (33.3%). Aura symptoms other than headache were complained by 62.6% of migraine patients and long-term prodromal symptoms were reported by 20.2%. The types of migraine are divided from the patterns of onset into cluster type: 18.2%, classic type: 38.4%, and common type 14.1%. Patients who had migraine before the onset of panic disorder when compared with those who had migraine after the onset of panic disorder showed a tendency to have younger onset of panic disorder (25.4 ± 5.9 vs 30.2 ± 4.8, p = 0.06) and longer duration of the illness (150.4 ± 127.1 vs 65.2 ± 72.0, p = 0.06).

NR162 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Efficacy and Safety of Pregabalin and Alprazolam in Generalized Anxiety Disorder

Karl Rickels, M.D., *3535 Market Street, Philadelphia, PA 19104-3309*; Mark H. Pollack, M.D., R. Bruce Lydiard, M.D., Robert J. Bielski, M.D., Douglas E. Feltner, M.D., Atul C. Pande, M.D., Richard J. Kavoussi, M.D.

Summary:

Objective: Pregabalin is a novel compound under development for the treatment of anxiety disorders, neuropathic pain, and epilepsy. Previous studies have shown pregabalin to be safe and effective in the treatment of generalized anxiety disorder (GAD). This study examined the efficacy of pregabalin in the treatment of GAD in comparison to alprazolam.

Method: Following a one-week screening phase, 455 patients with GAD were randomized to 4 weeks of double-blind treatment with either pregabalin 300mg/day, pregabalin 450mg/day, pregabalin 600mg/day, alprazolam 1.5mg/day, or placebo (all dosed TID).

Results: All doses of pregabalin and alprazolam produced a significantly greater reduction in the HAMA total score than placebo: pregabalin 300mg/day (−12.2 ± 0.77, p = 0.0004), pregabalin 450mg/day (−11.0 ± 0.78, p = 0.0169), pregabalin 600mg/day (−11.8 ± 0.80, p = 0.0022), alprazolam 1.5mg/day (−10.9 ± 0.78, p = 0.0209), and placebo (−8.4 ± 0.79). Improvement in all three pregabalin treatment groups was evident by the end of the first week of treatment and continued to the end of the study. Improvement was noted in the psychic anxiety subscale of the HAMA with all active treatments. The somatic subscale of the HAMA showed improvement for pregabalin 300 and 600 mg/day but no significant improvement for pregabalin 450 mg/day or alprazolam. The most commonly observed adverse events for both pregabalin and alprazolam were somnolence and dizziness (34–37% for pregabalin, 35–42% for alprazolam 1.5 mg/day). Withdrawal rates due to adverse events were low: pregabalin 300mg/day (3.3%) pregabalin 450mg/day (7.8%), pregabalin 600mg/day (14.6%), alprazolam 1.5mg/day (14.0%), and placebo (9.9%).

Conclusions: Along with previously reported studies, this study confirms the safety and efficacy of pregabalin in the treatment of generalized anxiety disorder.

NR163 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Individual Interpersonal Psychotherapy for PTSD

Kathryn L. Bleiberg, Ph.D., *Department of Psychiatry, Cornell University Medical College, 525 East 68th Street, Box 140, New York, NY 10021*; John C. Markowitz, M.D., Marylene Cloitre, Ph.D.

Summary:

Objective: This poster describes the pilot adaptation of Interpersonal Psychotherapy (IPT) as an individual treatment for posttraumatic stress disorder (PTSD). Since IPT is a life event-based, time-limited treatment empirically validated to treat mood disorders, and PTSD is a life event-based disorder that compromises interpersonal and social functioning, it seems intuitive to treat PTSD with IPT. Unlike most PTSD treatment, IPT is not exposure-based, but focuses on interpersonal sequelae of trauma.

Method: Male and female subjects (n = 8), recruited via clinical referral and local advertising, were treated in an open 14-week IPT trial Assessments included the Clinician-Administered PTSD Scale (CAPS). Posttraumatic Stress Scale-Self Report (PSS-SR), Social Adjustment Scale (SAS), Inventory of Interpersonal Problems (IIP) and other measures, at baseline, mid-treatment, end of treatment and 6 month follow-up.

Preliminary results: Treatment was well-tolerated. Most subjects reported a decline in PTSD symptoms and improved interpersonal functioning. PSS-SR scores (n = 8) fell from 72.1 (±25) at baseline to 25.1 (±18.7) at week 14, yielding an effect size of 1.79. All PTSD symptom clusters improved, with effect sizes of 1.30, 1.76 and 1.72 for clusters B, C and D respectively. Follow-up and treatment of subjects are ongoing; results will be updated. Nevertheless, the preliminary data are promising.

NR164 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Comparative Efficacy of Pharmacological Treatments for PTSD: A Meta-Analysis

Constance B. Portier, M.D., *Department of Psychiatry, Lt Lucas-Andreas, Jan Tooropstraat 164, Amsterdam, AE 1006, Netherlands*; Abraham Bakker, M.D.

Summary:

Objective: To compare the efficacy of the various pharmacological treatments of post-traumatic stress disorder (PTSD), a meta-analysis was conducted.

Method: Included were 46 studies (17 placebo-controlled and 29 open-label studies), pertaining to 2,126 patients at pretest and 1,453 patients at post test. Outcome was measured with pre/post Cohen's *d* effect sizes, calculated for selfrated and observer-rated PTSD outcome measures, as well as depression and anxiety ratings.

Results: There were differences between the investigated groups of pharmacological treatments on most effect sizes. Antidepressants, especially the SSRs, seem to be the most effective drugs in reducing PTSD symptoms, depressive symptomatology, and general anxiety.

Conclusion: Different medications can be effective in reducing PTSD symptoms, and pharmacotherapy should be considered part of the treatment of this disorder.

NR165 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Pregabalin: Efficacy in Generalized Anxiety Disorder Using a BID Regimen

Robert B. Pohl, M.D., *Department of Psychiatry, Wayne State University, 2751 East Jefferson, Suite 200, Detroit, MI 48207*; Daniel L. Zimbroff, James T. Hartford, M.D., Ronald R. Fieve, M.D., Douglas E. Feltner, M.D., Atul C. Pande, M.D., Richard J. Karoussi, M.D.

Summary:

Objective: Several studies have shown the novel compound, pregabalin, to be effective in the treatment of generalized anxiety disorder (GAD). Because of the 6-hour half-life of pregabalin, all previous studies have used a TID dosing regimen. The purpose of this study was to assess the efficacy and safety of pregabalin using a BID dosing regimen.

Method: Following a one-week screen period, 344 patients meeting DSM-IV criteria for GAD were randomized to 6 weeks of double-blind treatment with either pregabalin 100mg BID, pregabalin 200mg BID, pregabalin 150mg TID, or placebo.

Results: Pregabalin, whether dosed BID or TID produced a statistically significant reduction in the HAMA total score compared to placebo. Reductions in the HAMA total score by treatment group were: pregabalin 100 mg BID (−12.4 ± 0.84, p = 0.0063), pregabalin 200mg BID (−12.9 ± 0.78, p = 0.0010), pregabalin 150 mg TID (−12.4 ± 0.78, p = 0.0045), and placebo (−9.3 ± 0.79). Changes in the HAMA total score did not differ significantly between the BID and TID treatment groups. The response rate (defined as "very much improved" or "much improved" on the CGI-I) was significantly higher for 100 mg BID (56%), 200mg BID (55%), and 150mg TID (59%) than placebo (34%). Improvement in all the pregabalin treatment groups was evident by the end of the first week of treatment and continued to the end of the study. Pregabalin treatment was well tolerated; the percentage of patients who withdrew from study participation due to adverse events was similar in the pregabalin and placebo treatment groups.

Conclusions: This study demonstrates that pregabalin, whether dosed BID or TID, is efficacious and well tolerated as a treatment for GAD.

NR166 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Development and Validation of a Short Form of the Hamilton Depression Scale

Kenneth A. Kobak, Ph.D., *Health Care Technology Systems, 7617 Mineral Point Road, #300, Madison, WI 53717*; John H. Greist, M.D.

Summary:

Background: Recent evidence suggests shortened versions of the HDRS may have greater correlations with overall depression severity, as well as larger effect sizes in antidepressant trials. In addition, completion time limits the utility of the standard 17-item version. The current study was designed to develop and validate a shortened version of the HAMD and to corroborate previous findings.

Methods: 750 adults [major depression (310), dysthymia or atypical depression (40), anxiety disorders (n = 151), alcohol abuse (n = 14), other diagnoses (n = 61), or no diagnoses (n = 174)] were recruited from either clinical drug trial screenings or community ads and administered the 17 item HAMD. Short-form items were selected based on a) high item-to-total scale correlations; b) greatest differentiation of persons with depression from other diagnostic groups; and c) items providing the greatest factor loadings.

Results: Eight items (1, 2, 3, 7, 10, 11, 13 & 14) were identified that had a minimum item-total correlation of r = .60, a minimum factor loading of .60, and an F value of >200 in differentiating persons with major depression from other psychiatric disorders and from non-depressed community volunteers. Internal consistency reliability for the 8-, 17-, and 6-item (Bech) versions were .91, .90 and .87 respectively, and test-retest reliability (n = 120) was r = .953, r = .956, and r = .947. All 3 versions distinguished depressed subjects from subjects with other psychiatric disorders and controls, as well as subjects with major and minor depression (p < .0001).

Conclusion: The 6- and 8-item versions of the HDRS are valid and reliable measures of depression andcorroborate earlier studies. The ability of the 6- and 8-item scales to detect true differences between drug and placebo in clinical trials needs to be further examined. Given their similar psychometics, brevity may favor use of the 6-item version.

NR167 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

A Controlled Study of Exposure Therapy, Clomipramine, and Combination for OCD

Martin E. Franklin, Ph.D., *Department of Psychiatry, University of PA, 3535 Market Street, 6th Floor, Philadelphia, PA 19104*; Edna B. Foa, Ph.D., Raphael Campcas, M.D., Michael R. Liebowitz, M.D., Sharon Davies, R.N., Michael J. Kozak, Ph.D., Jonathan D. Huppert, Ph.D.

Summary:

Introduction: Cognitive-behavioral therapy using exposure and response (or ritual) prevention (EX/RP) and pharmacotherapy using serotonin reuptake inhibitors (e.g., clomipramine (CMI) and the SSRIs) are established treatments for obsessive compulsive disorder (OCD). However, their relative and combined efficacy has not been well studied. A two-center randomized controlled trial compared the acute efficacy of EX/RP, CMI, and combined treatment (EX/RP+CMI) to that of pill placebo (PBO).

Methods: One hundred twenty-two patients were randomly assigned to EX/RP, CMI, EX/RP + CMI, or PBO and entered the acute (12-week) phase of the study (29 EX/RP, 36 CMI, 31 EX/RP + CMI, 26 PBO). During this phase, patients' OCD and related symptoms were assessed monthly by an evaluator blind to condition.

Results: In completer analyses, all active treatments were superior to PBO at week 12. Additionally, EX/RP and EX/RP+CMI were superior to CMI, yet did not differ significantly from one another. Different measures of OCD symptom severity yielded similar results. Similar results were found for ITT analyses.

Conclusion: EX/RP, CMI, and EX/RP+CMI are efficacious treatments for adult OCD, and there is no clear advantage for combined treatment over EX/RP alone when EXRP is done intensively and CMI is started at the same time as EXRP.

NR168 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Combination of Pharmacotherapy and Behavior Therapy Is Superior to Pharmacotherapy Alone in OCD

Nienke H. Tenney, M.S., *Department of Psychiatry, UMC, Heidelbergiaan 100 HPAO1.126, Utrecht 3854 CX, Holland*; Damiaan Denys, M.D., Nie van der Wee, M.D., Harold J. Van Megen, M.D., Herman Westenberg, Ph.D.

Summary:

Background: Numerous studies have shown that behavior therapy and serotonergic agents are effective in the treatment of OCD. Approximately 50% of the patients, however, do not benefit from it or have only a small reduction in symptoms.

Objective: We tested the hypothesis that addition of behavior therapy would be beneficial in patients already responding to pharmacological treatment.

Method: Seventy-eight patients with a primary diagnosis of OCD (DSM-IV) who responded on a 12-week treatment with antidepressants were included (age 35.5 years; 70.5% female; illness duration 14.77 years). Before pharmacological treatment, mean Y-BOCS score for responders was 25.8 and after pharmacotherapy 16.2. Patients were subsequently randomized to receive six months medication only, or a combination of medication and behavior therapy.

Results: Sixty patients completed this study. After treatment the reduction in symptoms of patients receiving the combination therapy (n = 25) was 41%, while symptoms of patients treated with medication only (n = 35) increased with 18% (t = 4.73,p = .000). When repeating this analysis for the total sample (completers and dropouts), this was a reduction of 26% (n = 38) and an increase of 17% (n = 40), respectively (t = 3.77,p = .000).

Conclusion: These results suggest that administration of behavior therapy to patients, who have benefited already of a pharmacological intervention, enhances treatment effect considerably.

NR169 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Nefazodone Maintenance Treatment to Prevent Recurrence of Chronic Depression

Alan J. Gelenberg, M.D., *Department of Psychiatry, University of Arizona Health Science Center, 2320 East Adams, AZ 85719-1166*

Summary:

Objective: How would nefazodone compare to PBO in preventing depressive recurrence in recovered patients with chronic depression.

Background: Chronic major depression accounts for much of the illness burden associated with depression. Long-term treatment is recommended, but few studies have examined maintenance antidepressants for chronic depression. This study was a randomized, placebo-controlled evaluation of the efficacy and safety of nefazodone in preventing recurrence over the course of a 1-year maintenance treatment period for patients with chronic forms of MDD.

Method: 160 outpatients with chronic non-psychotic major depressive disorder (MDD), MDD plus dysthymic disorder ("double-depression"), or recurrent MDD with incomplete inter-episode recovery, who achieved and maintained a clinical response during acute and continuation therapy with either nefazodone or nefazodone combined with psychotherapy were randomized to 52-weeks of double-blind nefazodone (n = 76) (maximum dose 600 mg/d) or placebo (n = 84). The occurrence of episodes of major depressive disorder during maintenance treatment was assessed with (1) the 24-item Hamilton Rating Scale for Depression (HAM-D-24) and a DSM-IV MDD checklist, and (2) a blinded review of symptom exacerbations by a consensus committee. Relative to the nefazodone group, subjects in the placebo group were more than twice as likely to discontinue treatment for all reasons. Since, the likelihood of early discontinuation compeled with the observation for recurrence, a "competing-risk" statistical model was used.

Results: The competing-risk model revealed a significant (p = 0.043) difference between nefazodone and placebo, when the latter part of the one-year maintenance period was emphasized. At the end of one year, the conditional probability of recurrence was 30.3% with nefazodone compared to 47.5% with placebo. Discontinuations due to adverse events were 5.3% and placebo 4.8%.

Conclusions: Nefazodone is efficacious and well-tolerated as a maintenance therapy for chronic forms of MDD.

NR170 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Capsulotomy for Anxiety: Long-Term Efficacy and Safety

Christian Ruck, M.D., *Clinical Neuroscience, Karolinska Institute, Psykiatricentrum Karolinska, Stockholm, SE 17176, Sweden*; Sergej Andreewitch, M.D., Hakan Nyman, Ph.D., Karin Flyckt, M.D., Bjorn Meyerson, M.D., Gunnar E. Edman, Ph.D., Marie Asberg, M.D.

Summary:

Objective: There is evidence indicating that some cases of anxiety disorders may benefit from brain surgery, now referred to as Neurosurgery for Mental Disorders (NMD). Such operations include capsulotomy and cingulotomy and the main indication is OCD, other indications are less studied.

Methods: 26 patients that had undergone bilateral thermocapsulotomy were followed up after a mean of 13 years. Main diagnoses

were Generalized Anxiety Disorder (n = 13), Panic Disorder (n = 8) or Social Phobia (n = 5). Psychiatric methods include rating scales, neuropsychological testing as well as a personality inventory (KSP). Raitings were made by psychiatrists independent of patient selection and post op treatment. A quantitative MRI evaluation (1) was conducted to search for common anatomic denominators.

Results: The reduction in anxiety ratings was significant at both one-year and long-term follow-up. Seven patients were, however, rated as having significant adverse events, most prominent symptoms being apathy and dysexecutive behavior. Neuropsychological results and results of the personality inventory will be discussed. No common anatomic denominator could be found in responders in the analysis of MRI scans.

Conclusions: Thermocapsulotomy is an effective treatment of selected cases of non-obsessive anxiety but may carry a significant risk of impairment on cognition and personality. Future directions for research will be discussed.

NR171 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Galantamine Improves Cognition in Alzheimer's Cebrovascular Disease

Gary W. Small, M.D., *Department of Psychiatry, UCLA Neuropsychiatric Institute, 760 Westwood Plaza, Los Angeles, CA 90024;* Sean Lilienfeld

Summary:

Objective: To evaluate the sustained efficacy of continious galantamine in patients with Alzheimer's disease (AD), vascular dementia (VaD), and AD with cerebrovascular disease.

Methods: Open-label extensions of 3 double-blind, placebo-controlled trials assessed the long-term effects of galantamine. In 2 studies, mild-to-moderate AD patients received galantamine or placebo for 6 or 6.5 months, followed by open-label extensions (24 mg/day) for an additional 6 or 12 months, respectively. In a third trial, patients with probable VaD or AD with cerebrovascular disease received galantamine or placeboe for 6 months, followed by a 6-month, open-label extension (24 mg/day). The primary endpoint for all studies was the AD Assessment Scale-cognitive subscale (ADAS-cog).

Results: During the 12-month AD study, patients maintained cognition at or above baseline. Similarly, patients with AD who received galantamine for a total of 18.5 months demonstrated sustained cognitive benefit. Patients with VaD or AD with cerebrovascular disease with galantamine for 12 months also showed maintenance of or improvement in cognition.

Conclusions: Galantamine demonstrates long-term cognitive benefits in patients with dementia. Treatment is favorable and may be initiated, even before definitive diagnosis of dementia ubtype (ie, AD versus VaD versus AD with cerebrovascular disease).

NR172 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Role for NSAID on Interferon-Induced 5-HT Changes: Useful for Depression?

Richard De La Garza II, Ph.D., *Albert Einstein College, 1300 Morris Park Avenue, Forch 111, Bronx, NY 10461*; Rajendra P. Paladugu, M.D., Xinhe Liu, M.A., Gregory M. Asnis, M.D.

Summary:

Introduction: Chronic alpha-interferon (α-IFN) administration induces major depression in 40% of patients (Musselman et al., 2001). Recent reports suggest that major depression is associated with dysfunction of inflammatory mediators. We sought to establish the effect of a non-steroidal anti-inflammatory drug (NSAID), diclofenac acid, on monoamine turnover in brain induced by acute α-IFN exposure.

Methods: Twelve male, Wistar rats (N = 4/group) were pretreated with diclofenac (20 mg/kg, s.c.) or saline, followed by intracerebroventricular infusion of α-IFN (1000 IU in 5 μl) or vehicle. The prefrontal cortex was isolated and samples were assayed for monoamines and major metabolites by HPLC.

Results: α-IFN increased dopamine and serotonin turnover in prefrontal cortex, consonant with proposed brain alterations in depression. Pre-treatment with diclofenac completely blocked this response.

Conclusion: The data reveal altered serotonin/dopamine turnover in response to α-IFN, and reveal the ability of diclofenac to reverse this effect.

Discussion: Recent data in humans revealed that the NSAID indomethacin attenuated elevated levels of cytokines and stress hormones induced by IFN-β1a (Kumpfel et al., 2000). Additional findings suggest that the NSAID ketoprofen reduces α-IFN-induced "flu-like" symptoms in humans. The data presented here offer support for a novel role of NSAIDs in modulating depression induced by chronic α-IFN exposure.

NR173 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Effect of CCK-4 in Patients with Irritable Bowel Syndrome

Diana Koszycki, Ph.D., *Sacru, Royal Ottawa Hospital, Pital/ 1145 Carling Avenue, Ottawa, ON K1Z 7K4, Canada*; Jacques Bradwejn, M.D.

Summary:

Objective: Both clinical and community surveys suggest that irritable bowel syndrome (IBS) and panic disorder (PD) co-exist with a high frequency. However, the nature of this relationship remains obscure. The objective of this study was to elucidate the neurobiological link between IBS and PD and between the brain and the gut. Specifically, we explored whether these syndromes share a common dysfunction of the CCK-B receptor system.

Method: We compared panicogenic response to a 20 μg dose of the gut-brain hormone, CCK-4, in IBS (n = 6), PD (n = 8) and normal control (NC) (n = 12) subjects. IBS patients had no psychiatric history or history of panic attacks. The study used a double-blind, randomized, placebo-controlled design.

Results: None of the subjects panicked with placebo. PD patients were more prone to panic with CCK-4 than IBS and NC subjects (75% vs 0% vs 17%, $p < 0.004$). Significant diagnostic differences were also noted for the number ($p < 0.05$) and sum intensity ($p < 0.01$) of panic symptoms, with PD patients having higher scores than the other two groups. Interestingly, mean ratings of nausea and abdominal distress were lowest in IBS subjects and there was no evidence of symptom overendorsement. No significant diagnostic differences were noted for heart rate and blood pressure response to CCK-4.

Conclusion: These preliminary data indicate that a) CCK-B receptor activity may not be altered in IBS and b) hypervigilence to and amplification of internal stimuli are not relevant factors in IBS patients with no lifetime psychiatric diagnoses.

NR174 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Quantitative Tremor Characteristic in Lithium-Maintained Bipolar Patients

Rocco M. Zaninelli, M.D., *Department of Neurosciences, Novartis Pharmaceuticals, One Health Plaza Bldg, 419/2335, East Hanover, NJ 07936*; Michael Bauer, M.D., Zhengning Lin, Ph.D.

Summary:

Objective: To characterize quantitatively tremor in patients with bipolar disorder receiving lithium maintenance treatment.

Method: Resting tremor[1] was assessed by accelerometry[2] at Day 1 and Day 7 in three groups of subjects: 1) euthymic bipolar outpatients on lithium maintenance (BP-EU, N = 35); 2) bipolar outpatients maintained on lithium but experiencing breakthrough major depression (BP-MDE, N = 26); 3) healthy controls (N = 36). All groups were age- and gender-matched; lithium was the only psychoactive medication in the patient groups. Variables of interest were the mean tremor frequency and tremor activity. The data were analyzed using ANCOVA, with age as the covariate and gender and group as factors in the model.

Results: Mean tremor frequency ranged from 7.08 to 8.90 Hz, mean tremor activity from 3.8 to 12.2 cm/s^2 Hz. According to the ANCOVA, these variables were significantly influenced only by group and gender ($p < 0.01$). On both assessment days, the mean tremor frequency was highest in the control group, while mean tremor activity was highest in the BP-MDE group. Across the three groups, the values for both variables were consistently greater in men than in women, although the differences were significant only for mean frequency in the control group ($p < 0.05$).

Conclusions: Accelerometry offers a convenient approach to quantifying tremor characteristics. This method is recommended for psychopharmacology studies where resting tremor is an expected side-effect.

NR175 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Triptans and Immune Response

Aron D. Mosnaim, Ph.D., *Department of Pharmacology, FUHS, The Chicago Medical School, 3333 Green Bay Road, North Chicago, IL 60064*; Karla Hidalgo, Pharm.D., Javier Puente, Ph.D., Seymour Diamond, M.D., Marion E. Wolf, M.D.

Summary:

Recognition of the critical role played by serotonergic mechanisms in the etiology of migraine headaches has led to the introduction of "triptans", a class of pharmacological agents sharing serotonin's indole-like chemical structure and selective vascular serotonin 1B/1D receptor agonist properties. Individual triptans show significant differences in their cardiovascular side effects and hepatic toxicities; they also appear to produce important changes in the immune system. We have tested the effect of various triptans e.g., Alnitidan, Avitriptan, Naratriptan, and Sumatriptan on natural killer cell activity (NKCA) of peripheral blood mononuclear cells (PBMC; separated by centrifugation on Hystopaque 1077) and highly purified NKC preparations [$CD3^-CD56^+$ cells (over 95% $CD56^+$); immunomagnetic isolation procedure] obtained from thirteen drug free, adult, healthy volunteers. Human erythroleukemia K-562 cells served as target. Triptans (10^{-4} M), but not serotonin or tryptamine, significantly (arbitrarily considered as 20% below baseline values for the same sample) inhibited NKCA in each of the PBMC samples tested, however they had no significant effect on the cytotoxicity of HPNKC preparations. The magnitude of this immunodepressant effect appears to be dependent on the effector-to-target cell ratio (30:1; 50:1 and 70:1), drug concentration (10^{-4} to 10^{-7}) and individual triptan studied. It could be suggested that this observed "triptan effect" is partly mediated by their ability to release monocyte-derived chemicals, particularly a number of cytokines known to inhibit NKCA. Triptan-induced cytokine-elicited immunological changes could possibly mediate their therapeutic effects in migraine.

NR176 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

The Role of the Dopamine D4 Receptor (DRD4) Gene Variants in Novelty Seeking

Heon-Jeong Lee, M.D., *Department of Psychiatry, Korea University Ansan Hospital, 516 Go-Jan Dong, Ansan, Kyunggi-Do 425-020, Korea*; Hong-Seock Lee, M.D., Min-Soo Lee, M.D., Seung-Gul Kang, M.D., Kwang-Yoon Suh, M.D., Leen Kim, M.D., Dong-K Kwak, M.D.

Summary:

Polymorphism in exon III 48-bp repeats of the human dopamine D4 receptor (DRD4) gene has been associated with the human personality trait of novelty seeking (NS). More recently, the −521 C/T single nucleotide polymorphism (SNP) in the promoter region of the DRD4 gene has been shown to be associated with the NS scores of the temperament and character inventory (TCI) in Japanese and Hungarian populations. We have investigated the association between polymorphism in 48-bp repeats and −521 C/T SNP of the DRD4, and personality traits of the TCI in a young Korean female population (n = 101). We found no evidence of a direct association between the two DRD4 polymorphisms and personality traits. Nevertheless, the interaction effects of the two DRD4 polymorphisms on NS ($F = 4.88$, $P = 0.029$) and persistence (P) scores ($F = 5.05$, $P = 0.027$) were observed. In the presence of the −521 C allele, NS scores are higher and P scores are lower in the presence of the 48-bp long allele. In conclusion, we found that the 48-bp VNTR and −521 C/T SNP of the DRD4 gene have an interactive influence on high NS and low P personality traits. Further investigations are necessary to establish if this genetic interaction between two DRD4 polymorphisms influences the human personality in a larger group.

NR177 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

5HT2A Receptors in Different Psychiatric Disorders

Donatella Marazziti, M.D., *Department of Psychiatry, University of Pisa, Via Roma 67, Pisa 56100, Italy*; Annalisa Giromella, Gino Giannaccini, Elena Di Masso, Irene Masala, Stefano Baroni

Summary:

Much focus has been recently directed toward 5-HT_{2A} receptors whose density seems to be altered in brain tissues from both schizophrenic patients and suicide victims. Given these controversial findings, our study aimed to compare the specific binding of [^{3}H]-ketanserin in human frontal and parietal cortex obtained postmortem from bipolar, depressed, schizophrenic patients and normal controls. The human brain samples (60 frontal cortex and 41 parietal cortex), were donated by the Stanley Foundation Brain Collection, courtesy of Drs. Michael B. Knable, E. Fuller Torrey, Maree J. Webster and Robert H. Yolken. They were collected during autoptic session of 60 subjects (36 male and 24 female) of whom there were 15 healthy controls, 15 bipolar patients, 15 unipolar depressed patients, and 15 schizophrenic patients. The results of the present study showed the presence of a high-affinity and saturable binding of [^{3}H]-ketanserin to frontal and parietal brain membranes of all subjects. The overall data, showed that normal controls and depressed and schizophrenic patients had a higher density in the frontal than in the parietal cortex, while bipolar patients did not show any difference. When the data were analysed according to the two hemispheres, some additional, intriguing observations were made: it emerged that [^{3}H]-ketanserin binding sites did not show any difference in the two frontal cortices, while they were less represented in the right parietal cortex of normal and bipolar patients and more dense in schizophrenic patients. In conclusion, our study has demonstrated the presence of heterogenous alterations of [^{3}]H-ketanserin binding sites in healthy

controls and different psychiatric disorders that may be of help in a further elucidation of the specific role that 5-HT_{2A} receptors.

NR178 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Metachlorophenylpiperazine and PET in Impulsive Aggressive Personality Disorder Patients

Antonia S. New, M.D., *Department of Psychiatry, Mt. Sinai/ Bronx VAMC, Box 116A, 130 West Kingsbridge Road, Bronx, NY 10468*; Erin A. Hazlett, Ph.D., Harold W. Koenigsberg, M.D., Monte S. Buchsbaum, M.D., Vivian Mitropoulou, M.A., Marianne Goodman, M.D., Larry J. Siever, M.D.

Summary:

Background: Impulsive aggression is a prevalent problem and yet little is known about its neurobiology. Preclinical and human studies suggest that the orbital frontal and anterior cingulate cortex play an inhibitory role in the regulation of aggression.

Methods: Using positron emission tomography, regional metabolic activity in response to *meta*-chlorophenylpiperazine (m-CPP) was examined in 13 impulsive-aggressive and 13 normal subjects. The anterior cingulate and medial orbitofrontal regions were hypothesized to respond differentially to m-CPP in impulsive-aggressive patients and controls. In the frontal cortex, regional metabolic glucose response to m-CPP was entered into a Group (impulsive aggressive, control)×Slice (dorsal, middle, orbital)×position (medial, lateral)×location (anterior, posterior)×Hemisphere (right,left) mixed-factorial ANOVA design. A separate Group (impulsive aggressive, controls)×anteroposterior location (Brodmann Areas 25, 24, 31, 29)×Hemisphere (right,left) ANOVA was used to examine regional glucose metabolism in the cingulate gyrus. Confirmatory SPM analyses were conducted.

Results: Unlike normal subjects, impulsive-aggressive patients did not activate the left anteromedial orbital cortex in response to m-CPP. The anterior cingulate, normally activated by m-CPP, was deactivated in impulsive-aggressive patients; in contrast the posterior cingulate was activated in impulsive aggressive patients and deactivated in controls.

Conclusions: The decreased activation of inhibitory regions in patients with impulsive aggression in response to a serotonergic stimulus may contribute to their difficulty in modulating aggressive impulses.

NR179 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Event-Related Functional MRI in PSTD

Jong I. Park, M.D., *Department of Psychiatry, Eunpyong Hospital, San 6, Eungam Dong, Eunpyong GU, Seoul 122-913, Korea*; Jin Pyo Hong, M.D., Ji Hye Ha, M.D., Ji Kang Park, M.D., Ho Kyu Lee, M.D., Chang Yoon Kim, M.D., Oh Su Hahn, M.D.

Summary:

Objective: The purpose of this study is to measure regional change of brain upon exposure to fear stimulus and elucidate the probable relation between signal changes and fear response in PTSD.

Method: Event-related fMRI was performed during a task where traffic accident-related photos and checkerboards were presented in nine women with PTSD and nine women normal controls in unpredictable order. MRI data were acquired on a 1.5 T GE vision system with a head volume coil. Stimuli were presented on a mirror mounted on the head coil. A total of 200 functional images were taken during a 10-minute scanning session. TR was 3 seconds and inter-stimulus time was varing 4.5 to 11.5 seconds. Data were analyzed using SPM99.

Results: In PTSD group, the fear conditions versus the neutral conditions showed activations in both occipital cortex, both fusiform gyrus, left parietal lobule, both insula, right cerebellar tonsil, right putamen, right claustrum, but deactivations in both prefrontal gyrus($p < 0.001$).

In normal control group, activations were found for the fear conditions as compared with the neutral conditions in left fusiform gyrus, both occipital cortex, left parietal lobule, right frontal lobule($p < 0.001$).

Conclusions: Emotion provocation paradigm using event-related functional magnetic resonance imaging can be applied to illuminate fear response mechanism in PTSD. The result suggests that insula, limbic lobe, cerebellum may play a role in mediating fear response in PTSD.

NR180 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Brain Morphometry and Spectroscopy in Psychotic Youth

Mohamed M. El Sayed, M.D., *Psychiatry, University of North Carolina, CB 7160 UNC-Chapel Hill, Chapel Hill, NC 27599-7160*; Linmarie Sikich, M.D., Miranda H. Chakos, M.D., Cecil Charles, Ph.D., Jeffrey A. Lieberman, M.D., Guido Gerig, Ph.D.

Summary:

Objective: This presentation describes the results of morphometric and spectroscopic magnetic resonance imaging in twenty nine youth between 12 and 19 years of age who presented with significant psychotic symptoms.

Methods: Subjects had a thorough diagnostic and clinical evaluation using standardized tools and an extensive neurocognitive battery. Magnetic resonance imaging was done on a GE Signa Advantage System operating at 1.5T. Measurements of gray matter, white matter and cerebrospinal fluid (CSF) was performed using computer assisted segmentation. Measurements of the hippocampus were performed using manual segmentation. Measurements of N-acteylaspartate and creatine + phosphocreatine within selected voxels of the hippocampus and frontal cortex were made. Eighteen of the subjects were rescanned after 2–6 months of treatment.

Results: The youth in this study included 17 individuals with schizophrenia spectrum disorders and 11 with affective disorders. The grey matter volume and white matter volume did not differ significantly between the groups. However; the CSF volumes were significantly increased ($p < 0.006$) in the schizophrenic subjects (139.8 ± 37.3) compared to those with affective disorders (102.6 ± 15.1).

Conclusions: Youth with psychotic symptoms occurring in the context of schizophrenia spectrum illness have larger ventricular volumes than those with affective disorders.

NR181 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Decreased Left Frontal Lobe Gray Matter in Men with Bipolar-1 Disorder

Nathan F. Dieckmann, B.A., *Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94305*; Po W. Wang, M.D., Olga V. Becker, M.D., Nadia Sachs, M.S., Terence A. Ketter, M.D.

Summary:

Objective: To compare brain volumes and chemistry in an expanded sample of thirty-six bipolar disorder patients (BP) (18 BPI and 18 BPII) and twenty one healthy control subjects (HC).

Method: Subjects received magnetic resonance imaging (MRI) and spectroscopy (MRS) scans on a 1.5 Tesia 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: Male BPI tended to have a 10% decrease in left frontal lobe gray matter compared to male HC (Mann-Whitney $\mu = 35$; $P < 0.1$). DLPF N-Acetyl Aspartate (NAA) tended to be lower in BP than HC. Left DLPF NAA correlated with left frontal lobe gray matter in HC ($r = 0.46$, $p < .05$) and tended to correlate in BPI men ($r = 0.37$, $P < .08$). Right DLPF NAA correlated with right frontal lobe gray matter in HC ($r = 0.53$, $p < 0.02$), as well as in BP ($r = 47$, $p < 0.02$).

Conclusions: In this expanded sample we continued to find related structural and functional frontal lobe abnormalities in BP compared to HC, which were particularly evident in BPI men. These findings may be particularly robust as they emerged in this sample, while differences in ventricular and cerebellar volumes, which were expected in view of prior studies, were not significant.

NR182 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Brian Reactivity to Symptom Provocation in Sertraline-Treated OCD Subjects

Joseph Zohar, M.D., *Department of Psychiatry, Chaim Sheba Medical Center, Tel Hashomer 52621, Israel*; Talma Hendler, M.D., Elinor Goshen, M.D., Tzilla S. Zwas, M.D., Yehuda Sasson, M.D., Carol Austin, M.D.

Summary:

Objective: To identify patterns of brain activation and their relation to therapeutic response in OCD patients using functional brain imaging (SPECT SPM Method).

Method: Using behavioral challenge techniques, four-brain SPECT scans were obtained from 31 OCD patients prior to and following six months of sertraline treatment. SPECT data for prospective responders and non-responders were further analyzed and compared by Statistical Parametric Mapping Methods (SPM MEDx), to assess for regional brain activity differences between relaxing and symptom provocation conditions.

Results: Prior to treatment, under specific symptom provocation state, prospective responders showed significantly lower brain perfusion in the anterior cingulum and prefrontal cortex, and higher brain perfusion in the right caudate. Furthermore, only responders to sertraline treatment, showed significant changes in brain response during specific symptom provocation when pre- and post-treatment scans were compared; demonstrated as increased perfusion in the left anterior temporal cortex and prefrontal cortex following six months sertraline treatment.

Conclusions: Functional brain imaging and symptom provocation may illuminate brain circuits involved in responsiveness to sertraline treatment in OCD. Brain responses in anterior cingulum and right caudate during specific symptom provocation differentiated between prospective responders and non-responders to sertraline treatment. Moreover, only responders eventually showed brain changes during specific symptom provocation six months into sertraline treatment.

NR183 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Striatal and Ventricular Size in Good and Poor Outcome Schizophrenia

Lina S. Shihabuddin, M.D., *Department of Psychiatry, Mt. Sinai School of Medicine, One Gustave Levy Place, Box 1505, New York, NY 10029*; Adam M. Briokman, Radovan Prikryl, Michael Dorfmar, Zlatin Ivenov, M.D., Monte S. Buchsbaum, M.D., Kenneth L. Davis, M.D.

Summary:

Previous work from our department with CT scans has demonstrated that schizophrenia patients with poor outcome (i.e., "Kraepelinian") have relatively larger ventricles compared to good outcome (i.e., "non-Kraepelinian") patients. We are currently employing high-resolution magnetic resonance imaging on a cohort of good outcome patients, poor outcome patients, and normal controls to identify brain changes underlying our previous findings.

Methods: MR images of 118 patients with schizophrenia (56 non-Kraepelinian, 62 Kraepelinian) and 37 matched normal controls were acquired. The caudate nucleus and putamen were traced on axial slices from the most superior extent of the caudate to the most inferior point. Similarly, axial images of the ventricular system, including the anterior and temporal horns and lateral aspects, were traced for analysis. Patients were characterized as Kraepelinian or non-Kraepelinian based on longitudinal analysis of self-care deficits.

Results: Preliminary analyses with a subset of 37 patients (24 non-Kraepelinian, 13 Kraepelinian) and 37 controls indicated that non-Kraepelinians had larger relative mean putamen size than Kraepelinians or normal controls, but not caudate size. This enlargement was most marked for the dorsal putamen and right hemisphere. Striatal size was not related to whether patients had been predominantly treated with typical or atypical neuroleptics currently or over the past three years. Comparative analyses of the ventricular system and correlational analyses of striatal and ventricular size are currently underway.

Discussion: The findings suggest both anatomical and pathophysiological differences between good and poor outcome schizophrenia. Differences in the striatal and ventricular size in the good and poor outcome patients will be discussed.

NR184 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Preliminary Functional MRI Evidence of Visual System Dysfunction in Parkinson's Disease Patients with Visual Hallucinations

Suzanne Holroyd, M.D., *Department of Psychiatry, University of Virginia, Health Sciences/Box 800623, Charlottesville, VA 22908*; Frederick Wooten, M.D.

Summary:

Objective: Visual hallucinations (VH) are common symptoms and frequent causes of morbidity in Parkinson's disease (PD). Increasing evidence suggests that VH are not simply a medication effect, but may be associated with changes to the visual system in PD. In this preliminary study, visual system function was examined using functional magnetic resonance imaging (fMRI) in PD patients.

Method: Visual tasks were used to investigate activation of visual brain regions in six PD patients, three with VH and three without VH, matched on clinical variables.

Results: Patients with visual hallucinations demonstrated increased activation in visual association cortex, and deficits in primary visual cortex and retina, compared to patients without VH.

Conclusions: The results suggest that VH in PD are associated with increased activity of visual association cortex and diminished activity of both retina and visual cortex in response to visual input. A possible model is discussed.

NR185 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Effect of Lamotrigine on Neuronal Excitability as Determined by TMS/fMRI

Xingbao Li, M.D., *Department of Psychiatry, Medical University of South Carolina, 67 President Street, Room 502N, Charleston, SC 29425*; Charlotte C. Teneback, B.S., Ziad H. Nahas, M.D., Andrew F. Kozel, M.D., Charles Large, Ph.D., Jeff Cohn, Ph.D., Daryle Bohning, Ph.D., Mark S. George, M.D.

Summary:

Objective: To use functional MRI (fMRI) to image brain activity during transcranial magnetic stimulation (TMS) in order to examine

pharmacologically-induced changes in neuronal excitability with lamotrigine.

Methods: 12 healthy young men (mean age 25 years) were given, a single dose of lamotrigine 325 mg, or placebo in a randomized, blinded fashion on two separate days one week apart. On each testing day, the resting motor threshold (rMT) was assessed using TMS at baseline and 3 hours after administration of lamotrigine. Subjects were scanned with intermittent TMS over the left motor cortex and in a separate run, with TMS over the left prefrontal cortex.

Results: Lamotrigine caused a 15% increase (9.5 SD) in the rMT, compared with a 1% increase following placebo ($p < 0.01$). Lamotrigine, compared to placebo, diffusely inhibited TMS-induced activation in motor and prefrontal cortex. Interestingly, when TMS was applied over the prefrontal cortex, lamotrigine increased the TMS induced activation in limbic regions.

Conclusions: Lamotrigine has an inhibitory effect on cortical neuronal excitability as demonstrated by the rMT and cortical fMRI results. It may have a complex effect on prefrontal TMS, with cortical inhibition and limbic facilitation. TMS/fMRI may be useful for understanding regional brain effects of CNS active compounds.

NR186 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Current Density Map of P300 in Schizophrenia LORETA Using Realistic Head Models and 128-Channel EEG

Ji Soo Pae, M.D., *Department of Neuropsychiatry, Seoul National University Hospital, Yun-Gun-Dong 28, Seoul 110-460, South Korea*; Tak Youn, M.D., Hae-Jeong Park, Ph.D., Myung Sun Kim, Ph.D., Jae-Jin Kim, M.D., Jun-Soo Kwon, M.D.

Summary:

This study describes the application of a method for the statistical parametric mapping of current density images in order to investigate the characteristics of the P300 generators in schizophrenia.

The P300 generators, produced by rare target tone of 1500Hz (30 trials) under the frequent non-target tone of 1000Hz (170 trials), 80dB binaural stimuli with 1200msec of interstimulus interval, were measured in 15 right-handed schizophrenic subjects and controls.

LORETA (low resolution electromagnetic tomography), using a realistic head model of the boundary element method based on individual MRI, was applied to the 128 channel EEG. Three dimensional current density images were reconstructed from the LORETA intensity maps that covered the whole cortical gray matter, up to 20,000 points. Spatial normalization and intensity normalization of the smoothed current density images were used to reduce anatomical variance and subject specific global activity, and then statistical parametric mapping (SPM) was applied for statistical analysis.

We found that the sources of P300 were consistently localized at left superior parietal area in normal subjects, while those of schizophrenics were diversely distributed. With statistical comparison, schizophrenic patients, with global reduction of current density, showed a significant P300 reduction in the left parietotemporal junction ($P = 0.002$) and right superior temporal area ($P = 0.029$), while both frontal area were highly activated. These results implicate the P300 generator abnormalities in schizophrenia.

NR187 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Galantamine Improves Behavior in Alzheimer's Cerebrovascular Disease

William J. Burke, M.D., *Department of Psychiatry, University of Nebraska, P.O. Box 985575, Nebraska Medical Center, Omaha, NE 68198-5580;* Sean Lilienfeld

Summary:

Objective: To assess the effect of galantamine on behavior and caregiver distress in patients with Alzheimer's disease (AD), vascular dementia VaD), and AD with cerebrovascular disease.

Methods: Patients with mild-to-moderate AD (n = 978) were randomized to placebo or galntamine (8, 16, or 24 mg/day) in a double-blind, placebo-controlled trial for 5 months. In second double-blind, placebo-controlled trial, patients with probable VaD or AD with cerebrovascular disease (n = 592) were randomized to placebo or galantamine 24 mg/day for 6 months. In both studies, behavioral changes were assessed using the Neuropsychiatric Inventory (NPI), and their relationship to caregiver distress was measured using the NPI distress (NPI-D) scale.

Results: In the 5-month AD study, the 16-and 24-mg/day groups showed significantly better total NPI scores versus placebo)$p < 0.05$). Total NPI scores did not change significantly from baseline, and caregiver distress was significantly reduced ($p < 0.05$). In patients with Va D or AD with cerebrovascular disease, galantamine-treated patients demonstrated significantly better behavioral outcomes than placebo ($p < 0.05$) after 6 months of therapy. Caregiver distress decreased for patients recreased for patients receiving galantamine.

Conclusion: Galantamine delays the emergence of behavioral symptoms in patients with AD, Va D, or AD with cerebrovascular disease with subsequent reductions in caregiver distress.

NR188 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Pharmacogenetics of Drug-Induced Weight Gain in Schizophrenia

Gavin P. Reynolds, Ph.D., *University of Sheffield, Biomedical Science, Western Bank, Sheffield, UK S10 2TN, United Kingdom*; Zhijun Zhang, Ph.D., Xiaobin Zhang, M.D.

Summary:

Objective: Increased body fat, leading to further morbidity and poor treatment adherence, is a common consequence of the treatment of schizophrenia with antipsychotic drugs. Antagonism of the 5-HT2C receptor is one receptor mechanism implicated in this side effect. A recent study showed that genetic variants in the promotor region of the 5-HT2C receptor gene were associated with obesity and diabetes, and had functional effects on receptor expression. We determined whether one of these genetic polymorphisms influenced treatment-induced weight gain in a Chinese Han population with schizophrenia.

Method: Patients (n = 123) admitted to hospital following a first episode of schizophrenia were genotyped for the −759C/T polymorphism and had weight changes monitored after six and ten weeks' drug treatment.

Results: The mean increase in BMI (in kg/m^2) was 0.66 at six weeks and 1.15 at ten weeks. We found that the 27 patients with the −759T variant allele showed significantly less weight gain ($p < 0.001$); patients without this allele were six times more likely to develop substantial (i.e > 7%) weight gain ($p = 0.001$). The protective effect of the variant allele was also apparent by six weeks in the subgroups of patients receiving risperidone ($n = 46$, $p = 0.014$) and chlorpromazine ($n = 69$, $p = 0.003$).

Conclusion: These findings identify an important genetic factor associated with treatment-induced increases in weight in schizophrenia, and indicate the future potential of pharmacogenetics in understanding, and perhaps avoiding, a major side effect limiting antipsychotic drug use.

NR189 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Physically Ordered Markers Increase Genetic Linkage Evidence for Bipolar Disorder and Chromosome 18q

Thomas G. Schulze, M.D., *Department of Psychiatry, University of Chicago, 924 East 57th Street, Room R004, Chicago, IL*

60637; Yu-Sheng Chen, Ph.D., Judith A. Badner, M.D., Melvin G. McInnis, M.D., J. Raymond DePaulo, Jr., M.D., Francis J. McMahon, M.D.

Summary:

Background: We recently reported evidence of linkage of bipolar disorder to chromosome 18q, with a paternal lodscore of 4.67 in a clinically defined subset of families. Like other linkage studies, we relied on imprecise genetic maps to establish the marker order. Here we test for linkage in the same sample with a denser set of markers, now physically ordered according to the draft sequence of the human genome.

Method: Families were ascertained through probands with bipolar I disorder and diagnosed with reliable methods. Genotypes were generated for 12 microsatellite markers. Multipoint affected sib-pair linkage analysis was performed in a set of 16 pedigrees.

Results: Typing additional markers significantly increased the extractable amount of total genetic information in our sample. The peak paternal lodscore increased from 4.67 to 5.42. Linkage resolution also increased: The approximate 1-lod support interval changed from 12 to 9 male cM.

Conclusion: The results strengthen our previous findings and define a region suitable for genetic fine-mapping analysis on chromosome 18q. Our data suggest that using a both denser and physically ordered set of markers can increase the information value of linkage signals.

NR190 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Polymorphisms of the Interleukin-1 Gene Complex and Schizophrenia

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 Bousono-Garcia, M.D., Julio B. Bobes, Ph.D.

Summary:

Objectives: To determine the possible association between three polymorphisms of the interleukin-1 (IL-1) gene complex and schizophrenia.

Patients and Methods: We genotyped 126 schizophrenic outpatients (DSM-IV criteria) [mean age: 35.24 (11.49), 56.1% males] and 95 healthy volunteers (blood donors) [mean age: 43.01 (11.54), 75.8% males] from Asturias (Northern Spain). The following allelisms were analyzed: IL-1alpha gene: base exchange polymorphism at position –889; IL-1beta gene: base exchange polymorphisms at position –511 (relative to the transcriptional start site); IL-1 receptor antagonist (IL-1RA) gene: variable numbers of 86-base pair tandem repeats in intron 2.

Results: The frequency of the IL-1alpha (–889) allele 2 was higher in schizophrenic patients compared with controls (69.8% vs 60.0%, OR = 1.54, 95%CI = 1.04–2.29; p = .034). No association was detected between the IL-1beta (p = .171), or the IL-1RA (p = .284) polymorphisms and schizophrenia.

Conclusions: Our data suggest that polymorphic variations in the IL-1alpha gene might influence susceptibility to schizophrenia. In our population, there is no evidence that the IL-1beta, nor the IL-1RA genes are involved in schizophrenia.

NR191 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Estrogen Receptor Alpha Gene Polymorphism in Korean Schizophrenics

Tae M. Kim, M.D., *Huron Valley Women's Facility, 3511 Bemis Rd, Ypsilanti, MI 48197-9307*; Do-Hyung Kim, Jin-Kyung Park, M.D., Ji-Young Song, M.D., Joo-Ho Chung, M.D., Geon-Ho Bahn, M.D., Jong-Woo Kim, M.D.

Summary:

Objective: Schizophrenic women experience a less severe course of illness than schizophrenic men. This difference is thought to be partly due to the neuroprotective effect of estrogen. This study was designed to investigate the association between estrogen receptor alpha(ERα) gene polymorphism and schizophrenics.

Method: A total of 182 schizophrenics diagnosed by DSM-IV criteria and 233 age- and sex-matched normal controls in Korea were selected as study subjects. We determined ERα gene polymorphism using PCR of the relevant region followed by digestion with PvuII and XbaI and electrophoresis. All data were analyzed by χ^2 test.

Results: There were no significant differences in genotype distribution and allele frequencies of ERα gene polymorphism between schizophrenics and normal controls. In the study of PvuII polymorphism, there were significant differences in genotype distribution and allele frequencies of ERα gene polymorphism between female schizophrenics and female normal controls.

Conclusions: These results suggested that variation at these polymorphism in the ERα gene may not influence susceptibility to schizophrenia. However, we found the possible association between PvuII polymorphism in the ERα gene and female schizophrenics. Further studies with larger samples are needed to confirm this association.

NR192 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

A Possible New Genetic Syndrome Involving Panic Disorder and Interstitial Cystitis

Raz Gross, M.D., *Department of Epidemiology, Columbia University, 600 West 168th Street, PH-18 R 303, New York, NY 10032*; Abby Fyer, M.D., Gary A. Heiman, Ph.D., Matthew Schaenen, Myrna M. Weissman, Ph.D.

Summary:

Objective: We followed evidence from a genetic linkage study for a possible syndrome in some families with panic disorder (PD). This syndrome includes urinary bladder conditions, mostly interstitial cystitis (IC), and, possibly, headaches, thyroid disorders, and mitral valve prolapse.

Method: We studied 75 cases with IC and related disorders and 71 controls with other urological disorders. Urological diagnoses were made by urologists. Cystoscopy reports and urodynamic tests were available for >90% of the patients. PD was diagnosed with SADS-LA and confirmed by two clinicians. Family trees, and data on other anxiety disorders and on the medical conditions comprising the hypothesized syndrome among probands and their first and second-degree relatives were collected using a modified version of the Family History Screen.

Results: Preliminary analysis shows that lifetime prevalence of PD was significantly higher among patients with IC compared to controls (29.3% vs 8.4%, adjusted OR = 3.7, 95% CI = 1.23, 11.01; $P = .02$). Differences in prevalence of other anxiety disorders were not significant. A family history of PD was about twice as common among cases.

Conclusions: The increased frequency of PD in patients with IC is consistent with the findings from the linkage study in suggesting that, in a subgroup of patients, these two disparate disorders may be, in fact, part of the same syndrome.

NR193 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Blood Injection Injury Phobia in Primary Care

Raz Gross, M.D., *Department of Epidemiology, Columbia University, 600 West 168th Street, PH-18 R 303, New York, NY*

10032; Marc J. Gameroff, Ph.D., Mark Olfson, M.D., Adriana Feder, M.D., Myrna M. Weissman, Ph.D.

Summary:

Objective: Information on the epidemiology, presentation, and medical consequences of blood-injection-injury phobia (BIIP) in primary care is scarce.

Methods: We analyzed data from a survey conducted on a systematic sample (n = 211) of patients from an urban primary care practice to examine the prevalence of BIIP, its psychiatric comorbidity, impairment, and frequency of primary care visits, and to assess the likelihood that patients with BIIP will get serum cholesterol and glucose tests, and flu shot.

Results: Lifetime prevalence of BIIP was 7.1%. Patients with BIIP were more likely to have a lifetime history of mood disorders (64.3% vs 26.8%, $P = .005$), social phobia (28.6% vs 4.1%, $P = .005$), and natural environment phobias (53.3% vs 8.7%, $P < .0001$), and were more impaired on the SF-36 Mental Component Summary (40.1 ± 14.2 vs 48.6 ± 14.0, $P = .06$). During a12-months follow up, patients with BIIP made a similar number of primary care visits, but were significantly less likely to have a serum cholesterol test, than patients without BIIP (33.3% vs 60.2%, $P = .04$). This trend remained also after adjusting for age. No significant differences were found for glucose tests or flu shots.

Conclusions: BIIP is common in primary care patients, and is associated with mood disorders, social phobia, other specific phobias, and impairment. Patients with BIIP are possibly avoiding lab tests that involve withdrawing of blood.

NR194 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Exposure Therapy Effects Are More Durable Than Those of Clomipramine in OCD

H. Blair Simpson, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive Unit 69, New York, NY 10032*; Michael R. Liebowitz, M.D., Edna B. Foa, Ph.D., Michael J. Kozak, Ph.D., Andrew B. Schmidt, C.S.W., Eva Petkova, Ph.D., Jonathan D. Huppert, Ph.D., Martin E. Franklin, Ph.D., Sharon Davies, R.N., Raphael Campeas, M.D., Kevin D. Kjernisted, M.D., Vivienne Rowan, Ph.D.

Summary:

Introduction: There are two proven treatments for obsessive-compulsive disorder (OCD): cognitive-behavioral therapy using exposure and response (or ritual) prevention (EX/RP) and pharmacotherapy using serotonin reuptake inhibitors (e.g., clomipramine (CMI) and the SSRIs). However, the long-term efficacy of these treatments has not been well studied. A two-center randomized controlled trial compared the efficacy (the Acute Phase) and durability (the Discontinuation Phase) of these treatments. Results from the Discontinuation Phase are presented here.

Methods: During the Acute Phase (Weeks 0–12), 122 patients were randomly assigned to EX/RP, CMI, EX/RP + CMI, or pill placebo (PBO). Forty-six responders (18 EX/RP, 11 CMI, 15 EX/RP + CMI, 2 PBO) entered the Discontinuation Phase (Weeks 13–24), during which treatment was stopped, and patients were assessed for relapse by an evaluator blind to treatment.

Results: Responders to EX/RP or EX/RP + CMI during the Acute Phase were significantly less likely to relapse during the Discontinuation Phase than CMI responders (relapse rates: CMI = 45%; EX/RP = 11%; EX/RP + CMI = 13%). Different definitions of relapse gave similar results.

Conclusion: Those who responded to EX/RP and EX/RP + CMI had more lasting improvements 12 weeks after treatment discontinuation than those who responded to CMI alone.

NR195 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

PET Imaging of the Serotonin Transporter in Patients with OCD

H. Blair Simpson, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive Unit 69, New York, NY 10032*; Ilise D. Lombardo, M.D., Henry Huang, Ph.D., Mark Slifstein, Ph.D., Dah Ren Hwang, Ph.D., Ronald Van Heertum, M.D., Michael R. Liebowitz, M.D., Marc Laruelle, M.D.

Summary:

Introduction: Because of the efficacy of serotonin reuptake inhibitors in obsessive-compulsive disorder (OCD), dysfunction in serotonergic neurotransmission has been hypothesized to contribute to the pathophysiology of OCD. To test whether serotonin transporter (SERT) density is reduced in OCD, SERT binding potential (BP) was measured in the brains of OCD patients and healthy controls using positron emission tomography (PET) and the SERT radioligand [^{11}C](+)McN-5652.

Methods: Ten OCD patients (free of psychiatric medications and depression) and 11 matched healthy controls underwent PET scanning after [^{11}C](+)McN-5652 injection and MRI scanning for anatomical co-registration. Regional time activity curves were computed, and the BP for various brain regions of interest (ROI) with known high levels of SERT density (dorsal caudate, dorsal putamen, midbrain, thalamus, hippocampus, and anterior cingulate) was estimated using kinetic analysis (2 compartment model) and the arterial parent concentration as input function.

Results: There were no significant differences in [^{11}C](+)McN-5652 BP between 10 OCD patients and 11 matched controls in the ROIs examined. Within the OCD group, OCD severity and SERT BP were not significantly correlated.

Conclusion: This study suggests that OCD is not associated with major changes in SERT anatomical distribution in the examined brain regions.

NR196 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

A Double-Blind, Placebo-Controlled Study of Sertraline in the Prevention of Depression in Stroke Patients

Alice Rasmussen, M.D., *Department of Psychiatry, Bispebjerg Hospital, Bispebjerg Bakke 23, Copenhagen, NV DK-2400, Denmark*; Marianne Lunde, Karen Sorensen, M.D., Susanne Qvitzau, M.D., Per Bech, M.D.

Summary:

Objective: To test the antidepressant prophylactic efficacy of sertraline in the first year after an acute stroke.

Methods: Randomized, double-blind assignment to 12-months of treatment with sertraline (50–150 mg) vs. placebo in patients hospitalized for an acute ischemic stroke. Depression symptom severity was evaluated using the 17-item Hamilton Depression Rating Scale (HDRS) including the 6-item depression factor and the age-specific Geriatric Depression Scale (GDS). Occurrence of clinically significant depression was operationally defined by a HDRS total score ≥18. Cognitive function was assessed serially using the CAMCOG.

Results: A total of 137 patients were treated with either sertraline (N = 70; male, 51%; mean age, 72 years; mean dose, 63 mg) or placebo (N = 67; male, 53%; mean age, 67 years). A logistic regression analysis showed a significant ($p = 0.02$) treatment X time interaction effect in favor of sertraline on the GDS scale. Kaplan-Meier analysis of time-to-emergence of depression showed sertraline to have significantly ($p < 0.05$) superior prophylactic efficacy compared with placebo. There was a 20% depression-sparing effect due to sertraline treatment. By endpoint there was a 10-point improvement in the CAMCOG score on sertraline compared with a 5-point improvement on placebo (Wilcoxon p =

0.04). Prophylactic sertraline also appeared to reduce both medical and cardiovascular morbidity in the year post-stroke.

Conclusion: Sertraline significantly reduced the frequency of emergent depression, and improved cognitive function, in stroke patients over the course of one year of treatment.

NR197 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Sertraline-Induced Platelet Dysfunction May Protect Against Cardiovascular Comorbidity Post-Stroke

Alice Rasmussen, M.D., *Department of Psychiatry, Bispebjerg Hospital, Bispebjerg Bakke 23, Copenhagen, NV DK-2400, Denmark*; Erling Mellerup, M.D., Inge Hindberg, M.S.C.

Summary:

Objectives: Depression has been identified as an independent risk factor for increased cerebrovascular and cardiovascular morbidity. Research suggests that SSRIs such as sertraline may alter platelet function through a serotonergic mechanism, which may, in turn, reduce the cardiovascular comorbidity. The current exploratory analysis examined the correlation between altered serotonergic function and emergent cardiovascular mortality during one year of post-stroke treatment.

Method: In a double-blind study with prophylactic sertraline treatment, we examined the serotonin variables in 118 patients with a recent stroke. The comorbidity was measured by registration of admissions to hospital, and registration of the diagnosis that caused the admission to hospital in the follow-up period.

Results: At baseline no statistically significant difference between the treatment groups was found for any of the peripheral indices of serotonin activity. The effect of one year of treatment is summarized in the Table, below:

After one year	Treatment	Mean	Wilcoxons two sample test
Plasma-5-HT (nmol/l)	Placebo	7.4	P < 0.001
	Sertraline	3.3	
Platelet-5-HT (nmol/$10^4$9)	Placebo	3.4	P < 0.001
	Sertraline	1.2	
Emergent Comorbidity at 1 year post-stroke	Placebo	15 cases	(Fishers test)
	Sertraline	5 cases	P < 0.02

Conclusion: These results indicate that sertraline induced reductions in plasma-5-HT and platelet-5-HT may protect against cardiovascular comorbidity in stroke patients.

NR198 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Is the Serotonin Transporter a Biological Marker in Cerebral Stroke?

Alice Rasmussen, M.D., *Department of Psychiatry, Bispebjerg Hospital, Bispebjerg Bakke 23, Copenhagen, NV DK-2400, Denmark*; Erling Mellerup, M.D.

Summary:

Objectives: The number of serotonin transporters on platelets has been shown to be correlated with affective illness. The goal of the current study was to evaluate whether serotonin transporter status was correlated with depression in stroke patients, and we examined the number of serotonin transporters in platelets in patients with a recent stroke.

Method: Blood tests were taken from 113 patients with recent stroke and from 56 healthy controls matched for age and sex.

Results: As summarized in the table, below, we found no difference in the number of serotonin transporters (B-max) between patients who developed depression and patients who remained well. The stroke patients, however, had significantly lower number of serotonin transporters than the controls.

	Treatment	Sample size	Mean value	Depression Yes	Depression No	Logistic Regression
B-max (Fmol/mg prot)	Placebo	56	1099	1116	1090	P = 0.72
	Sertraline	57	1102	986	1133	P = 0.06

				Wilcoxons two sample test
B-max (Fmol/mg prot)	Patients	113	1101	
	Controls	56	1252	P = 0.0003

Conclusion: A low number of serotonin transporters does not appear to be associated with increased vulnerability to depression in stroke patients. However, the data do suggest that cerebral stroke is associated with a significant reduction in numbers of serotonin transporters.

NR199 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Elevated Apoptosis Marker BCL-2 in the CSF of Patients Schizophrenia

Henry A. Nasrallah, M.D., *Department of Psychiatry, University of Mississippi, 1500 East Woodrow Wilson Drive, Jackson, MS 39216*; Meng-Yang Zhu, Ph.D., David L. Garver, M.D.

Summary:

Introduction: There is now substantial evidence for brain tissue loss in schizophrenia (such as reduced cortical volume and enlarged cerebral ventricles (both at the onset of the illness (neurodevelopment) and progressively after recurring psychotic relapses (assumed to be neurodegenerative). The mechanism of neuronal loss remains unknown, but the lack of gliosis in post mortem brain studies in schizophrenia suggests a non-inflammatory process. We postulated that psychosis in schizophrenia may be associated with an acceleration of programmed all death (apoptosis), and that apoptosis markers should be elevated in schizophrenic patients.

Methods: We measured the CSF concentration of the proto-oncogene bcl-2, which is involved in the regulation of cell death, in 40 consenting subjects with schizophrenia in acute relapse (who were neuroleptic-free for > 10 days) as well as in 4 consenting health volunteers. The bcl-2 was measured using ELISA assay.

Results: The mean CSF bcl-2 in the controls was 2.73 ± 1.54 μ/ml (95% CI = 0.273 – 6.187). 14/40 (35%) of the schizophrenia sample had CSF bcl-2 levels in excess of the 95% CI of the controls and none of the schizophrenia patients had CSF bcl-2 levels below the 95% CI of controls. The 14 patients with very high bcl-2 levels had an earlier mean age of first hospitalization than the patients whose bcl-2 was within the controls' CI (23.1 ± 7.4 vs 28.1 ± 6.8 years; p = 0.056).

Discussion: This is the first report of elevation of the apoptosis marker bcl-2 in the CSF in a subgroup of schizophrenia patients. These findings point to the possibility that apoptosis is more likely than necrosis to be the underlying mechanism for the brain tissue loss observed in schizophrenia during a psychotic episode. The relationship to early onset of illness is intriguing and may indicate that the neurodevelopment neurobiology of the brain in schizophrenia may be associated with the apoptotic mechanisms that may be triggered or accelerated during acute psychosis. Other possible implications will be discussed.

NR200 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Safety and Efficacy of Bilateral Repetitive Transcranial Magnetic Stimulation in Major Depression: An Open Trial

Carl I. Cohen, M.D., *Department of Psychiatry, SUNY Health Sciences Center, 450 Clarkson Avenue, Brooklyn, NY 11203*; Bola O. Akande, M.D., Paul J. MacCabee, M.D., Vahe Amassian, M.B.

Summary:

Objectives: Studies using either fast (>1Hz) repetitive Transcranial Magnetic Stimulation (rTMS) to the left dorsolateral prefrontal cortex (DLPFC) or slow (<1Hz) rTMS to the right DLPFC have produced significant, albeit modest decreases in depressive symptoms among medication-resistant patients. Therefore, we examined whether bilateral rTMS, using both slow rTMS and fast rTMS to the right and left DLPFC, respectively, could be safely administered, and whether it would have greater efficacy than unilateral rTMS.

Methods: 10 consecutively referred medication-resistant outpatients with a DSM IV diagnosis of major depression and a HAM-D score of ≥16 were scheduled to receive 9 rTMS sessions consisting of 20 1.5-sec. trains at 20Hz to the left DLPFC followed immediately by 2 60-sec. trains to the right DLPFC.

Results: 7 of 10 subjects completed the study; all subjects completed at least 7 sessions. Using an intent-to-treat design, last assessment carried forward, a repeated measures ANOVA indicated a significant decline in the Hamilton Depression Rating Scale (HAM-D) scores (baseline: 21.9; follow-up: 15.7); 4 of 10 subjects showed a ≥50% decline on the HAM-D, with a strong trend for those under age 50($p = .076$). There were no adverse events or changes in cognitive status.

Conclusions: Improvement on the HAM-D scores were similar to results of unilateral treatment. Thus, bilateral treatment may afford no added benefits. Nevertheless, controlled trials with larger samples may be worthwhile because younger subjects responded more robustly, there is theoretical support for bilateral stimulation, and bilateral stimulation appears to be safe.

NR201 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Mandatory Depression Screening of Dementia Patients in Nursing Homes

Carl I. Cohen, M.D., *Department of Psychiatry, SUNY Health Sciences Center, 450 Clarkson Avenue, Brooklyn, NY 11203*; Kathryn Hyland, Ph.D., David Kimhy, M.A.

Summary:

Objectives: Depression continues to be under-recognized in nursing home patients. This study examines the process and impact of a mandatory depression screening program instituted for dementia patients in nursing homes.

Methods: The experimental group(EG) consisted of 2 nursing homes with 519 beds and the comparison group(CG) consisted of 2 nursing homes with 363 beds. One of the CG homes was a more typically staffed facility, whereas the other had an enriched staff of psychologists. Residents with dementia in the EG were screened for depression by social work staff using the Cornell Scale (CS). Those attaining a score of ≥5 were required to be referred to psychiatrists for assessment and treatment.

Results: In the EG, 100% of the referred dementia patients who had met screening criteria for depression were seen by the psychiatrists, and there was a significant increase in persons placed on antidepressants (15% vs. 30%). This was greater than the percentage of persons receiving antidepressants in the "typical" CG home (19%), but not the staff-enriched home (43%). On 12-week follow-up, there was a significant difference in the CS between persons receiving antidepressants in the EG (25% decline) and the CG homes (1% increase).

Conclusions: Nursing home staff can be easily trained to use a standardized depression scale and referrals based on a cut-off score did not place undue burdens on staff psychiatrists. This procedure can significantly increase the proportion of depressed dementia patients receiving treatment. Given its low costs, ease of administration, and favorable results, mandatory screening should be considered in all nursing homes.

NR202 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

A Placebo-Controlled Study of Pregabalin and Venlafaxine Treatment of GAD

Siegfried Kasper, M.D., *Department of General Psychiatry, University of Vienna, Wahringer Gurtel 18–20, Wien A-1090, Austria*; M. Blagden, M.D., S. Seghers, M.D., A. Veerman, M.D., H.P. Volz, M.D., Agnes Geniaux, Nathalie Strubb

Summary:

Objective: To compare the efficacy and safety of pregabalin, a novel anxiolytic, and venlafaxine in patients with generalized anxiety disorder (GAD) versus placebo.

Methods: A total of 426 patients (62% female, mean age = 44) were randomized to six weeks of double-blind treatment with pregabalin 400 mg/day (n = 98), pregabalin 600 mg/day (n = 111), venlafaxine 75 mg/day (n = 114) or placebo (n = 103), all given BID. The primary efficacy parameter was the mean change from baseline to endpoint in the Hamilton Anxiety Rating Scale total score. Safety was assessed through clinical and laboratory observations.

Results: Both pregabalin 400 mg/day ($p = 0.008$) and pregabalin 600 mg/day ($p = 0.026$), as well as venlafaxine 75 mg/day ($p = 0.027$) were statistically superior to placebo in improving the symptoms of GAD, as measured by the improvement on the HAM-A total score. No dose-response difference was evident for the two pregabalin doses. Adjusted baseline to end point mean changes in the HAM-A were 14.7, −14.1, −14.1 and −11.6 for pregabalin 400, pregabalin 600, venlafaxine and placebo, respectively. Efficacy on the HAM-A vs placebo was shown at week 1 for both pregabalin treatment groups and at week 2 for venlafaxine. The adverse event profiles were similar to those expected for both pregabalin and venlafaxine. Withdrawals due to adverse events were numerically more frequent in venlafaxine group (21%) compared to both pregabalin groups (6% and 16% respectively), and placebo (9%).

Conclusion: This study confirms the results of previous studies showing that pregabalin is an effective and safe treatment for GAD, and provides evidence for the efficacy and safety of a BID dosing schedule for pregabalin.

NR203 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Linear Relationship Between Severity of Anxiety and Comorbid Depression

Hogni Oskarsson, M.D., *12 Sudurgata, Reykjavik 101, Iceland*

Summary:

Objective: Exploration of the relationship between the severity of anxiety, as defined by the number of anxiety disorders per Index Case (IC), and depression.

Method: The study is based on the screening for anxiety in a population sample, followed by diagnostic work-up with the computerized version of the Composite International Diagnostic Interview (CIDI). ICs have to meet criteria for either an ICD-10 or a DSM 3-R anxiety diagnosis. The number of anxiety disorders for each IC was calculated and their Odds Ratio (OR) of receiving a diagnosis of depressive disorders.

Results: 444 cases were diagnosed with a lifetime diagnosis of anxiety disorders. The co-occurrence of other anxiety disorders is highest in Panic Disorder, with an average of 2.9 per IC, but lowest in Social Phobia, 2.2 per IC ($P < 0.001$). The comorbidity of anxiety with depressive disorder is also found to be high (56%); the highest OR is found in Generalized Anxiety Disorder (6.6) and Panic Disorder (4.5). With multiple anxiety disorders the risk of comorbid depressive disorder is increased, the difference between those with one or five disorders being highly significant ($P < 0.001$).

Conclusions: Co-morbidity between the anxiety disorders is high, a possible explanation being that the anxiety disorders have

common origins, with PD being the most severe form of these disorders. The linear relationship between depression prevalence and number of anxiety co-morbid conditions points to common etiological factors in the genesis of these disorders.

NR204 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Quality of Life in Anxiety and Mood Disorders

Mark H. Rapaport, M.D., *Department of Psychiatry, UCSD School of Medicine, 8950 Villa La Jolla Drive, Suite 2243, La Jolla, CA 92037*; Jean Endicott, Ph.D., Henry Chung, M.D., Cathryn M. Clary, M.D. *Supported by Pfizer Inc.*

Summary:

Background: The availability of QOL data using the same standardized instrument, the Quality of Life, Enjoyment, and Satisfaction scale (Q-LES-Q) across a range of depression and anxiety disorder diagnoses, provides a unique opportunity to obtain comparative data on the impact of anxiety disorders and depressive disorders on psychosocial functioning.

Method: Q-LES-Q data was analyzed from patients reporting moderate-to-severe illness intensity, prior to beginning double-blind treatment trials for MDD, Dysthymia, Panic Disorder, PTSD, Social Phobia, OCD, and PMDD. Subjects' were defined as significantly impaired if their Q-LES-Q scores were >2 standard deviations below the community norm on the Q-LES-Q.

Results: The proportion of patients with normative QOL (within 10% of community norms) vs. diminished QOL for each diagnosis, respectively, was as follows: MDD (6.7% vs. 63%), chronic MDD (1.7% vs. 85%), dysthymic disorder (6.7% vs. 56%), panic disorder (6.5% vs. 59%), OCD (22.8% vs. 26%), social phobia (32.2% vs. 21%) and PTSD (6.5% vs. 59%). Results of regression analyses identified both diagnosis-specific and nonspecific clinical variables that contribute to baseline QOL dysfunction.

Conclusion: Between 20–85% of affective or anxiety disorder patients as having significant QOL impairment, the degree of dysfunction is diagnosis-specific with, surprising, social phobia and OCD patients reporting less dysfunction than other disorders. We will discuss the relationship between clinical variables and levels of dysfunction on the Q-LES-Q.

NR205 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Quality of Life in Anxiety and Depressive Disorders

Mark H. Rapaport, M.D., *Department of Psychiatry, UCSD School of Medicine, 8950 Villa La Jolla Drive, Suite 2243, La Jolla, CA 92037*; Jean Endicott, Ph.D., Henry Chung, M.D., Cathryn M. Clary, M.D.

Summary:

Background: The availability of QOL data using the same standardized instrument, the Quality of Life, Enjoyment, and Satisfaction scale (Q-LES-Q) across a range of depression and anxiety disorder diagnoses, provides a unique opportunity to obtain comparative data on the impact of anxiety disorders and depressive disorders on psychosocial functioning.

Method: Q-LES-Q data was analyzed from patients reporting moderate-to-severe illness intensity, prior to beginning double-blind treatment trials for MDD, Dysthymia, Panic Disorder, PTSD, Social Phobia, OCD, and PMDD. Subjects' were defined as significantly impaired if their Q-LES-Q scores were >2 standard deviations below the community norm on the Q-LES-Q.

Results: The proportion of patients with normative QOL (within 10% of community norms) vs. diminished QOL for each diagnosis, respectively, was as follows: MDD (6.7% vs. 63%), chronic MDD (1.7% vs. 85%), dysthymic disorder (6.7% vs. 56%), panic disorder (6.5% vs. 59%), OCD (22.8% vs. 26%), social phobia (32.2% vs. 21%) and PTSD (6.5% vs. 59%). Results of regression analyses identified both diagnosis-specific and nonspecific clinical variables that contribute to baseline QOL dysfunction.

Conclusion: Between 20–85% of affective or anxiety disorder patients seeking treatment have significant QOL impairment. The degree of dysfunction is diagnosis-specific with social phobia and OCD patients reporting less dysfunction than other disorders. We will discuss the relationship between clinical variables and levels of QOL dysfunction as measured by the Q-LES-Q.

NR206 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Evaluation of Cognitive and Psychomotor Profile of Pregabalin Compared to Alprazolam in Normal Volunteers

Ian Hindmarch, Ph.D., H.P.R.U., *Surrey University, Egerton Road, Guildford, Surrey GU2 5XP, United Kingdom*; Jean Dawson, Neil Stanley

Summary:

Objective: Pregabalin is a novel centrally acting drug displaying anxiolytic properties, in addition to efficacy in neuropathic pain, that may modulate the Bz-GABAergic complex by its action on an allosterically-linked Ca^{2}♠ channel. The current study was designed to evaluate the cognitive and psychomotor effects of pregabalin (PGB) compared to placebo (PBO), and alprazolam (ALP).

Methods: A total of 24 volunteers were randomized, double-blind, to a three-way crossover study (including a seven-day washout). A standard battery of cognitive and psychomotor tests was administered, including brake reaction time, following training sessions to minimize practice effects.

Results: Repeated measures ANOVAs found significantly ($p < 0.001$) less impairment on PGB compared with ALP on the Hicks-Choice Reaction Time, the Compensatory Tracking Task, the Sternberg Short-Term Memory Task, the Rapid Visual Information Processing Task, and Brake Reaction Time. In contrast, PGB showed only modest and intermittently significant impairment compared to PBO, most notably on the Critical Flicker Fusion test, and the RVIP ($p < 0.05$), while Brake Reaction Time was significantly improved on PGB compared with PBO ($p < 0.05$).

Conclusion: Pregabalin appears to have a behavioral and cognitive profile that is distinctly different than the profile of benzodiazepines. Improved performance over placebo on tests such as Brake Reaction Time must be cross-validated.

NR207 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Rates of PTSD Symptom Remission in Patients Treated with Paroxetine

Jonathan R.T. Davidson, M.D., *Department of Psychiatry, Duke University Medical Center, Trent Drive, Room 4082B, Box 3812, Durham, NC 27710*; Katherine L. Beebe, Ph.D., Karen Hewett, Ph.D., Cornelius D. Pitts, R.P.H., Ali Adams, M.S.C., Lee D. Ruggiero, B.S.C.

Summary:

Objective: To evaluate symptom remission in adults with chronic PTSD who were treated for up to 12 weeks with either paroxetine or placebo.

Methods: Data from three placebo-controlled outpatient studies (paroxetine, n = 676; placebo, n = 504) were combined for these analyses. One study used a fixed dosage design (20mg, 40mg, placebo), and the other two studies were flexible dosage (20–50mg, placebo). On average, patients had moderately severe to severe PTSD at baseline. Two definitions of PTSD symptom remission were employed: CAPS-2 total score <20 (asymptomatic to very mild symptoms)[1] or CGI-Global Improvement score of 1 (very much improved)[2]. The incidence of remission were analyzed using logistic regression, controlling for study, baseline value and

treatment in the last observation carried forward (LOCF) datset which included all patients with at least one post-dose efficacy assessment.

Results: Patients treated with paroxetine consistently achieved significantly greater rates of PTSD symptom remission compared to placebo on both indices. Thirty-one percent (31%) of paroxetine and 16% of placebo patients achieved a CAPS-2 score <20 (Odds Ratio = 2.29, C.I.: 1.68–3.12, $p < 0.001$); 29% of paroxetine and 19.6% of placebo patients attained a CGI-I rating of 1 (Odds Ratio = 1.67, C.I.:1.26–2.21, $p < 0.001$).

Conclusion: Remission from chronic PTSD symptoms is achieved in a significant proportion of patients treated for up to 12 weeks with paroxetine.

NR208 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

The 35 Percent CO2 Challenge Test in Panic Disorder: Sensitivity and Reliability

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., Marco A. Mezzasalma, M.D., Fabiana L. Lopes, M.D., Walter Zin, M.D.

Summary:

Background: A number of studies have investigated the vulnerability of different groups of anxiety disorder patients to the 35% CO2 challenge, and most studies have confirmed that panic disorder (PD) patients are particularly vulnerable to it.

Objective: to verify the frequency of panic attacks in a sample of PD patients, after the 35% CO2 challenge test.

Methods: 27 PD patients (DSM-IV) were randomly selected and went double-blind through an inhalation of 35% CO2 and compressed gas (atmospheric air) on two occasions, with a two-week interval. During this period patients were drug free.

Results: 20 (74%) of 27 PD patients had a panic attack after at least one of the two CO2 challenges and of these, 19 (70.3%) had a panic attack in both CO2 challenges. Seven PD patients had no panic attacks after the two CO2 challenges and just one PD patient had a panic attack in one of the two CO2 challenges.

Conclusion: PD patients have high sensitivity to CO2. The CO2 challenge test is of good sensitivity and reliability in PD.

NR209 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Clonazepam in Carbon Dioxide-Induced Panic Attacks: A Six-Week 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 Zin, M.D.

Summary:

The 35% CO2 panic provocation challenge induces anxiety and panic attacks in most panic disorder patients. We aim to determine if an acute dose of clonazepam (2 mg) and if treatment for two and six weeks with clonazepam (2 mg/day) actually blocks panic attacks induced by a 35% carbon dioxide inhalation in panic disorder patients. Thirty-four panic disorder patients participated in a carbon dioxide challenge test for three times: an hour after a dose of either 2 mg of clonazepam or placebo and after two and six weeks of treatment with either placebo or clonazepam (2 mg/day), in a randomized crossover double-blind method. Panic disorder patients who received clonazepam (2 mg) one-hour prior to the CO2, or clonazepam (2 mg/day) for two and six weeks had significantly fewer panic attacks when compared with those who received placebo (Fisher Exact test, $p = 0.001$ and $p = 0.004$, respectively). There was a positive association between therapeutic response to clonazepam and efficacious blockade in carbon dioxide challenge tests. The CO2 challenge test might be a useful tool for screening psychotropic drugs with antipanic properties.

NR210 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Effects of Deficient Serotonergic Modulation on Chemoreflex Control of Breathing in Man

Lukasz Struzik, M.S.C., *Anxiety Clinic, Centre for Addiction and Mental Health, 250 College Street, 11th Floor, Toronto, ON M5T1R8, Canada*; James Duffin, Ph.D., Monica Verman, M.A., Katherine Hegadoren, Ph.D., Martin A. Katzman, M.D.

Summary:

Klein (1993) proposes that panic attacks are the results of a defective "suffocation alarm" threshold that presents with carbon dioxide (CO_2) hypersensitivity, exaggerated ventilatory response, and panic in panic disorder patients. Serotonin (5-HT) is expected to normalize the "suffocation alarm" threshold and associated CO_2 hypersensitivity. Current research supports both 5-HT-mediated increases and decreases of ventilatory output. To resolve this controversy and test Klein's theory, we assessed the effect of low 5-HT levels on ventilatory control in man. We hypothesised that if Klein is correct then CO_2 responsiveness should be increased. We used tryptophan depletion (TRP-) concurrently with a modified Read rebreathing test to determine the effect of deficient serotonergic modulation on central and peripheral chemoreflex threshold and sensitivity of response to CO_2 in eleven healthy men. TRP- did not affect central or peripheral chemoreflex threshold or sensitivity of response to CO_2. However, basal ventilation was significantly elevated during TRP-. In contrast to "suffocation alarm" theory predictions, deficient 5-HT neurotransmission does not significantly affect the respiratory chemoreflex response to CO_2, instead increasing non-chemoreflex drives to breathe. Panic associated respiratory abnormalities may be related to defective 5HT modulation of non-chemoreflex drives to breathe, unrelated to any respiratory chemoreflex abnormality.

NR211 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Duration of Treatment with Venlafaxine Extended Release in GAD

Philip T. Ninan, M.D., *Department of Psychiatry, Emory University, 1639 Pierce Drive, Suite 4000, Atlanta, GA 30322*; David Hackett, M.S.C., Vincent Haudiquet, B.Sc.

Summary:

Objective: Generalized anxiety disorder (GAD) is a chronic disorder. It is not known how long treatment should continue once a response is obtained, nor how long treatment should persist in the absence of response.

Method: In this analysis, data from two 1,2 placebo-controlled 6-month trials of venlafaxine ER (37.5–225 mg/day). In GAD patients (ITT population: 767) were pooled. Criteria of response (> = 50% improvement in HAM-A score) and remission (HAM-A score = <7) were used. The analysis aims to compare at each visit the percentage of nonresponders (or nonremitters) who become responders (or remitters) at month 6.

Results: The percentage of nonresponders who became responders at month 6 was statistically significantly greater with venlafaxine ER than with placebo up until week 8 of treatment, but not beyond. The percentage of nonremitters who became remitters at month 6 was statistically significantly greater with venlafaxine ER than with placebo at all time points.

Conclusion: Treatment of patients with GAD should persist for at least 8 weeks even in the absence of response, while treatment to obtain remission should continue beyond this time point.

NR212 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Long-Term Sertraline Treatment of Pediatric OCD: Remission and Functional Status

Karen D. Wagner, M.D., *Department of Psychiatry, University of Texas Medical Branch, 301 University Boulevard, Galveston, TX 77550-0188*; Edwin H. Cook, Jr., M.D., Henry Chung, M.D., Robert Wolkow, M.D., Michael Messig, Ph.D.

Summary:

Background: Given the chronicity and impairment associated with OCD, it is recommended that pharmacotherapy be continued for at least one year following a satisfactory acute treatment response (Grados et al, 1999). Few studies have evaluated the effectiveness of long-term treatment for pediatric OCD. The goal of the current analysis is to evaluate response and remission among children and adolescents with OCD treated with sertraline for 12 months.

Method: Children (6–12 years; n = 72) and adolescents (13–18 years; n = 65) with DSM-III-R OCD who had completed a 12-week, double-blind, placebo-controlled sertraline study (March et al, 1998) were administered open-label sertraline 50–200 mg for 52 weeks (Cook et al, 2001). Efficacy was evaluated by the Children's Yale-Brown Obsessive-Compulsive scale (CY-BOCS), NIMH Global Obsessive-Compulsive Scale (NIMH-GOCS), and Clinical Global Impression scores.

Results: At endpoint, 72% of children and 61% of adolescents met response criteria (>25% decrease in CY-BOCS *and* a CGI-I score of 1 or 2). Using LOCF-endpoint analysis, 47% of patients achieved a full remission (defined as a CY-BOCS ≤8) while an additional 25% achieved a partial remission (CY-BOCS ≤15, but > 8). Among study completers, full remission was achieved by 55% of patients, and partial remission by 31%. Only 66% of patients with severe OCD at baseline (CY-BOCS ≥ 26) achieved full or partial remission. Children were more likely to achieve a full remission than adolescents, although the difference was not significant. Improvement in functioning for those who had moderate to severe functional impairment was achieved by 69% of patients using an LOCF analysis.

Conclusion: Sertraline is effective in the treatment of childhood and adolescent OCD, with initial acute response converting to remission and improved functional status in a substantial proportion of patients. More research is needed to develop pharmacologic and psychotherapeutic strategies that provide full remission for patients with OCD.

NR213 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Underdetection of Anxiety Diorders in Depressed Patients and a Method to Improve Recognition

Iwona Chelminski, Ph.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Providence, RI 02905*; Mark Zimmerman, M.D.

Summary:

Objective: In this presentation we examine how often anxiety disorders are underdiagnosed in patients with a primary diagnosis of Major Depressive Disorder and whether patients want treatment for these comorbid disorders. We also examine diagnostic performance of the anxiety disorder subscales of the Psychiatric Diagnostic Screening Questionnaire (PDSQ) in cases where an anxiety disorder is not the principal reason for seeking treatment.

Methods: The Structured Clinical Interview for DSM-IV (SCID) was administered to 479 patients and a separate sample of 610 patients were evaluated clinically by psychiatrists. Clinicians' diagnoses written as "rule out" were included as present. Prior to the evaluation, SCID and non-SCID patients completed the PDSQ. All evaluations were conducted blind to the PDSQ results.

Results: Both groups scored similarly on the PDSQ subscales suggesting comparable level of psychopathology. The frequency of any anxiety disorder was more than two times higher in the SCID than the clinical sample (55% vs. 23%). Every anxiety disorder was significantly less often diagnosed in the clinical series. Overall, 81% of the depressed patients with at least one anxiety disorder wanted their treatment to address a comorbid anxiety disorder. The PDSQ performed as well in identifying additional diagnoses as it did in the entire cohort. The mean sensitivity and negative predictive value of the anxiety disorder subscales was 88.5% and 96.5% when all diagnoses were included, and 88.3% and 95.6% when only comorbid diagnoses were examined.

Conclusions: Our findings suggest that anxiety disorders are frequently unrecognized in patients with MDD and that patients consider them important enough to want treatment to address them. Feasibility of incorporating the PDSQ into clinical practice and its clinical implications will be discussed.

NR214 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

A Comparison of Haloperidol and Atypical Antipsychotics in the Treatment of Delirium

Martha M. Kato, M.D., *Department of Psychiatry, University of Miami, 1695 N.W. 9th Avenue, #2435, Miami, FL 33136*; M. Beatriz Currier, M.D., Joan Pop, M.D., Lacresha L. Hall, M.D., Marni Grant, German Molina, M.D.

Summary:

Objective: To determine the prevalence and etiology of delirium among patients referred to a psychiatric consultation service. To identify clinical variables of delirium associated with antipsychotic treatment response and to compare outcome in delirious patients treated with intravenous (IV) haloperidol and atypical antipsychotics.

Method: A retrospective chart review was conducted on 658 consecutive psychiatric consults. Delirium was diagnosed by clinical interview using the DSM-IV criteria and treatment outcome was assessed using the Clinical Global Impression (CGI) score as indicated in the chart. Responders were defined by a CGI score of "very much" or "much" improved.

Results: Thirty-nine percent (256/658) of the patients were diagnosed with delirium. The most frequent causes of delirium included hypoxia (23%), infection (17%), hypoperfusion (13%), medications (11%), and metabolic abnormalities (11%). Patients selected were treated with IV haloperidol (N = 81, dose range = 0.5–30 mg/day), risperidone (N = 30, dose range = 0.5–2.0mg/day), and olanzapine (N = 12, dose range = 2.5–20 mg/day). For purpose of analysis, patients on atypical antipsychotics were combined (N = 42). Fifty-seven percent of the patients were male, 69% were white, and 46% were Hispanics. Patients with comorbid dementia (haloperidol N = 8, atypical antipsychotics N = 17) were excluded from analysis. The mean age was 55.36 ± 16.28 for patients on haloperidol and 54.20 ± 15.35 for patients on atypical antipsychotics. Fifty-three percent of patients treated with haloperidol and 58% of patients treated with atypical antipsychotics responded. Response rate did not differ significantly between the 2 groups ($p < 0.677$). Treatment response was not associated with age, gender, race, ethnicity, antipsychotic dose, or medical etiology for delirium. However, severity of delirium as indicated by the pretreatment Mini-Mental Exam Score (MMSE) was significantly associated with treatment outcome ($p < 0.007$).

Conclusion: Delirium is common among medically ill patients referred for psychiatric consultation. Haloperidol and atypical antipsychotics were equally effective and safe in the treatment of delirious patients regardless of medical etiology. In this study the MMSE score was the only clinical variable significantly associated with treatment outcome.

NR215 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

The Profiles of Traumatic Brain Injury Patients on a Binomial Forced Test

Beilin Gao, M.D., *Shenzhen Kangning Hospital, Cuizhu Road #1080, Shenzhen Gungdon 518020, China*

Summary:

Objective: The forensic cases with compensations are increasing rapidly in China. The capacity to accurately assess the veracity of client-reported cognitive deficits is essential whenever settlement, litigation, or forensic issues are primary. However, so far there is no an objective method to assess malingered cognitive deficits in China. The present study explored the validity of a test used for malingered memory deficits. A binomial forced-choice test of digits memory with 24 items was edited in this study. Two levels of item difficulty were used which were based on Slick's Victoria Revision of the Hiscock Digit Memory Test.

Methods: The test was given to 66 traumatic brain injury (TBI) without compensations, 61 TBI with compensations and malingering, and 58 normal controls. The subjects with TBI and without compensation were divided into three categories based on degree of brain damage and included severe, moderate, and mild. The patients were tested 6–24 months post-injury. Calculated the cut-off score of detecting malingering from the subjects' performances, and distinguishing analysis was also made.

Results: The performance of TBI cases with malingering was significantly lower than that of TBI subjects without compensations and normal controls on both the easy and difficult items. The accuracy of distinction was 98.6% when the cut-off score was 11 on easy items and 7 on difficult item.

Conclusion: The binomial forced-choice test of digits memory with 24 items was useful for detecting dissimulated memory deficits.

NR216 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Increasing Rates of Homicide-Suicide in Older Persons

Donna Cohen, Ph.D., *Aging/Mental Health Department, University of South Florida, 13301 Bruce B. Downs Boulevard, Tampa, FL 33612-3899*; Carl Eisdorfer, M.D.

Summary:

Objective: The purpose was to determine the annual incidence of homicide-suicide (HS) from 1997–2001 in the State of Florida and to compare rates by age.

Methods: All cases of HS were ascertained from the 25 medical examiner districts in Florida for each of 5 years. Annual HS rates were calculated, age-adjusted by year, for total HS cases per 100,000 population, per 100,000 persons 55 years and older, and per 100,000 persons 54 years and younger.

Results: A total of 292 HS events were identified over the 5 years, with 40% among the older population. All perpetrators in the older group were male compared to 87% in the younger group. The annual incidence rates from 1997–2001 for the total population were 0.40, 0.36, 0.36, 0.40, 0.60 per 100,000. The annual incidence rates for the population 55 and older were 0.48, 0.43, 0.43, 0.50, and 1.07 per 100,000, consistently higher than the annual incidence rates for the population 54 and younger: 0.36, 0.32, 0.32, 0.36, 0.42.

Conclusions: This is the first statewide study of HS. Results replicate our initial report showing higher annual incidence rates in the older age group as well as the prominent role of men as perpetrators. The increasing rate of HS in the old group emphasizes the importance of better detection and preventive intervention.

NR217 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Depression as Determinant of Fatigue in Inflammatory Bowel Disease

Phillippe M.J. Persoons, M.D., *Department of Psychiatry, UZ Gasthuisberg, Herestraat 49, Leuven 3000, Belgium*; Benjamin Fischler, M.D., Joris Vandenberghe, M.D., Paul Rutgeerts, M.D.

Summary:

Objective: Fatigue is an important concern in inflammatory bowel disease (IBD). To assess the determinants of fatigue in IBD, and the importance of fatigue for quality of life (QOL).

Methods: Consecutive IBD patients completed a validated fatigue questionnaire (CIS-4), the Hospital Anxiety and Depression scale (HAD) Depression Score (DS) and Anxiety Score (AS) and QOL scale (SF-36). Disease activity parameters and disease characteristics were determined. Significant correlates ($p < .05$) were entered in a multivariate analysis with fatigue score (CIS) and next SF-36 mental factor (SF-36MF) and physical factor (SF-36PF) as dependent variables.

Results: 77 patients participated. 46.8% felt chronically fatigued over the last six months. Significant correlates of CIS were hematocrit($r = -.22; p = .05$), CRP($r = .25; p = .03$), weight($r = .25; p = .03$), HADAS ($r = .40; p < .01$) and HADDS ($r = .49; p < .01$). Significantly higher CIS scores were found in inpatients ($p < .01$), in women ($p < .01$) and in active IBD ($p = .01$). Stepwise multiple linear regression identified HADDS ($p < .01$), female gender ($p < .01$), and being inpatient ($p = .01$) as determinants of CIS ($R^2 = .37; p < .01$). Stepwise multiple linear regression identified CIS ($t = -3.52; p < .01$), being inpatient ($t = -4.32; p < .01$), and HADDS ($t = -2.95; p < .01$) as determinants of SF-36PF ($R^2 = .53; p < .01$). HADDS ($t = -3.16; p < .01$), CIS ($t = -3.50$; $p < .01$) and HADAS ($t = 3.33$; $p < .01$) were independent determinants of SF-36MF ($R^2 = .57; p < .01$).

Conclusion: In IBD, the most important determinant of fatigue are depressive symptoms. Together with psychological distress and physical factors, fatigue is an independent determinant of QOL in IBD.

NR218 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Alcohol Abuse Is Not Associated with Adverse Cardiac Surgery Outcomes

Thomas P. Beresford, M.D., *Department of Psychiatry, VAMC/ University of Colorado, 1055 Clermont Street, Denver, CO 80220*; Adrianne Casebeer, Maureen O'Brien, Ph.D., Karl Hammermeister, M.D., Frederick Grover, M.D., A. Laurie Shroyer, Ph.D.

Summary:

Introduction: Providing cardiac surgery procedures to alcohol abusing (AA) patients may generate controversy due to the nature of this addictive disorder and its related conditions. This study examined whether AA and non-AA patients differ in risk-adjusted 30-day operative mortality (RAOM) and major peri-operative complication rates.

Method: We analyzed data obtained from the VA "Processes, Structures, and Outcomes of Cardiac Surgery" (PSOCS) study. These described risk factors, procedural details, and clinical outcomes for cardiac patients before, during, immediately after, and six months following heart surgery. Using univariate statistical comparisons in combination with a multivariate logistic model for 30-day operative death, we compared the PSOCS outcomes for AA patients (identified by self report or study interview) and non-AA patients with statistical significance set at $p < 0.05$.

Results: For all clinical outcomes examined, the AA group ($N = 459$) did not differ significantly from the remaining non-AA patients ($N = 4333$). Clinical outcomes evaluated included observed 30-day operative mortality (4.6% vs. 4.8%), major complication rates

(stroke 3.4% vs. 2.8%, renal failure 0.9% vs. 2.2%, re-operation 4.0% vs. 3.5%, prolonged ventilation 10.9% vs. 10.9%, deep sternal wound infection 2.2% vs. 2.3%), and expected 30-day mortality rates (4.3% vs. 5.0%). Observed to expected 30-day operative mortality ratios (1.067 vs. 0.951) did not statistically separate the groups.

Conclusion: recognizing that a selection bias likely exists related to pre-screening of AA patients who receive cardiac surgery, AA as a risk factor does not predispose to adverse RAOM or major morbidity after holding all other risk factors constant.

NR219 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Paroxetine in Patients Irritable Bowel Syndrome: A Pilot Study

Prakash S. Masand, M.D., *Department of Psychiatry, Duke University Medical Center, Box 3391 Duke South, Room 3050B, Yellow Zone, Durham, NC 27710*; Subhdeep Virk, M.D., Thomas L. Schwartz, M.D., Sanjay Gupta, M.D., Kari Lockwood, R.N., Ahmad Hameed, M.D., Monica King, M.D., David S. Kaplan, M.D., Katherine L. Beebe, Ph.D.

Summary:

Irritable bowel syndrome is a common disorder and is the largest diagnostic cohort seen by gastroenterologists. There is a bi-directional co-morbidity of IBS and psychiatric illness. In the first study of any SSRI to treat IBS, 20 subjects with the Rome criteria diagnosed IBS were treated with 20 to 40 mg of Paroxetine for 12 weeks. We utilized a computer administered patient daily diary administered over the telephone using the interactive voice response (IVR) system. Sixty-five percent of patients reported improvement in abdominal pain and 55% in pain frequency. Constipation and diarrhea improved in 69% and 57% of patients respectively. Similarly there was significant improvement compared to the baseline week in the symptoms of incomplete emptying (53%) and bloating/abdominal distension (55%). On the clinical global impression scale (CGI) at week 12, 47% of the patients were much or very much improved. In our pilot open label study, paroxetine was very effective in alleviating the abdominal pain and associated symptoms of IBS. These results warrant further examination in a placebo controlled study.

NR220 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Depressive and Anxiety Symptoms in Patients with Subclinical Hypothyroidism

Jose C. Appolinario, M.D., *Department of Psychiatry, University of Rio de Janeiro, Visconde de Piraja 550 CJ 2002, Rio De Janeiro, RJ 22410-001, Brazil*; Leonardo F. Fontenelle, M.D., Rosita Fontes, M.D., Marcelo Papelbaum, M.D., Joao R. Bueno, M.D., Daniel Segenreich, M.D.

Summary:

Depressive and anxiety symptoms have been associated with subclinical hypothyroidism (SCH).

Objective: To assess the presence and the severity of depressive and anxiety symptoms in a SCH sample and to evaluate the correlation between these symptoms and the thyroid function.

Methods: 21 patients with SCH were evaluated. Control group: 18 individuals with normal thyroid function. Instruments: The Hamilton depressions scale (HD) and the Hamilton anxiety scale (HA) were used. Serum thyroid-stimulating hormone (TSH), triiodothyronine (T_3), free thyroxine (FT_4), antimicrossomials, and anti-peroxidase antibodies were determined in all participants.

Results: There was a statistically significant difference between the HD and HA scores from SCH group compared with the control group. The SCH patients displayed a median HD = 11.7 and the control group 5.5 ($p < 0.01$) and a median HA = 13.1 compared with 6.6 in the controls ($p < 0.01$). We did not find, however, a statistical correlation between the depressive and anxiety symptoms and the TSH levels ($c = 0.26$, $p = 0.22$; $c = 0.14$, $p = 0.40$).

Conclusion: Patients with SCH, in our sample, compared with individuals without SCH displayed an elevation of depressive and anxiety symptoms.

NR221 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Medication-Induced Psychiatric Emergencies in Older Adults

Daniel P. Chapman, Ph.D., *Health and Aging Branch, CDC, 4770 Buford Highway NE, MS K45, Atlanta, GA 30341*; Joan K. Miller, Glenn W. Currier, M.D.

Summary:

Objectives: Polypharmacy and increased sensitivity to adverse effects are frequently believed to increase the prevalence of medication-induced emergencies in older adults. However, previous investigations have largely been restricted to examination of emergency admissions precipitated by somatic complaints and have involved a limited number of medications. This investigation assessed the prevalence of medication-induced emergency hospitalizations for psychiatric disorders in persons aged 65 years or older involving all medications.

Method: Analysis of Medicare claims data for the primary diagnosis of a psychiatric disorder among adults aged 65 years and older who received emergency hospitalization in 1997.

Results: 96,359 psychiatric emergency admissions were reported among older adults in the U.S. in 1997, of which 0.7% ($n = 676$) were medication-induced. Medication-induced psychiatric emergency admissions were significantly more prevalent among systemic, analgesic, respiratory and anticonvulsant agents (35.8%, 24.7%, 19.7%, 11.7%, respectively) than among neuroleptics, sedative-hypnotics, or other psychotropics (1.0%, 1.9%, 1.5%, respectively). Comparison of comorbid medical diagnoses associated with medication-induced emergency admissions versus other psychiatric emergency admissions reveals that circulatory (44.2% vs. 34.3%), respiratory (6.9% vs. 4.2%), and neoplastic (3.2% vs. 1.6%) comorbidities were more common among medication-induced admissions.

Conclusions: These results indicate that the reported prevalence of psychiatric emergencies in older patients induced by medications is relatively low and that psychotropic agents were seldom precipitants of psychiatric emergency admissions. Medication-induced psychiatric emergency admissions are also characterized by different comorbidities than other psychiatric emergency admissions in older patients.

NR222 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

An Open Study of Bupropion Sustained Release in Adults with ADHD and Substance Use Disorders

Jefferson B. Prince, M.D., *Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC-725, Boston, MA 02114-3117*; Timothy E. Wilens, M.D., James G. Waxmonsky, M.D., Paul G. Hammerness, M.D., Michael C. Monuteaux, B.A., Sarah Goldman, B.A., Joseph M. Gonzalez-Heydrich, M.D.

Summary:

Introduction: Individuals with Attention Deficit/Hyperactivity Disorder (ADHD) are at a higher risk for developing a Substance Use Disorder (SUD). However, patients with SUD are frequently excluded from pharmacological trials. Because bupropion has been reported effective for treating ADHD and for reducing substance craving, we studied the efficacy and tolerability of sustained-release (SR) bupropion in ADHD adults with mixed SUDs

(12% alcohol abuse/dependence, 12% drug abuse/dependence, 76% alcohol + drug abuse/ dependence).

Method: This was a prospective, open, six-week trial of bupropion SR (up to 200 mg BID) in DSM IV diagnosed outpatient adults with ADHD and mixed SUD. Diagnoses were based on psychiatric evaluation and confirmed by structured diagnostic interview. Efficacy was based primarily on CGI and ADHD symptom checklist scores.

Results: Nineteen (mean age = 32 years) of 32 patients completed protocol (41% attrition). Three subjects dropped due to adverse events (panic, hypertension, hives), and 10 were lost to follow-up. At endpoint (LOCF), DSM IV ADHD Symptom Checklist scores were lowered by 46% compared to baseline ($p < 0.001$). Likewise, there was a 22% reduction in substance use by CGI ($p < 0.001$). No drug interactions with substances of abuse were noted.

Discussion: The results from this open trial suggest that bupropion SR is associated with significant reductions in ratings of ADHD symptoms and to a lesser extent substance use. While bupropion SR was well tolerated, the high attrition rate suggests the need to stabilize the addiction prior to pharmacological treatment.

NR223 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Follow-up of Children Exposed or not Exposed to Antidepressant Drugs During Pregnancy

Regina C. Casper, M.D., *Dept of Psychiatry, Stanford University, 401 Qarry Road, Stanford, CA 94305*; Barry Fleisher, M.D., Eugene Hoyme, M.D., Allyson Gilles, B.A.

Summary:

Background: This study compared the structural growth and developmental outcome of children, born to mothers diagnosed with major depressive disorder during pregnancy, who were exposed or not exposed to antidepressant drugs *in utero.*

Method: Children, whose mothers were diagnosed during pregnancy with major depressive disorder or bipolar disorder, depressed and elected not to take medication (N = 17) were compared to children of depressed mothers treated with antidepressant medication (N = 29) on birth outcome and postnatal neurodevelopmental functioning between ages 3 to 51 months. At follow-up, children underwent standardized pediatric and dysmorphology examinations and an evaluation of their mental and psychomotor development using the Bayley Scales of Infant Development (BSID II).

Results: Frequencies of major and minor anomalies and Bayley Mental and Psychomotor indices were similar in both groups. Children of mothers, who took antidepressant medication during pregnancy, had lower Apgar scores at 5 minutes ($t = 2.47$; $p < .02$) and scored lower on the motor quality factor (71.3 vs. 92.2; $t = 2.8$; $p < .01$) of the Bayley Behavioral Rating Scale.

Conclusions: The results confirm the relative safety of antidepressant drugs given during pregnancy. They suggest that antidepressant drugs acting during fetal development might have subtle effects on observed motor quality.

NR224 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

Divalproex Sodium Is Superior to Placebo for Impulsive Aggression In Cluster B Personality Disorders

Eric Hollander, M.D., *Department of Psychiatry, Mt. Sinai School of Medicine, One Gustave Levy Place, Box 1230, New York, NY 10029*; Alan C. Swann, M.D., Emil F. Coccaro, M.D., Katherine A. Tracy, M.D., Susan L. McElroy, M.D., David Burt, Ph.D., Elizabeth Peris, B.S., Kenneth Sommerville, M.D.,Charles B. Nemeroff, M.D.

Summary:

Objective: Cluster B Personality Disorders are common and highly disabling. Currently, no pharmacologic agent is approved for the treatment of these disorders. This study examines divalproex sodium versus placebo in the treatment of impulsive aggression in patients with Cluster B disorders.

Method: Ninety-one outpatients diagnosed with a Cluster B disorder and with a score of ≥15 on the Aggression scale of the Overt Aggression Scale- Modified (OASM-A) were followed weekly in a randomized, placebo-controlled, double-blind 12-week trial. The primary efficacy measure was the average of the last four OASM-A assessments.

Results: OASM-A scores were significantly improved ($P < 0.05$) for the divalproex group (n = 43) compared to placebo (n = 48), during the last four weeks on treatment (ITT). In the evaluable subset, there were statistically significant treatment differences favoring divalproex on OASM-A, including Verbal Assault, Assault Against Objects, and Irritability, as well as CGI-S at multiple timepoints. Overall, equal numbers discontinued from both groups (47% divalproex, 45% placebo), 17% of patients on divalproex discontinued from the study for adverse events versus 4% on placebo.

Conclusions: In the largest sample of Cluster B disorders studied, divalproex was superior to placebo in the treatment of impulsive aggression, irritability, and global severity.

NR225 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

History of Substance Abuse and Differential Treatment Response in Chronic Depression

Michael E. Thase, M.D., *Department of Adult Psychiatry, University of Pittsburgh-WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213-2593*; Edward S. Friedman, M.D., Philip T. Ninan, M.D., Bruce A. Arnow, Ph.D., Frances E. Borian, R.N.

Summary:

Objective: Approximately 50% of people with chronic depression have or have had problems with alcoholism or other substances of abuse. We evaluated the impact of prior alcoholism or substance abuse (A-SA) on the outcome of 641 chronically depressed patients treated in a multicenter trial comparing nefazodone ($\bar{x}$: 457 mg/day), Cognitive Behavioral System of Psychotherapy (CBASP; $\bar{x}$: 18 sessions), or their combination.

Method: All patients met SCID-P/DSM-IV criteria for one of the 3 forms of chronic major depression. History of A-SA was also determined by SCID-P; patients must have been in remission (abstinent) for at least 6 months to be study-eligible.

Results: The A-SA group (n = 226; 33%) was significantly younger and contained more men. The groups did not differ in terms of course of illness variables (e.g., age of onset, illness duration) or other Axis I or Axis II comorbidities. Nor did the groups differ in overall 12 week outcomes. The A-SA group did, however, have a better response to nefazodone (remission rate: 34%) than CBASP (remission rate: 16%), whereas the opposite pattern was observed among the non A-SA patients (15% vs 28%).

Conclusion: Chronically depressed patients with a history of A-SA may respond preferentially to pharmacotherapy, either alone or in combination with CBASP. It is not clear if these findings are specific to nefazodone or would generalize to other antidepressants.

NR226 Tuesday, May 21, 12:00 p.m.-2:00 p.m.

A Systematic Evidence-Based Review of Mood Stabilizers for Bipolar Disorder

Mark S. Bauer, M.D., *Department of Psychiatry, Providence VAMC, 830 Chalkstone Avenue, Providence, RI 02908*; Landis Mitchner, M.D.

Summary:

Background: Treatments for bipolar disorder have proliferated, and pharmaceutical industry marketing forces are being brought to bear to shape practice patterns without clear definition of the term "mood stabilizer." We propose that mood stabilizer be defined as an agent that has efficacy for acute manic and depressive symptoms, and prophylaxis of manic and depressive symptoms and evaluate available agents against this definition.

Methodology: Articles were reviewed that: (a) were published in peer-reviewed journals in English through 7/01, (b) reported quantitative results in a bipolar sample or subsample. Medline, PsychLit, and the Cochrane databases were reviewed, supplemented by discussion with US and European authors working in the field to identify further studies in press. Bibliography of each located article was reviewed until no further articles were found. Studies were categorized according to AHCPR/AHRQ evidence classification system.

Results: 401 articles were reviewed. Class A studies were identified for acute mania (n = 39), acute depression (n = 11), and prophylaxis (n = 22, including 5 reporting depression prophylaxis specifically). Currently, Class A data support the use of lithium, carbamazepine, valproate, olanzapine, and verapamil for acute mania; lithium and lamotrigine for acute depression; and only lithium for prophylaxis.

Conclusions: Only lithium currently fulfills the proposed definition for "mood stabilizer."

NR227 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Combination Lithium and Divalproex Sodium Treatment of Pediatric Bipolar Disorder

Robert L. Findling, M.D., *Department of Psychiatry, University Hospital, 11100 Euclid Avenue, Cleveland, OH 44106-5000*; Barbara L. Gracious, M.D., Nora K. McNamara, M.D., Robert J. Stansbrey, M.D., Joseph R. Calabrese, M.D.

Summary:

Objective: To examine the effectiveness of combination treatment with both divalproex sodium (VPA) and lithium carbonate (Li+) in the treatment of juvenile bipolarity.

Method: Patients between the ages of 5 and 17 years diagnosed with either bipolar disorder 1 or 2 (BP-1 or BP-2) are treated with combination VPA/Li+ therapy for up to 20 weeks. If subjects experience symptom remission they are randomized to receive either VPA or Li+ monotherapy.

Results: One hundred and two subjects have enrolled. Their mean age is 10.8 years (SD = 3.4 years). Changes in mood ratings and global assessment of functioning show significant improvement with VPA/Li+ when compared to baseline. Almost half the subjects who received study medicine had symptom remission and were randomized to receive medication monotherapy. Combination VPA/Li+ therapy was usually well tolerated.

Conclusions: Divalproex sodium and lithium carbonate treatment is generally safe and effective in pediatric bipolarity. Whereas the treatment resistant mood state in adults with bipolar disorder is depression, this does not seem to be the case in children or adolescents with this condition.

NR228 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Reboxetine and Sexual Side Effects

Anita H. Clayton, M.D., *Department of Psychiatry, University of Virginia, 2955 Ivy Road, Northridge Suite 210, Charlottesville, VA 22903*; John M. Zajecka, M.D., James M. Ferguson, M.D., Jacqueline K. Reisner, Mark T. Brown, Ph.D., Gerri E. Schwartz, M.D.

Summary:

Objective: Sexual side effects due to antidepressant treatment are an important consideration when selecting the most appropriate treatment regimen and may often influence patient compliance.

Methods: Recently, a multicentre, randomized, eight-week double blind study of reboxetine versus fluoxetine versus placebo was completed with 450 outpatients diagnosed with major depressive disorder (MDD). Sexual function was measured by the Rush Sexual Inventory (RSI) that was completed by male and female patients and administered at baseline, Day 28 and Day 56.

Results: Preliminary results indicate that reboxetine was comparable with placebo and superior to fluoxetine in its effect on overall sexual function. There was a greater overall degree of sexual satisfaction in the reboxetine group in comparison with fluoxetine ($p = 0.018$). Furthermore, the ability to become sexually excited for both males and females was significantly better for reboxetine compared with fluoxetine ($p = 0.038$).

Conclusion: These results suggest that reboxetine may be of particular benefit for patients at risk for sexual dysfunction with SSRIs.

NR229 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Refining Phenomenology of Bipolar Depression

Elie G. Hantouche, M.D., *Department of Psychiatry/Mood Center, Pitie-Salpetriere Hospital, 43 Bd Hopital, Paris 75013, France*; Hagop S. Akiskal, M.D., Jean-Francois Allilaire, M.D., Sylvie Lancrenon, Ph.D., Jean-Michel Azorin, M.D., Marc L. Bourgeois, M.D., Daniel Sechter, M.D.

Summary:

Clinical presentations in BP-II disorder are varied, inconsistent, and often confusing. The aim of the current report is to show the differences between unipolar and bipolar depressions. The data are deriving from the French National study EP DEP, which included a sample of 452 major depressives.

Methods: At inclusion during major depressive episode (DSM-IV), depression was assessed by the clinician (using HAM-D and Rosenthal Atypical Depression Scale) and by the patient (using the Multi-Visual Analog Scale of Bipolarity, MVAS-BP of Ahearn-Carroll—26 items). Principal component analyses (PCA) were conducted on HAM-D and MVAS-BP in the total population and separately in BP-II (n = 196) and UP (n = 256). We performed intergroup comparative tests (UP vs BP-II) on factorial scores and correlation tests between the two PCA.

Results: The PCA on "HAM-D + Rosenthal scale" showed the presence of six major factors: F1 "weight changes", F2 "sleep disturbances", F3 "sadness", F4 "retardation", F5 "somatic" and F6 "diurnal variation". The PCA on MVAS-BP revealed also the presence of six principal components: F1 "PM retardation", F2 "central pain", F3 "somatic", F4 "social contact", F5 "worry" and F6 "loss of interest". Despite uniformity in global intensity, significant differences were observed such as followed: Higher score on the "PM retardation" ($p = .03$), "loss of interest" ($p = .057$) and "insomnia" in the UP group ($p = .05$); Higher score on "hypersomnia" ($p = .008$) in BP-II group.

Correlation analyses between clinician- and self-ratings revealed the presence of higher number of significant coefficients in UP group (13 vs 6 in BP-II), which indicates more stability and less confusion in the clinical picture of UP depression.

Conclusion: Despite global uniformity, depressive phenomenology seemed to be different in bipolar-II disorder when compared to strict unipolar disorder.

NR230 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Changes in Glucose and Cholesterol in Schizophrenia Treated with Atypicals

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, Jan Volavka, M.D., Leslie L. Citrome, M.D., Brian B. Sheitman, M.D., Joseph P. McEvoy, M.D., Thomas B. Cooper, M.A.

Summary:

Background: Hyperglycemia and hypercholesteremia associated with treatment with atypicals have been extensively documented in open series. We present the effects of both typical and atypical antipsychotics on glucose and cholesterol levels during a randomized double-blind 14-week trial comparing clozapine, olanzapine, risperidone and haloperidol in hospitalized patients with schizophrenia or schizoaffective disorder.

Methods: The trial consisted of Periods 1 (fixed dose, 8 weeks) and 2 (variable dose, 6 weeks). Assessments included fasting blood samples, collected at baseline, Period 1 endpoint, and Period 2 endpoint.

Results: Of 157 subjects, 101 provided blood samples at baseline, Period 1 endpoint (x = 92), and Period 2 endpoint (x = 71). During Period 1, there was an overall significant increase in glucose levels ($F = 6.51$; $df = 4,99$; $p = 0.0001$). There were significant increases in glucose at Period 1 endpoint for clozapine (17.2 mg (30.5); $t = 2.92$; $p < 0.01$) and for haloperidol (8.4 mg (17.8); $t = 2.37$; $p = 0.03$). The olanzapine group showed a significant increase of glucose levels during the interval of baseline through Period 2 (14.3 (25.5), $t = 2.62$; $p < 0.02$). The proportion of subjects with a shift in glucose levels to abnormally high levels (>110mg/ml) in Period 1 was numerically higher for the clozapine group. Cholesterol levels increased during Period 1 for clozapine (14.7 (30.5); $t = 2.50$; $p < 0.02$), while they increased for olanzapine during Period 2 (20.1(26.8);$t = 3.52$; $p < 0.001$).

Conclusion: This is to our knowledge the first study comparing plasma glucose and cholesterol levels during prolonged treatment with three atypical medications. Clozapine, olanzapine, and haloperidol were associated with an increase of plasma glucose, while cholesterol levels were increased for the clozapine and olanzapine groups. Patients treated with clozapine showed a higher number of patients shifting from a normal glucose level to an abnormal level. Our findings confirm observations of open label series showing a higher liability for hyperglycemia for patients treated with clozapine.

NR231 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Dronabinol for Antidepressant-Induced Sexual Dysfunction

Alen J. Salerian, M.D., *Washington Psychiatric Center, 4228 Wisconsin Avenue NW, Washington, DC 20016*; Holly Motto, Ph.D., Antonia L. Baum, M.D.

Summary:

Background: Sexual dysfunctions have been reported to occur with many classes of antidepressants. Antidepressant-induced sexual dysfunction (AISD) may have profound negative consequences such as noncompliance with medication and premature discontinuation of pharmacotherapy. There have been anecdotal reports of cannabinoids sexual enhancing effects. Dronabinol is a cannabinoid, which has sympathomimetic activity.

Method: Twenty-one patients seen at the Washington Psychiatric Center who had been given dronabinol to treat AISD were included in the sample. The charts of these patients were retrospectively reviewed. The patients selected all had initial diagnosis of either major depression or bipolar disorder, depressed type by DSM-IV criteria, and had Arizona Sexual Experiences Scale (ASEX) and Salerian Sexual Symptom Scale (SSSS) administered prior to taking dronabinol and at each subsequent visit, as part of routine clinical care.

Results: At doses of 5 to 20 mg taken one to two hours before sex, 17 out of 21 patients reported significant improvement of their sexual functions. Eighty-five percent (N = 17) of the sample showed overall improvement on SSSS. Eighty-one percent (n = 17) of the sample showed overall improvement of the ASEX. Side effects were minimal and none of the patients showed any signs of abuse.

Conclusion: Dronabinol appears to be a drug with promise as a reverser of AISD. Clinicians must pay particular attention to abuse potential.

NR232 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Gender Differences in Bipolar Disorder: Systematic Treatment Enhancement Program First 500 (Step BD)

Claudia F. Baldassano, M.D., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, Philadelphia, PA 19104*; Deborah R. Kim, M.D., Hadine Joffe, M.D., Lauren B. Marangell, M.D., Kemal Sagduyu, M.D., Stephen R. Wisniewski, Ph.D., Lee S. Cohen, M.D.

Summary:

Objective: To determine if there are gender differences in bipolar disorder and to determine if these differences impact treatment.

Methods: The STEP-BD database from 20 participating sites of the first 500 patients enrolled was analyzed for gender differences. Data for this analysis was harvested from the MINI-International Neuropsychiatric Interview and a structured clinical interview based on DSM-IV.

Results: Women with bipolar disorder were significantly more likely to have a lifetime diagnosis of bipolar type II ($p < .01$), thyroid disease ($p < .05$), suicide attempts ($p < .01$), and antidepressant treatment ($p = .03$). There was a trend suggesting that bipolar women had greater antidepressant-induced manic/hypomanic switch ($p = .06$). Men were more likely to have a history of violence and legal problems ($p < .05$) and a history of head trauma ($p = .03$). No gender differences were found in the following areas: 1) Age of onset of illness, 2) Polarity at onset of illness, 3) Episode Pattern, 4) Number of lifetime episodes of Mania or depression, 5) Lifetime history of rapid cycling, and 6) quality of mania.

Conclusion: There has been a dearth of systematic studies evaluating gender-specific issues in mood disorder, especially bipolar disorder. Issues specific to women can impact on the course and treatment of bipolar illness.

NR233 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Having It All: Career Satisfaction and Family Demands in Women Physicians

Daniel P. Chapman, Ph.D., *Health and Aging Branch, CDC, 4770 Buford Highway NE, MS K45, Atlanta, GA 30341*; Erica Frank, M.D., Lisa Elon, M.P.H.

Summary:

Objectives: Previous literature suggests that balancing career and family demands is a source of stress among women physicians, who are traditionally the primary caretakers of children. This investigation examined the association between parenting responsibilities and self-reported stress among participants in the Women Physicians Health Study (WPHS).

Methods: WPHS surveyed a stratified random sample of U.S. women physicians listed in the American Medical Association Physician Masterfile and randomly selected 2,500 women who

graduated from medical school during each of four decades from 1950 through 1989.

Results: Comparing women physicians with children less than 7 years of age with those not having children younger than 7 revealed no significant differences between percentages reporting high home stress (8% vs. 11%), high work stress (11% vs. 15%), and being satisfied with their career (46% vs. 38%). Among respondents with children less than 7 years old, those who were their child's primary caretaker (n = 633) did not differ significantly from those who were not (n = 75) on percentages reporting high home stress (7% vs. 9%), high work stress (11% vs. 11%) and career satisfaction (46% vs. 46%).

Conclusions: These data reveal that neither the presence of children less than seven years of age nor assuming primary caretaking responsibility for them adversely affect women physicians' self-reported stress or career satisfaction.

NR234 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Symptom Pattern Analysis of PMDD

Teri B. Pearlstein, M.D., *Department of Psychiatry, Butler Hospital, 345 Blackstone Boulevard, Providence, R1 02906*; John A. Gillespie, M.D.

Summary:

Background: The advent of intermittent dosing strategies for the treatment of Premenstrual Dysphoric Disorder (PMDD) has highlighted the need for more detailed empirical data on the onset, duration and pattern of PMDD symptoms.

Method: Data was analyzed from 276 women who met DSM-IV criteria for PMDD and who prospectively charted 2 menstrual cycles off medication. The presence and severity of PMDD symptoms were rated using the Daily Rating of Severity of Problems (DRSP).

Results: The top PMDD symptoms (moderate-to-severe for ≥ 3 days) included anger/irritability (76%), anxiety/tens (71%), and mood swings (58%). DRSP scores peaked at day -2, but the day of onset of PMDD-level symptom severity was highly variable, differing from cycle-to-cycle by 3 or more days in ≥60% of women. Similarly, the duration of PMDD-level symptoms varied by 3 or more days in ≥50% of women. One day after the onset of menstruation, 34% of women continued to report PMDD-level of symptoms (≥ moderate severity of ≥5 out of 11 DSM-IV symptoms). The DRSP anger/irritability/conflict factor showed the earliest rise in symptom severity, and the slowest tail-off after the onset of bleeding.

Conclusion: The variable onset/offset pattern of PMDD symptoms suggests that care must be taken when utilizing luteal phase dosing to ensure adequate pharmacologic coverage of cycle-to-cycle episodes.

NR235 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

What Is the Optimal Duration of Luteal Phase Dosing?

Teri B. Pearlstein, M.D., *Department of Psychiatry, Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906*; John A. Gillespie, M.D.

Summary:

Background: Sertraline has demonstrated significant efficacy in the treatment of PMDD using an intermittent, luteal dosing strategy in terms of reducing symptoms prior to menses. Results of a recent pattern analysis of the onset and offset of PMDD symptoms in unmedicated women suggests that luteal phase dosing adequately covers the variability in onset of symptoms, but that more than one-third of women may continue to have PMDD-level of symptoms in the first 1–2 days after the start of menses.

Method: An exploratory analysis of Daily Rating of Severity of Problems (DRSP) data from day 0–2 in the cycle was conducted comparing efficacy across 2 studies with similar entry criteria, continuous dosing vs. luteal phase dosing (with discontinuation on day 0).

Results: A comparison of DRSP change scores (baseline luteal vs. day 0, day +1, day +2, successively) found no difference between patients receiving continuous treatment with sertraline and those receiving intermittent luteal dosing. The percent of women on day +1 who continued to report PMDD-level of symptoms (≥ moderate severity of ≥5 out of 11 DSM-IV symptoms) was similar on luteal dosing (22.0%) compared to continuous dosing (28.1%). Finally, abruptly stopping luteal phase setraline on day 0 across 3 cycles was not associated with any discontinuation symptoms.

Conclusion: Despite the delayed offset pattern of PMDD symptoms in some women, luteal phase dosing with sertraline provides adequate pharmacologic coverage of PMDD symptoms occurring after onset of bleeding.

NR236 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Lamotrigine or Lithium in the Maintenance Treatment of Bipolar I Disorder

Joseph R. Calabrese, M.D., *Department of Psychiatry, University Hospital of Cleveland, 11400 Euclid Avenue, Suite 200, Cleveland OH 44106*; Charles L. Boden, M.D., Denis Mee-Lee, M.D., Frederick Rheimherr, M.D., Alan H. Rosenbaum, M.D., Jeffrey S. Simon, M.D., Paul Montgomery, M.D.

Summary:

Objective: Two large maintenance studies have recently been completed using the anticonvulsant mood stabilizer, lamotrigine. Trials separately enrolled currently or recently depressed (GW605) or manic\hypomanic\mixed (GW606) patients into open-label treatment followed by randomization of stabilized patients to lamotrigine, lithium or placebo monotherapy for up to 18 months. The studies were prospectively designed to be combined for analysis of treatment outcomes.

Methods: 1315 currently or recently symptomatic bipolar I patients (DSM-IV) were enrolled in the preliminary phase of the studies, of whom 638 were stabilized and randomized to 18 months of double-blind monotherapy with lamotrigine (n = 280; 50–400mg/day fixed and flexible dose), lithium (n = 167; 0.8–1.1mEq) or placebo (n = 191). The primary outcome was time from randomization until intervention for an emerging mood episode or dropout from study unrelated to bipolar illness.

Results: In the combined analysis, both lamotrigine and lithium significantly delayed the time to treatment intervention, survival in study and time to any bipolar event. In separate analyses of manic/hypomanic/mixed vs. depressive events, lamotrigine significantly delayed time to intervention for both types of events compared with placebo. Lithium delayed time to intervention for manic/hypomanic/mixed but not depressive events.

Conclusions: Lamotrigine and lithium appear to have distinct and potentially complementary mood stabilizing properties.

NR237 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Factors Associated with Antidepressant Choice Survey Choosing Among SSRIs

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Michael A. Posternak, M.D., Naureen Attiullah, M.D., Scott E. Baymiller, M.D., Stacie L. Berlowitz, M.D., Robert J. Boland, M.D., Michael Friedman, M.D.

Summary:

Background: The SSRI's are equally effective, and there is little empirical support for predictors of preferential treatment response. Nonetheless, clinicians must make medication choices. The goal of the Rhode Island Factors Associated with Antidepressant Choice Survey (FAACS) was to prospectively examine the factors considered by psychiatrists at the time an antidepressant is selected. In the present report we focus on the factors used by psychiatrists when deciding which SSRI to prescribe.

Methods: The FAACS lists 43 items that might be considered when selecting an antidepressant. The list includes clinical factors (e.g. symptom profile/target symptoms, comorbid conditions), demographic variables, medication properties (e.g., side effects, half-life), 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 711 depressed outpatients, 362 (51%) of whom were begun on an SSRI.

Results: Patients prescribed citalopram were significantly older than patients prescribed the other 3 SSRI's, and the least likely to be prescribed the medication because of a prior positive response. The presence of PTSD was associated with preferential selection of sertraline and paroxetine. The presence of comorbid GAD was associated with preferential selection of paroxetine. Fluoxetine was less likely to be prescribed for patients with comorbid Axis I disorders. SSRI selection was also related to the profile of patient's depressive symptoms, and desire to avoid particular side effects.

Conclusions: Despite a lack of empirical evidence, psychiatrists routinely base their selection of an SSRI for depression on patients' clinical profile. These findings draw attention to gap between efficacy and effectiveness research, and have implications for conclusions that can be drawn from studies such as pharmacoeconomic analyses that are not based on random assignment to treatment.

NR238 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Exclusion Criteria Used in Antidepressant Efficacy Trials

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Iwona Chelminski, Ph.D., Michael A. Posternak, M.D.

Summary:

Background: The inclusion and exclusion criteria used to select subjects for participation in antidepressant efficacy trials (AETs) vary from study to study. Although it is well appreciated that exclusion criteria limit the generalizability of the results of these trials, it is unknown how much impact different sets of exclusion criteria have on the representativeness of subjects treated in AETs. In the present study we applied the inclusion and exclusion criteria used in 39 recently published AETs to patients evaluated in routine clinical practice to evaluate the range and extent of the representativeness of samples treated in AETs.

Methods: Nearly 600 individuals with DSM-IV major depressive disorder (MDD) or bipolar depression presenting for an intake appointment at a general psychiatric outpatient practice underwent a thorough diagnostic evaluation that included the administration of semi-structured diagnostic interviews. Inclusion and exclusion criteria used in AETs were applied to the depressed patients to determine how many patients from our sample would have qualified for each AET had they applied.

Results: Approximately one-sixth of the 596 depressed patients would have been excluded from an efficacy trial because they had a bipolar or psychotic subtype of depression. In the remaining 503 outpatients with nonpsychotic, unipolar MDD, the rates of exclusion based on the different AET exclusion criteria ranged from 0% to 95.0% (mean = 65.8%).

Conclusions: There is much variability in the generalizability of AETs, and subjects treated in AETs represent only a minority of patients treated for MDD in a routine clinical psychiatry practice. The implications of these findings are discussed.

NR239 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Gender Differences in Mood Patterns in Bipolar Disorder

Natalie L. Rasgon, M.D., *Department of Psychiatry, University of California at Los Angeles, 300 Medical Plaza, Suite 1544, Los Angeles, CA 90095-7057*; Michael Bauer, M.D., Tasha Glenn, Peter C. Whybrow, M.D.

Summary:

Objective: To evaluate gender differences in mood, sleep and medication patterns in a population with bipolar disorder (BP).

Methods: 38 patients (12 men, 26 women) with a diagnosis of BP I or II, entered mood, medications taken and sleep, daily into software (ChronoRecord) on a home computer. The patients' mean years of illness was 14.0 ± 12.0. Data (1118 days from men and 2828 days from women, mean 103 days) were analyzed by gender and by individual.

Results: No significant differences for age, diagnosis, sleep, hospitalizations, age of onset, years ill or medications taken were found between men and women. Overall mean mood was lower in women ($p \leq .0001$). Men were depressed 13.6% of study days versus 32.5% for women; men were euthymic 80.1% of study days versus 58.7% for women ($p \leq .0001$). The distribution of mood changes differed with women having more changes from euthymic to depressed, depressed to euthymic, and depressed to hypomanic ($p \leq .0001$). Analysis by individual showed women had a higher frequency of mood changes ($p = .021$), lower mean percent of days normal and higher mean percent of days with mood changes ($p = .014$).

Conclusions: Women with BP appear to be more depressed and have more mood changes than men.

NR240 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Increased Insulin Resistance in Women Bipolar Disorder

Natalie L. Rasgon, M.D., *Department of Psychiatry, University of California at Los Angeles, 300 Medical Plaza, Suite 1544, Los Angeles, CA 90095-7057*; Lori L. Altshuler, M.D., Shana Elman, M.A., Mark A. Frye, M.D.

Summary:

Objective: To evaluate insulin resistance in women with bipolar disorder (BPD).

Subjects: Forty-two women were recruited from the UCLA Mood Disorders Clinic. Fasting a.m. glucose and insulin levels were collected. Insulin resistance was estimated through calculation of homeostasis model assessment (HOMA)[1]. Type of mood stabilizer currently used for treatment of bipolar disorder was recorded. In addition, body mass and height were obtained to calculate the body mass index (BMI)[2].

Results: Out of 42 women, 7 (16.7%) were receiving VPA alone, 3 (7.1%) Lithium alone, 8 (19%) were on Lithium and VPA combination, 18 (42.9%) were on VPA and another anticonvulsant combination (i.e., neurontin, lamotrigine, topomax), 4 (9.5%) were on Lithium and another anticonvulsant combination, 2 (4.8%) were on another anticonvulsant alone. Seventeen (40.5%) women were overweight (BMI >27) and 6 (14.3%) were obese (BMI >30). Nineteen (45.2%) women had a HOMA ratio >2.3, indicating increased insulin resistance (IR).

Conclusions: IR is common among bipolar women treated with anticonvulsants. The question whether IR is inherently high in

women with bipolar disorder or is a result of its treatment remains to be elucidated.

NR241 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Are Time to Response and Degree of Response During Acute Treatment with Bupropion Sustained Release Related to Longer-Term Relapse?

Sidney Zisook, M.D., *Department of Psychiatry, UCSD, 9500 Gilman Drive, # 0603R, La Jolla, CA 92095*; Barbara Haight, Pharm.D., Carolyn B. Watson, Ph.D., Michael Ames, Ph.D., Carol Rockett, Pharm.D., Alan Metz, M.D.

Summary:

Objectives: We hypothesized that: (1) early responders (within 2 weeks) to Bupropion SR (SR) would not sustain their responses as long as patients with a more traditional response beginning after 3-4 weeks, and (2) patients in complete remission after acute treatment with SR would be less likely to relapse during continued treatment than patients with residual symptoms.

Methods: In the study on which this post-hoc analysis is based, 816 depressed patients were treated with SR for 8 weeks and responders randomized to SR or placebo for the next 12 months (N = 417). Time to sustained response (first week of >50% reduction in HAM-D 17) and remission (HAM-D 17 ≤6) in the acute phase were evaluated to determine if time to response or remission were related to relapse over the next year. The degree of symptomatic response, based on number of residual symptoms, was evaluated to determine whether residual symptomatology was related to later relapse.

Results: Neither hypothesis was confirmed. 24% of acute phase responders began their responses within the first 2 weeks of treatment. Of these, 91% were in full remission by the end of the acute phase. Neither time to response nor time to remission were significantly related to relapse during the continuation phase. Similarly, residual symptoms were not related to relapse. The only variable significantly related to relapse was treatment assignment during the continuation phase: SR patients had a significantly longer time to relapse than placebo patients (p = .003).

Conclusion: Early response to SR appears to be both real and enduring. Most early responders achieve full remission by the end of 8 weeks and early responders who continue treatment with SR are no more likely than later responders to relapse over the next year. Similarly, there is no relationship between degree of response and likelihood of relapse over the next year of treatment. Therefore, responders who continue to have residual symptoms after acute treatment with SR may be good candidates for continued treatment over the next year.

NR242 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Are Time to and Degree of Response with Bupropiion Sustained Release Related to Relapse?

Sidney Zisook, M.D., *Department of Psychiatry, UCSD, 9500 Gilman Drive, # 0603R, La Jolla, CA 92095*; Barbara Haight, Pharm.D., Carolyn B. Watson, Ph.D., Michael Ames, Ph.D., Carol Rockett, Pharm.D., Alan Metz, M.D.

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Conclusion: Early response to SR appears to be both real and enduring. Most early responders achieve full remission by the end of 8 weeks and early responders who continue treatment with SR are no more likely than later responders to relapse over the next year. Similarly, there is no relationship between degree of response and likelihood of relapse over the next year of treatment. Therefore, responders who continue to have residual symptoms after acute treatment with SR may be good candidates for continued treatment over the next year.

NR243 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Olanzapine-Fluoxentine Combination for Psychotic Major Depression

Sanjay Dube, M.D., *Eli Lilly & Company, Lilly Corporate Center, Indianapolis, IN 46284*; Scott W. Andersen, M.S., Todd M. Sanger, Ph.D., Judith Hostetler, R.N., Mauricio F. Tohen, M.D., Gary D. Tollefson, M.D.

Summary:

Background: Between 16 to 54% of adults with major depression have psychotic features[1] antidepressant combinations have been shown more effective than monotherapies for reducing depressive symptoms[2].

Methods: Two parallel, 8-week double-blind trials with an optional 48-week open-label extension phase compared olanzapine-fluoxetine combination (OFC) to olanzapine or placebo in psychotic depression (PD). PD patients (n = 249) were randomized to the three treatment groups. Efficacy was evaluated with the HAMD-24.

Results: Pooled data showed OFC patients achieved a greater mean total score decrease (–18.3) than olanzapine (–14.4, p = 0.072) and placebo (–11.4, p = 0.001) patients. The response rate for OFC patients at endpoint (≥50% total score decrease) was significantly greater (56%) than that of either olanzapine (36%) or placebo (30%) patients. The median time to response for OFC patients was significantly better (12 days) than placebo (20 days), and equal to olanzapine (12 days). In the open-label extension, 71% of OFC responders maintained response. Significantly more OFC partial responders (≥25% total score decrease at 2 weeks) attained a full endpoint response compared with olanzapine or placebo (64%, 35%, 32%) responders.

Conclusion: OFC demonstrated greater improvement in depressive symptoms and a greater rate of response than olanzapine or placebo. Approximately three-fourths of acute OFC responders maintained a long-term response.

NR244 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Meta-Analysis of Olanzapine-Fluoxetine in Treatment-Resistant Depression

Sanjay Dube, M.D., *Eli Lilly & Company, Lilly Corporate Center, Indianapolis, IN 46284*; Scott W. Andersen, M.S., Sofia Paul,

Ph.D., Sara A. Corya, M.D., Luann E. Van Campen, Ph.D., Todd M. Sanger, Ph.D., Gary D. Tollefson, M.D.

Summary:

Background: Up to 30% of patients with major depression are resistant to conventional antidepressant treatment[1]. Subsequent therapy may include augmenting an antidepressant with an antipsychotic to enhance treatment effect[2]. The efficacy of olanzapine-fluoxetine combination (OFC) was compared with component monotherapies for patients with treatment-resistant depression (TRD). TRD was defined as a retrospective SSRI failure and a prospective non-SSRI failure.

Methods: A metanalysis was performed on one 8-week, and one 12-week double-blind study. Subjects (n = 797) with non-bipolar, TRD without psychotic features were randomized to OFC, or olanzapine or fluoxetine monotherapy treatment groups. MADRS was the primary efficacy measure.

Results: OFC patients achieved significantly greater total score improvement at Week 1 (–7.31) than olanzapine (–5.18, $p = 0.013$) or fluoxetine (–5.26, $p = 0.004$) patients and maintained the significant effect throughout 8 weeks of treatment (–11.60; –7.55, $p < 0.001$; –8.73, $p < 0.001$). OFC patients had a significantly greater endpoint response rate than olanzapine (37.3%, 21.1%) patients and significantly greater endpoint remission rates than olanzapine or fluoxetine (24.9%, 13.1%, 15.2%).

Conclusion: OFC showed rapid improvement in depressive symptoms by Week 1 of treatment and sustained treatment effect throughout 8 weeks of therapy. The combination demonstrated significant advantage over either component monotherapy, and represents a promising treatment strategy for patients with TRD.

NR245 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Validity of the Mood Disorders Questionnaire in the U.S.

Robert M.A. Hirschfeld, M.D., *Psychiatry & Behavioral Science, University of Texas Medical Branch, 301 University Boulevard, Galveston, TX 77555-0188*; Charles Holzer, Ph.D., Joseph R. Calabrese, M.D., Mark A. Frye, M.D., Paul E. Keck, Jr., M.D., Myrna M. Weissman, Ph.D.

Summary:

Background: The Mood Disorders Questionnaire (MDQ), a screening instrument for bipolar spectrum disorders (BSD) (i.e. Bipolar I, Bipolar II, and Bipolar NOS), was previously validated in a psychiatric outpatient population.

Objective: To test the validity of the MDQ in the general United States (US) population.

Method: 695 subjects were selected from a nationally representative sample of 85,358 participants in a US epidemiology study of BSD. The sample was balanced for MDQ score (0–13) and 2000 US Census data. Subjects were contacted by telephone, from January to August 2001, and completed a SCID diagnostic interview with a researcher blinded to MDQ scores. Sensitivity and specificity, relative to SCID diagnosis, were calculated for each MDQ score and were plotted as a Receiver Operating Characteristics Curve. Sensitivity equaled the percent of criterion standard diagnoses correctly diagnosed by the MDQ, and specificity equaled the percent of criterion standard non-cases correctly identified by the MDQ.

Results: MDQ sensitivity was 0.81 and specificity was 0.65.

Conclusion: The MDQ is a valid screening instrument for BSD in the general US population.

NR246 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

The Early Efficacy and Safety of Oral Loaded Divalproex Sodium in the Treatment of Acute Mania in Bipolar Patients

Robert M.A. Hirschfeld, M.D., *Psychiatry & Behavioral Science, University of Texas Medical Branch, 301 University Boulevard, Galveston, TX 77555-0188*; Jeff D. Baker, Ph.D., Kenneth Sommerville, M.D.

Summary:

Objective: Although previous studies have examined the safety and tolerability of oral loaded divalproex sodium in the treatment of acute mania,[1,2] no studies have examined the efficacy of this dosing strategy. The purpose of this analysis was to evaluate the early efficacy of oral loaded divalproex.

Method: This study combined subjects from three randomized, double-blind, parallel group, active or placebo controlled studies to compare the efficacy, safety and tolerability of oral loaded divalproex compared with standard titration divalproex, lithium, olanzapine and placebo. Subjects were inpatients diagnosed with acute mania associated with bipolar disorder. Patients were administered oral loaded divalproex (20 or 30 mg/kg/day on days 1 and 2), standard titration divalproex (250 mg tid starting dose), lithium (900 mg starting dose), olanzapine (10 mg starting dose), or placebo. The oral loaded divalproex group was compared to all other groups on the Mania Rating Scale using analysis of variance. Safety and tolerability were assessed by monitoring adverse events, laboratory parameters, and weight gain.

Results: The results indicated an early efficacy advantage for oral loaded divalproex compared to standard titration divalproex at day 5, 7/8, and 10 and superior efficacy to lithium on days 5 and 7/8. There were no efficacy differences between divalproex loading and olanzapine. Divalproex loading was superior in efficacy to placebo at all data points. Divalproex loading was as well tolerated or better tolerated than all other groups.

Conclusions: These results suggest the oral loading of divalproex leads to a more rapid anti-manic effect when compared with standard titration divalproex, lithium, or placebo and is as well or better tolerated than each of these groups or olanzapine.

NR247 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Prevalence of Bipolar Spectrum Disorders in U.S. Adults

Robert M.A. Hirschfeld, M.D., *Psychiatry & Behavioral Science, University of Texas Medical Branch, 301 University Boulevard, Galveston, TX 77555-0188*; Joseph R. Calabrese, M.D., Myrna M. Weissman, Ph.D., Mark A. Frye, M.D., Paul E. Keck, Jr., M.D., Karen D. Wagner, M.D.

Summary:

Objective: To determine the prevalence of bipolar spectrum disorders (BSD) in the United States (US).

Methods: The Mood Disorder Questionnaire (MDQ) was mailed to a representative sample of 127,800 US adults. Samples were balanced with 2000 US Census data for age, gender, region, market size, and household size. A sub-sample of non-responders was re-surveyed by telephone. A positive MDQ was defined as seven or more symptoms, co-occurrence of two or more symptoms, and moderate or severe impairment.

Results: Response rate was 67% (85,358 returns). After weighting, the prevalence was 3.3%. Non-responders had a prevalence rate of 4.6% ($p < 0.05$). Adjusting for non-response bias, overall prevalence was 3.7%. Prevalence was highest among the young (18–24 years: 9%), American Indians (7.6%) and African-Americans (4.3%), rural areas (4%), small cities (4%), and lower incomes (<$20,000: 6%). Only 19.8% of MDQ-positive subjects

reported a diagnosis of bipolar disorder; 48% of MDQ-positive subjects reported a diagnosis of unipolar depression.

Conclusions: The US prevalence of BSD is three times that previously reported for Bipolar 1 Disorder. Only one in five positive subjects reported a diagnosis of BSD, nearly half reported a diagnosis of unipolar depression. These finding suggest that BSD is under-recognized and underdiagnosed.

NR248 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Double-Blind, Placebo-Controlled Study of Sertraline in Premenstrual Syndrome

Susan G. Kornstein, M.D., *Department of Psychiatry, Virginia Commonwealth University, P.O. Box 980710, Richmond, VA 23298*; John A. Gillespie, M.D.

Summary:

Objective: The objective of this study was to evaluate the safety and efficacy of sertraline in the treatment of premenstrual syndrome (PMS).

Methods: 314 women (mean age, 36 years) with PMS from 22 US sites were randomly assigned to fixed-dose treatment with sertraline (25 or 50 mg/day) or placebo for 4 menstrual cycles after a single-blind placebo lead-in cycle. Patients were treated sequentially using 3 different dosing strategies: luteal phase (2 cycles), followed by continuous dosing throughout the month (1 cycle), followed by dosing begun at the first onset of PMS symptoms (1 cycle of "symptom-onset" dosing). Assessments included the Daily Symptom Report (DSR) and the Clinical Global Impressions rating of Improvement (CGI-I).

Results: Both doses of sertraline showed significant ($p < 0.05$) efficacy compared to placebo on a repeated measures analysis of the DSR and CGI-1 for the 2 luteal phase dosing cycles. An ANCOVA found the 25 mg dose of sertraline to be significantly superior to placebo using both continuous dosing and symptom-onset dosing. In contrast, the 50 mg dose of sertraline did not consistently show significant efficacy using either continuous or symptom-onset dosing.

Conclusions: Overall, sertraline was a well-tolerated and significantly effective treatment of PMS even in doses as low as 25 mg.

NR249 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Gender Differences in Response to Combination Treatment for Chronic Depression

Susan G. Kornstein, M.D., *Department of Psychiatry, Virginia Commonwealth University, P.O. Box 980710, Richmond, VA 23298*; Alan F. Schatzberg, M.D., Michael E. Thase, M.D., Dace Svikis, Ph.D., Alan J. Gelenberg, M.D., Gabor I. Keitner, M.D., Frances E. Borian, R.N.

Summary:

Objectives: Previous studies have shown the benefit of combination treatment over psychotherapy alone in depressed men but not in depressed women. This difference may have been due to the use of tricyclic antidepressants in these studies, since women tend to respond poorly to this class of medication. This study examines gender differences in response to combination treatment with nefazodone and Cognitive-Behavioral Analysis System of Psychotherapy (CBASP) compared to either monotherapy for the treatment of chronic forms of major depression.

Methods: A total of 445 female and 236 male outpatients between the ages of 18 and 75 with chronic depression (i.e., chronic major depression, double depression, or recurrent major depression with incomplete interepisode recovery) were randomly assigned to 12 weeks of treatment with either nefazodone, CBASP, or their combination. All participants had a 24-item HAM-D score of at least 20 at baseline. Treatment response was defined as a 50% decrease in HAM-D score and HAM-D ≤15. Remission was defined as a HAM-D ≤8.

Results: In both males and females, response and remission rates for combination treatment were dramatically higher than for either monotherapy, and these differences were all highly statistically significant using both completer and intent-to-treat analyses. There were no statistically significant differences by gender in dropout rates or in response rates to each of the three treatments.

Conclusions: In contrast to previous studies, these results suggest that both men and women with chronic depression show an advantage to combination treatment with nefazodone and CBASP over either treatment alone.

NR250 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Effect of Antidepressant Drugs on Responses to Thyrotropin and Apomorphine Tests

Fabrice Duval, M.D., *Department of Psychiatry, Centre Hospitalier, 27 Rue du 4eme RSM, Rouffach 68250, France*; Jose Monreal, M.D., M. Claude Mokrani, Ph.D., Marc-Antoine Crocq, M.D., Jean-Paul Macher, M.D.

Summary:

Background: The aim of this study was to determine whether changes that may occur during antidepressant treatment in hypothalamic-pituitary-thyroid (HPT) activity and dopaminergic (DA) function are related to a direct effect of the drug or to a change in clinical state.

Method: We measured thyrotropin (TSH) and prolactin (PRL) responses to 8 AM and 11 PM TRH tests (200μg, IV), and PRL, adrenocorticotropin (ACTH), cortisol and growth hormone (GH) responses to the direct DA receptor agonist agent apomorphine (APO 0.75 mg, s.c.) in 10 drug-free, DSM-IV major depressed inpatients and 11 hospitalized healthy control subjects. Results at baseline were compared with those after two weeks and one month of antidepressant treatment with either veniafaxine or tianeptine.

Results: Clinical efficacy did not differ between the two antidepressant drugs. Compared with controls, patients demonstrated at baseline lower TRH-TSH responses (8 AM-ΔTSH, $p < 0.05$; 11 PM-ΔTSH, $p < 0.01$; and lower difference between 11 PM-ΔTSH and 8 AM-ΔTSH [ΔΔTSH], $p = 0.01$). Pretreatment TRH-PRL and APO responses were comparable between patients and controls. After two weeks of treatment, post-APO ACTH and cortisol levels were increased compared with pretreatment values ($p = 0.06$ and $p = 0.05$, respectively); however, after four weeks of treatment this difference was not found. ΔΔTSH values increased significantly after four weeks treatment ($p = 0.02$) and were negatively correlated with Hamilton Depression Rating Scale score ($rho = -0.83$; $p < 0.03$).

Conclusions: These results suggest that chronobiological changes in HPT axis activity are a state-related marker, while transient changes in dopaminergic function are related to an effect of the antidepressant drugs.

NR251 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

The Relationship Between Somatic Symptoms and Depression

John W. Denninger, M.D., *Department of Psychiatry, Massachusetts General Hospital, WACC 812, 15 Parkman Street, Boston, MA 02114*; Yasmin Mahal, B.A., Wedelien Merens, M.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Albert Yeung, M.D. Maurizio Fava, M.D.

Summary:

Background: Among patients suffering with major depressive disorder (MDD), physical and somatic symptoms are associated

with a high degree of disability and health care utilization; however, very little is known about the relationship between these symptoms and their changes during antidepressant treatment.

Objective: To evaluate the relationship between somatic symptoms and depression among outpatients with MDD.

Methods: We studied 148 outpatients with MDD (mean age = 40.9, 85 women and 63 men, mean initial HAM-D-17 score 19.6 ± 3.3) by administering the Symptom Questionnaire (SQ) Somatic Symptom Scale before and after 8 weeks of open treatment with fluoxetine 20 mg/day.

Results: The mean SQ Somatic Symptom Scale scores decreased significantly (paired $t = 7.2$, $p < .0001$) following fluoxetine treatment from a mean of 9.4 ± 5.8 to 6.2 ± 5.3. The degree of reduction in somatic symptoms was significantly ($R = 0.345$, $p < .0001$) correlated with the degree of improvement in depressive symptoms as measured by the HAM-D-17. Among responders (50% or greater reduction in HAM-D-17 from baseline), those who achieved remission (endpoint HAM-D-17 score ≤5, n = 50) had significantly ($F = 5.3$, $p < .03$) lower somatic symptom scores at endpoint (3.4 ± 3.4) compared to non-remitters (n = 45; 5.2 ± 4.2)

Conclusions: Our findings suggest that antidepressant treatment is followed by a significant reduction in somatic symptoms among MDD patients, and that the degree of somatic symptom improvement is related to the magnitude of depressive symptom reduction and to the likelihood of achieving remission.

NR252 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

A Double-Blind, Randomized Trial of St. John's Wort, Fluoxetine, and Placebo in MDD

Maurizio Fava, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WAC 812, Boston, MA 02114*; Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., David Mischoulon, M.D., Michael W. Otto, Ph.D., Harald Murck, M.D., John M. Zajecka, M.D., Jerrold F. Rosenbaum, M.D.

Summary:

Objective: To compare the antidepressant efficacy and safety of a standardized extract of St. John's Wort with both placebo and fluoxetine.

Method: Following a 1-week, single-blind wash-out, patients with SCID-diagnosed MDD were randomized to 12 weeks of double-blind treatment with LI 160 St.John's wort extract (900 mg/day), fluoxetine (20 mg/day), or placebo. The 17-item Hamilton Rating Scale for Depression (HAM-D) was the primary efficacy measure and ANCOVA was used to compare differences in endpoint HAM-D scores across the three treatment groups after adjusting for baseline HAM-D. Following an interim analysis of the study, conducted in two sites in the U.S. (Boston and Chicago), the sponsor (Lichtwer Pharma AG, Berlin, Germany) opted to close the study and to proceed with the final analyses carried out on a sample size smaller than the one originally planned (n = 180).

Results: 133 patients (56% women, mean age: 36.7; mean HAM-D: 19.8 ± 3.1) were randomized to double-blind treatment. ANCOVA analyses showed lower mean HAM-D scores at endpoint in the St. John's wort group (n = 47; 11.3 ± 6.9) compared to the fluoxetine group (n = 45; 14.4 ± 7.2; $t = 2.1$; $p < .04$) and a trend toward a similar finding relative to the placebo group (n = 41; 14.1 ±7.4; $t = 1.7$; $p = .086$). There was also a trend toward higher rates of remission (HAM-D < 8) in the St.John's wort group (32%) compared to the fluoxetine group (22%) and the placebo group (17%). Overall, St.John's wort appeared to be safe and well tolerated.

Conclusion: St. John's wort was significantly more effective than fluoxetine and showed a trend toward superiority over placebo. While a type I error and/or the relative underdosing of fluoxetine may have contributed to our findings with respect to the lesser efficacy of fluoxetine compared to St. John's wort, the (26%) smaller than planned sample size is likely to account for the lack of statistical significance for the advantage (indicating a moderate effect size, d = .45) of St.John's wort over placebo.

NR253 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Remission Rates During Long-Term of Depression Venlafaxine

Charles B. Nemeroff, M.D., *Department of Psychiatry, Emory University School of Medicine, 1639 Pierce Drive, Suite 4000, Atlanta, GA 30322*; A. Richard Entsuah, Ph.D., Nadia R. Kunz, Pharm.D.

Summary:

Objective: This reanalysis of data from a double-blind, multicenter recurrence prevention trial evaluated remission in outpatients with recurrent major depression who were treated with venlafaxine.

Methods: Patients who responded to venlafaxine 100 to 200 mg/day and remained relapse free during the 6-month, open-label period were randomly assigned to ≤12 months of venlafaxine or placebo. Of 495 patients entering acute treatment, 470 (95%) met intent-to-treat (ITT) criteria (baseline and ≥1 on-therapy 21-item Hamilton Rating Scale for Depression [HAM-D_{21}] score). In order to enter the double-blind phase, patients were required to have a HAM-D_{21} score <10, but after 180 days of acute treatment, the remission rate (HAM-D_{17}≤7) was 75% for the 286 completers and 53% for all patients (last observation carried forward [LOCF] analysis).

Results: Of 235 patients entering double-blind treatment, 213 (91%; 106 venlafaxine, 107 placebo) comprised the ITT group; LOCF analysis of 173 (81%; 91 venlafaxine, 82 placebo) with HAM-D_{17} score ≤7 at randomization showed remission was consistently significantly higher with venlafaxine than placebo after the first month. At the final on-therapy visit, in patients who remitted during open label, remission rates were 67% on venlafaxine vs 46% on placebo ($P < 0.01$).

Conclusion: Prophylactic venlafaxine treatment was significantly more effective than placebo substitution in maintaining achieved remission over 12 months.

NR254 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Duration of Untreated Illness and Clinical Course in Bipolar Disorder

Emanuela Mundo, M.D., *Department of Psychiatry, University of Milan, Ospedaleluigisacco Viagbgrassi 74, Milan 20145, Italy*; Daniele Salvadori, M.D., Donato Madaro, M.D., Roberta Bassetti, M.D., Carlo A. Altamura, M.D.

Summary:

Objective: The primary aim of this study was to investigate the effects of the duration of untreated illness (DUI) on the clinical course of bipolar disorder (BD). We hypothesized that a longer DUI was correlated with a more sever course of BD, as identified by a higher rate of comorbid Axis I diagnoses, and a higher number of hospitalizations.

Methods: Thirty-six patients (18 men, 18 women) with a DSM-IV diagnosis of BD I or BD II, with a mean age of 49.06 (12.9 sd) years, age at onset of 31.8 (10.3sd) years, and a well-documented good compliance to mood stabilizers were studied. All patients had been diagnosed with the administration of the SCID-I and gave their informed consent to participate into the study. The DUI was defined as the time between the onset of BD and the beginning of treatment with mood stabilizers. The main clinical variables were tabulated and compared between patients with DUI ≤1 year and patients with DUI >1 year (chi-square tests and t-tests).

Results: BD patients with DUI >1 year (N = 25) were more likely to have comorbid anxiety disorders (chi-square = 17.429, df = 1, $p < 0.0001$) or comorbid substance abuse or dependence (chi-square = 4.092, df = 1, $p < 0.05$). In addition, seven patients had a rapid cycling course and all had a DUI >1 year. With respect to the other clinical variables investigated no significant differences were found.

Conclusions: The clinical implications of these preliminary results with particular respect to the importance of early pharmacological intervention with mood stabilizers in BD will be discussed.

NR255 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Reboxetine Effects on Cognitive Functioning in Depressed Patients

James M. Ferguson, M.D., *Pharmacology Research Clinic, 448 East Winchester Street #, Salt Lake City, UT 84107–8525*; Keith A. Wesnes, Ph.D., Gerri E. Schwartz, M.D.

Summary:

Objective: There has been speculation that catecholamines might enhance cognitive functioning. The availability of reboxetine, a selective noradrenaline reuptake inhibitor, has provided an opportunity to test this hypothesis.

Methods: Seventy-four depressed patients were recruited as part of a large multicentre study comparing reboxetine to paroxetine and placebo. Patients were administered a selection of tests (including choice reaction time, digit vigilance, simple reaction time, numeric working memory and word recognition) from the Cognitive Drug Research computerised test system at screening, baseline, Day 14 and Day 56.

Results: Patients receiving reboxetine showed significant improvements in their speed of cognitive functioning ($p = 0.024$) and ability to sustain concentration ($p = 0.023$) at Day 56 compared to baseline. No significant changes or trends in this direction were seen in patients taking either placebo or paroxetine.

Conclusion: Despite the small number of patients tested, by Day 56 reboxetine had significantly improved performance on two composite scores, one reflecting the ability to sustain attention and the other the speed of cognitive processing. At this time point there was no statistical evidence that either placebo or paroxetine had altered performance. Reboxetine appears to have a more positive effect on cognitive function than was seen for either of the other conditions.

NR256 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Oxcarbazepine: Review of 200 Subjects Treated for Mania in a Hospital Setting

Michael J. Reinstein, M.D., *Department of Psychiatric Research, Forest Foundation, 4755 North Kenmore Avenue, Chicago, IL 60640*; John G. Sonnenberg, Ph.D., Sangarapillai C. Mohan, M.D., Maxim A. Chasanov, M.D., Arkady Koltun, M.D., Polina Reyngold, M.A., Robert M. Wishner, R.Ph.

Summary:

Oxcarbazapine (OXC), and anti-convulsant agent, has shown utility as an anti-manic agent. A retrospective review of 200 subjects undergoing initial treatment with OXC for acute mania in a hospital setting has affirmed previous positive findings. At the time of discharge, 194 of the original 200 subjects remained on OXC and demonstrated an improvement in manic symptoms. The dose range for OXC was 600–3000mg daily. No subjects were discontinued due to dose-related side effects or cognitive/neuropsychiatric adverse events. These included screening for psychomotor slowing, impaired concentration, speech or language problems, somnolence or fatigue, or coordination abnormalities including ataxia and gait disturbances. Of the 200 subjects, 3 were discontinued for hyponatremia (sodium < 125mmol/L) within 3 days of initiating treatment with OXC. Nineteen subjects were flagged for potential drug-drug interactions. Of these, 3 were discontinued due to concomitant treatment with oral birth control. The remaining 16 were on calcium channel blockers and were monitored for blood pressure changes. No significant blood pressure increases were measured and all 16 subjects remained on OXC and their calcium channel blockers. The hospital's director of pharmacy reported that the criteria for an Adverse Drug Reaction was not met for any of the 200 subjects treated with OXC. In sum, OXC merits continued study as an efficatious and well-tolerated option for the treatment of mania.

NR257 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Postmortem Dopamine Alterations in Human Cocaine Users Mood Disorders

Karley Y. Little, M.D., *Department of Psychiatry, University of Michigan, 116-A, Psychobiology, AAVAMC, Ann Arbor, MI 48105*; Joshua O. Scheys, B.S., Lian Zhang, Ph.D.

Summary:

Striatal dopamine transporter (DAT) binding sites are increased, while vesicular monoamine transporter (VMAT2) binding sites, VMAT2 immunoreactivity, and total dopamine levels are decreased in post mortem samples from human cocaine users. Increased DAT function may contribute to cocaine binging and withdrawal anhedonia, while overall dopamine neuronal dysfunction may contribute to less modulated reward experience and craving. The present study examined post mortem samples from 7 subjects with cocaine-induced mood disorders, 26 cocaine users without mood disorder, and matched controls. Clinically, cocaine dependent subjects with coexisting cocaine-induced mood disorders display more severe cocaine-induced behavioral disorders and may be at increased risk for suicide during withdrawal.

Striatal DAT binding was assayed autoradiographically employing [^{3}H]WIN 35428 (100 nM) while striatal VMAT2 binding was assayed with [^{3}H]DTBZ (10 nM). VMAT2 immunoreactivity was assayed using a highly specific antibody (Chemicon, Inc, Temecula, CA). Total striatal dopamine levels were assayed using HPLC. Cocaine dependent subjects who were not clinically depressed displayed mild dopamine alterations including increased DAT levels. Subjects with mood disorders showed greater dopamine dysfunction, including increased DAT synthesis and plasma membrane trafficking. Mood disordered subjects were not more cocaine dependent, but rather displayed a unique adaptation to cocaine exposure.

NR258 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Mood Changes in Patients with Bipolar Disorder Taking or not Taking Antidepressants

Michael Bauer, M.D., *Department of Psychiatry, UCLA, 300 UCLA Medical Plaza, Suit 2330, Los Angeles, CA 90024*; Tasha Glenn, Peter C. Whybrow, M.D.

Summary:

Objective: With the risk for antidepressants to induce mania or rapid cycling unclear, mood patterns in a population with bipolar disorder (BP) taking or not taking antidepressants were analyzed.

Methods: 38 patients (mean age 38.3, 12 males, 26 females) with a diagnosis of BP I or II entered mood, medications and sleep into software (ChronoRecord) on a home computer for 3 months. Data from 17 patients not taking antidepressants (1721 days) and 21 patients taking antidepressants (2201 days) were analyzed by group and by individual. The groups were compared for the frequency of switches between depressed, normal and manic, distribution of these switches, change in mood from one day to

the next for a lag of 1–3 days, overall percent of days normal and overall percent of days with no mood change. The individuals were compared for the total number of mood switches.

Results: There was no statistically significant difference in age, diagnosis and gender between the groups. The group taking antidepressants took more Depakote ($p = .018$); no other difference in medications was found. No patients took tricyclics. No statistically significant differences were found on any test of mood switches between the groups or individuals.

Conclusion: No statistically significant differences were found in the mood changes of those taking or not taking antidepressants.

NR259 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Meta-Analysis of Sertraline Versus Fluoxetine in Major Depression

Alan D. Feiger, M.D., *Feiger Health Research Center, 3555 Lutheran Parkway #320, Wheat Ridge, CO 80033-6021*; John A. Gillespie, M.D.

Summary:

Objective: To increase the power to detect efficacy in clinically relevant subgroups, a mega-analysis of pooled data was conducted.

Method: Data were pooled from 8 double-blind, head-to-head studies comparing sertraline and fluoxetine. A "mega-analysis" (Thase et al, Arch Gen Psych, 1997) was conducted on the anxious depression subgroup (defined by a HAM-D-anxiety-somatization factor score ≥ 7), and a high severity subgroup (defined by a 17-item HAM-D total score ≥ 26).

Results: A total of 1,706 patients (65% female; mean age, 49 yrs; baseline HAM-D, 22.7) were randomized to receive at least 6 weeks of double-blind treatment. In the anxious depression subgroup, HAM-D responders (>50% reduction in HAM-D) for sertraline vs. fluoxetine were 72% vs. 64% ($p < 0.05$). In the severe depression subgroup, HAM-D responder rates were 72% vs. 56% ($p < 0.02$). A Cox regression analysis found sertraline treatment to be associated with a significantly ($p < 0.05$) higher likelihood of response (CGI-I ≤ 2) and remission (CGI-I = 1) than fluoxetine.

Conclusion: Mega-analysis represents a promising new method for identifying meaningful clinical differences in the efficacy and tolerability of various antidepressants.

NR260 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Personality Disorders and Depression

Amy H. Farabaugh, M.A., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WAC-812, Boston, MA 02114*; Pamela A. Roffi, B.S., Nicole B. Neault, B.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Shamsah B. Sonawalla, M.D., Maurizio Fava, M.D.

Summary:

Objective: To evaluate changes in personality disorder traits among depressed outpatients undergoing treatment with the antidepressant fluoxetine.

Method: We assessed 307 consecutive outpatients (165 women; mean age: 40.0) with major depressive disorder diagnosed with the SCID-P. Patients were administered the clinician-rated SCID-II for personality disorders before and after 8 weeks of open treatment with fluoxetine 20 mg/day. Personality disorder traits were measured as the number of items endorsed for each specific diagnosis. The paired t-test was used to evaluate the change in number of items endorsed, while the simple linear regression method was used to evaluate the relationships between the change in number of items endorsed and the percent change from baseline in depression severity (as measured by the HAM-D-17). The Bonferroni correction was used to adjust for multiple comparisons.

Results: Following treatment with fluoxetine, we observed a statistically significant (after Bonferroni correction) reduction in the number of items endorsed for the following personality disorder diagnoses: avoidant, dependent, obsessive-compulsive, passive-aggressive, self-defeating, paranoid, schizotypal, narcissistic, and borderline. We also found a statistically significant relationship (after Bonferroni correction) between the change in number of items endorsed and the percent change from baseline in HAM-D-17 score for the following diagnoses (avoidant, r:0.18; dependent, r:0.24; paranoid, r:0.18; narcissistic, r:0.22; borderline, r:0.25).

Conclusions: Our results suggest that significant reductions in personality disorder traits occur among depressed outpatients following treatment with the antidepressant fluoxetine. These reductions appear to be somewhat related to the change in depression severity, but other factors, including a direct effect of fluoxetine itself, may contribute to such changes.

NR261 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Functioning and Interpersonal Relationships as Predictors of Response in Treatment-Resistant Depression

George Papakostas, M.D., *Department of Psychiatry, Massachusetts General Hospital, WACC 812, 15 Parkman Street, Boston, MA 02114*; Timothy J. Petersen, Ph.D., David Mischoulon, M.D., Megan E. Hughes, B.A., Jonathan E. Alpert, M.D., Maurizio Fava, M.D., Andrew A. Nierenberg, M.D.

Summary:

Objective: The purpose of this study is to examine whether occupational functioning or the quality of interpersonal relationships is predictive of clinical response to a 6-week open trial of nortriptyline (NT) in patients with treatment resistant depression (TRD).

Methods: 92 subjects with TRD were treated openly with NT for 6 weeks. The longitudinal interval follow-up evaluation (LIFE) scale was administered at baseline. A logistic regression was performed using occupational functioning and interpersonal relationships (over the past month and over the past 5 years) as predictors of treatment response. Unpaired t-tests were performed to examine mean composite LIFE score values between responders and nonresponders. The composite scores that were statistically significant were used as single predictors of treatment status in separate logistic regression equations.

Results: Better occupational function over the past five years predicted better response to treatment with NT in patients with TRD.

Conclusions: Beyond a history of non-response to antidepressants, long-term occupational function may be a predictor of outcome in the treatment of TRD.

NR262 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Dysthymia and Quality of Life: Review of Data from Controlled Treatment Studies

Arun V. Ravindran, M.D., *Department of Psychiatry, University of Ottawa, 451 Smyth Road Room 3207, Ottawa, ON K12 7K4, Canada*; John A. Gillespie, M.D.

Summary:

Objective: One of the least well-studied dimensions of dysthymia is its impact on quality of life and functioning. We report here the results of a critical review of the published dysthymia literature relating to its effect on QOL and functioning, and their improvement with treatment.

Method: A search of the dysthymia literature was conducted back to 1966 using both Medline and Embase for reports of randomized, double-blind treatment studies. Studies were included in this review if any validated quality of life or functioning measure was utilized.

Results: The literature review yielded seven published studies that met search criteria, and one that is yet to be published, but has been presented as a poster. Baseline QOL and functional assessments consistently found impairments. Treatment yielded improvement in both QOL and functional measures that was surprisingly rapid given the chronicity of the depression. Cognitive-behavioral therapy was also associated with QOL improvement, but did not substantially enhance the efficacy of sertraline, which is the antidepressant that has the most well-established efficacy in the treatment of dysthymic disorder.

Conclusion: Dysthymic disorder is associated with a moderate impairment in QOL that is rapidly responsive to acute treatment intervention despite the chronicity of the illness. Much more research is needed to establish optimal treatment strategies for this often overlooked and understudied illness.

NR263 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Comorbid Medical Illness and Relapse of MDD

Dan V. Iosifescu, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114*; Robert L. Gresham, B.A., Heidi D. Montoya, B.A., Christina M. Dording, M.D., Andrew A. Nierenberg, M.D., Roy H. Perlis, M.D., Maurizio Fava, M.D.

Summary:

Objective: We examined the impact of medical comorbidity on the rate of relapse of major depressive disorder (MDD) and on changes in psychological symptoms during 28-week continuation therapy with the antidepressant fluoxetine.

Methods: We studied 114 outpatients meeting DSM-IV criteria for MDD (52 women and 62 men; mean age: 39.8 years) who entered the continuation phase of an antidepressant treatment study. Patients had achieved remission [defined as a 17-item Hamilton Rating Scale for Depression (HAM-D-17) score <8] after eight weeks of treatment with fluoxetine 20 mg/day. We utilized the Cumulative Illness Rating Scale (CIRS) to measure the baseline severity of medical comorbidity (SMC) for each patient, blind to treatment outcome. Patients were followed for 28 weeks of continued treatment with fluoxetine 40 mg/day to monitor for possible depressive relapses and for possible changes in psychological symptoms, measured by the HAM-D-17 and by Kellner's Symptom Questionnaire (including four scales of anxiety, depression, anger/hostility, and somatic symptoms). We used logistic regression to assess the relationship between relapse and severity of medical comorbidity (range: 0–8) and we used the simple linear regression to evaluate the relationship between severity of medical comorbidity and changes in severity of psychological symptoms (HAM-D-17 and SQ scale scores) from the beginning of the continuation phase to endpoint.

Results: 43 patients (38%) did not complete and 8 patients (7%) relapsed during the 28-week continuation phase. Higher scores on the CIRS (indicating greater severity of medical comorbidity) significantly predicted relapse of MDD ($p < .02$), and were also significantly related to higher endpoint Ham-D-17 scores ($p < 0.003$) and to increases in Ham-D-17 scores ($p < .002$), SQ Depression scores ($p < .004$), and SQ Anger/Hostility scores ($p < .008$) during the continuation phase of fluoxetine treatment.

Conclusion: Comorbid medical illness appears to increase the rates of relapse of major depressive disorder during continuation therapy with the antidepressant fluoxetine. The severity of medical comorbidity is also directly related to worsening of depressive and anger/hostility symptoms during follow-up.

NR264 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Prevalence of Major Affective Disorders in Persons with Epilepsy

David Blum, M.D., *GlaxoSmithkline, 5 Moore Drive, Res. Triangle Pk, NC 27709*; Robert M.A. Hirschfeld, M.D., Joseph R. Calabrese, M.D., Michael Reed, Ph.D., Alan Metz, M.D.

Summary:

Background: Depressive symptoms are common in persons with epilepsy (PWE). The prevalence of bipolar symptomatology is unknown.

Methods: We conducted a mail survey of subjects selected from the US general population. The MDQ questionnaire can indicate a likelihood of bipolar based on presence and severity of manic and/or hypomanic symptoms. 180,996 persons or proxies responded. 2,281 indicated a diagnosis of either "epilepsy" or "seizure disorder." Responses were tested by chi-square statistic.

Results: 39% of PWE had been diagnosed with major depression. This was higher than the rates for the general population (8.7%), diabetes (17%) or asthma (16%), $p < 0.00001$. Bipolar depression had been diagnosed in 9.8% of PWE, higher than in the general population (1.2%), diabetes (2.6%) or asthma (2.7%), $p < 0.0001$ each. PWE had substantially higher positive responses to all surveyed manic/hypomanic symptoms, with 8.1% of PWE reaching a diagnostic threshold on the MDQ compared with 2.1% in the general population, 3.9% in asthma, 3.0% in diabetes ($p < 0.0001$ each).

Conclusions: Affective disorders and bipolar symptoms are more common in epilepsy than in the general population or than in some other chronic ailments. Manic/hypomanic symptomatology is more common in PWE than in any of the other groups studied.

NR265 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Lithium as a Mood Stabilizer: Fifty Years Later

Ronald R. Fieve, M.D., *Columbia Univ/Psychiatry, New York State Psych Inst, 722 West 168th Street Unit 118, New York, NY 10032-2603*; Lenard A. Adler, M.D., Michael H. Allen, M.D., John M. Zajecka, M.D., Vivek Kusumakar, M.D., John A. Ascher, M.D., Nancy L. Earl, M.D.

Summary:

Objective: Two 18-month, double-blind trials (GW605/GW606) were conducted to assess the efficacy and tolerability of lithium and lamotrigine versus placebo as maintenance treatments in bipolar I patients.

Methods: Study design was identical for both trials with one enrolling recently manic or hypomanic patients and the second trial enrolling recently depressed patients. During the 8- to 16-week open-label phase lamotrigine therapy was initiated while other psychotropic drugs were discontinued. Patients were then randomized to lithium (0.8 to 1.1mEq/L), lamotrigine (50mg, 200mg or 400mg daily), or placebo. Individual study results were prospectively designed to be combined for analysis.

Results: Of the 1315 patients meeting screening criteria, 588 patients met stabilization criteria and were randomized to a maintenance treatment ($n = 167$ for lithium). Lithium was superior to placebo at prolonging the time to intervention for any mood episode and overall survival in study. Lithium was also superior to placebo at prolonging the time to a manic, hypomanic or mixed episode but not for depressed episodes.

Conclusions: Lithium continues to be an effective mood stabilizer particularly in patients experiencing a manic, hypomanic or mixed episode. These are the first successful long-term maintenance studies for lithium that avoid enrichment for lithium responders.

NR266 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Sustained Cognitive Benefits of Galantamine in Alzheimer's Disease

Murray A. Raskind, M.D., *Department of Psychiatry, VA Puget Sound Medical Center, 1660 South Columbian Way, 116A, Seattle, WA 98108*

Summary:

Objective: To evaluate the cognitive efficacy of galantamine over 36 months in mild-to-moderate AD patients.

Methods: In 2 double-blind trials (6-month US and 3-month international trial), AD patients were randomized to placebo or galantamine (24 or 32 mg/day). At the end of the double-blind period, all patients in the US trial and all US participants in the international trial were eligible to receive galantamine (24 mg/day) for an additional 30 and 31.5 months, respectively, in an open-label extension study. The primary efficacy measure was the AD Assessment Scale-cognitive subscale (ADAS-cog). ADAS-cog scores were compared against a 36-month extrapolation of the natural cognitive decline observed in a 12-month historical placeboe group with similar patient entry criteria and baseline characteristics and an estimation of decline using the Stern equation.

Results: Patients receiving galantamine showed sustained cognitive benefits for the 36-month period. Patients treated with galantamine maintained ADAS-cog scores at or above baseline for the first 12 months, and gained approximately 18 months in preservation of cognition versus the decline projected for untreated patients.

Conclusions: The cognitive benefits of galantamine are sustained for at least 36 months versus the expected decline in untreated AD patients. At endpoint, cognitive decline was delayed by approximately 18 months versus the expected decline in untreated patients.

NR267 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Negative Affective Traits and Openness Have Differential Relationships to Creativity

Connie M. Strong, M.S., *Department of Psychiatry, Stanford University, 401 Quarry Road, Room 2124, Stanford, CA 94305-5723*; Terence A. Ketter, M.D.

Summary:

Objective: To investigate relationships between temperament/personality traits and creativity in a heterogeneous sample of 48 euthymic bipolar disorder patients (BP), 25 euthymic (unipolar) major depressive disorder patients (UP), 47 healthy controls (HC), and 32 creative discipline graduate student controls (CC).

Method: Five personality/temperament factors derived from 16 variables from the NEO Personality Inventory, Cloninger's Temperament and Character Inventory, and Akiskal's Affective Temperament Scale were correlated with Barron-Weish Art Scale (BWAS), Adjective Check List Creative Personality Scale (ACL-CPS), and the Torrance Tests of Creative Thinking scores, covarying for age and gender effects.

Results: Two factors, "Negative Affective Traits" (NAT, including neuroticism, dysthymia, cyclothymia, and irritability), and "Openness" (from the NEO) had significant relationships with creativity. NAT had equal and opposite ($r = .35$, $r = -.35$) correlations with BWAS and ACL-CPS. Openness correlated with ACL-CPS ($r = .48$), and NAT ($r = .34$).

Conclusion: NAT appeared related to better BWAS performance, but worse ACL-CPS scores. Openness was associated to better ACL-CPS scores, consistent with its relationship to diverse creativity measures in prior studies. NAT, although associated with Openness, appeared to have dramatically differential relationships with creativity measures, and thus could be an important additional factor amongst the complex contributors to creativity.

NR268 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Outcome of DSM-IV MDD in Psychiatric Care

Tarja K. Melartin, M.D., *Department of MHAR, NPHI, Mannerheimintie 166, Helsinki 00300, Finland*; Heikki K. Rytsala, M.D., Ulla S. Leskela, M.A., Paula S. Lestela-Mielonen, M.A., Petteri Sokero, M.D., Erkki T. Isometsa, M.D.

Summary:

Background: Previous studies show patients with depression to be at significant risk of developing chronicity, relapse, or recurrence. However, as most published naturalistic cohort studies have been conducted on inpatient populations in tertiary-level treatment centers, and during the era of tricyclic antidepressant use, the generalizeability of their findings to present-day psychiatric settings is questionable.

Method: In the Vantaa Depression Study, six- and 18-month outcomes were prospectively assessed in a sample of 269 secondary-level care psychiatric patients with DSM-IV MDD, effectively representing psychiatric patients of a Finnish city. SCAN 2.0 and SCID-II interviews were used for repeated diagnostic assessments, and outcome was measured at six and 18 months. Possible predictors, of time to remission, and of recurrence, were investigated.

Results: The median time to remission was 1.5 months (95% CI 1.3–1.8); 36% of the cohort achieved at least partial remission by one month, 76% by three months, and 94% by 18 months. Only 6% suffered from chronic depression over 18 months. However, over 40% had a recurrence during the follow up. Previous episodes, severity of depression, and partial remission from the index episode were the most significant predictors of recurrences.

Conclusion: In a representative sample of psychiatric patients with MDD treated during the current therapeutic era, the prognosis of a treated major depressive episode appears better than in earlier reports. However, the risk of a recurrence remains high, and is most effectively predicted by the severity and previous course of depression.

NR269 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Clinical Profile of Major Depression in India

Sumant Khanna, M.D., *Department of Psychiatry, N. I. M. H. A. N. S., P O Box 2900 Hosur Road, Bangalore 560029, India*; Sunita Rajadhyaksha, M.D., Chitra Lele, Ph.D., Depression Study Group

Summary:

Various proponents over time have expressed opinions that the clinical profile of depression is culture bound or culture specific. Most of these statements have unfortunately not been backed by data. One thousand one hundred and seventeen subjects diagnosed with major depression according to DSM-IV were assessed on various rating scales, to determine the phenomenological constellation of their profiles. There were 659 females and 450 males with a mean age of 38.06 years. The data were from six centers across India. The rating scales used were the Hamilton Depression Rating Scale (HDRS), Montgomery Asberg Depression Rating Scale (MADRS), Brief Psychiatric Rating Scale (BPRS), and Hamilton Anxiety Rating Scale (HARS). The item scores on each of these scales, were factor analysed, and those factors with an eigen value greater than unity the underwent a Varimax rotation. On the HDRS, three meaningful factors emerged—the first incorporating endogenous symptoms, the second depressive and somatic symptoms, and the third biological disturbances associated with depression. These three factors accounted for 47% of the variance. On the MADRS, there were two factors, depression and guilt, which were extracted. The three meaningful factors on the BPRS were mood disturbances, disorganisation and psychotic symptoms. The HARS revealed two factors with high loadings for

anxiety symptoms and depressed symptoms respectively. Such a large exercise on the psychometric profile of depressed patients has not been undertaken so far to the best of our knowledge. This study points to many similarities in the presentation of depression across cultures. Of cross-cultural interest are the first two factors on the HDRS—the fact that endogenous symptoms constitute the first factor; and that somatic symptoms combine with depressive symptoms in the second factor. These findings are relevant in the context of increasing international boundaries for clinical research across the world.

NR270 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Cocaine Addicts Show Impaired Ability to Supress Negative Emotional States

Karen G. Drexler, M.D., *Department of Psychiatry, Emory University, VAMC-Atlanta 1670 Clairmont Rd, Decatur, GA 30033*; Jennifer L. Casarella, M.D., Kristi Walker, B.A., Clinton D. Kilts, Ph.D.

Summary:

Introduction/hypotheses: Cocaine addiction is associated with dysfunction in the orbitofrontal cortex a region implicated in emotion regulation. [1] Guided imagery-induced anger is associated with decreased activity in the orbitofrontal cortex in cocaine dependent men. [2] The current project investigates whether cocaine-dependent men demonstrate deficits in emotion regulation.

Methods: 5 cocaine-dependent men and matched controls were screened for major psychiatric disorders using the Structured Clinical Interview for DSM-IV (SCID-NP version), the SCID-II, the Conners Adult ADHD Rating Scale (CAARS), and the vocabulary and block-design portions of the WAIS and the Folstein MMSE. Guided imagery scripts were constructed for anger, sadness, and an emotionally neutral scene using the methods described in ref 2.

Emotional scripts were presented three times each in a counterbalanced fashion. Sixty seconds into the emotion scripts subjects were instructed to enhance, maintain or suppress the induced emotion. Subjects rated their emotional responses using a Likert scale with anchor points of "0" for "none at all" and "10" for "most ever".

Results: Cocaine-dependent subjects had a significantly more robust anger response (self-rated anger-6.0 vs. 2.0, $p < 0.05$), and more difficulty suppressing the anger response (50% vs. 90% decrease in self-rated anger, $p < .10$). Cocaine-dependent subjects experienced more severe self-rated sad response (6.1 vs. 2.0, $p < .10$) and significantly more difficulty suppressing the sad response (+19% (increase) versus –50% (decrease) in self-rated sadness, $p < 0.05$).

NR271 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Gepirone Extended Release (ER) in the Treatment of Major Depression

Michael Gibertini, Ph.D., *Organon Inc., 375 Mt. Pleasant Avenue, West Orange, NJ 07052*; Alan D. Feiger, M.D., Jon F. Heiser, M.D., Ram K. Shrivastava, M.D., Kenneth J. Weiss, M.D., Ward T. Smith, M.D., A.D. Sitsen, M.D.

Summary:

Objective: To assess the efficacy and tolerability of the 5-HT_{1A} agonist, gepirone extended-release (gepirone-ER) in patients with major depressive disorder.

Methods: Eligible patients were aged 18 to 70 years with major depressive disorder and a baseline HAMD-17 score ≥20. Patients were randomized to placebo or gepirone-ER for 56 days. The initial dose was gepirone-ER 20 mg/day, and the dose was adjusted within the range of 40 mg to 80 mg daily. The primary efficacy variable was the absolute change in the HAMD-17 total score from baseline.

Results: Among 204 patients, the mean change from baseline in the HAMD-17 was significantly greater with gepirone-ER than placebo at weeks 3 ($p = 0.013$) and 8 ($p = 0.018$). Significantly ($p \leq 0.05$) more patients on gepirone-ER were HAMD-17 responders at weeks 3 and 4 and HAMD remitters at weeks 6 and 8. Discontinuation for adverse events occurred in 9.8% of the gepirone-ER group and 2.8% of the placebo group. Common adverse events included dizziness, headache, and gastrointestinal symptoms. Gepirone-ER did not cause weight gain, sedation, or sexual dysfunction. No serious adverse events were reported.

Conclusion: Gepirone-ER is effective for the treatment of major depressive disorder and is well tolerated.

NR272 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Effects of Lamotrigine Versus Valporate Monotherapy on Mood and Weight Gain: A Randomized, Double-Blind Clincal Trial

Alain Vuong, B.S., *GlaxoSmithKline, 5 Moore Drive, Resh Triangle Park, NC 27709*; Keith R. Edwards, M.D., Victor Biton, M.D., Anne E. Hammer, Pamela S. Barrett, Pharm.D., Alan Metz, M.D.

Summary:

Background: In patients with epilepsy comorbid depressive symptoms are underrecognized and undertreated.

Methods: LAMICTAL® (LTG) was compared to DEPAKOTE® (VPA) for weight gain. Mood assessments (Beck Depression Inventory, BDI; Cornell Dysthymia Rating Scale, CDRS; Profile of Mood States, POMS) were secondary measures. Patients were ≥12 yrs with partial or generalized seizures, randomized 1:1 to LTG or VPA, entered an 8-week Escalation, then a 24-week Maintenance phase. Target doses were 200–500 mg/day (LTG), 20–60 mg/kg/day (VPA).

Results: LTG: n = 65, 42% male, mean age 35yrs, mean dose = 254mg/day. VPA: n = 68, 46% male, mean age 30yrs, mean dose = 822mg/day. Mean screen BDI scores = 10.4 (LTG), 11.9 (VPA); greater improvements were noted at weeks 10, 32 with LTG (2.2, 2.6) than VPA (–0.1, 0.7). Mean screen CDRS scores = 51.7 (LTG), 52.9 (VPA); greater improvements were observed with LTG (1.4, 3.6) than VPA (–0.3, 0.5) at weeks 10, 32. Mean Total Mood Disturbance scores = 36.5 (LTG), 35.8 (VPA); at week 32 greater improvement was noted for LTG (13.8) than VPA (–0.4). Mean weight gain at weeks 10, 32 was negligible with LTG (1.4, 1.3 lb), higher ($p \leq 0.002$) with VPA (5.8, 12.8 lb).

Conclusion: LTG has mood elevating effects in patients with epilepsy and comorbid depressive symptoms.

NR273 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Increased LPS-Stimulated Levels of IL-6 in Patients with Major Depression

Ziad A. Kronfol, M.D., *Dept of Psychiatry, Univ of Michigan Medical Center, 900 Wall Street, Ann Arbor, MI 48109-0722*; Mohamed Aziz, M.D., Daniel Remick, M.D.

Summary:

Introduction: There is now overwhelming evidence that cytokines, in addition to their traditional role as communicators between immune and inflammatory cells, play a role as neuromodulators. Their role in psychiatric illness in general and affective disorders in particular has been somewhat controversial. This study investigates the role of various cytokines and their receptors in patients with major depression.

Methods: In this study, we measured cytokine levels in 21 patients with major depression and 21 healthy controls. The cytok-

ines and their receptors studied were: IL-1β, IL-1sr2, IL-6, TNFα, TNFsr1 and TNFsr2. All cytokine measures were obtained at baseline and following 24-hour cultures with PHA or LPS. Comparisons between the groups were made using ANOVA.

Results: There were no significant differences in baseline levels or PHA-stimulated levels of cytokines between the two groups. LPS-stimulated IL-6 levels however were significantly ($p < .006$) higher in the depressed group (41,386 ± 20, 961 pg/ml) compared to the control group (20,576 ± 13,616 pg/ml).

Conclusions: These results indicate an increase in the secretion of the pro-inflammatory cytokine IL-6 in patients with major depression. The clinical implications of this finding are yet to be determined.

NR274 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Cytokine Profile (IL-1 and IL-6) in Subtypes of MDD

Andrea H. Marques, M.D., *Department of Psychiatry, University of Sao Paulo, Rua Simao Alvares 765 AP71, Sao Paulo, SP 05417-030, Brazil*; Francisco Lotufo-Neto, M.D., Euthimia B.A. Prado, Ph.D., Wagner V. Dominguez, B.Sc.

Summary:

Introduction: Major depressive disorder (MDD) may be associated with cytokines alterations. We focused on a subclassification of MDD, comparing patients with melancholic and nonmelancholic, acute and chronic, severe and moderade presentations, by measuring plasma concentration of IL-1 and IL-6.

Hyphotesis: Different cytokine profile should discriminate subtypes of MDD.

Methods: 27 outpatients (19 women and 8 men) from the department of psychiatry, University of São Paulo were enrolled. Diagnosis was made with SCID (DSM-IV) and Halmiton Depression Rating Scales (HDRS,21). All patients were free of antidepressants. IL-1β and IL-6 were measured before and after treatment (decrease of HDRS < 50%) using whole blood in culture after stimulation with LPS (1μg/ml). Severity was considered when HDRS>25 and Chronicity when duration >2 years. Treatment was done with sertraline or imipramine.

Results: IL-1 and IL-6 levels were shown in the table. Significant increase in IL-1β was seen in MDD, Non-melancholic, severe and acute patients. IL-6 was significantly increased in all groups after treatment (except non melancholic).

See chart at top of next page.

Conclusion: Increase in IL-6 was associated to clinical improvement, independently of subtype of MDD. IL-1 increase discriminated the non-melancholic, severe and acute groups.

NR275 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Occupational Patterns of Three Groups of Sex Offenders

Lauren S. Magidson, *Department of Psychiatry, Beth Israel Medical Center, 16th Street at 1st Avenue Room 6K42, New York, NY 10003*; Lisa J. Cohen, Ph.D., Soenke Boettger, M.D., Carrie Weaver, M.A., Enid C. Gertmenian-King, B.A., Kenneth Cullen, M.S.W., Igor I. Galynker M.D.

Summary:

Background: Sexually aggressive offenders are extremely dangerous to society and highly difficult to treat. Therefore, any further information that characterizes the different subgroups may be of interest.

Method: The occupational patterns of three groups of sexual offenders and one group of non-sexual, violent offenders were assessed; 174 convicted of child molestation, 91 convicted of rape of adult and adolescent women, 58 convicted of miscellaneous paraphilias, 39 convicted of domestic violence. All of the subjects were currently on probation or parole and in outpatient treatment. The subjects' access to children, access to the public, and general occupational status according to Hollingshead's Index of Social Position were evaluated.

Results: Child molesters did not vary from other groups with regard to access to the public or access to children. Only 3% of the total had special access to children, ranging from 2–6% across the groups. There was a significant difference across groups with regard to employment status—72% of rapists were employed while 84–87% of the other groups were employed. Of the employed subjects, groups did not differ with regard to their Hollingshead occupational status.

Conclusion: That pedophiles did not differ from other offender groups in access to children and occupational status argues against the notion that child molestation is opportunistic and impulsive and offers greater support that it is planned. The greater unemployment rate of adult rapists, however, may speak to more pervasive functional impairment in that population relative to other offender groups.

NR276 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Admission and Coersion Among Sexually Aggressive Paraphilics

Carrie Weaver, M.A., *Department of Psychiatry, Beth Israel Medical Center, 16th Street at 1st Avenue Room 6K42, New York, NY 10003*; Lisa J. Cohen, Ph.D., Soenke Boettger, M.D., Enid C. Gertmenian-King, B.A., Kenneth Cullen, M.S.W., Igor I. Galynker, M.D.

Summary:

Objective: Sexually aggressive paraphilias are notoriously treatment refractory. Better characterization of the different sexually aggressive behaviors could potentially lead to development of more effective treatments. In this light, we compared admission of the charged crime and degree of force used in four offender groups.

Method: Subjects were recruited from CAP Behavioral Health Associates, a clinic for the treatment of male sexual and violent offenders. Of the 348 subjects included in this study, 170 were charged with child molestation, 87 with rape, 52 with miscellaneous paraphilias (i.e., non-pedophilic sexually aggressive behavior), and 39 with domestic violence. Data was obtained from the clinic database in which information from the in-take evaluation (clinical and legal information included) was utilized. The degree of force used and the degree to which the subject admitted the crime was analyzed with Chi-Square tests. Method of coercion was divided into 6 categories, none, bribe, manipulation, threat, force, and assault. The coercion method was only compared in the 3 groups of sexual offenders.

Results: Forty percent of the child molesters and 41% of the rapists denied their crime, while only 21% of the miscellaneous paraphilias and 18% of the domestic violence offenders did ($x^2 = 27.43$ (6, 348), $p < .001$). Among the offenders who admitted their crime, 22% of the child molesters admitted use of force compared to 51% of the rapists. Forty-two percent of child molesters, however, reported use of manipulation.

Conclusions: The admission of the crime and method of coercion varied across different offender groups. Of note, sex offenders are less likely to admit to their crime than are domestic violence offenders. Moreover, child molesters are less likely than rapists to use force. These findings suggest that treatment planning and public health preventive strategies should vary according to the specific offense.

	IL-1β (ng/ml) Median min-max				IL-6 (ng/ml) Median min-max			
	N	BT	AT	P#	N	BT	AT	P#
MDD All patients	26	**29.2** 9.7-79.8	**42.7** 11.8-115.8	0.0089 *	27	**95.5** 44.6-279.3	**160.0** 56.3-340.9	0.0003 *
Melancholic	17	**21.9** 9.7-79.9	**37.4** 11.8-80.7	0.15 n.s.	18	**78.9** 44.6-279.3	**167.1** 56.3-340.9	0.0017 *
Non Melancholic	9	**42.6** 15.0-66.3	**55.6** 29.7-115.8	0.019 *	9	**117.7** 70.9-157.9	**154.2** 111.9-192.9	0.055 n.s.
Severe	15	**25.0** 9.7-75.8	**51.3** 26.6-115.8	0.0026 *	15	**87.4** 47.3-279.3	**170.3** 56.3-340.9	0.0012 *
Moderate	11	**29.3** 16.5-79.9	**35.7** 11.8-80.7	1.00 n.s.	12	**106.6** 44.6-157.9	**119.0** 78.6-283.0	0.0042 *
Chronic	14	**43.3** 15.0-79.9	**51.7** 18.1-80.7	0.23 n.s.	15	**117.7** 44.6-279.3	**164.0** 56.3-340.9	0.0103 *
Acute	12	**19.7** 9.7-58.2	**35.8** 11.8-115.8	0.034 *	12	**86.1** 47.3-134.9	**139.6** 78.6-308.3	0.0049 *

Wilcoxon matched pairs; * $p < 0.05$; n.s.: not significant.

NR277 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Pregnancy Outcomes Following Exposure to Lamotrigine

Patricia S. Tennis, Ph.D., *Glaxosmithkline, 5 Moore Drive, RTP, NC 27709*

Summary:

Objective: To monitor pregnancy outcomes in women exposed to lamotrigine.

Methods: This study monitors pregnancy outcomes in women exposed to lamotrigine for major birth defects (BD). Data on exposure to lamotrigine are collected from physicians of patients registered with the Lamotrigine Pregnancy Registry preferably before prenatal testing. Pregnancy outcomes were obtained through the reporter, and each birth defect reviewed by an independent pediatrician. The percentage of pregnancies with major BD was calculated for first-trimester lamotrigine monotherapy and for lamotrigine polytherapy. All conclusions are developed by an advisory committee with members largely external to the sponsor.

Results: The number of patients with major BD following lamotrigine monotherapy was 3/168 (2.5%[95%CI:0.5,5.5%]), following lamotrigine polytherapy involving valproic acid (VPA) was 5/50(10%[95%CI:3.7,22.6%]), and following lamotrigine polytherapy without VPA was 5/116(4.3%[CI:1.6,10.3]).

Conclusion: Although the data on monotherapy with lamotrigine have not suggested a concern, the numbers for any regimen including lamotrigine are too small to rule out increased frequency of all or specific major BD. Although, in published literature, VPA is associated with major BD, interpretation of this data on the lamotrigine/VPA combination is problematic without internal data on VPA monotherapy.

NR278 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Timing of Recurrence of Postpartum Depression

Katherine L. Wisner, M.D., *Department of Psychiatry, Case Western Reserve University, 11400 Euclid Avenue, Suite 280, Cleveland, OH 44106*; Kathleen S. Peindl, Ph.D., James Perel, Ph.D., Barbara H. Hanusa, Ph.D.

Summary:

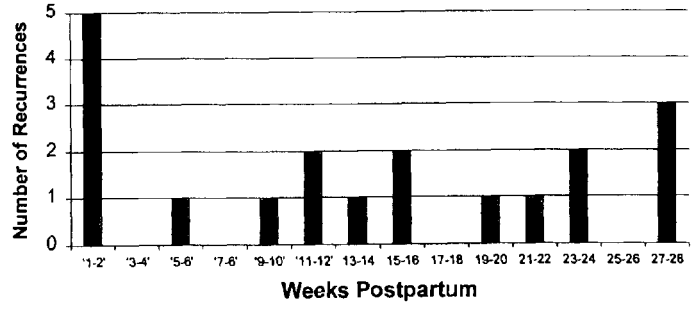
Background: Women who have suffered from one episode of postpartum-onset major depression (PPMD) experience increased risk for recurrence in the year following another birth.

Methods: Non-depressed women who had at least one past episode of PPMD were recruited during pregnancy. The subjects were assessed prospectively for 20 weeks with the Hamilton Rating Scale for Depression and Research Diagnostic Criteria for recurrence of major depression. Evaluations were performed at 24, 36, and 52 weeks to assess for episodes beyond 20 weeks postpartum.

Results: The data (*Figure*) revealed a clustering of cases, with 5 of the 21 recurrences (24%) occurring in the first two weeks. Thirteen of the 21 recurrences (67%) and 19/21 recurrences (90%) occurred in the first 20 and 28 weeks following birth, respectively.

Conclusions: The one-year recurrence rate was 21/51 or 41%, with a clustering of cases near delivery. All recurrences except two occurred by 28 weeks postpartum.

Frequency of Recurrence of Postpartum Major Depression



NR279 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Birth Complications and Neonatal Outcomes in Women Depression

Jan Berle, M.D., *Department of Psychiatry, University of Bergen, Haukeland University Hospital, N-5021 Bergen,*

Norway; Arnstein Mykletun, Anne K. Daltveit, Ph.D., Susanne I. Steinberg, M.D., Alv A. Dahl, Ph.D., Fred Holsten

Summary:

Objective: Depression during pregnancy is a problem for the mother and poses a threat to the health of the fetus. Prospective studies are necessary to evaluate the association between exposure to prenatal psychiatric symptoms and birth outcome. Some older studies may be biased in retrospective reporting of pregnancy events by mothers of children with birth complications.

Method: We examined relations between maternal depression in pregnancy with neonatal outcome and birth complications in a prospective design. Taking into account the high degree of comorbidity between depression and anxiety, the prevalence of anxiety among these women were also rated. The study was based on a cohort of pregnant women aged 20 years and above selected from a large population-based study in Norway where a total of 33,260 women participated. Psychiatric symptoms were assessed by Hospital Anxiety and Depression Scale, a valid and reliable self-rating instrument. Birth complications and neonatal outcome were assessed by information from the Medical Birth Registry of Norway.

Results: Psychiatric symptoms in pregnant women increase the risk for some birth complications.

Conclusion: Recognition of depression and anxiety during pregnancy is particularly important as psychiatric illness in this period may have implications for the offspring.

NR280 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Antidepressants in Pregnancy, Minimizing Fetal Exposure: Preclinical and Clinical Data

Sandra Graybeal, B.A., *Department of Psychiatry, Emory Clinic, 1365 Clifton Road NE, 6100, Atlanta, GA 30322*; D. Jeffrey Newport, M.D., Angela D. Fisher, B.S., Amy L. Hostetter, B.A., Zachary N. Stowe, M.D.

Summary:

Antidepressant use in pregnancy has generated a myriad of retrospective, case series, and teratology/toxicology center reports. The literature is replete with review articles regarding perinatal antidepressant medication; nonetheless, fetal central nervous system (CNS) exposure has yet to be quantified. Clinical data from umbilical cord samples (n = 125) and amniotic fluid (n = 10) demonstrates a highly variable placental passage of antidepressants. Tightly protein bound medicines with short elimination half lives and molecular weights have significantly less placental passage and potentially less absolute (ng/ml) fetal exposure. Pregnant rodent models with continuous antidepressant administration via osmotic minipump provide similar sample sources (amniotic fluid, umbilical cord blood) and permits fetal CNS quantification and receptor binding profiles. Presently, the fetal fluoxetine brain concentrations associated with pregnancy exposure were greater than 50% that of maternal brain. Concentrations for sertraline (N = 10 maternal, n = 80 pup brain, amniotic fluid) and paroxetine (N = 3 maternal, n = 32 pup brain, amniotic fluid) also are being analyzed. The neonatal clearance of norfluoxetine, demonstrated concentrations >20% of maternal brain at 3 weeks after delivery. Similar experiments with sertraline (N = 8 maternal, n = 64 pup brain, amniotic fluid) and paroxetine (N = 2 maternal, n = 16 pup brain, amniotic fluid) have been complete and analyses are pending. The clinical data (placental passage) indicates that the physicochemical properties of antidepressants determine absolute (ng/ml) fetal exposure. Should the CNS animal data parallel these findings, the selection of medication could be scientifically derived to provide minimal fetal exposure.

NR281 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

A Placebo-Controlled Trial Exploring the Efficacy of Paroxetine in PMDD

Mikael Landen, M.D., *Department of Psychiatry, Institute of Clinical Neuroscience, S-431 80 SU/Molndal, Molndal, Sweden*; K. Sorvik, C. Ysander, C. Allgulander, B. Nissbrandt, B. Gezelius, Elias Eriksson, Ph.D.

Summary:

Background: Continuous treatment with paroxetine has been shown to alleviate the symptoms of PMDD. Intermittent treatment, i.e., during the luteal phase only, may also be effective. The current placebo-controlled study compared continuous and intermittent treatment of paroxetine with that of placebo in PMDD.

Methods: Patients meeting DSM-IV criteria for PMDD were randomly allocated into continuous treatment with 20 mg paroxetine, intermittent treatment with 20 mg paroxetine (administered for the last 14 days of the cycle), or placebo, for three menstrual cycles. Primary efficacy was assessed by daily recording of symptoms using visual analog (VAS) scales. Other efficacy assessments included the Clinical global improvement (CGI) and severity of illness scales (CGS).

Results: From 274 women screened, 186 were randomized to treatment (placebo n = 62, intermittent n = 61, continuous n = 63). Groups were balanced for demographic and medical history variables. The percentage change from baseline on the VAS irritability item was significant for both continuous (difference in medians −43.0; 95% confidence intervals[CI] −53.7, −29.1; $p < 0.001$, treatment minus placebo) and intermittent treatment (−39.4; 95% CI −51.8, −26.1; $p < 0.001$). The proportion of responders on the CGI was 29.8% for placebo, 84.8% for continuous treatment (Odds ratio [OR] 15.6; 95% CI 5.7, 48.8; $p < 0.001$) and 68.1% for intermittent treatment (OR 5.4; 95% CI 2.3, 13.8; $p < 0.001$). Using a composite "VAS-Mood" score based on all four core items of PMDD, both continuous (adjusted mean difference −21.3; 95% CI −28.6, −13.9; $p < 0.001$) and intermittent (−17.3; 95% CI −24.6, −9.9; $p < 0.001$) treatment were significantly superior to placebo. Fewer adverse events (AEs) were seen with intermittent treatment compared with continuous treatment, there were slightly more withdrawals due to AEs in the continuous treatment arm (continuous 8.3%, intermittent 5.1%, placebo 1.7%).

Conclusion: These results demonstrate that both intermittent and continuous treatment with paroxetine are highly effective for the treatment of PMDD.

NR282 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

PMDD: Social Functioning Improves with Paroxetine Treatment

Kevin M. Bellew, B.S., *Department of Neuroscience, GlaxoSmithKline, 1250 South Collegeville Road, Collegeville, PA 1426-0989*; Mikael Landen, M.D., Brian Hunter, Ph.D., James P. McCafferty, B.S.

Summary:

Background: Previous reports suggest that premenstrual dysphoric disorder (PMDD) is associated with a marked reduction in social functioning[1]. We have now examined if this aspect of the condition is influenced by treatment with paroxetine.

Method: Women with PMDD (n = 186) were randomized to one of three arms: paroxetine continuously (20 mg) (n = 63), paroxetine intermittently (20 mg) (n = 61), or placebo (n = 62). Treatment was double-blind and continued for three cycles. Functional impairment was assessed using the Sheehan Disability Scale (SDS)[2]. PMDD symptoms were assessed using diary cards containing visual analog scales (VAS).

Results: At baseline, the three groups were balanced for demographic and medical history variables. The mean (SD) SDS scores

at entry were 5.4 (2.5) (work); 5.8 (2.6) (social life), and 7.0 (2.1) (family life). At endpoint, the VAS mood score was significantly reduced in both paroxetine groups compared to placebo ($p < 0.001$). The reduction in SDS scores was significantly larger in both the intermittent group—work: –3.1 (0.4); social life: –3.5 (0.4); family life: –4.4 (0.5)—and in the continuous group—work: –4.7 (0.4); social life: –5.0 (0.4); family life: –6.0 (0.4)—than in the placebo group—work: –1.3 (0.5); social life: –1.8 (0.4); family life: –2.3 (0.4). p-value was <0.001 vs placebo for both paroxetine groups and all subscales.

Conclusion: The results support previous studies suggesting that PMDD is accompanied by a considerable functioning impairment and that this aspect of the condition is markedly improved by paroxetine.

NR283 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

A Pilot Study of Extended Sertraline Treatment for Severe PMS and PMDD

Ellen W. Freeman, Ph.D., *Department of OBGYN/Psychiatry, University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104*; Steven J. Sondheimer, M.D., Karl Rickels, M.D., Roxellen Auletto, M.S.N.

Summary:

Objectives: Efficacy of sertraline has been demonstrated in the short term treatment of premenstrual dysphoric disorder (PMDD) and severe premenstrual syndrome (PMS), but there is little information about long term treatment for this chronic disorder. To determine whether improvement was maintained in patients who continued sertraline beyond the 2–3 months of treatment trials and whether symptoms returned after discontinuing medication.

Methods: A 1-year follow-up of 67 women with severe PMS or PMDD who requested sertraline prescriptions after completing double-blind treatment protocols. Trained interviewers completed a brief telephone questionnaire.

Results: After 1 year, 48% (32/67) continued sertraline, mean dose 65 mg/day. Relief was reported by 50% of continuers vs 23% of discontinuers ($P = 0.017$, Fishers exact test). Of the sertraline discontinuers during the follow-up period, 67% worsened vs 20% of the continuers ($P = 0.036$). Of those who worsened, all reported that PMS symptoms returned within 3 months of discontinuing sertraline. Symptom levels at the outset were nearly identical between the continuers and discontinuers and did not account for differences in symptom levels at follow-up.

Conclusions: About half the women continued to medicate their PMS for 1 year after the acute treatment trial, most with perceived benefit. Among those who discontinued medication, symptoms returned swiftly within 3 months, consistent with other pilot data. Further controlled studies that address the appropriate length of drug treatment for this disorder are warranted.

NR284 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Risk of Recurrence Among Pregnant Women Bipolar Disorder

Adele C. Viguera, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WACC 812, Boston, MA 02114*; Lee S. Cohen, M.D., Alison Reminick, Christina Psaros, B.A.

Summary:

Pregnancy poses major challenges for the treatment of bipolar disorder, and information to guide clinical care remains sparse. The specific aim of this study was to determine the recurrence risk for women with bipolar disorder during pregnancy who discontinued mood stabilizer proximate to conception.

Method: Pregnant women with DSM-IV bipolar disorder were followed prospectively and systematically during pregnancy and the first year postpartum. Recurrence was defined by SCID criteria for hypomania, mania, or depression.

Results: Crude rate of recurrence during pregnancy was 73% in the overall sample (32/44). Among the 33 subjects who discontinued their mood stabilizer during pregnancy, 26 relapsed (78.8%). Subjects who abruptly (1 day to < 2 weeks) discontinued maintenance mood stabilizer appeared to be at highest risk for relapse (n = 10; 100%) compared to subjects who gradually discontinued maintenance mood stabilizer (>2 weeks) (n = 21; 62%). Other predictors of recurrence will be presented.

Conclusions: These preliminary prospective data suggest that subjects, who discontinue mood stabilizer proximate to conception, especially abruptly, are at very high risk for recurrence during pregnancy.

NR285 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

A Randomized, Placebo-Controlled Trial of Sertraline for Prophylactic Treatment of Highly Recurrent Major Depressive Disorder

Patrice Boyer, P.R., *Hopital de la Salpe, Triere Bd Del Hopital, 47 La Force, Paris 75013, France*; Vincent F. Caillard, M.D., Jean-Pierre Lepine, M.D., Jean-Llaude Bisserbe, Jean-Michel Mottom, Sylvie Troy

Summary:

Objective: To determine if sertraline prevents the recurrence of major depressive disorder among patients with recurrent depression.

Methods: It was a 20 months, randomized, double-blind study. Patients presenting with at least three documented episodes of major depressive disorder within the last four years and currently in full remission were eligible. The last episode must have been treated for at least four months with any antidepressant except sertraline. Patients initially received two months of single-blind, placebo (n = 371) to confirm the stability of the remission during a no antidepressant period, then were randomized double blind (n = 288) to 50 mg or 100 mg of sertraline (Ser) or to placebo (Pbo) during 18 months. Patients were evaluated at selection, randomization, and months 4, 5, 8, 11, 14, 17, and 20. The primary criteria was the occurrence of a recurrence definied as MDE according to the DSMIV criteria, and/or appearance of symptoms which, in the opinion of the clinician, required the administration of another antidepressant treatment.

Results: 61/371 patients discontinued prior to the double-blind phase, including 33 who relapsed. Of 288 patients (full analysis set) who entered the double-blind prophylactic phase, 123/288 discontinued, including 64 for recurrences. Recurrences were significantly ($P = 0.001$) lower in the sertraline groups compared with placebo (ser 50 mg, 16/95 [16.8 %]; ser 100 mg 15/94 [16.0 %]; placebo 33/99 [33.3 %) Pbo versus Ser 50 mg $p = 0.008$. Pbo versus Ser 100 mg $p = 0.005$ time to recurrence was shorter in the placebo group compared to sertraline; 10% of the patients presented a recurrence after 70 days in Pbo group; 150 days in Ser 100 mg and 300 days in Ser 50 mg. Sertraline was well tolerated, the number of adverse event was slightly lower in the 50 mg group.

Conclusion: This study is the first one to prove a real significant efficacy of an antidepressant i.e. sertraline in the prevention of recurrences of depressive episodes.

NR286 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Maternal Depression and the Risk for Adverse Neonatal Outcomes: Is There an Association?

Amy K. Lyster, B.A., *Department of Psychiatry, Massachusetts General Hospital WACC 812, 15 Parkman Street, Boston, MA*

02114; Adele C. Viguera, M.D., Allison R. Fraer, B.A., Lee S. Cohen, M.D.

Summary:

This study examines the association between depressive symptoms in pregnancy and adverse neonatal outcome.

Method: Between 1996–2000, 1,917 women in a prenatal clinic were screened for depression during the second trimester with a questionnaire which included the Center for Epidemiological Studies Depression Scale (CES-D) and questions about past/current psychiatric history including antidepressant use. A CES-D cutoff score of >24 was used in the analysis as indicative of DSM-IV major depressive disorder.

Results: No significant association was found between CES-D score >24 and adverse neonatal outcome (i.e. birthweight <2500g; gestational age <37 weeks at delivery; Apgar <5 or transfer to NICU). However, women who reported a past (n = 118) or current (n = 81) history of medication treatment for mood/anxiety disorders were at increased risk for adverse neonatal outcomes vs. those with no prior history of mood disorder or medication use: RR 1.7(95% CI, 1.1–2.7) g.a<37 weeks and RR 1.8(95% CI, 1.1–3.1) b.w<2500 grams.

Conclusions: Depressive symptoms in pregnancy were not associated with adverse neonatal outcomes. However, women who reported either a current or past history of medication treatment may be at increased risk for adverse neonatal outcome. These data suggest that history of medication treatment (past/current) may be a marker of illness severity and clinically may be an efficient screening question to identify a high risk group.

NR287 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

A Randomized Single-Blind Trial of the Efficacy of Group Psychoeducation in the Prevention of Relapses in Remitted Bipolar Patients

Francesc Colom, Ph.D., *Department of Psychiatry, Hospital Clinic, Billarroel 170, Barcelona 08036, Spain*; Anabel Martinez-Aran, Ph.D., Maria Reinares, Carla Torrent, Jose M. Goicolea, M.D., Merce Comes, Eduard Vieta, M.D.

Summary:

Background: Studies on individual intervention have recently proved that this kind of psychotherapy may reduce the number of relapses in bipolar patients (Perry et al., 1999). However, there is a lack of randomized, blind controlled studies demonstrating the efficacy of group psychoeducation to prevent relapses in bipolar I and II patients (Colom et al, 1998).

Methods: One hundred twenty bipolar I and II outpatients in remission (YMRS<6, HDRS<8) for at least a six-month period prior to inclusion in the study who were receiving standard pharmacological treatment were included in a controlled trial. Subjects were matched for age and sex and randomized to receive, in addition to standard psychiatric care, 20 sessions of group psychoeducation or 20 sessions of non-structured group meetings. Subjects were assessed monthly during the 20-week treatment period and throughout the two-year follow-up.

Results: At the two year follow-up, group psychoeducation significantly reduced the number of relapsed patients ($p < 0.0008$), the number of relapses per patient ($p < 0.0001$) and the time to depressive (0.0001), manic or hypomanic (0.008) and mixed ($p < 0.048$) relapses. The number and length of hospitalizations per patient were also significantly lower in psychoeducated patients.

Conclusions: Group psychoeducation is an efficacious intervention to prevent relapse and diminish length of hospitalizations in pharmacologically treated bipolar I and II patients.

NR288 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

ADHD in Adults with Bipoplar Disorder in the Systematic Treatment Enhancement Program for Bipolar Disorders

Andrew A. Nierenberg, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114-3117*; Leslie J. Yan, B.A., Stephanie L. McMurrich, B.A., Thomas J. Spencer, M.D., Stephen R. Wisniewski, Ph.D., Dan V. Iosifescu, M.D., Gary S. Sachs, M.D.

Summary:

Objective: Systematic studies of children and adolescents with a diagnosis of bipolar disorder show that rates of Attention Deficit Hyperactive Disorder (ADHD) range from 60% to 90% in pediatric patients with mania, but the prevalence of ADHD in adult bipolar patients is less clear. The purpose of this study is to assess the prevalence of ADHD in a large cohort of adults with bipolar disorder.

Methods: The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) is a multi-center, NIMH study that assesses, treats, and follows a large cohort of patients with bipolar disorder. All patients with a diagnosis of bipolar disorder are eligible for STEP-BD, regardless of comorbid conditions. At the time of entry, patients are evaluated for current and past psychiatric disorders by staff certified on a battery of standardized evaluation procedures. ADHD was diagnosed with the Mini International Neuropsychiatric Interview (MINI).

Results: The prevalence of ADHD in 919 patients was 9.8% (95% confidence interval from 8.0% to 11.9%) with 7.1% current (95% CI from 5.6% to 8.9%).

Conclusions: ADHD is a frequent comorbidity in adults with bipolar disorder that is probably underdiagnosed and undertreated. We will present further detailed results on the first 500 STEP-BD subjects.

NR289 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Age at Onset as a Predictor of Outcome in Bipolar Disorder

Tasha D. Cate-Carter, B.A., *Neurogenetics, CAMH, Clarke Site, 250 College Street, Tortonto, ON M5T 1R8, Canada*; Emanuela Mundo, M.D., Sagar V. Parikh, M.D., James L. Kennedy, M.D.

Summary:

Objective: The primary purpose of our study was to investigate the effect of the age at onset of bipolar disorder (BD) on the clinical course of the illness.

Method: We studied 336 subjects with a diagnosis of BD 1, BD 11, or schizoaffective disorder, bipolar type were recruited. All patients gave their informed consent to participate in the study. The sample was mostly comprised of an outpatient population. Each subject was interviewed by using the diagnostic Structured Clinical Interview for DSM-IV Axis 1 disorders (SCID 1). The main clinical variables were compared between subjects with early (<18 years) and later (≥18 years) age at onset of BD (chi square and t-tests for independent samples). In addition, the age at onset of BD was analyzed as a continuous variable and analyzed with respect to clinical subgroups of BD.

Results: We found a significant difference in the AAO between subjects with and without Axis 1 comorbidity ($t = 2.68$, $p = .008$), the presence of an Axis 1 anxiety disorder ($t = 2.19$ $p = .029$), substance use disorder ($t = 2.14$, $p = .033$), and rapid cycling ($t = 3.00$, $p = .003$). When we compared different clinical characteristics between early and late onset of BD, significant differences were found between early AAO and lifetime occurrence of suicidal behaviour ($X^2 = 16.18$, df 4, $p = .003$), suicidal ideation ($X^2 = 11.76$, $p = .001$), Axis 1 comorbidity ($X^2 = 8.2$, $p = .004$), substance

use disorders (X^2 = 6.0, p = .014) and rapid cycling (X^2 = 9.66, p = .002).

Discussion/Conclusion: The clinical implications of these findings, with particular respect to the role of AAO as a significant predictor of poor outcome in BD, will be discussed.

NR290 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Patient Response in Depression Overeating and Oversleeping to Gepirone Extended Release

Frederick M. Quitkin, M.D., *Department of Psychiatry, New York State Psychiatric Institute, 1051 Riverside Drive, New York, NY 10032-2603*; Michael Gibertini, Ph.D.

Summary:

Gepirone is a 5-hydroxytryptamine receptor (1A) agonist in the azapirone class. In a recent pivotal trial of gepirone-ER in outpatients with Major Depressive Disorder (MDD) of any subtype (N = 202; HAMD-17 >20 at baseline; mean dose = 70 mg/day), the majority (136, 67%) had symptoms which included overeating, oversleeping or both on the HAMD-25. For this analysis, a subset of patients with probable atypical depression who presented with overeating or oversleeping at baseline were defined as "probably atypical". The comparison group was patients with chronic or recurrent MDD without overeating or oversleeping. Atypical patients treated with gepirone-ER had a larger therapeutic response than atypicals treated with placebo or nonatypicals receiving either drug or placebo (2x2 Factorial ANOVA). This effect was significant at several time points across a number of standard parameters. The difference in the response rate (defined as 50% reduction HAMD-17) on drug vs placebo for the atypicals (16%) was greater than the nonatypicals (3%). Specifically, for atypicals on gepirone-ER, 43.3% vs 27.5% on placebo were judged responders. For nonatypicals on gepirone-ER, 33.3% vs 30% on placebo were judged responders. These results suggest that gepirone-ER is effective in patients with MDD and may be particularly effective in those with atypical features.

NR291 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Increased Obesity in Women Bipolar Disorders

Terence A. Ketter, M.D., *Department of Psychiatry, Stanford University School of Medicine, 401 Quarry Road, Room 2124, Stanford, CA 94305–5723*; Po W. Wang, M.D., Gary S. Sachs, M.D., Carlos M. Zarate, Jr., M.D., Lauren B. Marangell, M.D., Joseph R. Calabrese, M.D., Joseph F. Goldberg, M.D.

Summary:

Objective: Obesity, a body mass index (BMI) over 30 kg/m^2, affects 20% of Americans, and is associated with a profile of increased medical risks, which overlaps that seen in bipolar disorders (BD).

Method: BMI was assessed in relationship to other clinical measures in 321 (62% female, 69% BPI) Systematic Treatment Enhancement Program for BD (STEP-BD) patients.

Results: Mean ± SD BMI was 27.5 ± 6.2, and thus in the overweight (25–30) range, and similar in women (27.8 ± 7.1) and men (27.1 ± 4.6). However, significantly more women (31%) than men (20%) were obese. Obesity risk was significantly increased with compared to without prior valproate (31% vs 16%), prior antipsychotic (31% vs 22%), and current lithium (32% vs 23%) treatment, current caffeine use (31% vs 16%), suicidal ideation at intake (43% vs 17%), and psychomotor retardation at intake (35% vs 23%), but was decreased with current alcohol use (16% vs 32% without).

Conclusion: Women with BD have an obesity risk which is increased 50% not only compared to the general American population, but also compared to men with BD. Medications, substance use, suicidal ideation, and psychomotor retardation also influenced obesity rates. Obesity could thus be related to increased psychiatric (suicide) and medical (cardiovascular, respiratory) mortality in BD.

NR292 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Rates of Axis II Comorbidity in Remitted Patients Melancholic and Non-Melancholic MDD

Joyce R. Tedlow, M.D., *Department of Psychiatry, Massachusetts General Hospital, WAC 815/15 Parkman Street, Boston, MA 02114*; Wendelien Merens, M.A., Pamela A. Roffi, B.S., Amy H. Farabaugh, M.A., Timothy J. Petersen, Ph.D., Jerrold F. Rosenbaum, M.D., Maurizio Fava, M.D.

Summary:

Introduction: Patients with the melancholic subtype of major depressive disorder have often been considered to have lower rates of premorbid personality disorder than patients who develop nonmelancholic major depression. The purpose of our study is to assess rates of axis II comorbidity in patients who are in remission from melancholic depression compared to patients in remission from non-melancholic depression.

Methods: We assessed consecutive patients in remission (defined as a 17-item Hamilton Rating Scale for Depression score <8) from melancholic depression (n = 46 mean age 38 years, 41% female) and from non-melancholic depression (n = 63; mean age 39 years, 49% female). Patients were treated for 8 weeks with open-label fluoxetine 20 mg/day and they were assessed as baseline and endpoint for major depressive disorder (MDD) using the SCID-P and for personality disorders with the SCID-II.

Results: For patients in remission from major depressive disorder there were no significant differences in rates of Cluster A, B, or C personality disorders in those who had had melancholic depression compared to those who had had non-melancholic depression. The rate of Cluster A personality disorders was 17% in melancholic compared to 16% in non-melancholic patients. Cluster B personality disorder rate was 17% in both groups. The rate of Cluster C personality disorders was 43% in melancholics and 38% in non-melancholics.

Conclusions: In our study sample of patients in remission from their major depressive disorder, we found no differences in rates of personality disorders in any cluster between those who had had melancholic subtype and those who had not. Our results contradict the often held belief that patients who develop melancholia have lower rates of premorbid personality disorder than those who do not.

NR293 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Psychosocial Functioning in Pregnant Bipolar Women

Alison Reminick, B.A., *Massachusett General Hospital WACC 812, 15 Parkman Street, Boston, MA 02114*; Adele C. Viguera, M.D., Christina Psaros, B.A., Lee S. Cohen, M.D.

Summary:

The specific aim of this study was to examine the association between psychosocial functioning and risk for relapse in bipolar women during pregnancy.

Method: Pregnant women with DSM-IV bipolar disorder were followed prospectively and systematically during pregnancy. Recurrence was defined by SCID criteria for hypomania, mania, or depression. Psychosocial functioning was assessed by the Social Adjustment Scale (SAS) at baseline during the first trimester in 25 subjects. For this analysis, only subjects who had been euthymic at the time of completion of the baseline SAS were included (n =

20). Five subjects were excluded from this analysis because they had relapsed at the time of their baseline assessments.

Results: A significant association ($t = 4.03$;$df = 13$; $p < 0.001$) was found between high (impaired) SAS baseline scores and risk for relapse during pregnancy.

The overall, mean baseline SAS score among subjects who relapsed during pregnancy was 2.07 compared to 1.54 in subjects who remained euthymic throughout pregnancy. Scores on specific subscales of the SAS and their association with risk for relapse will also be presented.

Conclusions: These preliminary data suggest that among pregnant bipolar women, poor psychosocial functioning at baseline predicts high risk for relapse during pregnancy.

NR294 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Reactions to the World Trade Center Disaster in New York City Bipolar Patients

Carrie J. Endick, C.S.W., *Psychiatry, New York Presbyterian Hospital, 525 East 68th Street, New York, NY 10021*; Joseph F. Goldberg, M.D.

Summary:

The role of stress in exacerbating bipolar disorder remains controversial regarding symptom relapse. We assessed reactions to the 9/11 catastrophe in a previously studied New York City bipolar cohort.

Method: We interviewed 25 NYC DSM IV bipolar patients with pre-existing Post Traumatic Stress Disorder (PTSD) and 25 without PTSD. Subjects were evaluated for affective symptoms, substance abuse, and clinical status in the three month aftermath of 9/11.

Results: About one-third of subjects directly witnessed or lost friends in the World Trade Center (WTC) collapse. Nearly half of all subjects noted intensified affective symptoms, though most perceived no connections with 9/11 events; increased fears of being alone, taking risks, transportation, explosions, fires, or air travel were evident in most subjects (17–44%) and did not differ between those with vs. without prior PTSD. Increased suicidal thoughts and increased alcohol or drug use were more prevalent among bipolars with than without previous PTSD. More than 2/3 of bipolars without PTSD identified the WTC collapse as significantly influencing their global attitudes and perspectives, as contrasted with < 1/3 of non PTSD bipolars. Reactions to 9/11 events in bipolar patients directly affected by the catastrophe generally fell within the expectable range of normal responses. Pre-existing PTSD conferred some increased risk for greater substance abuse but did not markedly promote maladaptive or psychopathologic responses.

NR295 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Lamotrigine Delays Mood Episodes in Recently Depressed Bipolar I Patients

Charles L. Bowden, M.D., *Department of Psychiatry, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284-7792*; S. Nassir Ghaemi, M.D., Laszlo Gyulai, M.D., Leighton Y. Huey, M.D., Arifulla Khan, M.D., Paul Montgomery, M.D., John A. Ascher, M.D.

Summary:

Objective: A double-blind, placebo-controlled, 18-month study (GW 605) was conducted to assess the efficacy and tolerability of lamotrigine as maintenance treatment in currently or recently depressed bipolar I patients.

Methods: Lamotrigine was initiated during an 8- to 16-week open-label phase while other psychotropic drugs were discontinued. Stabilized patients were then randomized to lamotrigine (50mg, 200mg or 400mg daily), lithium (0.8 to 1.1mEq/L), or placebo for up to 18 months double-blind treatment.

Results: 966 qualified patients entered the open-label phase. 463 met stabilization criteria and were randomized to double-blind maintenance treatment (221 lamotrigine, 121 lithium, 121 placebo). Lamotrigine (both 200mg and 200/400mg combined) and lithium were superior to placebo at prolonging the time to intervention for any mood episode ($p = 0.029$ lamotrigine versus placebo, $p = 0.029$ lithium versus placebo) and overall survival in study ($p = 0.003$ lamotrigine versus placebo; $p = 0.022$ lithium versus placebo). Lamotrigine was superior to placebo at prolonging the time to a depressive episode ($p = 0.047$), lithium was not ($p = 0.209$). The most common adverse event reported for lamotrigine was headache. There were no reports of serious rash.

Conclusions: Lamotrigine and lithium were superior to placebo in delaying relapse or recurrence of mood episodes in recently depressed bipolar I patients.

NR296 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Drug-Use Patterns and Relapse Rates for Patients on Selective SSRIs

Stella Chang, M.P.H., *MEDSTAT, 4301 Connecticut Avenue N.W. Suite 330, Washington, DC 20008*; Sean Kennedy, B.A., Roma Tretiak, M.H.A., Amy Grundzinski, Pharm.D.

Summary:

Introduction: Despite clear treatment guidelines for the treatment of depression the average duration of therapy in actual practice is less than recommended. This study investigated the evolution of drug use patterns, treatment length, and their impact of relapse or recurrence in patients treated for depression with SSRIs in the UK from 1996–99.

Methodology: Data from primary care settings in the United Kingdom (DIN-LINK) for the years 1996–1999 were collected. Drug use and therapy length were assigned using prescription records. Demographic and physician encounter data were utilized to control for confounding effects.

Results: Mean days of SSRI treatment among the 6,334 patients increased during 1996–1999 from 83.65 to 93.54 in 1999 ($p < .0001$). The overall rate of relapse/recurrence was 13.6%. Risk of relapse/recurrence decreased by approximately 4% with each monthly increase in treatment (OR = 0.96, CI = 0.921–0.994). Relapse/recurrence was more likely to occur in patients who had less than 120 days of treatment, augmented, switched, or increased dose than stable users ($p < .05$). Additional factors significantly associated with risk of relapse/recurrence included anxiety, younger age, male gender, and certain depression diagnoses.

Conclusions: Longer lengths of treatment were associated with decreased risk of relapse. While the mean length of SSRI treatment increased, it nevertheless fell short of the 120 days of SSRI therapy recommended in treatment guidelines.

NR297 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Determinants of Duration of Major Depressive Episodes in the General Population

Jan Spijker, M.D., *De Gelderse Roos and TR IMBOS Institute, P.O. Box 725, Utrecht, AS 3500, Netherlands*; Ron de Graaf, Ph.D., Rob V. Bijl, Aartjan T.F. Beekman, Hans Ormel, Willem A. Nolen, M.D.

Summary:

Background: Data on determinants of duration of major depressive episodes (MDE) in the general population are sparse.

Aims: To asses duration of MDE and its sociodemographic, psychosocial, and clinical determinants in subjects from the gen-

eral population (N = 250) with newly originated episodes of DSM-III-R major depression.

Method: The Netherlands Mental Health Survey and Incidence Study is a prospective epidemiologic survey in the adult population (N = .7076), using the Composite International Diagnostic Interview (CIDI). Duration of MDE was assessed with a life chart interview (LCI).

Results: Median duration of MDE was 3.0 months; 50% recovered within three months, and nearly 20% had not recovered at 24 months. Determinants of persistence were longer duration of previous episodes, presence of depressive symptoms, history of somatic illness, and lack of social support. Determinants early and late in episode differ, with a negative influence of higher age and higher neuroticism later in episode.

Conclusions: Although half of those affected with MDE recovered fast, the risk of chronicity (duration ≥24 months) was considerable, underlining the need for diagnosing and treating those at risk. Predictors for persistence were clinical characteristics, somatic illness, higher age, and high neuroticism.

Declaration of interest: NEMESIS is supported by the Netherlands Ministry of Health, Welfare and Sport (VWS), the Medical Sciences Department of the Netherlands Organization for Scientific Research (NWO), and the National Institute for Public Health and Environment (RIVM).

NR298 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Bipolar II Depressive Mixed State

Franco Benazzi, M.D., *Department of Psychology, University of Bologna, Via Pozzetto 17, Cervia, RA 48015, Italy*

Summary:

Objective: Depressive mixed state (DMX) (major depressive episode [MDE] with some hypomanic symptoms) was found common in depressed outpatients. Study aim was to find a clinically useful definition of DMX. A useful definition could be one increasing the probability of making the correct diagnosis of bipolar II.

Method: Consecutive 206 bipolar II and 130 unipolar MDE outpatients were interviewed with DSM-IV Structured Clinical Interview-Clinician Version. Different DMX definitions were tested, based on factor analysis, multivariate regression, discriminant analysis, and logistic regression analysis results. Sensitivity, specificity, correctly classified, and ROC area for bipolar II diagnosis were compared.

Results: Two factors were found (F1, including irritability, psychomotor agitation, and more talkativeness, and F2, including racing thoughts, irritability, and distractibility), significantly associated with bipolar II diagnosis. Of the hypomanic symptoms most common in bipolar II DMX, only irritability and racing thoughts were significantly associated with bipolar II diagnosis on discriminant analysis. DMX3 (DMX with three or more hypomanic symptoms) was strongly associated with bipolar II diagnosis. Comparisons of sensitivity, specificity, correctly classified, and ROC area of DMX definitions (F1, F2, DMX3, irritability during MDE, racing thoughts during MDE) for diagnosis of bipolar II, showed that F1 had the best combination of sensitivity and specificity (74.2%, 60.0%), and high correctly classified (68.7%) and ROC (0.70), but DMX3 has the highest specificity (80.0%) (sensitivity 55.8%), and slightly lower correctly classified (65.1%) and ROC (0.67) than F1.

Conclusions: A DMX definition having the highest specificity (DMX3) for bipolar II diagnosis may be more useful to clinicians, leading to few false positives. Bipolar II diagnosis has important treatment and clinical implications, but misdiagnosis is common because diagnosis is often based on history of hypomania (dependent on memory and clinical skills). A cross-sectional marker like DMX3 may increase the probability of making the correct diagnosis of bipolar II, and therefore may be a useful definition of DMX.

NR299 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Depression and Plasma Fibrinogen Concentration in Middle-Aged Women

Ruby C. Castilla-Puentes, M.D., *Department of Epidemiology, University of Pittsburgh, 3811 O'Hara Street, SWAN-Study, Pittsburgh, PA 15213*; Joyce T. Bromberger, Ph.D., James Perel, Ph.D., Karen Matthews, Ph.D.

Summary:

Objective: To compare the fibrinogen levels in depressed women (CES-D>16) vs. non-depressed women (CED-D≤16) using the baseline data from the Study of Women's Health Across the Nation.

Method: Fibrinogen levels of 3,198 women obtained during the baseline visit, were compared with their CES-D scores provided during the same visit. We examined the differences of fibrinogen levels with depressive symptoms. For comparisons, independent T-Test was calculated and significant *P* values were derived.

Results: In 778 (24.32%) women with depression (CES-D>16) the mean of fibrinogen levels was 304.14 (SD ± 72.24). Non depressed women showed lower plasma fibrinogen levels (Mean = 290.56, SD ± 66.83) compared with the depressed. Significant differences in the fibrinogen levels, $p < 0.001$ were associated with the presence of depressive symptoms.

Conclusions: Data suggest that women with depression have significant high levels of fibrinogen compared with non-depressed women. This data underline the importance of considering depressive symptoms a risk factor in the increase of fibrinogen levels.

NR300 Tuesday, May 21, 3:00 p.m.-5:00 p.m.

Direct Effect of Quetiapine on the Negative Symptoms of Schizophrenia

Rajiv Tandon, M.D., *Department of Psychiatry, University of Michigan Health System, 1500 East Medical Center Drive, Ann Arbor, MI 48109-0120*

Summary:

Introduction: Quetiapine improves the negative symptoms of schizophrenia[1] but whether this improvement is the result of a direct or indirect effect is unclear.

Objective: To determine the extent to which improvements in negative symptoms result from a direct effect of quetiapine activity or are secondary to quetiapine's efficacy against positive symptoms and reduced propensity to cause extrapyramidal symptoms.

Methods: Data from patients (n = 1106) in four 6-week, placebo-controlled, double-blind, randomized trials[2–5] were evaluated using a path analysis model. Change from baseline to Week 6 in the Scale for the Assessment of Negative Symptoms total score was used to assess the direct effect on negative symptoms. Changes from baseline in BPRS positive cluster score, BPRS depressive score, and Simpson-Angus total score were used to assess secondary, indirect effects via positive, depressive and extrapyramidal symptoms, respectively.

Results: The path analysis showed that negative symptoms improved more with quetiapine than placebo and that 44.2% of this improvement could not be explained by other effects and might represent a direct effect of quetiapine ($p < 0.001$).

Conclusions: Quetiapine appears to possess a direct effect on the negative symptoms of schizophrenia. This knowledge may be useful in evaluating treatment strategies for patients with prominent negative symptoms.

NR301 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

A Quantitative Review of Adherence to Mental Health Practice Guidelines

Mark S. Bauer, M.D., *Department of Psychiatry, Providence VAMC, 830 Chalkstone Avenue, Providence, RI 02908*;

Summary:

Background: Mental health clinical practice guidelines have proliferated, but there is little evidence regarding the degree to which they are actually implemented in clinical practice.

Methods: Search strategy identified peer-reviewed articles published through 2000 that reported quantitative adherence rates via Medline search, review of the Cochrane Collaboration evidence-based medicine database, review of bibliographies of relevant articles, and location of recently published studies via dialogue at scientific meetings.

Results: Studies (n=41) were classified as cross-sectional after guideline release (n=26), pre- and postrelease of guideline without specific intervention (n=6), or controlled trial of a specific intervention (n=9). Only 37% were conducted in the mental health specialty sector. Adequate adherence was found in only 27% cross-sectional and pre/post studies, but in 67% controlled trials. Successful interventions tended to be complex, involving system redesign or additional resources. Only 6 of 13 studies that also measured patient outcome (46%) showed that better outcome was associated with greater guideline adherence. Several studies indicate that after cessation of interventions adherence rates return to pre-intervention levels.

Conclusions: Evidence indicates that interventions can improve guideline adherence and that this may improve outcome; the public health challenge is to design and implement interventions that are sustainable in general clinical practice.

NR302 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Improvement in Health-Related Quality of Life was Associated Antidepressive Property: Evidence from an Acute Manila Clinical Trial of Olanzapine Versus Divalproex

Lizheng Shi, Ph.D., *Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285*; Baojin Zhu, Madhav Namjoshi, Ph.D., Sandra L. Tunis, Ph.D., Robert W. Baker, M.D., Mauricio F. Tohen, M.D., Alan F. Breier, M.D.

Summary:

Objective: To determine the associations between long-term quality of life (QOL) and clinical symptomatic outcomes in a 47-week double blind clinical trial.

Methods: Patients (N=251) with acute mania were randomized to olanzapine 5–20 mg/day or divalproex 500–2500 mg/day during a three-week acute phase. Only 167 patients, who entered a 44-week double blind maintenance phase, were included in the analysis. QOL improvement was measured by the changes from baseline to week 47 in Psychological General Well Being (PGWB) using last-observation-carried-forward (LOCF). Symptomatic improvements were measured by the LOCF changes from baseline to week 47 in Young-Mania Rating Scale (Y-MRS) and Hamilton Depression Rating 21-item Scale (HAM-D) as well as Clinical Global Impression-Bipolar (CGIBP). Pearson correlation analysis was used to test the associations between QOL and clinical measures (Y-MRS, HAM-D and CGIBP).

Results: Significant associations were found between changes in depression measures (HAM-D total and CGI depression severeity score) and changes in dimension PGWB scores while mania measures (Y-MRS total and CGI mania severity score) was only spuriously associated with PGWB.

Conclusion: Long-term QOL improvement was closely associated with the anti-depressive property, suggesting a potential for a clinically meaningful translation of improvement in QOL in the treatment of acute mania.

NR303 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

The Treatment of Schizophrenia Across Europe: Between-Country Baseline Differences in the Schizhophrenia Outpatient Health Outcome Study

Eric T. Edgell, Pharm. D., *Eli Lilly And Company, Lilly Corporate Center, Indianapolis, In 46285*; Josep Haro, M.D., P. Frewer, Ph.D., Padraig Wright, M.D., Diego Novick, Ph.D., Madhav Namjoshi, Ph.D.

Summary:

Objectives: To describe between country differences in schizophrenia treatment patterns.

Methods: SOHO is a three-year, prospective, observational study targeted to enrol 10,800 outpatients across 10 European countries. Patient characteristics in terms of resource utilization, antipsychotic use patterns, and symptomatology were compared between countries.

Results: Six countries had sufficient enrolment for analyses. Total enrolment was 4,570 patients. In the six-month period prior to the study, 34% of patients were admitted to hospital ranging from 19% in Greece to 38% in Germany. Day-hospital use was highest in Italy (42% of patients), and lowest in Greece (4%). Germany (42%) had the highest and Italy (23%) the lowest, proportion of patients involved in a relationship. The proportion living independently was also highest in Germany (66%) and lowest in Italy (33%). The UK/Ireland and Italy had the highest use of depot medications (more than 30% of patients in the previous six months). The UK/Ireland and Spain had the highest use of atypical antipsychotics (greater than 40% of patients in the previous six months).

Conclusions: European countries show important differences in patterns of care for schizophrenia. The impact of these differences on long-term outcomes requires examination.

NR304 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Aggression Screening to Predict and Prevent Use of Seclusion in Acutely Ill Inpatients.

Geetha Jayaram, M.D., *Department of Psychiatry, Johns Hopkins University School of Medicine, 600 North Wolf Street, M-101, Baltimore, MD 21287*; Gary Dunn, M.S.N.

Summary:

Background: Joint Commission regulations on seclusion use require systematic assessment and documentation of seclusion/restraint use. We did not find an intake tool used to prevent seclusion in the literature. The Short-Stay Psychiatric Service of the Johns Höpkins Hospital admits acutely ill patients. To decrease length-of-stay, safe safely/appropriately treat patients, our team devised an Aggression Screening Tool, administered within 48 hours of admission, which alerts nurses to potential for patient-related data for analyses of outcomes.

Method: Clinical data were collected on 229 consecutive admissions in 2000. Seclusion details were systematically recorded. Demographics, case-mix severity, outcomes were examined. Parametric tests were used for analyses.

Results: Sixty-eight acts of verbal/physical aggression occured among 22 patients, all of whom were identified by the Screening scale. The scale was more sensitive than specific. No gender or age differences were noted between aggressive and non-aggressive patients; significant differences were noted at the 0.004, 0.006, and 0.005 levels for length-of-stay, cost of hospitalization and illness complexity respectively. Interventions, outcomes, resolution of aggression are discussed.

NR305 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Does Illness Complexity Impact on Outcomes?

Geetha Jayaram, M.D., *Department of Psychiatry, Johns Hopkins University School of Medicine, 600 North Wolf Street, M-101, Baltimore, MD 21287*; Gary Dunn, M.S.N.

Summary:

Background: Illness complexity for hospitalized patients is determined by a careful consideration of all clinical data using the All Patient Refined-Diagnosis Related Groups (APR-DRGS) system. Within this system, besides the primary diagnosis, secondary factors such as severe psychotic symptoms, increased nursing management, complications of treatment such as delirum, medical problems, and functional difficulties add to the computation of severity. Also, the system is useful for comparative hospital profiling, measuring casemix and for prospective payments.

Method: The Johns Hopkins Hospital Short-Stay-Service (using screening/data collection instruments) collected clinical data for 193 of 1088 consecutive admissions and compared them to 192 standard-stay admissions. Besides descriptive statistics, we also collected intake and discharge information on symptom as well as functional impairment, length of stay, and illness complexity.

Results: We found that short-stay patients differed from standard-stay patients in average length-of-stay, illness complexity, functional impairment, symptom impairment, and overall charges at the p=0.01 level. The services fulfilled their missions in fully treating patients as measured by the Global Assessment of Function at discharge (p=0.01). Measuring outcomes enables precision in documentation and improves quality of care.

NR306 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

D-Fenfluramine and Apomorphine Tests and Antipsychotic Treatment Outcome

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, Marc-Antoine Crocq, M.D., Jean-Paul Macher, M.D.

Summary:

Background: Criteria for selection of an appropriate antipsychotic compound are lacking.

Method: We measured prolactin (PRL), adrenocorticotropin (ACTH) and cortisol responses to the selective 5HT releasing agent D-fenfluramine (D-FEN, 45 mg, p.o.) and the direct DA receptor agonist agent apomorphine (APO, 0.75 mg, s.c.) in 31 drug-free schizophrenic inpatients (SCZs) and 23 hospitalized healthy controls (HCs). Patients were subsequently treated for six weeks with haloperidol (HAL: n=16; mean daily dose±SD; 15±7 mg) or risperidone (RIS: n=15; 6±2 mg/day), and were then classified as responders or non-responders according to whether or not their scores on the Brief Psychiatric Rating Scale decreased by > 50% with treatment.

Results: Responders to HAL (n=11) showed lower pretreatment ACTH (p=0.02) and PRL (p<0.0006) responses to D-FEN, and lower ACTH (p<0.03) responses to APO than nonresponders (n= 5) and HCs. Nonresponders to RIS (n=5) showed lower PRL response to D-FEN (p<0.01) and to APO (p<0.03) than responders (n=10) and HCs.

Conclusions: Patients with blunted responses to D-FEN, which may reflect decreased central 5-HT tone, and to APO, which may reflect decreased D2-like receptor function possibly secondary to increased DA turnover, respond preferentially to haloperidol rather than to risperidone, whereas patients with normal responses to D-FEN and APO respond preferentially to risperidone rather than to haloperidol. If confirmed in randomized studies, these findings could aid clinicians in the selection of an antipsychotic drug.

NR307 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

The Relation Between Body Fat Distribution and Card Iovascular Risk Factors in Patients with Schizophrenia

Martha M. Kato, M.D., *Department of Psychiatry, University of Miami, 1695 N.W. 9th Avenue, #2435, Miami, FL 33136*; Mercedes Gonzalez-Blanco, M.D., Lacresha L. Hall, M.D., Orlando Santana, M.D., Marni Grant, M. Beatriz Currier, M.D.

Summary:

Aim: To examine body fat distribution and its relation to cardiovascular risk factors in schizophrenics.

Methods: Cross-sectional study of 36 subjects (17 females and 19 males) aged 20–73 years, on stable dose of one antipsychotic, were recruited from an outpatient clinic. They had no history of chronic illness and were on no medications known to affect glucose or lipids. Of the 36 subjects, 83% were white and 64% were Hispanics. Fasting glucose and lipids were obtained.

Results: Pearson correlations in males showed an association of the waist-to-hip ratio (WHR) with cholesterol (r=0.52, p<0.022), body mass index (BMI) with cholesterol (r=0.59 p<0.008), and waist circumference (WC) with cholesterol (r=0.53 p<0.020), triglycerides (r=0.50, p<0.028) and pulse (r=0.54, p<0.017). In females Pearson correlations showed an association between WHR with triglycerides (r=0.60, p<0.010) and WC with high-density lipoprotein (HDL) (r=0.55, p<0.021), pulse (r=0.50, p<0.041), and diastolic blood pressure (DBP) (r=0.69, p<0.002). Regression coefficients revealed the same associations as the Pearson correlations. The association between WC with pulse, DBP, and HDL and WHR with triglycerides remained significant after controlling for age, gender, ethnicity, race, smoking, BMI, and antipsychotic medications.

Conclusion: Data suggest that WC is a stronger predictor of cardiovascular risk factors, in both male and female patients with schizophrenia, than BMI or WHR. WC is an indicator of visceral abdominal fat, which is associated with insulin resistance. With the recent concern about increased risk of obesity and diabetes mellitus in patients with schizophrenia, this data suggests that the WC, a simple measure to obtain, is a significant screening tool for coronary heart disease.

NR308 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Olanzapine Causes Greater Increases in Serum Lipids Than Risperidone

Herbert Y. Meltzer, M.D., *Department of Psychiatry, Vanderbilt University, 1601 23rd Avenue South, Suite 306, Nashville, TN 37212-8645*; John H. Gilliam, M.D., Clifford Nasdahl, M.D.

Summary:

Background: Differences among antipsychotic drugs for risk of atherosclerotic cardiovascular disease (ACD) and diabetes mellitus (DM) are important to the long term analysis of risk/benefit ratios for this class of drugs.

Methods: We are conducting a 1 year multicenter, randomized trial comparing the effect of switching patients from other psychotropic drugs to olanzapine and risperidone on weight, serum lipids and serum glucose measures in patients with schizophrenia or related disorders.

Results: With data from 47 patients, olanzapine produced significantly greater increases in cholesterol, triglycerides, and LDL and a trend for increased glycohemoglobin levels at 1 or 3 months, or both, than did risperidone. Thus, serum cholesterol increased from 184.8±41.7 to 197.2±42.7 mg/dl in the olanzapine group while it decreased from 181.6±42.7 to 167.9±34.6 mg/dl in the risperidone group (effect size = 0.76). The increases in lipids were independent of changes in weight. There were no differences in the extent of weight gain, changes in HDL, or fasting plasma

glucose. The lack of difference in weight gain may be related to the mild or moderate obesity at baseline in the entire sample.

Conclusions: These findings, if enduring, suggest differential risk for the development of ACD and possibly type II diabetes.

NR309 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

The Intersept Trial: Reduced Suicidality with Clozapine Treatment

Herbert Y. Meltzer, M.D., *Department of Psychiatry, Vanderbilt University, 1601 23rd Avenue South, Suite 306, Nashville, TN 37212-8645*; Larry Alphs, M.D., A. Ravi Anand, M.D., M. Zahur Islam, Steven G. Potkin, M.D.

Summary:

Objective: Approximately 50% of patients with schizophrenia or schizoaffective disorder attempt suicide and about 10% die from suicide. Several lines of evidence suggest that clozapine significantly reduces the suicide attempt and completion rates in these patients.

Method: A multi-center, randomized, international study comparing the effects of clozapine and olanzapine on suicidality was conducted in 980 patients with schizophrenia or schizoaffective disorder who were at high risk for suicide. Suicidal behavior was assessed at regular visits by blinded raters. Subsequent to randomization, unblinded clinicians were allowed to make any interventions necessary to prevent the occurrence of suicide attempts. Suicide attempts and hospitalizations to prevent suicide were reviewed by a blinded expert Suicide Monitoring Board that identified all study endpoints.

Results: The risk for a suicide attempt or hospitalization to prevent suicide was significantly less in patients treated with clozapine compared to olanzapine (hazard ratio=0.74, p=0.02, 95% CI = (0.57, 0.95)). In addition, in comparison to treatment with olanzapine, clozapine-treated patients showed fewer suicide attempts (p= 0.03); required fewer rescue interventions to prevent suicide (p= 0.01); required fewer hospitalizations to prevent suicide (p=0.05); and required fewer concomitant medications, e.g., antidepressants (p=0.02) and anxiolytics/soporifics (p=0.03).

Conclusions: Clozapine was demonstrated to be superior to olanzapine, a widely used atypical antipsychotic therapy, for the prevention of suicide attempts in patients with schizophrenia and schizoaffective disorder at high risk for suicide.

NR310 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Switching to Aripiprazole Monotherapy

Daniel E. Casey, M.D., *Mental Health Department, Portland VA Medical Center, 3710 S.W., U.S. Veterans Hospital Road, Portland, OR 97201*; Anutosh R. Saha, Ph.D., Mirza W. Ali, Ph.D., Darlene Jody, M.D., Mary J. Kujawa, M.D., Elyse G. Stock, M.D., Gary G. Ingenito, M.D.

Summary:

Objectives: To assess the safety and tolerability of switching patients from current antipsychotic therapy to aripiprazole, a newly developed antipsychotic, with a unique mechanism of action (dopamine-serotonin system stabilizer). The impact on efficacy was also evaluated.

Methods: This Phase III study involved 311 patients with chronic, stable schizophrenia or schizoaffective disorder who had received monotherapy with a typical (haloperidol or thioridazine) or atypical (risperidone or olanzapine) antipsychotic for ≥1 month. Patients were randomized for 8 weeks into 3 groups: Group 1 - Immediate initiation of 30mg/d aripiprazole with simultaneous abrupt discontinuation of current antipsychotic (n=104). Group 2 - Immediate initiation of 30mg/d aripiprazole while tapering off current antipsychotic over 2 weeks (n=104), Group 3 - Titration of aripiprazole over 2 weeks (from 10mg/d to 30mg/d) while tapering off current antipsychotic (n=103).

Results: Safety and tolerability results were similar across treatment groups. There was no difference in discontinuations due to adverse events across the three groups. Antipsychotic efficacy was maintained in all groups throughout the study and improvement was seen from baseline in PANSS-total, -negative, -positive subscales, and CGI-Improvement Score.

Conclusions: Switching to aripiprazole is safe and well tolerated and can be initiated at an efficacious dose without having to gradually increase the dose of aripiprazole.

NR311 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Quality of Life in Schizophrenia

Patricia Russo, Ph.D., *ORE, The Medstat Group, 4301 Connecticut Avenue NW, Suite 330, Washington, DC 20008*; Mark Smith

Summary:

Objective: Examine relationship between self-reported and clinically assessed quality of life (QoL) among participants in the U.S. Schizophrenia Care and Assessment Program (SCAP).

Methods: Data obtained at 12-month assessment (n=908). Clinical instruments: Quality of Life Scale (QLS), Montgomery-Asberg Depression Rating Scale (MADRS), Positive and Negative Symptoms Scale (PANSS), Abnormal Involuntary Movement Scale (AIMS). Self-report instruments: Life Satisfaction (LifeSat) scale and Depression scale (SCAP Health Questionnaire). Regression analyses conducted.

Results: Correlation between subjective and objective scales were significant (magnitudes: 0.2 to 0.6). QLS was inversely impacted by PANSS ($p<0.001$) and MADRS ($p<0.001$). Self-reported LifeSat was impacted by MADRS ($p<0.001$) and not symptoms (PANSS). MADRS effect was 38% greater on LifeSat than QLS. QLS sub-scales (common objects; activities, interpersonal relations) were significantly related to LifeSat ($p<0.01$; $p<0.001$). In the presence of MADRS, significance of clinical and QLS subscales diminished and R-squared increased. Clinically assessed and self-reported depression were related (0.38; $p<0.001$).

Conclusions: Findings demonstrate: 1) self-reports and clinical assessments are interrelated (QoL and depression), 2) clinical symptoms and side effects are not important drivers of self-reported QoL; 3) depression is an important factor in patients' own sense of life satisfaction; and 4) depression exhibits a mediating effect between psychiatric symptoms and QoL.

NR312 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Safety and Tolerability of IM Ziprasidone: Review of Clinical Trial Data

Daniel L. Zimbroff, *Pacific Clinical Research, 1317 West Foothill Boulevard, Suite 200, Upland, CA 91786*; Shlomo Brook, M.D., Isma Benattia, M.D.

Summary:

Objective: To evaluate the safety and tolerability of IM ziprasidone, as demonstrated in randomized clinical trials.

Methods: We reviewed data from three fixed-dose and two flexible-dose trials that included 940 adult patients with acute psychosis who received IM ziprasidone at doses up to 20 mg a maximum of four times daily.

Results: Discontinuation rates for treatment-emergent adverse events (AEs) in IM ziprasidone groups ranged from 1.1% to 6.1%. The most common AEs among patients receiving 10- or 20-mg doses for up to 3 days were headache, nausea, dizziness, insomnia, and anxiety. The vast majority of treatment-emergent AEs in all studies were mild or moderate in severity. Compared with

haloperidol, IM ziprasidone was consistently associated with a lower movement disorder burden (eg, akathisia, dystonia, EPS, hypertonia) at all doses investigated. In all studies, clinically significant changes in blood pressure and heart rate associated with IM ziprasidone were isolated and transient; treatment-emergent postural hypotension was observed in one ziprasidone-treated patient in one study. There were no QTc values ≥500 msec with IM ziprasidone.

Conclusion: In clinical trials, IM ziprasidone in divided doses up to 80 mg/day was well tolerated, with low incidences of AE-related discontinuations and movement disorder AEs.

NR313 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Olanzapine Improves Tardive Dyskinesia in Patients with Schizophrenia

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., Khanhn T. Thi

Summary:

Objective: We report preliminary findings of the effects of olanzapine (OLZ) treatment upon tardive dyskinesia TD.

Methods: Eligible schizophrenic subjects met restricted Research Diagnosis Tardive Dyskinesia criteria (restricted RD-TD) that specified for abnormal involuntary movements to be of at least moderate severity. Subjects received OLZ, 5–20 mg/day for 8 months within a double-blind design that included up to 2 medication reduction (75%) periods of 2 weeks duration. TD was assessed with the Abnormal Involuntary Movement Scale (AIMS) and psychopathology with the Positive and Negative Syndrome Scale (PANSS).

Results: A significant reduction in mean AIMS Total score was demonstrated (N=95; BL=11.9; EP=7.5; p<.001; LOCF). Nearly 70% of subjects no longer met the restricted RD-TD criteria after up to 8 months of treatment, with greater than 50% improving as early as 8 weeks. No statistically significant rebound worsening of TD was found during the blinded drug reduction periods. A significant improvement in the PANSS occurred (BL=68.2; EP= 59.7; p<.001, LOCF).

Conclusion: These data, suggesting an ameliorative, rather than masking effect, and the concurrent further improvement in clinical status suggests that OLZ may offer a potential treatment alternative for managing the schizophrenic patient with pre-existing TD.

NR314 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Aripiprazole Versus Placebo in Acute Mania

Paul E. Keck, Jr., M.D., *Biological Psychiatry Department, Univ. of Cincinnatti College of Medicine, 231 Albert Sabin Way, ML559, Cincinnati, OH 45267-0559*; Anutosh R. Saha, Ph.D., Taro Iwamoto, Ph.D., Darlene Jody, M.D., Stavros Tourkodimitris, Ph.D., Donald G. Archibald, M.Phil., Ronald N. Marcus, M.D.

Summary:

Objective: To compare the efficacy and safety of aripiprazole, the first next-generation atypical antipsychotic with a unique mechanism of action (dopamine-serotonin system stabilizer) to placebo in patients with acute bipolar mania.

Methods: This Phase III, multicenter, double-blind, placebo-controlled study randomized 262 patients with acute mania to aripiprazole 30 mg (reduced to 15 mg if unable to tolerate) or placebo for 3 weeks. Patients remained hospitalized for a minimum of two weeks of the treatment phase. The primary measure of efficacy was the change in Y-MRS Total score. Response was defined as a decrease of ≥50% in Y-MRS Total score.

Results: Aripiprazole produced statistically significant improvements in Y-MRS Total score (–8.15 vs. –3.35, p≤0.01) compared to placebo. The response rate was significantly higher in the aripiprazole group than the placebo group (40% vs. 19%, p≤0.01). For all efficacy variables, aripiprazole separated from placebo by day 4. Discontinuations due to adverse events did not differ between the aripiprazole and placebo groups, and there were no significant changes in weight versus placebo.

Conclusion: Aripiprazole was effective and well tolerated in the treatment of acute mania in patients with bipolar disorder in this randomized, placebo-controlled trial.

NR315 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Ziprasidone Versus Olanzapine in Schizophrenia: Six-Month Continuation Study

George M. Simpson, M.D., *Department of Psychiatry, LAC/ USMC Medical Center, 2020 Zonal Avenue, IRD Room 20, Los Angeles, CA 90033*; Peter J. Weiden, M.D., Teresa A. Pigott, M.D., Steven J. Romano, M.D., Cynthia Siu, Ph.D.

Summary:

Objective: To compare long-term efficacy and tolerability of ziprasidone and olanzapine in schizophrenia or schizoaffective disorder.

Methods: This 6-month, blinded continuation study followed hospitalized patients who had completed a 6-week randomized trial with satisfactory clinical response (CGI-I ≤2 or ≥20% reduction in symptom severity by PANSS Total) and were discharged on olanzapine 5–15 mg QD (n=71) or ziprasidone 40–80 mg BID (n= 62). Primary efficacy measures were BPRS and CGI-S; secondary variables included PANSS Total and Positive and Negative Subscale scores. Tolerability assessments included fasting lipids, insulin, glucose, and weight.

Results: Ziprasidone- and olanzapine-treated patients demonstrated comparable changes in BPRS, CGI-S, and PANSS Total and Subscale scores from baseline of 6-week study to endpoint of 6-month continuation. Changes during continuation phase did not differ significantly between groups. Olanzapine-treated patients exhibited significant mean increases versus ziprasidone in endpoint weight (P<0.001) and BMI (P=0.001), and significant median increases versus baseline in LDL-C (P<0.01), insulin (P<0.05), glucose (P=0.05), and fasting liver enzymes (P<0.05). Both agents displayed low incidence of movement disorders. No patients had QTc ≥500 msec.

Conclusions: Ziprasidone and olanzapine demonstrated comparable antipsychotic efficacy in long-term treatment. Olanzapine patients alone exhibited sustained weight gain and deleterious metabolic changes.

NR316 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Antipsychotic Monotherapy Versus Combination Treatment with Valporate in Hospitalized Patients with Acute Schizophrenia: A Double-Blind, Multi-Center Study

Leslie L. Citrome, M.D., *Clinical Research/CREF, Nathan Kline Institute, 140 Old Orangeburg Road, Building 37, Orangeburg, NY 10962-2210*; David G. Daniel, M.D., Adel A. Wassef, M.D., Katherine A. Tracy, M.D., Patricia Wozniak, Ph.D., Daniel E. Casey, M.D.

Summary:

Objective: This study compared the efficacy and safety of atypical antipsychotic monotherapy (olanzapine or risperidone) versus combination treatment with valproate (divalproex sodium) in patients with an acute episode of schizophrenia.

Methods: A total of 249 inpatients with schizophrenia were randomly assigned to receive olanzapine plus placebo, olanzapine plus divalproex, risperidone plus placebo, or risperidone plus divalproex in a double-blind 28-day multi-center trial. Target daily dose was 15 mg for olanzapine, 6 mg for risperidone, and up to 30 mg/kg (minimum 15 mg/kg) for divalproex. The Positive and Negative Syndrome Scale (PANSS) was the principal efficacy measure.

Results: The PANSS Total and the PANSS Positive subscale scores of patients receiving combination therapy with divalproex indicated significantly greater improvement than those of patients receiving antipsychotic monotherapy. This was evident as early as Day 3 (ANOVA, $p<0.05$) and was present throughout the 28 days as demonstrated using repeated measures ANOVA (PANSS Total Score $p=0.020$; PANSS Positive Subscale $p=0.0020$). Adverse events and rates of discontinuation were similar between the treatments.

Conclusion: Divalproex significantly enhances antipsychotic efficacy in patients with schizophrenia. Combination therapy with divalproex was as well tolerated as monotherapy with olanzapine or risperidone.

NR317 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Pharmacokinetics and Safety of Aripiprazole and Concomitant Mood Stabilizers

Leslie L. Citrome, M.D., *Clinical Research/CREF, Nathan Kline Institute, 140 Old Orangeburg Road, Building 37, Orangeburg, NY 10962-2210*; Richard Josiassen, Ph.D., Nigel M. Bark, M.D., Karen S. Brown, M.S., Suresh Mallikaarjun, Ph.D., Daniel F. Salazar, Ph.D.

Summary:

Objective: To assess the safety profile and pharmacokinetics of aripiprazole, an antipsychotic with a unique pharmacologic profile of dopamine D_2 partial agonism, serotonin $5HT_{1A}$ partial agonism and $5HT_{2A}$ antagonism, when coadministered with lithium or divalproex sodium.

Methods: Two open-label, sequential treatment design studies were conducted in chronically institutionalized patients with schizophrenia or schizoaffective disorder requiring treatment with lithium (n=7) or divalproex sodium (n=6). Patients received aripiprazole 30 mg/day on Days 1–14 and aripiprazole with concomitant therapy on Days 15–36. Lithium was titrated from 900 mg until serum concentrations reached 1.0–1.4 mEq/L for ≥5 days. Divalproex sodium was titrated to 50–125 mg/L.

Results: Coadministration with lithium increased mean C_{max} and AUC values of aripiprazole by about 19% and 15%, respectively, while the apparent oral clearance decreased by 15%. There was no effect on the steady state pharmacokinetics of the active metabolite of aripiprazole. Coadministration with divalproex sodium decreased the AUC, C_{max} and C_{min} of aripiprazole by 24%, 26%, and 22%, respectively, with minimal effects on the active metabolite.

Conclusion: Aripiprazole can be administered safely with therapeutic doses of lithium or divalproex sodium in patients with schizophrenia or schizoaffective disorder.

NR318 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

The InterSept Scale for Suicidal Thinking: Reliability and Validity

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, Larry Alphs, M.D., Ann-Marie Nathan, M.A., Ravi Anand, M.D., Zahur Islam, Ph.D., James C. Chou, M.D.

Summary:

Background: The InterSePT Scale for Suicidal Thinking (ISST) is a 12-item instrument for the assessment of current suicidal ideation in patients with schizophrenia or schizoaffective disorder. We report the psychometric characteristics of this new scale based on two studies.

Method: In Study 1, 22 inpatients with schizophrenia or schizoaffective disorder who had recently attempted suicide or engaged in suicidal ideation were rated by 3 trained independent raters to calculate interrater reliability. In Study 2, 980 patients with schizophrenia or schizoaffective disorder with a history of suicidal ideation in the past 36 months were enrolled in a 2-year industry-sponsored suicide prevention study. At baseline, these patients were administered the ISST by the Principal Investigator (PI) and by a blind rater (BR), the Positive and Negative Symptom Scale (PANSS), the Calgary Depression Scale (CDS), and the Clinical Global Impression Scale for Severity of Suicidality (CGI-SS). Indices of internal reliability, construct and discriminant validity were examined.

Results: The interrater agreement (ICC) for the total ISST score for in Study 1 was 0.90 and mean weighted item kappa coefficients ranged from 0.66–0.92. In Study 2 internal reliability (Cronbach alpha) for all items was 0.88. The ISST (PI) total score was highly correlated with the CGI-Severity of Suicidality by the blind rater ($r=0.86$, $p<0.0001$). ISST total scores significantly differentiated the different levels of CGI-SS ($F=519.3$; $df=4,955$; $p<0.0001$). Results of construct and discriminant validity analyses are also presented.

NR319 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Do Atypicals Change the Syndromal 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*; Jan Volavka, M.D., Jeffrey A. Lieberman, M.D., Leslie L. Citrome, M.D., Brian Sheitman, M.D., Joseph P. McEvoy, M.D., Thomas Cooper, M.A.

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 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. 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 excitement, cognitive, positive and depression/anxiety factors explaining 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 explaining 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. The implications of these findings in comparison with results from studies with treatment responsive patients are discussed.

NR320 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Structural MRI Findings in Child Autism

Michal Hrdlicka, M.D., *Department of Child Psychiatry, Charles University, V Uvalu 84, Prague 5 15006, Czechoslovakia*; Lukas Propper, M.D., Jiri Lisy, M.D., Tomas Belsan, M.D., Marek Blatny, Ph.D., Tomas Urbanek, Ph.D.

Summary:

Introduction: The previous research has suggested aberrant development in several brain structures in autistic patients. The aim of our study was to explore the relationship of selected brain structures to the basic symptoms of autism.

Methods: We examined the group of 34 autistic children (27 boys, 7 girls) with an average age 9.0±5,4 years. Approximately 80% of these children were mentally retarded. The rating scale CARS, structured interview ADI-R, IQ testing, and structural MRI imaging (1,5 Tesla) were performed. In the MRI scans, qualitative observations (gross pathology) as well as quantitative planimetric measurements were analyzed. Quantitative measurements were focused on cortex thickness, size of corpus callosum (CC - genu, corpus and splenium), amygdala (feet - head size), hippocampus (feet - head size), and caudate nucleus (caput).

Results: The total CARS score was 38,3 ± 6,9, no significant correlation with MRI measurements was found. Some ADI-R subscores correlated significantly with the size of caudate nucleus, hippocampus, corpus callosum and amygdala.

Conclusion: Our findings support a possible involvement of the caudate nucleus, hippocampus, corpus callosum, and amygdala in the pathogenesis of child autism.

NR321 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Eating Behavior Correlates with Drinking Behavior in Adolescent Females

Carol A. Beresford, M.D., *Department of Psychiatry, Children's Hospital, 1056 East 19th Avenue, Denver, CO 80218*; Elizabeth Siewert, Robin Corley, Ph.D., John Hewitt, Ph.D., Thomas P. Beresford, M.D.

Summary:

Objective: we previously observed significant associations between behaviors related to eating disorders and alcohol use in a mixed sample of adolescents. For the present study, we hypothesized that the reported eating behaviors would correlate with alcohol use for females but not for males.

Method: the sample consisted of 1141 twins from our state registry; ages ranged from 12 to 18,649 (56.9%) were female and 492 (43.1%) male. Each answered seven items associated with eating disorders and two items on frequency and quantity of alcohol use. The data were analyzed using chi Square tests in two-by-two tables.

Results: among the females, three of the eating behavior items were related to frequent alcohol use (3+ drinking episodes in the past 30 days): feeling fat ($p<0.05$), eating to relieve stress (0.0001), and not eating to relieve stress (0.01). These items were also associated (0.01, 0.0001, 0.001 respectively) with high quantity of alcohol per episode (3+ standard drinks) as were two other items: finding it hard to stop eating (0.03) and thinking about thinness (0.04). None of the eating behavior reports bore an association to drinking reports in the male group.

Conclusion: these data suggest that problem eating behaviors in adolescent females are associated with frequent and heavy drinking. This, in turn, may be related to development of problem drinking. If so, it would appear that a link between eating and drinking behaviors at this age represents a path to problem drinking that is unique to females.

NR322 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Language Skills and Child Psychopathology: Negative Association in Bilinguals

Claudio O. Toppelberg, M.D., *Judge Baker Children's Center, Harvard Medical School, 3 Blackfan Circle, Boston, MA 02115-5794*; Laura Medrano, M.A., Alfonson Nieto-Castanon, M.S.

Summary:

Objective: To investigate: the relationship of language skills and psychopathology, in Spanish-English bilingual children referred to child psychiatry, important as most prior studies only focused on monolingual children.

Method: Bilingual Latino children (n=50, ages 5–16) consecutively referred to psychiatric services are studied. Data on language skills [Spanish/English Woodcock Language Proficiency Battery (WLPB-R)], emotional/behavioral problems [Child Behavior Check List (CBCL); Teacher's Report Form (TRF)], sociodemographics, immigration, acculturation and non-verbal IQ, is collected. Correlational analyses are conducted.

Results: In children with clinically significant emotional/behavioral problems, bilingual language skills are strongly and inversely correlated with problem scores, particularly global problems ($r=-.67$, $p<.001$); social, thought, and attentional problems ($r=>-.54$; $p<.004$); delinquency ($r=-.66$, $p<.001$); and aggression ($r=-.52$, $p<.01$). These correlations remain significant after IQ-adjustment.

Conclusions: The data strongly suggests the clinical importance and feasibility of language assessment in psychiatrically-referred bilingual children and provides unprecedented evidence for the close relationship of low language skills and psychopathology in bilingual children.

NR323 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Language Disorder: Deficit Prevalence in Referred Bilingual Children

Claudio O. Toppelberg, M.D., *Judge Baker Children's Center, Harvard Medical School, 3 Blackfan Circle, Boston, MA 02115-5794*; Laura Medrano, M.A., Alfonson Nieto-Castanon, M.S.

Summary:

Objective: To study the prevalence of language disorders and language deficits in psychiatrically-referred bilingual children to compare it to findings in similarly referred monolingual children.

Methods: Spanish-English bilingual children consecutively referred to child psychiatry (n=50, ages 5–16), undergo an intensive language evaluation [Woodcock Language Proficiency Battery (WLPB-R), Spanish and English versions]. Language deficits, conservatively defined as standard scores below 82 (−1.25 SD) in both languages, are classified into expressive, receptive and mixed receptive-expressive types. Language disorders are defined as language deficits with language scores at least 15 standard points below a child's non-verbal IQ scores.

Results: Language disorder prevalence for this sample is 41%, while language deficit prevalence is 48%. Mixed receptive-expressive is the most common language deficit type (82.3%, Chi-Square=9.783, df=1, p=.002).

Conclusions: The prevalence of language disorders and language deficits, particularly of its mixed receptive-expressive type, is quite high and comparable to that found in prior literature on monolingual children, even when using highly conservative definitions. These unprecedented findings, highly relevant for clinical and educational purposes, justify efforts for the early detection and remediation of language problems in psychiatrically referred bilingual children. A safe approach is to fully assess language skills, rather than misattributing these children's language delays to normal bilingual acquisition processes.

NR324 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

High-Resolution Brain SPECT Imaging in ADHD Using Statistical Parametric Mapping

Eun-Young Oh, M.D., *Department of Psychiatry, Ajou University, San5 Wonchon-Dong, Paldal-Gu, Suwon, Kyunggi-Do 442-749, South Korea*; Seok-Nam Yoon, M.D., Young-Ki Chung, M.D.

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. And we revised our previous study by increasing the normal control subjects.

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 16 normal controls (M:F=14:2, 10.09+2.2y). ADHD group is 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 compaired individual and patient group's SPECTs with those of 16 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 significant hypoperfusion in total ADHD patients (n=85) when compared with control subjects (n=16)($p<0.01$). (2) Only left temporal area showed significant hypoperfusion in ADHD patients without comorbidity (n=60) when compared with control subjects (n=16). (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=25) when compared with control subjects (n=16).

Conclusion: Left temporal area rCBF was decreased in ADHD group whether subjects have comorbidity or not, when compared with control groups. According to these results, the left temporal dysfunction may mediate ADHD symptoms in children.

NR325 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

The Symptom of Irritability in Adolescent Affective Disorder

Paul J. Ambrosini, M.D., *Department of Psychiatry, MCP Hahnemann University, 3200 Henry Avenue, Philadelphia, PA 19129*;

Summary:

Objectives: The DSM IV uses Irritability synonomously with depressed mood for child diagnostic ascertainment. This conceptualization is not validated. This study assesses the influence of irritability on clinical and diagnostic issues in outpatient adolescents.

Methods: N=407 adolescents were interviewed with K-SADS. A Major Depressive Disorder (MDD) or Minor Depression/Dysthymic Disorder (MD/DD) was made *only* if significant depressed mood or pervasive anhedonia was present. All Irritable subjects without depressed mood/pervasive anhedonia were non-depressed Psychiatric Controls (PC).

Results: Irritability was more common in MDD (65.2%) than MD/DD (35.7%). Among Irritable PC, 84.6% (33/39) met symptom count criteria for an affective disorder. Irritable MD/DD was more prevalent than Irritable MDD (69.2% vs 15.4%). Irritable MD/DD (IRR MD/DD) subjects were younger, less severely depressed, more likely had Disruptive Behavior Disorders, and less likely previously depressed. The male/female prevalence ratio was converging. There was no evidence of Bipolar Disorder.

Conclusions: These data supports the uniqueness of an Irritable Minor Depressive/Dysthmic Disorder subtype. It is suggested this cohort could be misclassified as a Bipolar subtype rather than an Depressive Disorder subtype. Whether Irritable MD/DD represents a Bipolar diathesis remains to be answered by follow-up studies.

NR326 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

An Open-Label, Community Assessment Trial of Adderall XR in Pediatric ADHD

Paul J. Ambrosini, M.D., *Department of Psychiatry, MCP Hahnemann University, 3200 Henry Avenue, Philadelphia, PA 19129*; Frank A. Lopez, M.D., Mark C. Chandler, M.D., Simon J. Tulloch, M.D., M. Alex Michaels, M.D.

Summary:

Objective: This study has been conducted to evaluate the tolerability and effectiveness of Adderall XR in the treatment of pediatric ADHD in the community practice setting.

Method: A prospective, open-label, 7-week study conducted at >350 sites. >2500 children (mean age 9.5 years) with a DSM-IV diagnosis of ADHD and currently taking stable doses of immediate-release Adderall® or any methylphenidate formulation were enrolled. Efficacy was assessed by the Conners' Global Index Scale-Parent version (CGIS-P) at 12-hours after a single AM dose and by the Clinical Global Impression Scale (CGI).

Results: There was a statistically significant improvement from baseline in the mean CGIS-P scores at week 7 (baseline = 11.6, week 7 = 7.2; mean change = −4.4 [N = 1371, STD = 8.6], $p < 0.0001$). CGI-improvement scores revealed 57.2% of subjects were much improved or very much improved; only 2.1% were much worse or very much worse. The most frequently reported AEs for Adderall XR were headache (5.7% of subjects reporting), infection (3.0%), insomnia (2.9%), abdominal pain (2.7%), and anorexia (2.6%).

Conclusion: Children with ADHD, well controlled on stimulant therapy, showed significant improvement in symptoms after switching to treatment with Adderall XR. The medication was well tolerated. Adderall XR appears to be a safe and efficacious once-daily treatment for pediatric ADHD.

NR327 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Efficacy and Safety of Sertraline for Treatment of Pediatric Major Depressive Disorder

Karen D. Wagner, M.D., *Department of Psychiatry, University of Texas Medical Branch, 301 University Boulevard, Galveston, TX 77550-0188*; Christopher Wohlberg, M.D.

Summary:

Background: Major depressive disorder (MDD) is a pervasive and disabling disorder in pediatrics, affecting up to 8% of the adolescent population.

Methods: Pooled data was analyzed from two identical ten-week multicenter, double-blind, placebo-controlled, flexible-dose studies of sertraline (50–200 mg/day) in the treatment of outpatient children (6–11 years old) and adolescents (12–17 years old) with MDD.

Results: A total of 376 subjects were randomized (177 children, 199 adolescents) to receive either sertraline (n=189) or placebo (n=187). Subjects treated with sertraline showed significantly greater improvement on the primary endpoint, the Children's Depression Rating Scale - Revised (CDRS-R) total scores compared with placebo ($p<0.05$). In the treatment by visit week analysis, significantly greater improvement in the CDRS-R, CGI-I, and CGI-S scores were noted in sertraline-treated subjects beginning at week 1 and effect was seen at most visits. A significant ($p<0.05$) difference was noted for completers on all 3 rating scales. Sertraline was generally well-tolerated. Adverse events occurring in

greater than 5% of sertraline-treated subjects and twice that of placebo-treated subjects included diarrhea, vomiting, agitation, and anorexia. No clinically meaningful differences in laboratory data, electrocardiograms, or vital signs were noted between treatment groups.

Conclusions: These data support the safety and efficacy of sertraline in the treatment of pediatric MDD.

NR328 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Efficacy of Citalopram in the Treatment of MDD in Children and Adolescents

Karen D. Wagner, M.D., *Department of Psychiatry, University of Texas Medical Branch, 301 University Boulevard, Galveston, TX 77550-0188*; Adelaide S. Robb, M.D., Robert L. Findling, M.D., James Jin, Ph.D., Paul J. Tiseo, Ph.D.

Summary:

Objective: Citalopram is a safe and effective antidepressant in adults. Recently, citalopram was evaluated in a double-blind, placebo-controlled, flexible dose study in children (age 7–11) and adolescents (age 12–17) with depression.

Method: A total of 83 children and 91 adolescents with MDD (confirmed using the Kiddie Schedule for Affective Disorders and Schizophrenia [KSADS]-Present and Lifetime) were randomized to placebo or citalopram for 8 weeks. Dosing started at 20 mg/day and could be increased to 40 mg/day if needed after 4 weeks of treatment. The primary outcome measure was the Children's Depression Rating Scale - Revised (CDRS-R); response was defined as a CDRS-R score <= 28.

Results: Compared to placebo, mean CDRS-R scores decreased significantly from baseline in the citalopram group beginning at week 1 ($p < 0.02$) and continuing to week 8 ($p < 0.04$). Significant differences at week 4 indicate that citalopram 20 mg/day (which all patients received up to week 4) was an effective dose. The difference in response rate at week 8 between placebo (24%) and citalopram (36%) was significant ($p<0.05$). Adverse events seen more frequently in the citalopram group were nausea, influenza-like symptoms, and rhinitis.

Conclusion: These results demonstrate that citalopram is a safe and effective treatment for depression in children and adolescents.

NR329 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Comorbidity and Functioning in Preschoolers and School-Aged Youth with ADHD

Timothy E. Wilens, M.D., *Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114*; Joseph Biederman, M.D., Sarah A. Brown, B.A., Sara E. Tanguay, B.A., Christie S. Blake, B.S., Michael C. Monuteaux, B.A., Thomas J. Spencer, M.D.

Summary:

Objective: Although the literature documents that Attention Deficit Hyperactivity Disorder (ADHD) commonly onsets prior to age six, little is known about the disorder in preschoolers. We evaluated the clinical characteristics, psychiatric comorbidity, and functioning of preschoolers and school aged youth with ADHD referred to a pediatric psychiatric clinic.

Methods: Structured psychiatric interviews assessing lifetime psychopathology by DSM-III-R criteria were completed with parents about their youth. Family, social, and overall functioning were also assessed at intake.

Results: We identified 165 children with ADHD aged 4 to 6 years (preschoolers), and 381 youth aged 7 to 9 years (school aged) with ADHD. Preschoolers had similar rates of comorbid psychopathology compared to school aged youth with ADHD. There was an earlier onset of ADHD in the preschoolers compared to school aged youth. Both preschoolers and school aged youth had substantial impairment in school, social, and overall functioning.

Conclusions: These results suggest that despite being significantly younger, clinically referred preschoolers with ADHD are reminiscent of school aged youth with ADHD in the quality of ADHD, rates of comorbid psychopathology, and impaired functioning. Follow-up of these clinically referred preschoolers with ADHD evaluating the stability of their diagnoses, treatment response and their long-term outcome are necessary.

NR330 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Prevalence and Predictors of Depression During Pregnancy

Lee S. Cohen, M.D., *Department of Psychiatry, MGH Center for Women's Health, 15 Parkman Street, WACC 812, Boston, MA 02114*; Adele C. Viguera, M.D., Amy K. Lyster, B.A., Allison R. Fraer, B.A., Bernard L. Harlow, Ph.D.

Summary:

Introduction: While pregnancy has frequently been described as a time of emotional well-being, a growing literature supports a significant prevalence of mood disturbance in gravid women. This investigation was designed to assess the prevalence and predictors of significant depressive symptoms in a clinical series of women presenting for routine obstetrical care.

Method: A questionnaire including the Center for Epidemiologic Studies Depression Scale (CES-D) was administered to 1917 pregnant women during a second trimester routine antenatal visit at the Massachusetts General Hospital. Information regarding demographic characteristics of this sample and past history of mood disturbance and/or use of psychiatric medications was also obtained.

Results: Sixteen percent (N=309) of the sample reported CES-D scores of 16 or greater while 4.4% (N=85) reported more severe depressive symptoms with CES-D scores greater than 24. Relative to women with CES-D scores less than 16, those with scores of 16 or greater were more often younger (<30 years of age), non-caucasian, and unmarried. Significant depressive symptoms during pregnancy (CES-D > 24) was most strongly associated with a past history of mood disturbance or previous use of antidepressants (OR=11.7, 95% CI 6.8–20.1, OR=7.4, 95% CI 3.3–16.8, respectively).

Conclusion: Pregnancy is not "protective" with respect to risk for mood disturbance. Identification of populations of women at greatest risk for depression during pregnancy may allow for appropriate therapeutic interventions either during pregnancy and/or the postpartum period.

NR331 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Bipolar Spectrum Disorder: A Pilot Validation Study

S. Nassir Ghaemi, M.D., *Department of Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139*; James Y. Ko, Claudia F. Baldassano, M.D., Nicholas J. Kontos, M.D., Frederick K. Goodwin, M.D.

Summary:

Objective: To assess validity of a proposed definition of bipolar spectrum disorder (BSD) in which patients exhibit bipolar features without spontaneous mania or hypomania.

Methods: Depressive features reportedly characteristic of BSD were assessed in patients with bipolar disorder (BP) and unipolar depression (UP). 36 patients with BP I or II were compared to 38 patients with UP. Clinicians assessed mood features through systematic patient interview and chart review.

Results: Four features of major depressive episodes were statistically significantly more common in BP than UP: Recurrence (> 5 episodes; 92% vs 19%), brief episodes (<3 months duration; 86% vs 14%), increased sleep or appetite (97% vs 16%), and early age of onset (16.7 for BP vs 28.4 for UP). There was a statistical trend for increased postpartum depression in BP (26%) vs UP (6%, p=0.08), and increased family history of BP (38% in BP vs 13% in UP). Hyperthymia and psychotic depression did not differentiate statistically, though both were twice as frequent in the BP group.

Conclusion: Features more common in BP I and II than in UP may be characteristics of BSD. This preliminary naturalistic study supports most of the proposed features of BSD. These pilot data need to be assessed prospectively.

NR332 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Bipolar Disorder: Chronicity and Relapse Risk Despite Expert Care

Michael E. Thase, M.D., *Department of Adult Psychiatry, University of Pittsburgh-WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213-2593*; Stephen R. Wisniewski, Ph.D., Gary S. Sachs, M.D.

Summary:

Objective: To evaluate the risk of relapse during treatment according to Expert Guidelines in the multicenter STEP-BD project.

Method: The outcomes of 500 patients with bipolar disorder were evaluated across up to one year of treatment, which was provided by specialists according to expert consensus guidelines. Recovery was defined by 8 consecutive symptom free weeks.

Results: Three-hundred and twenty-four patients presented symptomatic, of which 150 (46%) have *not* yet recovered from the index episode. Among those who did recover (n = 178), 60 (34%) have relapsed despite ongoing expert care. Relapse risk was not associated with age, sex, other sociodemographic factors, or Bipolar I/II subtype. A significant difference (p=.03) was noted for episode polarity, with more relapses among patients who entered in mixed episodes (40%) as compared to those who were "just" manic or depressed (33%).

Discussion: Rates of chronicity, treatment resistance, and relapse are remarkably high in bipolar disorder despite the efforts of specially trained psychiatrists to provide expert care.

NR333 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Escitalopram Is a Well Tolerated SSRI

Ivan Gergel, M.D., *Medical Department, Forest Laboratories, 909 Third Avenue, New York, NY 10022; Heikki Hakkarainen, Ph.D., Gwen Zornberg, M.D.*

Summary:

Introduction: Escitalopram, the single isomer of citalopram, has been shown in several clinical trials to have antidepressant efficacy at a dose of 10 mg/day.

Objective: To assess the treatment emergent adverse events associated with short term escitalopram treatment.

Methods: A total of 715 depressed outpatients (male or female, aged 18-80 years) received acute treatment (up to 8 weeks) with escitalopram (10-20 mg/day) in randomized, placebo-controlled, double-bling, multicenter studies. Spontaneously reported adverse events (AEs) were recorded at each study visit; vital sign, ECG and laboratory value observations were taken at baseline and endpoint.

Results: Only one AE (nausea) occurred in escitalopraqm-treated patients at a greater rate than placebo, with an incidence exceeding 10%. Reports of somnolence and "activation" AEs (such as insomnia, agitation and nervousness) were notably low. Overall, less than 6% of iscitalopram-treated patients discontinued due to AEs. No clinically significant changes occurred in vital sign, ECG or laboratory values. Two fixed dose trials included an escitalopram 10 mg/day arm; in both trials, discontinuation due to AEs did not differ between escitalopram 10 mg/day and placebo.

Conclusion: In conlusion escitalopram was safe and well tolerated at the doses used in these studies.

Funding Source: Forest Laboratories.

NR334 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Methylphenidate Hydrochloride Extended Release Capsules: Once-Daily Therapy for ADHD

Joseph Biederman, M.D., *Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC-725, Boston, MA 02114*; Declan Quinn, M.D., Sharon Wigal, Ph.D., Margaret D. Weiss, M.D., S. Markabi, M.D., Kathryn Edson, Ph.D., G. Karlsson, Ph.D.

Summary:

Objective: To assess the safety and efficacy profile of methylphenidate hydrochloride extended-release capsules (Ritalin®-LA) as compared with placebo as a treatment for children with attention-deficit/hyperactivity disorder (ADHD)

Methods: One hundred sixty children, 6 to 12 years old, meeting DSM-IV criteria for ADHD, were enrolled in a multicenter, double-blind study comparing methylphenidate hydrochloride extended-release capsules to placebo. A screening period of 6 weeks was followed by a single-blind titration phase to optimize dosing of study medication (2 to 4 weeks), a single-blind placebo washout period (1 week), and 2 weeks of double-blind treatment with either study medication or placebo. One hundred thirty seven subjects were then randomized to receive either a once-daily, morning dose of methylphenidate hydrochloride or placebo. The primary outcome variable was the change from baseline to the final rating in Conners ADHD DSM-IV Scale (CADS) Teacher total subscale score.

Results: The study was completed in 130 of 137 subjects. All primary and secondary efficacy variables reflect superiority of methylphenidate hydrochloride extended-release capsules over placebo. The incidence of adverse events (AEs) was similar for methylphenidate modified-release capsules and placebo (24.6% versus 23.9%), and the (AEs) were consistent with the known side-effect profile of methylphenidate hydrochloride.

Conclusion: Methylphenidate hydrochloride extended-release capsules are safe and efficacious as a once-daily treatment for children with ADHD compared with placebo.

NR335 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Parent Preference for OROS MPH qd Over MPH t.i.d.

Adelaide S. Robb, M.D., *Child National Medical Center, 111 Michigan Avenue N.W., Washington, DC 20010*; Mark A. Stein, Ph.D.

Summary:

Objective: To evaluate parent/caregiver preference for OROS® MPH qd compared to MPH tid in a double-blind, double-dummy setting.

Background: Objective measures of ADHD symptoms have shown OROS® MPH qd to be comparable to that of immediate-release MPH tid.

Methods: Parent/caregiver preference for OROS® MPH qd, MPH tid, and placebo was assessed in a three-period, double-blind, double-dummy randomized crossover study in 64 children with ADHD. In a second, open-label, multicenter study 1082 patients (aged >6 years) with ADHD received OROS® MPH for 9

months. Parent preference for OROS® MPH over previous medical treatments was assessed at the end of the study.

Results: Over half (54.1%) of parents preferred OROS® MPH qd over MPH tid or placebo ($p<0.05$). Only 26.2% of parents preferred MPH tid. In the open-label study, 76.8% of parents preferred OROS® MPH to previous pharmacological ADHD treatments; reasons for this preference included: convenience, 86%; duration of treatment, 75%; and smoothness of effect, 71%.

Conclusion: OROS® MPH qd was statistically preferred to MPH tid in the double-blind, double-dummy situation. This may result from the smooth delivery profile of OROS® MPH, which could minimize fluctuations in efficacy and potential rebound effects.

NR336 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Efficacy of Once-Daily Transdermal Methylphenidate in Children ADHD

William E. Pelham, Jr., Ph.D., *Department of Psychology, SUNY at Buffalo, 373 Park Hall, Buffalo, NY 14260-4110*; Michael J. Manos, Kate E. Tresco, Elizabeth M. Gnagy, B.S., Martin T. Hoffman, M.D., Adia N. Onyango, Andrea M. Chronis

Summary:

Objective: Once-daily methylphenidate transdermal system (MTS) releases methylphenidate (MPH) continuously and provides sustained levels of MPH throughout the day. This study evaluated the effects of 3 doses of once-daily MTS on daily behavior in children with ADHD.

Methods: Thirty-six children aged 6 to 12 years with ADHD participated in this 8-day, crossover study in a summer treatment program. Children received either placebo or MTS 6.25 cm^2, 12.5 cm^2, or 25 cm^2 applied at 6 am or 7 am and removed at bedtime. Behavioral measures were recorded in recreational and classroom settings.

Results: MTS was superior to placebo in the majority of measures. Compared with placebo, all MTS doses significantly improved daily report card percentages, behavior (noncompliance, complaining, negative verbalizations), ability to follow rules, and peer-tutoring rules. MTS 12.5 cm^2 and 25 cm^2 significantly improved interruption and conduct problems, ability to follow seatwork rules, and seatwork productivity. Counselor and teacher daily ratings were also significantly better for all doses of MTS, with the exception of MTS 6.25 cm^2 for oppositional/defiant rating. MTS was well tolerated and most adverse events were mild to moderate.

Conclusions: Once-daily MTS has a good safety profile and significantly improves a range of behaviors in children with ADHD.

NR337 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Onset and Offset Time-Course of a Methylphenidate Transdermal System

Gregory A. Fabiano, M.A., *SUNY, 318 Diefendorf Hall 3435 Main Street, Buffalo, NY 14214*; Elizabeth M. Gnagy, B.S., Lisa Burrows-MacLean, Ph.D., Martin T. Hoffman, M.D., William E. Pelham, Jr., Ph.D., Gene Morse

Summary:

Objectives: This study examined the onset and offset time-course of 2 doses of a once-daily methylphenidate transdermal system (MTS) on children with ADHD in a laboratory analogue classroom.

Methods: Twenty-seven children aged 6 to 12 years with ADHD participated in this study. Each dose (placebo, 18.75 cm^2 MTS, 37.5 cm^2 MTS) was given on one of three Fridays over 6 weeks in a crossover design. The MTS was applied at 7:00 am and removed at 1:00 pm. A timed-math task was administered at 9:00 am, 11:00 am, 1:00 pm, 3:00 pm, and 5:00 pm. Rule violations and math problems completed correctly were dependent measures.

Results: The 37.5 cm^2 MTS significantly improved children's behavior during the math task over the day, and both doses of MTS improved math task performance overall. Means indicated that the lower dose peaked at 4 hours postapplication; the effects were steady until the removal time and then tapered off following the removal. The highest dose produced larger effects that remained relatively stable throughout the entire day.

Conclusion: The MTS produced improvement in behavior and productivity on a timed-math task throughout the day. The time-course appeared to differ for the different doses with the higher dose taking effect more quickly and staying active for a longer time after removal.

NR338 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Long-Term Safety of Atomoxetine in Children and Adolescents with ADHD

Joachim F. Wernicke, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Christopher J. Kratochvil, M.D., Denai R. Milton, M.S., David W. Dunn, M.D., Thomas J. Spencer, M.D., John H. Heiligenstein, M.D., David Michelson, M.D.

Summary:

Objective: This study assesses 12-month safety and tolerability data of atomoxetine in children and adolescents with ADHD.

Methods: Patients met DSM-IV criteria for ADHD and completed a 10-week open-label, dose-titration trial to establish efficacy, followed by a one-year extension study.

Results: 258 children (7 to 11 years) and 67 adolescents (12 to 17 years), received at least one atomoxetine dose, and 112 (43%) and 30 (45%) were treated for at least one year. Atomoxetine was well tolerated; only 9 children (3.5%) and 2 adolescents (3.0%) discontinued due to an adverse event. A slight increase in mean diastolic blood pressure (DBP) and pulse (HR) was observed for both children (DBP = 3.64 mm Hg; HR = 4.28 BPM) and adolescents (DBP = 3.43 mm Hg; HR = 2.58 BPM). Mean weight and height increased in children (2.17 kg, 4.01 cm) and in adolescents (4.35 kg, 5.81 cm). Effects on ECG parameters were consistent with an increased heart rate for both subgroups. No evidence of a drug related QTc prolongation was observed.

Conclusions: Atomoxetine was well tolerated and long-term therapy mean weight increased for both subgroups. These results support the use of atomoxetine for treating children and adolescents with ADHD.

NR339 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Sociodemographic Factors Do Not Influence Child Emotional Abuse Rates

Stephanie Hamarman, M.D., *Department of Psychiatry, New Jersey Medical School, 215 South Orange Avenue, UBHC B43, Newark, NJ 07103*; Sally J. Czaja, Ph.D.

Summary:

Objective: Rates of child emotional abuse (CEA), distinct from other forms of abuse, vary widely (300-fold) with states having inclusive civil laws reporting higher rates (One-way ANOVA $F(2,42)=3.8$, $p=0.03$). We sought to determine if sociodemographic factors might account for variations.

Methods: Retrospective review of 1998 data from US DHHS Child Maltreatment Reports, US Census Bureau, Kids Count, Urban Institute.

Results: None of 23 factors correlated. *Individual measures:* Race (Caucasian rho=–0.08, p=0.61; African-American rho=0.2, p=0.18; Hispanic rho=–0.03, p=0.83; Asian rho=0.13, p=0.41),

Household makeup (Married couple rho=–0.07, p=0.67; Single parent rho=0.02, p=0.9), Divorce rate (rho=0.2, p=0.22), Educational level (rho=–0.04, p=0.78), Births to teenage mothers (r= 0.02, p=0.92); *Individual economics:* Income per person (r=0.01, p=0.97); Income per household (rho=0.06; p=0.72),); Unemployment (rho=–0.16, p=.29); Retail sales per household (rho=–0.02, p=0.89), Homeownership (rho= 0.08, p=0.59); *State factors:* Geography (East, West, Midwest, South (F (3,42)=0.55, p=0.65), Population density (rho=0.21, p=0.17); Child population (r=–0.07, p=0.64), Violent crimes (rho=0.03, p=0.85); Gross state product (rho=0.10, p=0.49); Revenue per capita (rho=–0.09, p=0.56); *Social programs:* Federal, local, state welfare spending per child (r= –0.10, p=0.52; r=–0.17, p=0.33; r=–0.79, p=0.62, respectively).

Conclusions: In the absence of correlations with sociodemographic factors, civil laws on CEA among US states appear to drive reported rates. Thus, child advocates should concentrate on legal reform.

NR340 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Impact of ADHD Treatment Once-Daily OROS Formulation of MPH on Tics

Donna R. Palumbo, Ph.D., *Department of Neurology, University of Rochester, 601 Elmood Avenue Room 5-5237A, Rochester, NY 14642*;

Summary:

Objective: To assess the impact on tics of treatment with a once-daily OROS® formulation of methylphenidate HCl (OROS® MPH) in children with attention-deficit/hyperactivity disorder (ADHD).

Methods: 407 children with ADHD, ages 6 to 13 years, were enrolled in this open-label, multicenter study and received OROS® MPH qd for up to 12 months. All children had participated in previous short-term, controlled studies of OROS® MPH qd. Parental assessments of tics were recorded at baseline (prior history) and monthly during the study.

Results: Of 48 children with a history of tics, 3 (6.3%) experienced only worsening of tics, while 30 (62.5%) experienced either improvement in their tics (n=10) or no tics (n=20) during the study. Twenty-three (6.4%) of the 359 children with no known history of tics reported new onset of tics. Of these 23 children, 12 reported tic(s) at a single monthly assessment and 11 reported tics at more than one assessment. Seven children discontinued treatment because of tics. Of these, 5 had no history of tics, 1 had new onset in the previous controlled trial, and 1 had a history of tics.

Conclusions: Once-a-day dosing with OROS® MPH had minimal impact on tics in this sample of children with ADHD.

NR341 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Withdrawal Trial of Dex-Methylphenidate HCL Focalin in Children with ADHD

Scott A. West, M.D., *Psychiatric Institute of Florida, 5401 South Kirkman Road Suite 480, Orlando, FL 32819*; Diane Johnson, Ph.D., Sharon Wigal, Ph.D., Jerome Zeldis, M.D.

Summary:

Objectives: (1) To compare the efficacy of *dex*-methylphenidate hydrochloride (*d*-MPH) Focalin® and placebo in maintenance of ADHD symptom reduction. (2) To assess the safety of long-term treatment with *d*-MPH. (3) To determine the duration of action of d-MPH.

Methods: 89 patients between ages 6 and 17 years, all meeting DSM-IV criteria for ADHD, were enrolled in this three-phase study. First, they were treated open-label with optimal doses of *d*-MPH. Next, they were randomized, double-blindly, to either placebo or continuation of their current dosages. Lastly, participants received open-label treatment with *d*-MPH for up to forty-four weeks.

Results: Patients treated with *d*-MPH demonstrated significant reduction of ADHD symptoms, followed by substantial worsening upon medication discontinuation. Symptom assessments indicate 6 hours duration of action. Results reflect a favorable safety profile of *d*-MPH. No serious adverse events related to treatment were reported, and all adverse events were consistent with familiar reactions to methylphenidate-containing products.

Conclusions: Symptoms of ADHD, substantially reduced during treatment with *d*-MPH, resume significantly following its withdrawal. Treatment with *d*-MPH is safe, with adverse events consistent with those of other methylphenidate preparations. Duration of action of *d*-MPH extends up to six hours.

NR342 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Interim Results: Long-Term Safety of Paroxetine in Pediatric Patients

Diane Gallagher, M.S., *GlaxoSmithKline, 1250 Collegeville Road, Collegeville, PA 19426-0989*; Christel Gardiner, M.S.C., David J. Carpenter, M.S.

Summary:

Objective: Assess the safety and tolerability of long term paroxetine (PAR) treatment in children and adolescents with OCD or major depressive disorder (MDD).

Method: OCD or MDD patients 7–17 years of age who had completed an acute placebo-controlled PAR trial participated in this ongoing 6-month extension study. Extension phase dosing began at 10mg/day (open-label), with 10mg/day increases permitted at weekly intervals (max 50mg/day). Safety was primarily assessed via adverse event (AE) incidence. Maintenance of efficacy was assessed via the proportion of Clinical Global Impression (CGI) Global Improvement responders (very much or much improved), along with other instruments. All completed patients (including drop-outs) and all ongoing patients with at least 4 weeks of follow-up data were included.

Results: Data were available for 221 patients (116 MDD, 105 OCD; 119 < age 12 and 102 ≥ age 12). The overall mean duration of PAR exposure (including taper) was 28.5 weeks for patients receiving PAR in the acute studies (n=94) and 14.5 weeks for patients receiving placebo in the acute studies (n=127). The mean daily dosage was 22.2 mg/day. No serious unexpected AEs were reported. Common (≥10%) extension phase AEs were headache (21.7%), respiratory disorder (18.1%), infection (12.7%), and trauma (10.0%). The proportion of CGI responders at extension phase Week 24 was 92% for both the OCD and MDD populations (68% and 67%, respectively, in the LOCF datasets).

Conclusion: Long term Paroxetine treatment (10–50mg/day) was safe and generally well-tolerated in children and adolescents in this interim evaluation.

NR343 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Improved Nightly Parent Ratings Once-Daily Transdermal Methylphenidate

Lisa Burrows-MacLean, Ph.D., *Department of Psychology, SUNY, 318 Diefendorf Hall 3435 Main Street, Buffalo, NY 14214*; William E. Pelham, Jr., Ph.D., Martin T. Hoffman, M.D.

Summary:

Objectives: Once-daily methylphenidate transdermal system (MTS) releases methylphenidate (MPH) continuously and provides sustained levels of MPH throughout the day. To compare three dose strengths of MTS to placebo on the effect on evening parent ratings while being monitored during the day in a controlled, naturalistic setting.

Methods: This was a single-center, double blind, randomized, six-week study conducted in 27 pediatric patients aged 6 to 12 years, diagnosed with ADHD and attending a summer treatment program. Children received either placebo, or MTS 12.5 cm^2, 25 cm^2 or 37.5 cm^2 for 8.5 hours from Monday to Thursday. Each day, parents rated their children's behavior for the entire evening well after the patch had been removed.

Results: All MTS (12.5 cm^2, 25 cm^2 and 37.5 cm^2) doses were associated with a significant improvement versus placebo ($P<0.01$) in the parent ratings for Pittsburgh Modified Conners-Inattention/Overactivity, Oppositional/Defiant and Abbreviated Conners. MTS treatment was well tolerated and adverse events were mild to moderate in most cases.

Conclusion: Once daily application of MTS for 8.5 hours significantly improves the behavior of children with ADHD during the evening and is well tolerated.

NR344 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

ADHD Treatment with Once-Daily OROS Formulation of MPH: Effect on Growth

Thomas J. Spencer, M.D., *Department of Child Psychiatry, Massachusetts General Hospital, Fruit Street 725 ACC Building, Boston, MA 02114*;

Summary:

Objective: To assess the long-term effect on growth of a once-daily OROS® formulation of methylphenidate HCl (OROS® MPH) in children with attention-deficit/hyperactivity disorder (ADHD).

Methods: 407 children with ADHD, ages 6 to 13 years, were enrolled in this open-label, multicenter study. Children received OROS® MPH qd for up to 12 months. All children had participated in previous short-term, controlled studies of OROS® MPH qd. Children's height and weight were recorded at baseline and every month. Children's growth was compared with that of the general population, adjusted for age and sex, using z-score transformations.

Results: Mean absolute weight increased by 2.6 kg (baseline, 34.2 kg; Month 12, 36.8 kg) and mean absolute height increased by 5.2 cm (baseline, 137.1 cm; Month 12, 142.3 cm). Subjects were slightly taller (0.31) and heavier (0.67) than historical controls. Weight z-scores decreased over the first 3 months (baseline, 0.67; Month 3, 0.46) but stabilized over the remainder of the study (Month 6, 0.40; Month 12, 0.38); height z-scores decreased slightly (baseline, 0.31; Month 6, 0.30; Month 12, 0.22).

Conclusions: Once-a-day dosing with OROS® MPH produced no clinically meaningful changes in height, and had minimal impact on weight in this sample of children with ADHD.

NR345 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Randomized Trial of d-MPH Focalin and d,1-MPH in Children with ADHD

C. Keith Connors, Ph.D., *Duke University Medical Center, Durham, NC 27705*; C. Casant, M.D., Josephine Elia, M.D., D. Covey, M.D., N. Telew, M.D., Jerome Zeldis, M.D., James M. Swanson, Ph.D.

Summary:

Objective: To compare the efficacy and safety of *dex*-methylphenidate hydrochloride (*d*-MPH) (Focalin®) versus placebo in the treatment of attention deficit/hyperactivity disorder (ADHD) and to determine the comparative duration of action of *d*-MPH and *d,l*-MPH versus placebo.

Methods: This randomized, double-blind study treated 132 children ages 6 to 17 years with *d*-MPH, *d,l*-MPH or placebo at 8 am and 12 pm daily for 4 weeks. A placebo lead-in phase familiarized teachers and parents with the Swanson, Nolan and Pelham (SNAP)-ADHD Rating Scale and disqualified children who responded to placebo.

Results: Significant improvements of Teacher SNAP-ADHD ratings followed treatment with *d*-MPH versus placebo (P=.0004) and *d,l*-MPH versus placebo (P=.0042). Likewise, parent scores were significantly better at both 3 pm and 6 pm versus placebo. With *d,l*-MPH, scores improved at 3 pm but not at 6 pm, for which time the *d*-MPH scores were superior. Adverse effects were consistent with the known effects of MPH-containing agents.

Conclusions: d-MPH effectively treats symptoms of ADHD at approximately one half the milligram dose of *d,l*-MPH. *d*-MPH also has a longer duration of action than *d,l*-MPH, offering the potential to prolong improvement in home and school behavior.

NR346 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Venlafaxine Extended-Release for GAD Treatment in Children and Adolescents

Nadia R. Kunz, Pharm.D., *Wyeth-Ayerst, 145 King of Prussia Road, Radnor, PA 19087*; Arifulla Khan, M.D., Elizabeth Nicolacopoulos, R.N., Lisa Jenkins, Ph.D., Paul P. Yeung, M.D.

Summary:

Objective: To evaluate efficacy, safety, and tolerability of venlafaxine XR in treating GAD in children and adolescents.

Methods: One hundred fifty-eight (158) pediatric patients (6–17 yrs) were randomly administered venlafaxine XR (dose adjusted for body weight) or placebo for ≤8 weeks. The primary efficacy variable was the Columbia KIDDIE-SADS GAD total score for 9 delineated items (range, 0–55; higher scores indicating greater anxiety and/or impairment); the primary endpoint was the week-8 LOCF evaluation. Secondary efficacy variables were C-KIDDIE-SADS GAD (complete) total score and individual Severity (5 delineated items) and Impairment (4 delineated items) component scores of primary efficacy variable, PARS total score, HAM-A total score, SCARED Parent and Child Forms total score, and CGI-S and CGI-I scores.

Results: Children and adolescents receiving venlafaxine XR had a mean 18.6-point decrease on the primary efficacy variable vs a 12.4-point decrease with placebo (P<0.001). Similar results were obtained on secondary measures. On the CGI-I, 49/76 (64%) venlafaxine XR patients responded, indicated by a score <3 vs 31/77 (40%, P=0.004) with placebo. Two of 77 (3%) venlafaxine XR patients discontinued treatment because of adverse events vs 5/79 (6%) placebo patients. The most common treatment-related adverse events were asthenia, anorexia, weight loss, hyperkinesia, somnolence, and epistaxis.

Conclusion: Venlafaxine XR is an effective and well-tolerated treatment of GAD in children and adolescents.

NR347 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Topiramate Use for Pediatric Bipolar Disorder: A Retrospective Chart Review

Melissa P. Del Bello, M.D., *Department of Psychiatry, University of Cincinnati, 231 Bethesda Avenue, ML559, Cincinnati, OH 45267*; Robert A. Kowatch, M.D., Juliet Warner, B.A., Stephan M. Strakowski, M.D.

Summary:

Introduction: To our knowledge, there have been no studies evaluating the use of the antiepileptic agent, topiramate, for the treatment of pediatric bipolar disorder (BPD), although previous investigations suggest its effectiveness in adults with BPD. The aim of this study was to assess the safety, tolerability, and effectiveness of topiramate for the treatment of BPD in children and adolescents.

Methods: Outpatient medical charts of youths with a DSM-IV diagnosis of BPD I or II who had been treated with topiramate were reviewed. The primary outcome measures were the CGI-improvement and CGAS scores. A responder was defined as a CGI-improvement score of ≤2 (much or very much improved).

Results: Twenty-six youth (ages 6–20 years) with BPD I or II who were treated with topiramate were identified (mean treatment=4.1 months, mean dose=104 mg/day). Nineteen (73%) patients had a mania CGI-improvement score of ≤2 and sixteen (62%) had an overall CGI-improvement score of ≤2. CGAS scores increased from 40±12 to 59±16 (t=7.1, df=25, p ← 0.0001, effect size= 2.8). No severe adverse events occurred during treatment. Only 3 (12%) patients discontinued therapy secondary to side effects.

Conclusions: Preliminary results indicate that topiramate is effective, safe and well-tolerated for pediatric BPD.

NR348 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Efficacy of Atomoxetine in Children and Adolescents with ADHD

Albert J. Allen, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; David Michelson, M.D., Donald R. Harder, M.S., Nancy J. Trapp, B.A., Douglas K. Kelsey, Ph.D.

Summary:

Objective: Two recently completed clinical trials assessed efficacy of atomoxetine in children and adolescents with ADHD.

Methods: Patients enrolled in 6- to 8- week, double-blind, placebo-controlled trials received either atomoxetine or placebo. ADHD symptoms were assessed by change from baseline-to-endpoint total ADHD RS scores. Similar analyses for the ADHD RS inattentive and hyperactive/impulsive subscales, CGI-S, and CPRS-R-ADHD Index were examined.

Results: 296 children (6 to 11 years of age, 179 atomoxetine, 117 placebo) and 120 adolescents (12 to 18 years of age, 71 atomoxetine, 49 placebo), participated. Children and adolescents receiving atomoxetine reported significant reduction in ADHD RS Total scores compared to placebo ($p < .001$, $p = .009$, respectively). Similar results were observed for the inattentive ($p < .001$, $p = .012$, respectively), and hyperactive/impulsive ($p < .001$, $p = .024$, respectively), ADHD RS subscales, CGI-S ($p < .001$, $p = .002$, respectively), and CPRS-R ADHD Index ($p < .001$, respectively) for children and adolescents treated with atomoxetine compared to placebo. No significant differences were found between children or adolescents for either treatment.

Conclusions: These studies suggest that atomoxetine is effective for treating children and adolescents with ADHD and is an alternative to more traditional interventions.

NR349 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Efficacy of Paroxetine in Pediatric OCD: Results of a Multicenter Study

Daniel A. Geller, M.D., *Department of Pediatrics (OCD), McLean Hospital, 115 Mill Street, Belmont, MA 02478*; Karen D. Wagner, M.D., Diane Gallagher, M.S., Graham J. Emslie, M.D., Christel Gardiner, M.S.C., Tanya Murphy, M.D., David J. Carpenter, M.S.

Summary:

Objective: To evaluate the efficacy and safety of paroxetine (PAR) in children and adolescents with moderate to severe obsessive-compulsive disorder (OCD).

Method: Outpatients 7–17 years of age with OCD and a Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) total score ≥16 were enrolled in this 10 week, double-blind, placebo-controlled trial. PAR dosing began at 10mg/day, with increases of 10mg/day permitted at weekly intervals (max of 50mg/day). The primary efficacy measure was CY-BOCS total score change from baseline to week 10 (LOCF endpoint).

Results: The intention-to-treat (ITT) population consisted of 203 patients (n=115 < age 12; n=88 ≥ age 12) randomized to PAR (n=98) or placebo (n=105). Mean CY-BOCS total scores were 24.4 and 25.3 at entry for PAR and placebo, respectively, and 15.1 and 19.4 at week 10 (LOCF), respectively. The adjusted mean difference between PAR and placebo in change from baseline in CY-BOCS total score at week 10 (LOCF) was −3.45 points in favor of PAR (95% confidence interval [−5.60, −1.29], p=0.002), demonstrating the effectiveness of PAR. Data from several secondary endpoints supported this finding. The most common adverse experiences (≥10%) in the PAR group were headache (24.5%), abdominal pain (17.3%), nausea (16.3%), respiratory disorder (12.2%), somnolence (12.2%), hyperkinesia (12.2%), and trauma (10.2%). For only hyperkinesia and trauma was this incidence at least twice that for placebo.

Conclusion: Paroxetine is a safe and effective treatment for OCD in pediatric patients (7–17 years of age) over the dosage range studied (10–50mg/day).

NR350 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

The Use of Herbal Medicines in Children with ADHD or Depressive Disorders

Suzanne O. Cala, *4000 Horizon Hill 1505, San Antonio, TX 78229*; M. Lynn Crismon, Pharm.D., Jennifer Baumgartner, Pharm.D.

Summary:

Objective: To examine the use of herbal medicines by children or adolescents receiving care for depression or ADHD.

Methods: A 23-item questionnaire was administered in five community mental health centers in Texas. Parents or primary caregivers of children who received a psychiatric assessment were sought for participation. 117 caregivers completed the questionnaire. The main outcome measure was primary caregivers' self-report of the use of herbals in their children.

Results: The prevalence of herbal use in patients was 20%. Of the children who had used herbals, 18% had taken herbals during the past year. Recommendations from a friend or relative resulted in the administration of herbals by 60% of caregivers. Herbals were most frequently given for a behavioral condition, with ginkgo biloba, echinacea, and St. John's wort used most often. Almost 83% of caregivers gave herbals alone, whereas 13% gave herbals with prescription medications. Most caregivers (78.3%) supervised the administration of herbals in their children, and the children's psychiatrists (70%), pediatricians (56.5%), or pharmacists (73.9%) were not aware.

Conclusions: A majority of caregivers self-supervised the use of herbals in their children without communication with a health professional. There is a need for better communication between health professionals and caregivers regarding the use of herbals.

NR351 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Aripiprazole Versus Placebo in the Treatment of Chronic Schizophrenia

Teresa A. Pigott, M.D., *Department of Psychiatry, CNS, Inc, 4701 Willar Avenue, Suite 105, Chevy Chase, MD 20815*; Anutosh R. Saha, Ph.D., Mirza W. Ali, Ph.D., Robert D. McQuade, Ph.D., Anne F. Torbeyns, Ph.D., William H. Carson, Jr., M.D., Elyse G. Stock, M.D.

Summary:

Objective: To assess the time to relapse with aripiprazole, compared to placebo, over 26 weeks in stable patients with chronic schizophrenia.

Methods: A multicenter, randomized, double-blind, placebo-controlled study was conducted in 310 patients with chronic schizophrenia considered stable (no significant improvement or worsening in last 3 months and baseline PANSS = 82), randomized to aripiprazole 15 mg/day or placebo. Efficacy included time to relapse, PANSS Total Score, and CGI-Improvement Score.

Results: Treatment with aripiprazole resulted in significantly fewer patients relapsing at endpoint versus placebo (34% vs. 57%, respectively). Aripiprazole also significantly increased the time to relapse by two-fold. Aripiprazole produced a small but significantly greater improvement in PANSS-total score relative to placebo. Aripiprazole was generally well tolerated with an adverse event profile comparable to placebo. No clinically significant changes occurred in SAS, AIMS, and Barnes Akathisia scores in either group. Weight gain associated with aripiprazole was comparable to placebo.

Conclusion: Aripiprazole provides effective and safe antipsychotic treatment in patients with chronic schizophrenia, representing an important addition to the current antipsychotic armamentarium.

NR352 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

T Cells in the CSF of Patients with Major Depression Are Clonally Expanded

Emilia L. Oleszak, Ph.D., *Temple University, Fels Institute, 3307 North Broad Street, AHB 205, Philadelphia, PA 19140*; Wan Lu Lin, Ph.D., J. Robert Chang, Xiaoying Zhang, Sibylle Herzog, Ph.D., Meena Bhattacharjee, M.D., Glenn Rudner, Chris D. Platsoucas, Ph.D., Karl Bechter, M.D.

Summary:

Introduction: Infectious agents including viruses have long been implicated in the etiology of certain psychiatric diseases.

Hypothesis: The objective of our studies was to determine, whether T cells present in the CSF of patients with bipolar disorder and schizophrenia are clonally expanded, suggesting antigen-driven proliferation.

Methods: We have analyzed the T-cell receptor (TCR) repertoire in the CSF of two patients with bipolar disorder, one patient with schizophrenia and two "normal" individuals by non-palindromic adaptor PCR/V beta specific PCR amplification, followed by cloning and sequencing of TCR transcripts.

Results: Clonally expanded TCR transcripts were found in several V beta families in the CSF of two patients with bipolar disorder and schizophrenia. In contrast, TCR repertoire in the blood of these patients was polyclonal, as expected. We have detected 12 V beta TCR families in the CSF of two "normal" controls, and all TCR transcripts were polyclonal.

Conclusions: We have demonstrated clonally expanded T cells in the CSF of patients with bipolar disorder and schizophrenia. In contrast, T cells in the peripheral blood of these patients, and of normal donors, were polyclonal. These results suggest an immune response to as yet unidentified specific antigen (s) in the CSF of these patients. These T cells may recognize either viral antigen or host epitope, perhaps due to molecular mimicry.

NR353 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Meta-Analysis of the Efficacy of Aripiprazole in Schizophrenia

Jeffrey A. Lieberman, M.D., *Department of Psychiatry, Univ. of North Carolina School of Medicine, Room 7025, Neurosciences Hospital, CB7160, Chapel Hill, NC 27599*; William H. Carson, Jr., M.D., Anutosh R. Saha, Ph.D., Joseph C. Stringfellow, M.S., Donald G. Archibald, M. Phil., Mary J. Kujawa, M.D., Taro Iwamoto, Ph.D.

Summary:

Objective: Aripiprazole is novel antipsychotic therapy, with a unique mechanism of action (dopamine-serotonin system stabilizer). A meta-analysis of efficacy data is presented.

Methods: Four 4- to 6-week multicenter, double-blind, fixed-dose, placebo-controlled studies were done in 1545 patients hospitalized with acute relapse of schizophrenia or schizoaffective disorder. Patients were randomized to aripiprazole (n=898), placebo (n=381), or active control (haloperidol 10 mg/day [n=167] or risperidone 6 mg/day [n=99]). Daily aripiprazole doses ranged from 2–30 mg. Weekly efficacy assessments included PANSS and CGI.

Results: Aripiprazole demonstrated statistically superior antipsychotic efficacy to placebo at doses over 2 mg. In the meta-analysis, aripiprazole doses over 2 mg produced significant improvement in PANSS-total score by week 1 ($p<0.05$). In individual studies, aripiprazole 15, 20 and 30 mg consistently produced significant improvements in PANSS-total score, with similar changes from baseline observed for all aripiprazole treatment groups. Aripiprazole 15, 20 and 30 mg consistently produced significant improvements in other efficacy scores compared with placebo. In studies with active control, haloperidol and risperidone separated from placebo.

Conclusion: These data demonstrate that aripiprazole improved positive and negative symptoms of schizophrenia, with significant effects one week after starting treatment. Aripiprazole represents an important new option for the treatment of schizophrenia.

NR354 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Safety and Tolerability of Aripiprazole at Doses Higher Than 30mg

Anutosh R. Saha, Ph.D., *Otsuka Maryland Research Institute, 2440 Research Boulevard, Rockville, MD 20850*; Mirza W. Ali, Ph.D., Gary G. Ingenito, M.D., Richard Wilber, M.D., Xiaolong Luo, Ph.D., Steven Bramer, Ph.D.

Summary:

Objective: To evaluate the safety, tolerability, and pharmacokinetics of escalating doses of aripiprazole from 30 mg to 90 mg.

Methods: A randomized, double-blind, parallel-group, inpatient, pilot study was conducted in 40 patients with stable schizophrenia or schizoaffective disorder (mean baseline PANSS 43-64) randomized to aripiprazole 30mg/d (control in each dosing group, n= 12), 45mg/d (n=7), 60mg/d (n=7), 75mg/d (n=7), and 90mg/d (n= 7) over 15 days for each dose.

Results: There were no clinically significant changes from baseline in SAS, AIMS, and Barnes Akathisia across all groups. There was an increased incidence of akathisia and tachycardia in the 90 mg dose-group, however, there were no discontinuations due to adverse events in this group. There was no dose-dependent increase in weight. There were no clinically relevant ECG changes and no significant changes in protactin levels. Plasma concentrations of aripiprazole and its metabolites increased proportionately with dose. Patients in all dose groups maintained a stable symptom profile, based on PANSS Total Score, positive and negative subscales, and the CGI Severity of Illness Score.

Conclusion: Aripiprazole is safe and well tolerated at doses of 30 mg to 90 mg/day. Escalating doses of aripiprazole demonstrated linear pharmacokinetics following multiple doses and consistent control of schizophrenic symptoms.

NR355 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

The Segmented Volumes of Cerebrum in First-Episode Schizophrenia with Auditory Hallucinations

Sang-Eun Shin, M.D., *Department of Psychiatry, Inha University, 7-206, 3-GA, Shinheung-Dong Chung-GU, Incheon 400-103, Korea*; Jeong-Seop Lee, M.D., Min-Hee Kang, M.D., Chul-Eung Kim, M.D., Jae-Nam Bae, M.D.

Summary:

Objective: Many studies on the brain structure of schizophrenia in relation with psychopathology have been performed. In this study, the volumes of cerebral and cerebellar regions were measured in patients with auditory hallucination (AH) and without AH in first-episode schizophrenia by brain magnetic resonance imaging.

Method: Brain magnetic resonance images were obtained in 17 patients with AH and eight patients without AH in first episode schizophrenia. Cerebral and Cerebellar regions were segmented to gray and white fractions using algorithm for semi-automated fussy tissue segmentation. They were defined using the semi-automated Talairach atlas-based parcellation method.

Results: Patients with AH had larger frontal and temporal lobe volume than patient without AH. In gray matter, patients with AH had larger frontal and temporal lobe volume. And in white matter, patients with AH had a larger temporal lobe volume.

Conclusion: These findings suggest that patients with schizophrenia with AH may have neuropathological abnormalities in frontal and temporal lobes.

NR356 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

The Experience of Stigma in 150 Relatives of Patients with a Psychotic Disorder

Kirsten Catthoor, M.D., *Department of Psychiatry, UPC St-Jozef, Osystraat 13, Antwerpen B2060, Belgium*; Marc De Hert, M.D., Phillippe M.J. Persoons, M.D., Jozef Peuskens, M.D.

Summary:

Objective: To assess the degree of stigmatisation experienced by relatives of psychotic disorder (PD) patients, and its determinants.

Methods: A total of 150 relatives of PD patients were interviewed with the validated "Familial Burden Interview" and the stigma questionnaire of the Family Interview Schedule. Correlates of total stigma score (StS) were determined. Determinants of severe StS(score>10) were assessed.

Results: Mean StS was 6.1 (±5.6; range:0–30;18.7% with StS> 10). Higher StS was experienced by parents (p=.03) and if worsened relationship (p=.01), interfering behavior (p=.02), residential setting (p=.04), nuisance for respondent (p<.01), and receiving clarification by mental health professionals (MHP;p=.06) was present. Attributions concerning the origin of PD, associated with higher StS, were hereditariness (p<.01), patient's character (p<.01), and biological dysfunction (p=.05). Negative correlates of StS were patient's age (p=.02) and hours of contact over the last two weeks (p<.01). Logistic regression identified younger patients, residential setting, clarification by MHP, attributions to biological dysfunctioning and patient's character, worsened relationship, and the interaction of parents attributing PD to hereditariness as independent determinants of severe StS (c-statistic=91% Nagelkerke R^2=.53).

Conclusions: Average subjective stigma in relatives is not high. Attribution, patient characteristics observable by outsiders, relationship with patients, clarification by MHP and fear for hereditariness by parents determine relatives' heightened subjective stigma.

NR357 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Transition from IM to Oral Ziprasidone: Clinical Efficacy and Safety Data

David G. Daniel, M.D., *Broniche Development, P.O. Box 7137, McLean, VA 22106-7137*; Shlomo Brook, M.D., Isma Benattia, M.D.

Summary:

Objective: To evaluate the efficacy and tolerability of ziprasidone during the transition from intramuscular (IM) to oral treatment in patients with psychosis.

Methods: Data were analyzed from three studies in which 1005 patients received sequential IM and oral ziprasidone (n=725) or haloperidol (n=280): two 7-day, open-label, randomized studies (one using flexible dosing; the other, fixed dosing) and a 6-week, flexible-dose, randomized trial in acute schizophrenia. Efficacy measurements in all studies included BPRS Total and CGI-S.

Results: In all three studies, improvements in BPRS Total score and CGI-S observed during IM treatment with ziprasidone were sustained or increased through the transition to oral drug. In the 7-day studies, fewer ziprasidone- than haloperidol-treated patients were discontinued for any reason (3.7% vs 7.5%). Discontinuations due to adverse events were comparable (1.5% vs. 0.7%). In the 6-week trial, during the first 2 weeks of oral treatment, the rate of discontinuation due to adverse events was lower with ziprasidone than with haloperidol (4.2% vs. 9.6%). Rates of discontinuation from lack of efficacy were low in both groups (3.5% and 1.5%).

Conclusions: In these studies, transition from IM to oral ziprasidone was well tolerated, with sustained or increasing improvement in symptoms.

NR358 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Weight-Loss Program for Overweight Subjects on Atypical Antipsychotics

Franca Centorrino, M.D., *Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02478*; Judith J. Wurtman, Ph.D., Karen Duca, Ph.D., James P. Kelleher, M.D., Veronica H. Fellman, B.A., Judith M. Berry, M.A., Matthew Romeling, M.A.

Summary:

Objective: To assess the effects of a comprehensive six-month weight loss program (TRIAD), on psychotic disorder patients.

Method: 10 women and 7 men (41 ± 8.5 yrs) with schizophrenia (N=1) or schizoaffective disorder (N=16) completed the study. Inclusion criteria included increases in weight of ≥10 lbs and BMI (kg/m^2) of ≥5% during antipsychotic treatment. Subjects participated in a 24-week, twice weekly program of dietary and lifestyle counseling, and physical exercise tailored to each subject.

Results: Average baseline BMI was 36.6 ± 4.6 (231.4 ± 40.6 lbs.). BMI decreased in 16/17 subjects: 2.1 ± 2.0 (13.1 ± 13.1 lbs.). Women's BMI decreased more than men's (2.2 ± 1.9 vs. 1.9 ± 2.2), however, men lost more weight (13.5 ± 16.1 vs. 12.9 ± 11.4 lbs.). BMI losses ranked: olanzapine > risperidone > clozapine > ziprasidone. All subjects showed a slowing of resting heart rate (2.5 ± 9.5 beats/min) or lowering of systolic and diastolic BP (13.0 ± 13.4 and 9.3 ± 9.8 mm Hg, respectively; statistically significant).

Conclusions: These results demonstrate that weight gain among atypical antipsychotic-treated patients can be controlled and even reversed through weight management programs. This study is limited by small sample size and limited duration.

NR359 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Cortical Blood Flow and Preservative Errors: SPECT Study in Schizophrenia

Felipe Ortuno, M.D., *Department of Psychiatry, University Hospital, Apdo 4209, Pamplona, NA 31080, Spain*; Miguel Moreno-Iniguez, M.D., Ernesto Sol, M.D., Cesar A. Soutullo, M.D., Salvador Cervera-Enguix, M.D.

Summary:

Background: We studied relative cortical blood flow (relCBF) patterns associated with correct performance (CP) and perseverative errors (PE) during Wisconsin Card Sorting Test (WCST) performance, in controls and patients with schizophrenia.

Method: We measured relCBF (regional cortical blood flow (rCBF)/whole cortex blood flow) of well defined cortical regions in 18 male patients with schizophrenia and 13 healthy controls by a Technetium^{99}-HMPAO-SPECT, at rest and during WCST performance.

Results: Patients made significantly more PE during WCST performance than controls ($p<0.001$). We found a significant positive correlation between CP and relCBF in right prefrontal cortex in controls. We found a less important correlation in patients between CP and relCBF in right prefrontal cortex. However, in patients, EP was correlated with relCBF in right parietal and occipital cortex and inversely correlated with relCBF in left frontal cortex.

Conclusions: Successful WCST performance is associated to higher prefrontal activity in controls and patients with schizophrenia. In patients with schizophrenia, the severity of PE during WCST performance is correlated with relCBF in temporal-parietal-occipital cortex and inversely correlated with relCBF in prefrontal cortex. This may represent a cortical activity redistribution pattern related to perseveration in schizophrenia.

NR360 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Schizophrenia Care and Assessment Program: Treatment by Race

Mark Tami, Ph.D., The Medical Group, *4301 Connecticut Avenue, NW, #330, Washington, DC 20008*; Lisa Palmer, Ph.D., Patricia Russo, Ph.D., Joseph Vasey, Ph.D.

Summary:

Objective: Examine schizophrenia treatment differences among African-Americans and Non-African Americans enrolled in the U.S. SCAP.

Methods: Baseline data examined for differences by race and race-gender (n=2239). Schizophrenia severity measured by symptomology and functionality scores. Utilization measured by service type. Antipsychotic agents coded for first-generation only, any second-generation, Clozapine, and no antipsychotic use. Presence of Antiparkinson/Anticholinergic medications and depot administration examined. Descriptive and logistic regression modeling employed.

Results: ***Descriptive Analysis:*** African-Americans more likely diagnosed with paranoid schizophrenia, no more likely than Non-African Americans to present with greater positive symptoms. African-Americans more negative symptoms, lower QLS, and higher AIMS. African-Americans had less individual therapy, less day treatment and more rehabilitation than Non-African Americans. African-Americans less likely than Non-African Americans to be prescribed second-generation antipsychotics and more likely prescribed Antiparkinson/Anticholinergic agents. Proportion of African-American males receiving depot formulation greater than other race-gender pairings. ***Multivariate Analysis:*** African-Americans more likely to be prescribed only a first-generation antipsychotic. Presence of depot administration positively associated with first-generation antipsychotics; differences by race remained after controlling for depot administration.

Conclusions: Symptom profiles of African-Americans indicate prescribing second-generation antipsychotics clinically appropriate. Adjusted results corroborate that race, rather than clinical presentation, significant determinant of antipsychotic choice for schizophrenia treatment.

NR361 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Managing Atypical Antipsychotic-Associated Weight Gain: The Healthy Living Program

Elizabeth Vreeland, APN, *Department of Psychiatry, UMDNJ-RWJMS-UBHC, 2245 Rt 130, Suite 106, Dayton, NJ 08810-1413*; Matthew A. Menza, M.D., Shula Minsky, Ed.D., Diane Rigassio Radler, R.D., Beatrix Roemheld-Hamm, M.D., Robert G. Stern, M.D., Riva Touger-Decker, Ph.D.

Summary:

Introduction: Atypical antipsychotics have improved psychiatric treatment for people with serious mental illness. However, weight gain associated with these medications, and the complications that result from the weight gain, have been receiving critical attention. This study tested the hypothesis that subjects who participated in a structured weight control program would lose more weight than patients who received psychiatric care as usual.

Methods: Thirty-one obese subjects with schizophrenia, with atypical antipsychotic-induced weight gain, participated in a 24-week weight control program. Measures of BMI, weight, hunger level, exercise level, nutrition knowledge, B/P, pulse, lipids, FBS, hemoglobin A1C, and stage of change, were compared from baseline to endpoint. Weight and BMI changes in the intervention group were compared to changes in a non-intervention group ($n = 14$).

Results: 25 of the 31 subjects completed the program. There was a mean weight loss of 3.0 kg (–6.7 pounds, –3.0%) in the intervention group and a mean gain of 3.7 kg (+8.1 pounds, +3.9%) in the non-intervention group. The difference was statistically significant; $F(1,42)=12.32$, $p=.0011$). The corresponding change in the BMI was a drop from 34.3 to 33.2 (–1.1; –3.2%) in the intervention group and an increase from 33.4 to 34.9 (+ 1.5; +4.5%) in the non-intervention group. This difference was also statistically significant; $F(1,42)=12.52$, $p=.0010$. Other secondary measures also improved.

Conclusions: Participation in the structured weight control program resulted in a significant reduction in weight, BMI, and hunger level, and also resulted in significant changes in behavior and nutrition knowledge, as well as other measures. Patients who did not receive weight intervention continued to gain weight. These pilot data suggest that professionals treating patients on atypicals should assist them with weight control activities. Further studies are required to develop strategies that will optimize long term weight control in this population that are likely to improve overall physical health status and reduce the risk of complications associated with obesity.

NR362 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

IM Ziprasidone and IM Haloperidol Have Comparable Effects on QTC at CMAX

Jeffrey J. Miceli, Ph.D., *Department of Central Research, Pfizer, Incorporated, Building 260, Eastern Point Road, Groton, CT 06340*; Richard J. Anziano, M.S., Rachel H. Swift, M.D., Thomas M. Shiovitz, M.D.

Summary:

Objective: To characterize the effects of multiple IM injections of ziprasidone and haloperidol on corrected QT interval (QT_c) at observed peak concentrations (C_{max}).

Methods: In this single-blind, randomized study, individuals with schizophrenia or schizoaffective disorder received 2 injections of

ziprasidone (20 mg followed by 30 mg, the second dose being 50% above maximum recommended) or haloperidol (7.5 mg followed by 10 mg) 4 hours apart. ECGs and blood sampling for pharmacokinetic measurements were performed at 15-minute intervals within 2 hours after each injection to capture C_{max} and times on either side of C_{max}. Mean QT_c (with baseline correction factor of 0.33) at C_{max} was calculated as the average of three measurements obtained at and on either side of C_{max} for each injection for each subject.

Results: Among study completers, mean increases at C_{max} were 4.6 msec for ziprasidone (n=25) and 6.0 msec for haloperidol (n= 24) after injection 1, and 12.8 msec and 14.7 msec after injection 2. Mean (95% CI) QT_c increases over 24 hours after initial injection were 3.4 msec (0.86, 5.92) for ziprasidone and 6.3 msec (3.58, 8.95) for haloperidol. No subject had $QT_c \geq 500$ msec.

Conclusions: IM ziprasidone and haloperidol exhibited comparable effects on QT_c at Cmax.

NR363 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Risperidone-Refractory OCD: Positron Emission Tomography Imaging

Monte Buschbaum, M.D., *PET Laboratory, Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY 10029*; Eric Hollander, M.D., Stefano Pallanti, M.D., Nicolo Baldini-Rossi, M.D., Jimcy Platholi, M.S., Erica Sood, B.A., Rachel Bloom, M.D.

Summary:

Objective: To evaluate the efficacy of risperidone in patients with obsessive-compulsive disorder (OCD) not responsive to selective serotonin reuptake inhibitors (SSRIs) and image associated patterns of metabolic change in the brain.

Method: In a double-blind, parallel-group trial, patients received risperidone or placebo. Positron emission tomography (PET) and magnetic resonance imaging scans were obtained at baseline and 8 weeks.

Results: Fifteen of 16 patients completed the study. Risperidone was associated with significant increases in relative metabolic rate in the striatum, cingulate gyrus, and prefrontal cortex, especially in the orbital region. Four of 9 risperidone patients showed clinical improvement (CGI score of 1 or 2 at 8 weeks); none of the 6 placebo patients showed improvement. Patients with low relative metabolic rates in the striatum and high relative metabolic rates in the anterior cingulate gyrus were more likely to show a clinical response. The metabolic response in the striatum with neuroleptics and cingulate gyrus with SSRIs is consistent with earlier PET studies showing these effects when these treatments were administered individually. Our results are consistent with a fronto-striatial circuit change related to both dopaminergic and serotonergic systems and the presence of psychopharmacologic subtypes within OCD.

Conclusions: Risperidone significantly normalizes brain metabolic patterns in OCD patterns not responsive to SSRIs. Patients who had low relative metabolic rates in the striatum and high metabolic rates in the cingulated gyrus at baseline were more likely to respond.

NR364 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Meta-Analysis of Cardiac Safety with Aripiprazole

Elyse G. Stock, M.D., *Bristol-Myers Squibb Company, 5 Research Parkway, Wallingford, CT 06492-7660*; Anutosh R. Saha, Ph.D., Robert Brunell, Ph.D., Donald G. Archibald, M. Phil., Taro Iwamoto, Ph.D., Robert D. McQuade, Ph.D.

Summary:

Objective: A meta-analysis was done to assess the short and long-term cardiac safety of aripiprazole, as measured by prolongation of the QT interval.

Methods: Short-term effects were based on five 4- to 6-week double-blind, controlled studies in 1648 patients, randomized to aripiprazole, placebo, or active control (haloperidol 10 mg/day or risperidone 6 mg/day). Long-term effects were based on a 52-week haloperidol-controlled study (n= 1294) and a 26-week open-label olanzapine-controlled study (n= 255). Data is presented as the mean change from baseline to study endpoint using a fractional exponent correction method.

Results: In the short-term studies, aripiprazole was comparable to placebo across all doses regardless of gender or race. Mean changes in QT_c with aripiprazole and placebo were –4.4 msec and –3.5 msec, respectively; changes with haloperidol and risperidone were –1.04 msec and + 2.15 msec, respectively. In these studies, incidence at endpoint of a 30 msec increase in QT_c with aripiprazole was 4.3% compared to 5.5% for placebo; values for haloperidol and risperidone were 7.8% and 10.5%, respectively. In the long-term studies, aripiprazole was not associated with significant increases in QT_c.

Conclusion: Aripiprazole is not associated with QT_c prolongation following short and long-term administration.

NR365 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Social Anxiety Symptoms in Schizophrenia are Common, Severe, and Unrelated to Psychosis: A Replication Study

Robert G. Stern, M.D., *Department of Psychiatry, UMDNA-RWA Medical School, 189 New Street, New Brunswick, NJ 08901*; Sohaila Farooq, M.D., Denise Frank, B.A., Michelle Beyer, B.A.

Summary:

Objectives: This study tested the hypothesis that social phobia symptoms are common, often severe, but not correlated in any way with psychotic symptom severity among patients suffering from schizophrenia or schizoaffective disorder.

Design and Methods: After giving informed consent, neuroleptic treated patients with DSM IV schizophrenia or schizoaffective disorder were interviewed and rated on the "Liebowitz Social Anxiety Scale" [LSAS] (Liebowitz 1987), the PANSS and CGI and GAF as part of a larger study. Binomial correlation analysis assessed the relationship between PANSS and CGI, GAF scores and LSAS scores.

Results: The study fully replicated our previous findings. As a group these patients (CGI mean± SD: 2.7±8; GAF: 58.2± 7.9; PANSS: 68.7±16.9) had high LSAS (61.7±30.4) scores. A large proportion (60%) of the patients had LSAS total scores in the range of at least moderate social anxiety and half of them (30%) had LSAS scores in the severe range (81<). LSAS total scores did not correlate with PANSS total (r=–.05; p=.78), or PANSS general (r=05; p=.77) or PANSS positive scores (r=03; p=.86), or with PANSS negative scores (r=–.05; p=.81).

Conclusions: The study confirms that social anxiety symptoms are common, and of considerable severity in schizophrenia. Routine screening for social phobic symptoms in patients with schizophrenia appears warranted. Future studies should assess the efficacy of various strategies in treating those symptoms.

NR366 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Effect of Smoking Status on Olanzapine-Induced Weight Gain

Robert A. Lasser, M.D., *Novartis Pharmaceutical Corp, Building 419 Room 2349, 59 Route 10, East Hanover, NJ 07936*; Georges Gharabawi, M.D.

Summary:

Objective: To examine weight gain in smokers and nonsmokers in comparison trials of olanzapine and risperidone.

Method: We analyzed data from 2 large 8-week multicenter trials comparing olanzapine and risperidone in adult and elderly patients with schizophrenia. We recorded smoking status, demographics, and vital signs at baseline and 8 weeks. Variables included medication and nicotine status compared on continuous and categorical measures of weight gain and body mass index.

Results: At baseline, olanzapine- and risperidone-treated smokers and nonsmokers were well matched with regard to age, sex, race, and weight variables. Both adult and elderly smokers and nonsmokers were equally affected by olanzapine-induced weight gain on all measures. Slightly more elderly olanzapine-treated smokers, expected to have physiologic factors biased against weight gain, gained > 7% of baseline body weight compared with elderly olanzapine-treated nonsmokers. Physiologically expected differences in weight gain among risperidone-treated smokers and nonsmokers were maintained.

Conclusions: Olanzapine-induced weight gain was equally high in smokers and nonsmokers, despite known physiologic differences that occur with tobacco use. The adverse metabolic effects of olanzapine may overpower the physiologic bias toward weight loss usually observed in smokers. Risperidone does not appear to affect the physiologic difference between smokers and nonsmokers.

NR367 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Meta-Analysis of Weight Effects with Aripiprazole

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

Darlene Jody, M.D., *Bristol-Myers Squibb Company, PO Box 4000, Princeton, NJ 08543-4000*; Anutosh R. Saha, Ph.D., Taro Iwamoto, Ph.D., Bebjit Biswas, Ph.D., Chin-Lu Lin, Ph.D., Ronald N. Marcus, M.D., Robert D. McQuade, Ph.D.

Summary:

Objective: A meta-analysis was done to assess the short-term and long-term effects on weight (≥7% increase from baseline) of aripiprazole, a newly developed antipsychotic with a unique mechanism of dopamine D2 and serotonin 5-HT_{1A} partial agonism, and 5-HT_{2A} antagonism.

Methods: Short-term effects were based on five 4- to 6-week double-blind, controlled studies in 1648 patients with schizophrenia or schizoaffective disorder, randomized to aripiprazole, placebo, or active control (haloperidol 10 mg/day or risperidone 6 mg/day). Long-term effects were based on a 52-week haloperidol-controlled study (n= 1294) and a 26-week open-label olanzapine-controlled study (n=255).

Results: In the short-term studies, aripiprazole was associated with a 0.7 kg increase in weight; haloperidol and risperidone produced 0.6 kg and 1.3 kg increases, respectively. In the long-term haloperidol study, patients with a baseline BMI < 23 experienced weight gain with both haloperidol and aripiprazole, while patients with BMI > 27 experienced weight loss. In the olanzapine-controlled study, aripiprazole led to a 2.2 kg weight loss versus a 4.4 kg increase with olanzapine at 26 weeks. In all BMI categories, aripiprazole resulted in weight loss and olanzapine in weight gain.

Conclusion: Aripiprazole is associated with minimal weight gain, comparable to haloperidol and less than olanzapine.

NR368 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Corpus Callosum Abnormalities in Schizophrenia: A DTI Study

Melissa Frumin, M.D., *Department of Psychiatry, Brockton VA Medical Center, 940 Belmont Street, Brockton, MA 0240*; Carl-Fredrik Westin, Ph.D., Stephan Maier, M.D., Marek Kubick, M.D., Ron Kikinis, M.D., Robert V. McCarley, Martha E. Shenton, Ph.D.

Summary:

This study investigated white matter abnormalities in patients diagnosed with chronic schizophrenia using diffusion tensor imaging.

Methods: Sixteen subjects with chronic schizophrenia were recruited from the VA Boston Healthcare System and 18 comparison subjects were recruited from the general community. Subjects were male, right handed and grouped matched for age and parental SES. Subjects were scanned on a 1.5 Tesla GE Echospeed scanner with the following parameters. A rectangular field of view 220x165mm; 128x128 scan matrix (256x256 image matrix); 4mm slice thickness, 1 mm interslice thickness; received bandwidth +-4kHz; echo time (TE) 64 ms; effective repetition time (TR) 2592ms; scan time 60 seconds/slice section. Five sagittal slices were acquired with the middle slice aligned along the interhemispheric fissure. T2 weighted images were acquired simultaneously. Using the T2 weighted images; the corpus callosum was segmented manually and then co-registered with the diffusion data. Fractional anisotropy maps were calculated for the entire segmented corpus and for the front, middle and back sections.

Results: Mean fractional anisotropy was decreased in the schizophrenia group compared to the normal controls for the whole corpus ($F(2,32)p<0.001$), for the front third of the corpus ($F(2,32)p<0.001$), for the middle third ($F(2,32)p=0.01$) and for the back third ($F(2,32)p=0.01$)

NR369 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Olanzapine for Social Cognition in Patients with Schizophrenia

Kimberly H. Littrell, M.S., *The Promedica Research Center, 3562 Habersham at Northlake J200, Tucker, GA 30084*; Richard G. Petty, M.D., Nicole M. Hilligoss, M.S., Carol D. Kirshner, M.S., Craig G. Johnson, M.D.

Summary:

Objective: To evaluate the effect of olanzapine on the interpretation of nonverbal communication and social perception in patients with schizophrenia.

Method: Fifty-two (31 M, 21 F) patients meeting the DSM-IV criteria for schizophrenia or schizoaffective disorder were evaluated for interpersonal perception. From this preliminary cohort, a subset of 22 (14 M, 8 W) consented to a 12-month open-trial of olanzapine. All patients were receiving conventional antipsychotic medications at entry. The subset was cross-titrated to olanzapine, while the remaining patients (n = 30) continued treatment with their current conventional antipsychotic. Patient's social cognition was evaluated at baseline, interim (olanzapine patients only), and endpoint using the Interpersonal Perception Task (IPT). The IPT contains 30 brief videotaped scenes, each 30 to 60 seconds in length, with each scene paired to a multiple choice question. The viewer is asked to "decode" something important about the people he or she has just seen. Domains of kinship, intimacy, status, competition, and lying are assessed.

Results: At endpoint, the olanzapine group demonstrated significant ($p < .0001$) increases in scores when compared with the conventional group. In addition, the olanzapine group had statistically significant ($p < .0001$) improvements in scores from baseline to endpoint. Gender differences were noted at baseline and endpoint.

Conclusions: This preliminary study suggests that olanzapine has a positive effect on social cognition. Continued study is needed to determine the effect of prolonged olanzapine treatment on social cognition. Additionally, larger, controlled trials are needed to more

fully understand the impact that atypical antipsychotic treatment may have on improving this aspect of cognitive functioning.

NR370 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Hippocampal Volumes and Cognitive Deficits in Schizophrenia

Cheryl M. Corcoran, M.D., *Department of Psychiatry, NYSPI, 1051 Riverside Drive, Unit 2, New York, NY 10032*; Jack M. Gorman, M.D., David Leitman, B.A., Lawrence S. Kegeles, M.D., Dolores Malaspina, M.D.

Summary:

Background: Cognitive functioning in schizophrenia has variably been related to prefrontal, mediotemporal and total brain volumes. In a sample of 46 well-characterized schizophrenia patients, we examined if cognitive functioning and clinical symptoms were related to hippocampal volumes.

Methods: MRI images were acquired and the hippocampus was manually drawn using criteria based on Kates et al., 1997.

Results: In a sample of schizophrenia patients, left hippocampal volumes were associated with IQ and attention, whereas right hippocampal volumes correlated with performance across a broad array of cognitive functions, including IQ, attention, executive function, and explicit memory. Further, volumes of both left and right hippocampi were associated with global functioning and the PANSS autism scale.

Conclusion: These findings suggest that hippocampal abnormality may contribute to dysfunction in the distributed neural network that subserves cognition and is related to functioning and symptoms in schizophrenia patients.

NR371 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Effect of Olanzapine and Risperidone Use on Diabetes Risk in Patients with Schizophrenia

Robert W. Buchanan, M.D., *Department of Psychiatry, Maryland Psychiatric Research, PO Box 21247, Baltimore, MD 21228-5567*; Carol E. Koro, Ph.D., Sheila Weiss, Ph.D., Gilbert J. L'Italien, Ph.D., Laurence S. Magder, Ph.D., Donald O. Fedder

Summary:

Introduction: The newer class of antipsychotic agents exhibits a superior safety profile compared to conventionals. However, case studies suggest an association between use of these agents and diabetes. We sought to quantify this association using a large health care database.

Methods: The study was derived from 19,637 schizophrenia patients in the UK General Practice Research Database between 1987–2000. We used a 6:1 matched nested case-control design. Conditional Logistic Regression was used to derive adjusted odds ratios controlling for gender, age, and co-medications. Exposure to antipsychotic was defined as ≥ 1 prescription for anti-psychotic medication within two months prior to the date of diagnosis.

Results: We found 451 incident cases of diabetes matched to 2,696 controls. Olanzapine use was associated with a significantly increased odds for diabetes (OR=5.2, 95% CI 1.8–14.6, p=.002) compared with nonuse of antipsychotics and conventionals (OR= 3.8, 95% CI: 1.3–10.6, p=.001). Risperidone showed a lesser increased odds of diabetes (OR=2.1, 95% CI 0.88–5.00, p=.095) compared to nonuse, and conventionals (OR=1.5, 95% CI=0.64–3.63, p=.34).

Conclusions: Our study demonstrates a strong association between the use of olanzapine and the development of diabetes in schizophrenic patients. The metabolic consequences of atypical therapy should be given serious consideration by physicians:

NR372 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

The Dose Effect of Clozapine on Working Memory in Schizophrenia

Myung A. Lee, M.D., *Department of Psychiatry, Vanderbilt University, 1601 23rd Avenue South Suite 306, Nashville, TN 37212*; Herbert Y. Meltzer, M.D., Karu Jayathilake, Ph.D.

Summary:

Objective: We have reported that 6 weeks but not 6 months treatment with clozapine worsens verbal working memory (VWM; Hagger et al., 1993; Lee et al. 1999) while it improved verbal fluency (VF) and other cognitive measures in patients with schizophrenia (SCH) or schizoaffective disorder (SAD). We examined the relationship between improvement in VF and worsening in VWM with clozapine; we also examined clozapine dose and baseline VWM as predictors of the effect of clozapine on VWM.

Methods: Neurocognitive tests were administered to 131 patients (105 drug free) with SCH or SAD at baseline, and after 6 weeks and 6 months of clozapine treatment.

Results: Worsening in VWM was negatively correlated with improvement in VF. Worsening in VWM was not related to baseline VWM, indicating that the worsening was not regression to the mean. Lower clozapine dose was related to improvement in tests of executive function (Wisconsin Card Sorting Test and WISC-R Maze) at 6 months; there was a trend in the same direction for VWM but not VF.

Conclusions: These data indicate that the effects of clozapine to worsen VWM and improve VF may be related to similar neurochemical processes, e.g. effects on cortical dopaminergic activity, and that the short term worsening in VWM with clozapine treatment may be related to dose.

NR373 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Differential Effects of Antipsychotics on Brain Structure in Schizophrenic Patients

Miranda H. Chakos, M.D., *Department of Psychiatry, UNC at Chapel Hill, CB 7160, Chapel Hill, NC 27599-7160*; Scott Schobel, M.D., Jeffrey A. Lieberman, M.D., Hongbin Gu, Ph.D., Guido Gerig, Ph.D.

Summary:

We utilized quantitative 1.5 Tesla MRI T1 and spin echo brain examinations to investigate differential treatment effects of typical and atypical antipsychotics on hippocampal and cortical white matter volume in a cross sectional study of 32 male schizophrenic patients who were ill for less than five years. Patients treated with atypical antipsychotics prior to assessment had larger hippocampal volumes than those treated with typical antipsychotics (F = 6.67, p=0.01; mean hippocampal volume atypical antipsychotics = 5.81 cc; mean hippocampal volume typical antipsychotics 5.10 cc]. In addition, patients with longer duration of illness who had been treated with atypical antipsychotic medication had larger hippocampal volumes (F=5.23; p=0.03). Patients who had been treated with atypical antipsychotic medications also had more cortical white matter than did patients treated with typical antipsychotic medications antipsychotics [F=4.8, p=0.036; mean volume atypical antipsychotics = 383 cc; mean volume typical antipsychotics 362 cc). Patients with longer duration of illness who had been treated with typical antipsychotic medications had reductions in cortical white matter, compared to those treated with atypical medications, who had increases in cortical white matter volume (F= 4.7, p=0.04). These finding may suggest a neuroprotective effect of atypical antipsychotic medications on hippocampal volume and cortical white matter volume.

NR374 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

The Impact of Duration of Untreated Psychosis: A Two-Year Follow-Up

Jean M. Addington, Ph.D., *Department of Psychiatry, University of Calgary, FMC 1403 29th Street, NW, Calgary, AB T2N 2T9, Canada*; Donald E. Addington, M.D., Sarah Van Mastright, B.Sc., Eliana L. Coldham, B.S.C.

Summary:

Objectives: To determine if there is an association between a long duration of untreated psychosis (DUP) and longer-term outcome in a first-episode sample.

Method: Sample was 203 individuals who were being treated in an early psychosis program. The majority had a diagnosis of schizophrenia or schizophreniform. Symptoms were assessed every three months and functional outcome, neurocognitive functioning, and relapse rates were assessed annually. Median DUP was 26 weeks and the mean 80 weeks. The median was used to divide the sample into long and short DUP. Secondly, we compared those who were in remission (i.e., no positive symptoms score greater than 3 on the PANSS) with those who had failed to achieve remission by six months.

Results: There were no differences between the groups in functional outcome, neurocognition, or relapse rates at the different assessment times. The long DUP group had significantly more positive symptoms at each assessment period ($p<0.05$). Subjects who had failed to achieve remission of positive symptoms after six months of a comprehensive treatment approach had a significantly longer DUP ($p<0.01$).

Conclusions: DUP does not seem to predict functional or cognitive outcome but may have an impact on recovery from symptoms.

NR375 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Gray Matter Volume Abnormalities in Older Bipolar Patients

John L. Beyer, M.D., *Duke Univ Med Ctr, Box 3519, Durham, NC 27710*; Maragatha Kuchibhatla, Ph.D., James R. MacFall, Ph.D., Martha E. Payne, M.P.H., Elana L. Engstrom, B.S., Ranga K. Krishnan, M.D.

Summary:

Objective: Structural changes in the brain may be critical in the pathogenesis of bipolar disorder. Previous research in younger populations has suggested that bipolar disorder may be associated with decreases in the frontal lobe, a larger third ventricle, smaller cerebellum, and smaller temporal lobes. This study examined changes in regional brain volumes of older bipolar patients.

Method: We conducted a MRI study measuring regional and whole brain volumes of 40 older subjects (>50 years age) with bipolar disorder recruited from inpatient and outpatient psychiatry programs. A bivariate analysis was performed comparing the bipolar group with a non-psychiatric, older control group.

Results: Significant differences between bipolar subjects and controls were found in a decreased total brain gray matter ($p=0.0061$), decreased volume of the right caudate ($p=0.0303$), enlarged right lateral ventricle ($p=0.0431$), and enlarged left total cerebral spinal fluid volume ($p=0.0256$). No significant differences were seen in the orbital frontal cortexes or white matter.

Conclusions: Preliminary results support findings of a decrease in gray matter in older patients with bipolar disorder compared to controls. Regional variations of loss are noted in the right caudate. Our findings did not support a decrease in orbital frontal volumes for older bipolar subjects compared with controls.

NR376 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Aripiprazole for Long-Term Maintenance Treatment in Schizophrenia

Mary J. Kujawa, M.D., *Bristol-Myers Squibb Company, 777 Scudders Mill Road, Plainsboro, NJ 08536*; Anutosh R. Saha, Ph.D., Gary G. Ingenito, M.D., Mirza W. Ali, Ph.D., Xiaolong Luo, Ph.D., Donald G. Archibald, M.Phil., William H. Carson, Jr., M.D.

Summary:

Objective: To evaluate the maintenance of effect and long-term efficacy, safety and tolerability of aripiprazole, a dopamine-serotonin system stabilizer, compared with haloperidol when administered for 52 weeks.

Methods: A multicenter, randomized, double-blind study was conducted in 1294 patients with acute relapse of chronic schizophrenia randomized to aripiprazole 30 mg (n=861) or haloperidol 10 mg (n=433) daily. A one-time dose reduction was allowed to aripiprazole 20 mg and haloperidol 7 mg. Efficacy evaluations included PANSS and MADRS scores.

Results: A significantly greater proportion of patients treated with aripiprazole and demonstrated response and remained on treatment at weeks 8, 26, and 52 compared to haloperidol (Week 52: 40% vs. 27%, $p<0.001$). Aripiprazole produced statistically significant improvements in the PANSS negative subscale and in depressive symptoms as shown in the MADRS, compared to haloperidol. The overall incidence of EPS-related adverse events was significantly lower with aripiprazole than with haloperidol ($p<0.001$). Both treatments resulted in comparable weight gain. There was no significant difference in QT_c interval between both groups.

Conclusion: Aripiprazole may represent the next-generation antipsychotic leading to increased compliance in schizophrenia due to significantly greater improvements in negative and depressive symptoms and a superior safety and tolerability profile compared to haloperidol.

NR377 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Thioridazine and Haloperidol Appear to Have Similar Risks of Cardiac Arrest

Sean Hennessy, Pharm.D., *Department of Epidemiology, University of Pennsylvania, 423 Guardian Drive, 803 Blockley Hall, Philadelphia, PA 19104-6021*; Warren Bilker, Ph.D., Jill S. Knauss, M.S., David J. Margolis, M.D., Stephen E. Kimmel, M.D., Mary F. Morrison, M.D., Dale Glasser, Ph.D.

Summary:

Objective: To compare rates of cardiac arrest and ventricular arrhythmia associated with thioridazine and haloperidol.

Methods: We used 1987 to 1999 data from the General Practice Research Database in the United Kingdom to perform a cohort study of individuals receiving thioridazine or haloperidol. The primary outcome was diagnosis of ventricular arrhythmia or cardiac arrest. We used Cox regression to estimate rate ratios and 95% confidence intervals (CIs) for thioridazine vs. haloperidol, adjusted for age and sex, and to evaluate potential confounding by diagnoses and concomitant medications.

Results: We observed 450 events in 81,016 individuals with 50,354 person-years of follow-up, for an event rate of 9 per 1000 person-years. The adjusted rate ratio for thioridazine, using haloperidol as the reference category, was 0.9 (0.7 to 1.1). The rate did not appear to increase with dose with either drug.

Conclusions: Thioridazine and haloperidol were associated with similar rates of cardiac arrest and ventricular arrhythmia. These results cannot rule out arrhythmogenic effects in individual patients. Nevertheless, they suggest that a neuroleptic's ability to prolong the electrocardiographic QT interval to the degree shown

by thioridazine may not necessarily confer an increased rate of cardiac arrest or ventricular arrhythmia in the population.

NR378 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Quetiapine Produces Preferential Occupancy of Extrastriatal D2 Receptors

Robert M. Kessler, M.D., *Department of Radiology, Vanderbilt Medical Center, 1161 21st Ave South, Ste CCC-1121MCN, Nashville, TN 37232-2675*; M. Sib Ansai, M.D., Rui Li, Herbert Y. Meltzer, M.D.

Summary:

Background: Previous PET and SPECT studies of elozapine and quetiapine, two atypical antipsychotic drugs (APD), have reported conflicting results regarding the question of preferential occupancy of cortical dopamine (DA) D2r by these drugs. The current study evaluated the effects of quetiapine, olanzapine and clozapine, compared to haloperidol, atypical APD, on extrastriatal DA D2r occupancy.

Methods: We utilized $^{[18F]}$fallypride to determine regional levels of DA D2r occupancy in subjects with schizophrenia treated with quetiapine (N=6, 200–700 mg/day), clozapine (N=5, 400–900 mg/day), olanzapine (N=4 10–20 mg/day), and haloperidol (N=6, 150 mg haloperidol (H) decanoate or oral H, 10 mg/day.

Results: Quetiapine and clozapine showed the lowest occupancy of striatal and extrastriatal regions [temporal cortex, amygdala, ventral striatal, thalamic, and substantia nigra/ventral tegmental (SN/VTA)] D2r. D2r occupancy of olanzapine and haloperidol of striatal and extrastriatal regions were very similar to each other, with the exception of the SN/VTA. All of the atypical APDs had lower occupancy of the SN/VTA, with clozapine, the lowest. Otherwise, quetiapine had the lowest occupancy of any drug in all other brain regions. Some cognitive tests performance inversely correlated with D2r occupancy in the quetiapine-treated patients only. Quetiapine and clozapine preferentially occupy cortical D2r whereas there is no difference in striatal and extrastriatal D2r occupancy for haloperidol and olanzapine are similar.

Conclusion: Extrastriatal D2r occupancy provides a new dimension for comparing differences in APD. Higher doses of quetiapine which produce greater occupancy of extrastriatal D2r may further enhance its efficacy.

NR379 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Odor Identification and Deficit Syndrome Schizophrenia

Dolores Malaspina, M.D., *Department of Psychiatry, Columbia University-NY Psychiatric Institute, 1051 Riverside Drive, New York, NY 10032*; Cheryl M. Corcoran, M.D., Eliza Coleman, M.A., Raymond Goetz, Ph.D., Scott A. Yale, M.S.W., Jack M. Gorman, M.D., Jill M. Harkavy-Friedman, Ph.D.

Summary:

Background: Schizophrenia patients who have primary and enduring negative symptoms that predominantly affect social functioning are designated as having the deficit syndrome (DS), which predicts certain course and biological features. Because social affiliation is highly related to olfactory function in other mammals, we theorized that the DS might also be associated with smell identification.

Method: 50 patients had DS assessments using the Schedule for the Deficit Syndrome (SDS), and had their odor identification measured using the University of Pennsylvania Smell identification Test (UPSIT).

Results: DS patients had significantly worse mean UPSIT performance than the non-DS patients. Conversely, categorizing the patients by better or worse UPSIT scores also showed that those with greater UPSIT impairments were more likely to have the deficit syndrome: of patients with poor odor identification the deficit syndrome was present in 17/36 (47.2%), versus 1/14 (7.1%) of the patients with normal odor identification.

Conclusion: We found an association between the DS and smell identification. This suggests that the neural substrates of olfaction may be related to social affiliation in humans, as they are in other mammals, and that dysfunction in the neural circultry of olfactory processing may contribute to the deficit syndrome of schizophrenia.

NR380 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Neuroprotection by BCL-2 in a Subgroup of Schizophrenia

David L. Garver, M.D., *Department of Psychiatry, University of Louisville, 500 South Preston Building A Room 210, Louisville, KY 40292*; Meng-Yang Zhu, Ph.D., James D. Christensen, Ph.D., Jennifer Holcomb, M.D., Henry A. Nasrallah, M.D.

Summary:

Introduction: Changes of brain volume at rates greater than found in controls[1] suggests an active process within some patients with disorders of the schizophrenia spectrum. Endogenous attempts to resist such active processes include the release of neuroprotective factors. The proto-oncogene bcl-2 has been shown to act as a neurotrophic factor and impede programmed cell death (apoptosis). Herein we assess the relationship of CSF bcl-2 during psychotic exacerbation to illness course, and to total brain volumetrics.

Method: Forty neuroleptic-free patients with psychotic exacerbation of schizophrenia spectrum illnesses were assessed for onset history, for symptoms at admission, for brain volumes, and for CSF bcl-2.

Results: Fourteen of the 40 patients (35%) had CSF bcl-2 values above the 95% confidence level of normal controls. These 14 subjects evidenced a trend toward greater psychosocial deterioration during adolescence (p=0.103), had earlier initial hospitalization (age 23 vs age 28 [p=0.056]), and had larger total brain volumes (1620 cc vs 1490 [p=0.0101]) at psychotic exacerbation than the 26 patients with CSF bcl-2 levels within the confidence interval of controls. Following treatment with a conventional antipsychotic differences of total brain volume between the two groups vanished (p=0.246).

Discussion: An *active process* evidenced by progressive withdrawal during adolescence, by early initial hospitalizations, and by enlarged brain volumes during periods of psychotic exacerbation appears to be associated with a physiological response to protect the CNS through release of the protective neurotrophic factor, bcl-2 from tissues into the CSF. A deficit of bcl-2 was previously reported within temporal lobe in post mortem brain[2].

NR381 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Ziprasidone's Effects on Weight and Lipids in Patients with Schizophrenia

Steven J. Romano, M.D., *Pfizer, Incorporated, 235 East 42nd Street, New York, NY 10017*; Neal R. Cutler, M.D., Peter J. Weiden, M.D., George M. Simpson, M.D.

Summary:

Objective: To assess ziprasidone's effects on weight and lipids in patients with schizophrenia.

Methods: Data from five short-term studies (n=703; 40–160 mg/day): 6-week, double-blind comparison of ziprasidone and olanzapine; open-label comparison of ziprasidone, risperidone, olanzapine, quetiapine, thioridazine, and haloperidol (14–24 days' mean duration); three 6-week, open-label studies of outpatients

switched to ziprasidone from olanzapine, risperidone, or conventional agents. Additionally, pooled analysis of >900 patients exposed to ≥28 weeks of ziprasidone (10–160 mg/day).

Results: Weight: Ziprasidone patients gained significantly less weight than olanzapine patients ($P<0.0001$). Weight gain >7% of baseline was 10–23% with olanzapine, risperidone, quetiapine, and thioridazine versus 6% with ziprasidone. Weight loss was significant in patients switched to ziprasidone from olanzapine ($P<0.0001$) or risperidone ($P<0.05$). Pooled analysis showed mean weight change of −1.13 to +1.70 kg. *Lipids:* Ziprasidone improved fasting lipid measures in short-term studies, with significant changes for TChol ($P<0.001$) and triglycerides ($P<0.001$). Changes were significant versus olanzapine for TChol, triglycerides, and LDL-C ($P<0.01$). Significant reductions in median TChol and triglycerides occured in patients switched from olanzapine ($P<0.0001$) or risperidone ($P<0.01$).

Conclusions: Ziprasidone exhibits a weight-neutral profile and favorable effects on serum lipids. These effects have important implications for patients' overall health.

NR382 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Use of Antipsychotics in Schizophrenic Patients in the Veterans Health Administration

Xinhua S. Ren, Ph.D., *Department for Health Quality Outcomes and, Economic Research, 200 Springs Road, Bedford, MA 01730*; Austin F. Lee, Ph.D., Alaa Hamed, M.D., Yu-Hui Huang, M.P.H., Donald R. Miller, Sc.D., Ann M. Hendricks, Ph.D., John A. Gardner, Ph.D., Lewis E. Kazis, Sc.D.

Summary:

Objective: To describe use of atypical antipsychotics among schizophrenic patients in the Veterans Health Administration (VA).

Methods: We identified 89,107 schizophrenic patients (≥ 1 inpatient or ≥2 outpatient ICD-9-CM codes ≥ 7 days apart) during 7/1/98-6/30/99, of whom 74,715 were on antipsychotics. To describe switching patterns, we defined a prior (1/1/99 to 6/30/99) and post (10/1/99 to 12/31/99) period.

Key Findings: About half of schizophrenic patients on antipsychotics were prescribed atypical antipsychotics. More patients (22.7%) were prescribed Olanzapine than Risperidone (19.7%) ($p < 0.001$ for all comparisons). Among those not prescribed atypical antipsychotics in the prior period (N=36,498), 10% more patients subsequently initiated Olanzapine than Risperidone. About 8% more patients continued on Olanzapine from the prior to the post period, as compared to Risperidone, and 10% more patients on Risperidone switched to Olanzapine than vice versa. Among those on ≥ 2 atypical antipsychotics, 31.1% (N=1,040) switched to monotherapy with Olanzapine as compared to 18.7% (N=625) with Risperidone.

Conclusions: Among atypical antipsychotics, Olanzapine was widely prescribed (both in terms of initiation and switching). Given that Olanzapine is often prescribed for treating schizophrenia in the VA, there is a need to assess the cost-effectiveness associated with each of the atypical antipsychotics.

NR383 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Theory of Mind Performance Symptom and Neuropsychological Correlates

Tamasine C. Greig, Ph.D., *Department of Psychiatry, Yale University, CMHC 34 Park Street Room 527, New Haven, CT 06519*; Morris D. Bell, Ph.D., Gary Bryson, Psy.D.

Summary:

Objective: A large, representative group of people with schizophrenia was studied to determine the relationship between Theory of Mind (ToM) performance and (1) symptom subgroups of schizophrenia, (2) specific neuropsychological test variables, and (3) the age of onset of schizophrenia.

Method: One hundred and twenty-seven stable outpatients with DSM-IV diagnosis of schizophrenia or schizoaffective disorder were assessed using neuropsychological and symptom measures.

Results: Results indicated that ToM performance differed significantly by schizophrenia diagnosis, with disorganized schizophrenia performing the most poorly ($p<.05$). ToM performance was also highly correlated with measures of thought disorder including Gorham's Proverbs ($r=.48$, $p<.0001$) and the cognitive component of the PANSS ($r=.44$, $p<.0001$). ToM performance was significantly correlated with measures of verbal memory and with age of onset. Significant regression analysis revealed that Gorham's Total (a measure of thought disorder) explained 24% of the variance, while Logical Memory II explained 10% and the PANSS cognitive component accounted for the remaining 5%.

Conclusions: Findings suggest that there is ToM variance in the schizophrenia population, and ToM is strongly related to thought disorder, verbal memory, and cognitive disorganization.

NR384 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Remediating Working Memory in Impaired and Less-Impaired Schizophrenia

Morris D. Bell, Ph.D., *VA Connecticut Healthcare, 116B, 950 Campbell Avenue, West Haven, CT 06516*; Gary Bryson, Psy.D., Bruce E. Wexler, M.D.

Summary:

Objectives: Working memory impairments in schizophrenia may be responsive to retraining. We wanted to learn whether patients with severe cognitive impairments could improve as much as those whose general level of impairment was less severe.

Methods: Ninety-six patients with schizophrenia or schizoaffective disorder were categorized as severely or less severely cognitively impaired based on neuropsychological testing and randomly assigned to receive Neurocognitive Enhancement Therapy plus Work Therapy (NET+WT) or Work Therapy (WT) alone. NET consisted of cognitive retraining exercises in attention, memory, executive function, and social information processing, and WT was a 6-month VA Incentive Therapy program.

Results: Comparison on Digits Backwards, a task of working memory, from intake to follow-up revealed significantly greater improvement for participants receiving NET+WT but no interaction with severity group. Significantly more patients in NET+WT improved: 34 (72.3%) showed large or small effect-size improvements and 20 (42.6%) showed large effect-size improvement.

Conclusions: Results indicate that NET+WT improved working memory for most participants and that it was similarly effective for those with severe impairments. Findings support continued exploration of cognitive remediation for people with schizophrenia or schizoaffective disorder.

NR385 Wednesday, May 22, 12:00 p.m.-02:00 p.m.

Evaluation of a Weight Watchers Program at a Clubhouse for SPMI: Pilot Study

Stephen R. Holt, *350 A West 49th Street, New York, NY 10019*; Rebecca P. Smith, M.D., Paula C. Zimbrean, M.D., Marianne Emanuel, R.N., Lawrence Rothschild, Ralph Aquila, M.D.

Summary:

Although weight gain is a common side effect associated with the use of psychotropic drugs, particularly atypical and typical antipsychotic agents, there is little available in the literature either describing or evaluating programs for weight loss among psychiat-

ric patients. We report preliminary results of a pilot weight loss program in a population of predominantly SPMI patients. Twenty-six participants with previous diagnoses of major depressive disorder, schizophrenia or bipolar disorder were enrolled in a 12 week Weight Watcher's program, funded by Fountain House. Twenty four participants were on psychiatric medications whose most common side effects include weight gain. Starting BMI's ranged from 25–53 (mean=36.7). The average starting weight was 107.2 kg. At the end of 12 weeks, the attendance rate of the group at weekly meetings was 70%. The average weight loss at 12 weeks was 2.78 kg with an average loss in BMI of 1.01 kg/m2. Additional data on weight loss and attendance through 26 weeks will be presented. These results will be compared with those obtained in a population of moderately overweight individuals taken from the general population who underwent 26 weeks of Weight Watchers in the context of a controlled study. At the end of 26 weeks, subjects in the general population study had an attendance rate of 80% and had lost, on average, 4.8 kg.

NR386 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

The Community Reentry Program for Chronic Psychiatric Inpatients

Odulia Brown, B.S., *Department of Psychology, Eastern State Hospital, P.O. Box 8791 Ironbound Road, B12, Williamsburg, VA 23185*; Daniele Longo, Ph.D., Robert Thompson, Jane Czajka

Summary:

Goal: To show the effectiveness of a community re-entry program in teaching community living skills to psychiatric inpatients.

Methods: Sixteen-week skill training modules were designed to teach basic community living skills and expose patients to the community. A baseline measurement of each patient's skill level was taken on 16 different measures pre-skill training and compared to skill level following completion of the training modules.

Results: Pre and post measurement comparisons indicate that all participants in the CRP program demonstrated improved functioning level in all areas of skill training.

Conclusion: The overall findings support that a community re-entry program can be an effective tool in building community living skills, and can improve successful reintegration of patients back into the community.

NR387 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Patient-Reported Outcomes in Inpatients with Melancholic Depression

Dwight L. Evans, M.D., *Department of Psychiatry, University of Pennsylvania, 305 Blockley Hall, 423 Guardian Drive, Philadelphia, PA 19104*; Charles B. Nemeroff, M.D., Michael E. Thase, M.D., George J. Wan, Ph.D., Jessica M. Panish, Marc Cantillon, M.D.

Summary:

Objective: To compare patient-reported outcomes of patients treated with venlafaxine and fluoxetine with major depression and melancholia.

Methods: The study design was a six-week, double-blind, placebo-controlled flexible dose study of venlafaxine (75 to 375 mg/day) and fluoxetine (20 to 80 mg/day) in 285 intent-to-treat adult inpatients with melancholic depression.

Results: Venlafaxine was significantly superior to placebo based on the total scores of General Life Functioning (GLF) ($p<0.01$), social activity ($p<0.001$), cognitive functioning ($p<0.01$), general health perceptions ($p<0.001$), and vitality ($p<0.05$). Venlafaxine was also significantly superior to fluoxetine on measures such as GLF ($p<0.01$), social activity ($p<0.05$), cognitive functioning ($p<0.05$), and vitality ($p<0.01$). Patients treated with venlafaxine reported better general health than fluoxetine-treated patients, but this difference did not reach statistical significance. Fluoxetine was significantly superior to placebo on only one measure, general health ($p<0.05$).

Conclusions: Adult inpatients with melancholic depression displayed statistically significant superior improvement with venlafaxine vs. fluoxetine and placebo on the majority of the patient-reported outcome measures. This data suggest that treatment with venlafaxine may improve GLF, social activity, cognitive functioning, and vitality.

NR388 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Interventions to Improve Treatment of Depression in Ob-Gyn Practices

Roger F. Haskett, M.D., *University of Pittsburgh School of Medicine, Western Psychiatric Institute & Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213-2593*; Sarah Hudson Scholle, D.P.H., Barbara H. Hanusa, Ph.D.

Summary:

Introduction: Five effort to improve care of depression in primary care practices (PCP) have focused on internal medicine and family practices. Application of successful interventions to ob/gyn practices is likely to require adaptation. We conducted a feasibility study of depression screening and care management in 3 diverse ob/gyn practices: a suburban private practice serving primarily privately insured women, a large hospital-based clinic and suburban satellite serving low-income patients.

Methods: Depressed women were identified by routine screening with the Patient Health Questionnaire (PHQ; Spitzer, 2000) ($PHQ \geq 10$). A depression care manager (CM, a licensed social worker) completed a clinical and psychosocial assessment of depressed women, and provided education about depression and its treatment, and assistance with referral.

Results: 1090 women completed the screening and 81.7% agreed to the research. Prevalence of depression was higher in the hospital clinic (20.2%) than in the satellite clinic (10.6%) or private practice (8.2%). More depressed women in the private practice reported mental health counseling or taking psychotropic medication in the past 6 months compared to clinic patients (52.1% vs 36.4%). The private and clinic patients endorsed the same top 3 barriers to care: cost (41% vs 58%), time (46% vs 52%) and stigma (41% vs 51%). At 1-month follow-up, 28.2% of depressed clinic patients and 38.5% of private had made or scheduled a new mental health appointment.

Conclusions: Compared to private patients, clinic patients had twice the prevalence of depression as well as lower income, greater family demands, and fewer ties to general medical providers; yet the two groups were similar in clinical needs. Despite socioeconomic differences, the two groups endorsed similar barriers to care.

NR389 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Increasing Return Rate by a Post-Intake Debriefing of Patient Expectations

Katherine A. Kaiser, M.S., *Department of Psychiatry, Johns Hopkins Bayview, 4940 Eastern Avenue D3 East, Baltimore, MD 21224*; Karen L. Kaufman, M.S.W., Gerard Gallucci, M.D.

Summary:

Objective: This study was conducted to learn if a "debriefing" session about patient expectations would increase the rate of return for treatment. A brief post-intake session, specifically addressing a patient's expectations of treatment, was added at the

conclusion of the usual intake format and compared with a control condition of the usual intake format.

Method: All patients were adults who had called for an intake at Johns Hopkins Bayview's Outpatient Community Psychiatry Program in Baltimore City. Patients were randomly assigned to the usual intake format condition (N = 30) or to the expectations "debriefing" condition (N = 30). The "debriefing" intervention consisted of three questions immediately following intake designed to engage the patient in a dialogue about expectations of treatment. The outcome variables reviewed were, patients who expressed a desire to return but "dropped-out" and patients who returned for at least one appointment.

Results: Of the patients, 83 percent who received the "debriefing" session returned for at least one appointment, compared with 57 percent who received only the usual intake format.

Conclusions: Community outpatient clinics can increase the rate of return and moreover increase patient participation in treatment by engaging in a dialogue about the patient's expectations *after* the intake.

NR390 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Quality of Care, Persistent Depression, and Short-Term Disability

Ronald J. Ozminkowski, Ph.D., *The Medstat Group, 777 East Eisenhower Pkwy, #803R, Ann Arbor, MI 48108*; Thomas W. Croghan, M.D., Kevin Hawkins, Ph.D., Shaohung Wang, Ph.D., Ron Z. Goetzel, Ph.D., William H. Crown, Ph.D., Robert L. Obenchain, Ph.D.

Summary:

Objective: To compare patterns of service use and disability outcomes for depression patients on short-term disability (STD).

Method: 787 newly diagnosed patients with depression who used any STD services in 1997–1999 were selected from The MEDSTAT Group's Health and Productivity Management Database®, composed of medical, pharmacy, and disability claims from six large US employers. Treatment success was defined as receipt of care consistent with clinical practice guidelines and movement off STD in the last 3 months of the 6-month treatment episode following diagnosis. Treatment failure was defined by receipt of care according to guidelines and remaining on STD throughout the episode, or beginning STD during the last three months of the episode. Demographics, health status, and service use were compared across the groups via t-test.

Results: 392 patients received care consistent with clinical practice guidelines, and treatment success occurred in 178 cases. Compared to those with successful treatment, those with treatment failure were more likely to be in capitated insurance plans, to have medical comorbidities, to attempt suicide, and to use hospital services. Those whose care was not consistent with guidelines were significantly more likely to have a diagnosis of depressive disorder NOS, be treated first by primary care doctors, and be in capitated plans.

Conclusions: More than half of the depression patients who used any STD services received care that was not consistent with clinical practice guidelines. Those who failed treatment used more hospital services and were more likely to attempt suicide.

NR391 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Collaboration with Mental Health Professionals: A Survey of Family Physicians

Chantal M. Brazeau, M.D., *Department of Family Medicine, New Jersey Medical School, 185 S Orange Avenue Room MSB-B646, Newark, NJ 07103-2714*; Christina Yick, Susan Rovi, Ph.D., Mark Johnson, M.D.

Summary:

Purpose: To assess family physicians (FP's)'s opinion about collaboration with mental health professionals (MHPs). Background: Because mental health problems are frequent in primary care, collaboration between MHPs and primary care physicians is advocated. This survey explores the opinion of community FPs regarding MHPs working directly in FP's office.

Hypotheses: Most FPs will not have an in-office MHP; most FPs would be interested in having an in-office MHP.

Methods: Members of the New Jersey Academy of Family Physicians (N=709) were sent a 25 item questionnaire about collaboration with MHPs. Three mailings were sent, with a 65% response rate.

Results: 13.5% of FP's reported having an in-office MHP. Of those who did not, 60.2% responded that they would consider having one. Physicians with an in-office MHP and those who would consider one felt that: 1. They were more likely to utilize services of an MHP if that person was based in their office 2. Patients were more likely to accept a referral to an in-office MHP 3. An in-office MHP is advantageous for detection and treatment of mental illness ($p<0.001$)

Conclusions: Many FPs wish to collaborate with a MHP in their primary care office and recognize benefits of such collaboration.

NR392 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Do PRN Orders Expose Psychiatric Inpatients to Unnecessary Psychotropics?

Purushottam Thapa, M.D., *Dept of Psych Slot 554, Univ of AR for Med Sciences, 4301 W Markham Street, Little Rock, AR 72205-7101*; Shanna L. Palmer, M.D., Andrea Huntley, M.P.H., James A. Clardy, M.D., Richard R. Owen, Jr., M.D., Laurence H. Miller, M.D.

Summary:

Objectives: To compare the frequency of unscheduled psychotropic medication use during a period when standing PRN ("as needed") orders were allowed and during one when they were not to evaluate whether the practice of writing standing PRN orders exposes psychiatric inpatients to unnecessary psychotropic medications. This is the first study addressing this question.

Methods: Medical records of 223 new admissions between July 15, 1999 and October 15, 1999 when PRN orders were allowed (Yes PRN) and 224 new admissions between November 15, 1999 and February 15, 2000 when PRN orders were not allowed (No PRN) were reviewed from 3 acute adult psychiatric units of the Arkansas State Hospital, Little Rock. Detailed data were collected on demographic and clinical characteristics, scheduled and unscheduled medications from the medication administration records (MAR), and use of restraints, seclusions, and incident reports of physical aggression. The mean numbers of unscheduled medication doses administered during the two periods were compared in the analysis.

Results: The number of unscheduled psychotropic medications administered during the Yes PRN period decreased from 1812 to 976 during the No PRN period (unadjusted means of 8.1 to 4.4, $p=0.0001$; adjusted means 7.8 to 4.3, $p=0.0005$). The decrease in use of unscheduled medications in the No PRN period was not associated with corresponding increases in adverse events: no changes in scheduled psychotropic medication use, use of fewer restraints (N = 4 vs 8), fewer seclusions (N=41 vs 48), and fewer incidents of physical aggression (N=40 vs 61).

Conclusions: The data suggest that the use of PRN orders may expose psychiatric inpatients to unnecessary psychotropic medications.

NR393 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Coprescribing Improves Antidepressant Treatment Adequacy Rates

Jeffrey B. Weilburg, M.D., *Psychiatry, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114*; Randall S. Stafford, M.D., James B. Meigs, M.D., Kathleen M. O'Leary, B.A.

Summary:

Background: Antidepressants (ADs) produce optimal outcomes when provided at adequate dose and duration, yet AD treatment is often inadequate (1). Improving treatment adequacy is an important health policy goal. To date, most effective improvement efforts have used structured prospective programs (2).

Methods: Retrospective analysis of pharmacy claims made by 1754 patients in a managed care plan with a PCP at our academic medical center between 1996–2000. No depression management program was operating during this time. Treatment adequacy was defined as any period of average dose equivalent to fluoxetine ≥ 20 mg/day for ≥ 90 continuous days. We evaluated the independent impact of prescriber type on treatment adequacy using logistic regression.

Results: Patients prescribed ADs solely by, PCPs had an adequacy rate = 26%. Patients prescribed ADs by both psychiatrists and PCPs had an adequacy rate = 61% ($p < .0001$). The increased adequacy of such co-prescribing was confirmed in our regression analysis (OR 3.7 95%CI 2.2–6.2 vs. PCP only).

Conclusions: Co-prescribing conducted under "usual care" conditions, absent a structured QI program significantly improved adequacy rates. Exploration of factors involved, which may have included effective communication between PCPs and psychiatrists and judicious selection of referrals, may inform future care improvement efforts.

NR394 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Family Functioning in the Caregivers of Patients with Dementia

Alison M. Heru, M.D., *Department of Psychiatry, Brown University/Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906-9980*; Christine E. Ryan, Ph.D., Asma Iqbal, M.D.

Summary:

This study examines the role of family functioning in family members caring for a patient with dementia. Depression, caregiver burden and satisfaction are measured as well as the quality of life experienced by the caregivers. 63% of caregivers were female with a mean age of 62 years. Patient mean age was 73 years. Caregivers were more likely to be spouses (61%) than children (29%) or other relatives (11%). Caregivers in this study reported more satisfaction than burden. However, compared to caregivers with good family functioning those with poor perceived family functioning reported significantly higher strain ($t(36) = -2.20$, $p<.05$), more depressive symptoms ($t(14.5)=-3.07$, $p<.01$) and tended to have lower satisfaction ($t(25)=1.90$, $p<.10$). Female caregivers' perception of family functioning was significantly related to depression scores ($r=.53$, $p<.05$). In contrast, male caregivers' perception of family functioning was somewhat related to perception of burden only ($r=.54$, $p<.10$). Family dysfunction occurred in all areas of family life and was more disturbed the more depressive symptoms the caregiver reported ($p=.007$). While most (71%) caregivers reported receiving some type of support, 29% of the caregivers reported no support at all. Examing the relationship by gender suggest that women may be more vulnerable to the strains and satisfactions associated with caregiving when compared to men.

NR395 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Longitudinal Study of Deinstitutionalized Veterans: Interim Results

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., Katrine Enrile, B.A., Craig W. Davis, Psy.D., David A. Smelson, Psy.D.

Summary:

Introduction: Despite large and rapid deinstitutionalization in the VA and public health care systems, few longitudinal studies have focused on the quality of life of discharged long-term hospitalized veterans. This study examined the effects of deinstitutionalization on veterans' quality of life at several NY/NJ VA hospitals.

Methods: Veterans with at least 90 consecutive psychiatric hospitalization days are rated for two years following discharge. Functional and psychiatric status is assessed using a 16-item scale rated by their clinician.

Results: On hundred twenty-three veterans have been rated. Ninty-seven percent had at least one rating within six months of discharge. Symptom severity was moderate in this group (mean CGI=4.29). 25% were in nursing homes, while 48% were in supervised group homes. Employment of any type was low (8%). Most patients not in nursing homes required a case manager (92%). Rehospitalization was low (10% within 30 days). Patient satisfaction with social setting was good (60% satisfied or better).

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.

NR396 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Parental and Adolescent Roles in Adolescent Films: 1987–1989 Versus 1997–1999

Stephen A. Young, M.D., *1202 Woodrow Street, Columbia, SC 29205*; Danielle C. Young, M.A., Stefan Schulenberg, Ph.D., Kathleen R. Rafter, R.N., Kristin M. Wieduwilt

Summary:

Objective: Media images impact adolescent behaviors in complex ways. This study evaluated how adolescent and parental roles are depicted in films targeted to teenage audiences.

Method: Films were selected from two study periods, I (1987–89) and II (1997–99). Inclusion required 1) the primary theme involves adolescent issues and/or 2) the main character(s) are adolescents. Parental characters were rated by quantity (absent, peripheral, or main characters) and quality (wise/helpful, unwise/not helpful, abusive/malignant). Adolescents were rated for the presence of: importance of academics, substance use, smoking, employment, primary control of a vehicle, and sexual activity. A series of 2×2 cross tabulation analyses were performed comparing the described characteristics of both the adolescent and adult characters.

Results: Parents were significantly more likely to be portrayed as wise/helpful in the films for study period I than period II ($p=.04$). Adolescents were significantly more likely to be to be portrayed as being sexually active ($p=.003$), alcohol users ($p=.0000$), drug users ($p=.0000$), and smoke cigarettes ($p=0.01$) in study period II.

Conclusions: In studied films, parents are increasingly being depicted as unhelpful in the lives of the adolescent characters. Conversely, adolescents are depicted as increasingly adult in terms of sexual behavior and substance use.

NR397 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Impact of Social Anxiety Disorder on Work Success in Welfare Recipients

James L. Abelson, M.D., *Department of Psychiatry, University of Michigan, 1500 East Medical Center Drive, Ann Arbor, MI 48109-0118*; Joseph A. Himle, Ph.D., Michelle L. Vanetten, Ph.D., Richard M. Tolman, Ph.D.

Summary:

Background: Studies in clinical and community samples document that Social Anxiety Disorder (SocAD) is common, disabling, and costly. It reduces educational attainment and job success, and thus may undermine economic self-sufficiency. We examined SocAD as an obstacle to successful employment in a longitudinal epidemiological study of women receiving welfare in an urban Michigan county, testing the hypothesis that SocAD would predict greater levels of reliance on welfare for economic support.

Methods: Psychiatric diagnoses were established using CIDI Short Forms. Bivariate and logistic regression analyses were conducted on data from 624 respondents who completed the study's third wave.

Results: The data demonstrated that respondents with SocAD worked fewer months, spent more months on welfare, and were more likely to be welfare reliant rather than wage reliant in the past year. The impact of SocAD was independent of the effects of depression.

Conclusion: By undermining efforts to obtain or maintain employment, SocAD poses a significant, unrecognized impediment to efforts to reduce welfare costs and help recipients achieve economic self-sufficiency. Because recipients may lose benefits if they fail to return to work rapidly or exceed time limits, those suffering from SocAD are at risk of extreme economic hardship. Improved access to effective treatments in this population could have significant public health and economic benefits.

NR398 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Treatment-Resistant Depression in Primary Care

Patricia Corey-Lisle, Ph.D., GEA, *Eli Lilly and Company, Lilly Corporate Center, DC 1834, Indianapolis, IN 46285*; Rowena Nash, B.S., Paul Stang, Ph.D., Ralph Swindle, Ph.D.

Summary:

Background: Depressive disorders are one of the most common reasons for visits to primary care physicians (PCPs)[1]. Prevalence rates and treatment outcomes for treatment-resistant depression (TRD) in PCP settings are unknown. The study objectives were to identify TRD-likely patients and evaluate clinical response in a PCP setting.

Methods: A prospective, Randomized Trial Investigating SSRI Treatment (ARTIST) compared effectiveness of SSRI therapy in PCP settings. Eligible depressed patients were randomized to treatment (n=601) and naturalistically followed for 9 months. Medication use was determined by self-report questionnaire. Adequate treatment was defined as six months continuous medication. TRD-likely patients were classified using a treatment algorithm. Clinical response was determined by use of the SCL-20. Patients were classified as achieving remission (score $\leq$ 6), partial response (50% decrease in symptoms), or non-response.

Results: Thirteen percent of patients continuously on medication for 6 months had treatment patterns consistent with TRD. Clinical response in this setting was less than optimal with 45% of adequately treated patients classified as non-responders.

Conclusions: TRD patients are being managed in PCP settings. A substantial number of patients considered adequately treated did not achieve clinical response. These patients may be considered under-treated according to current treatment guidelines recommending dose increases or medication switches for non-responders.[2]

NR399 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Validation of a Treatment Algorithm for Treatment-Resistant Depression

Patricia Corey-Lisle, Ph.D., GEA, *Eli Lilly and Company, Lily Corporate Center, DC 1834, Indianapolis, IN 46285*; Roxanna Farinpour, Ph.D., S. Rae Starr, M.Phil.

Summary:

Objective: Treatment-resistant depression (TRD) has been studied retrospectively by identifying patients through treatment pattern algorithms[1,2]. TRD-likely patients were found to be higher and more costly utilizers of health care services. The study objectives were to replicate a previously developed algorithm in a large managed care data set and to compare utilization and costs for TRD-likely and TRD-unlikely patients.

Methods: Data for members in a large East Coast managed care organization (n=2M) was used for this retrospective analysis. Depressed plan members (n_{DEP}=17,283, were classified as TRD-likely (n_{TRD}= 1,561) or TRD-unlikely by use of the treatment-pattern algorithm. Resource utilization and costs were compared between TRD-likely and TRD-unlikely patients for year 2000 data.

Results: In this plan, 9% of the depressed sample was classified as TRD-likely with average annual health care costs of $6061.63 for TRD-likely patients and $3686.95 for TRD-unlikely patients. The average number of health claims among TRD-likely patients was almost twice that of TRD-unlikely patients (69.89 vs. 35.83).

Conclusion: Findings are consistent previous retrospective studies of TRD, underscoring that the high costs associated with TRD are comparable across different health care plans. These findings highlight the need for effective therapies for this subset of depressed patients.

NR400 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Antipsychotic-Induced Type-Two Diabetes: Evidence from a Large Health Plan Database

Frank D. Gianfrancesco, M.D., *Hecon Associates, 15831-B Branch Crabbs Way, Rockville, MD 20855*; Richard E. White, Ph.D.

Summary:

Objective: To evaluate the association of antipsychotic treatment with type 2 diabetes in a large health plan database.

Methods: Claims data for patients with psychosis within a health plan of nearly 2 million patients were analyzed using statistical models. Frequencies of newly treated type 2 diabetes in patients untreated with antipsychotics and among patients treated with quetiapine, risperidone, olanzapine, and conventional antipsychotics were compared.

Results: Based on exposure measured in months of antipsychotic treatment, quetiapine and risperidone had estimated odds of receiving treatment for type 2 diabetes that were lower than those of patients untreated with antipsychotics (not statistically significant); conventional antipsychotics had estimated odds that were virtually equivalent to those of patients untreated with antipsychotics; olanzapine alone had odds that were significantly greater than those of patients untreated with antipsychotics (P<0.05). Odds ratios based on 8 months of prescreening for preexisting type 2 diabetes and assuming 12 months' antipsychotic treatment were: quetiapine=0.953 (95% CI, 0.408-2.227); risperidone=0.652 (95% CI, 0.306-1.393); olanzapine=1.426 (95% CI, 1.049-1.945); and conventional antipsychotics=1.024 (95% CI, 0.669-1.564).

Conclusions: Case reports have increasingly implicated olanzapine as causing or exacerbating type 2 diabetes, while few have implicated quetiapine and risperidone. This study supports these findings.

NR401 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Effects of ECT on Psychopathology, Quality of Life, and Social Function in Patients with Refractory Schizophrenia

Worrawat Chanpattana, M.D., *Department of Psychiatry, Srinakharinwirot University, 681 Samsen Dusit, Bangkok 10300, Thailand*;

Summary:

Objective: To determine the effects of ECT combined with neuroleptic therapy on psychopathology, quality of life, and social functioning in patients with refractory schizophrenia.

Method: An open acute (Phase I) and maintenance (Phase II) study of the combination of ECT and flupenthixol in the treatment of 46 schizophrenic patients. Scales used: the Brief Psychiatric Rating Scale (BPRS), the Quality of Life Scale (QLS), Social and Occupational Functioning Assessment Scale (SOFAS), and Global Assessment of Functioning (GAF). The duration of Phase II was one year.

Results: In Phase I, there were marked reductions in the BPRS scores, and substantial increases in the QLS, SOFAS, and GAF scores. During Phase II, the BPRS negative symptoms worsened. Changes in other outcome measures were negligible.

Conclusions: Improvement in patients' psychopathology, quality of life, and social functioning were impressive in Phase I, and generally sustained during Phase II in patients who had remitted.

NR402 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Trichotillomanina Treatment: Medication Effectiveness and Predictors of Outcome

Shani H. Osbourne, B.A., *Department of Psychiatry, Yale University, 100 York Street Suite 2H, New Haven, CT 06511*; C. Neill Epperson, M.D., Suzanne Wasylink, R.N.

Summary:

Objective: Enthusiastic support for the hypothesis that serotonin reuptake inhibitors (SRIs) are more effective in the treatment of trichotillomania (TTM)[1] than noradrenergic antidepressants has been dampened by recent reports of their limited and/or short-lived efficacy.[2] In an attempt to confirm the preferential efficacy of SRIs in the treatment of TTM, the authors conducted a controlled study comparing the *selective* SRI fluvoxamine (FVX) versus the predominantly noradrenergic agent desipramine (DMI).

Methods: Twenty psychotropic medication-free women meeting DSM-IV criteria for TTM of at least moderate severity [based on the Psychiatric Institute Trichotillomania Scale (PITS)] were enrolled in this ongoing 12-week outpatient double-blind study. Medication was titrated to final mean FVX and DMI doses of 255 mg/d and 210 mg/d, respectively. Severity of TTM, depression and anxiety were assessed biweekly.

Results: Repeated measures analysis of variance revealed no significant group by time interaction ($p = 0.88$) with respect to total PITS score (main outcome variable). Regardless of medication group assignment, treatment responders were found to have significantly lower baseline anxiety (Students t-test; $p = .01$) and depression ($p = .01$) scores as assessed using standard rating scales.

Conclusions: Although cautious interpretation is warranted given the preliminary nature of these findings, this study does not support the hypothesis that FVX is more efficacious than DMI in the treatment of TTM. However, these results are consistent with the general opinion that comorbid depressive and anxiety symptoms which are common in TTM can impede *acute* as well as long-term treatment response.[2]

NR403 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Type-Specific Alpha EEG Biofeedback Improves Residential Substance Abuse Treatment

William M.W. Scott, M.D., *2300 Peachtree St NW # 3100-3, Atlanta, GA 30309-1146*; Thomas M. Brod, M.D., Stephen I. Sideroff, Ph.D., David Kaiser, Ph.D., Meredith L. Sagan, M.D.

Summary:

Objective: To evaluate the addition of an advanced EEG biofeedback protocol to a substance abuse residential treatment program.

Methods: Sixty one (61) control and 60 experimental volunteers undergoing an inpatient 12-step based program were randomly assigned to the EEG biofeedback or control group. The experimental group received a 40-session biofeedback protocol in addition to the standard residential treatment. Abstinence rates as well as psychometric measures were compared at set intervals for both groups, with both tester and subject blind as to group. The experimental group received beta/SMR training, followed by alpha training (divided into alpha suppression or augmentation training empirically based on initial alpha amplitudes). UCLA's HSPC approved the study design.

Results: The experimental group demonstrated significant improvements on all psychometric tests, with subgroup differences noted in the alpha-attenuation and alpha-augmentation subgroups. Experimental subjects stayed in treatment significantly longer compared to the control group ($p < 0.005$). At one year post study 36 of the 47 completing experimental subjects were abstinent compared to 12 of 27 control subjects.

Conclusion: We have confirmed and extended earlier EEG studies indicating the addition of an enhanced EEG biofeedback protocol to standard chemical dependency improves treatment outcome in a residential setting.

NR404 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Computer Assessment of Undiagnosed Mental Disorders in Emergency Room Patients

Michelle H. Biros, M.D., *Hennepin County Medical Center, 701 Park Avenue, Minneapolis, MN 55415*; Kenneth A. Kobak, Ph.D., James Risser, M.D., Monica Mandell, Ph.D.

Summary:

Background: The emergency department is the entry point into the medical system for many people who do not have primary health care providers. The brief and complaint-directed focus of ER visits may preclude the detection of underlying psychiatric illness. The current study examined the prevalence of undiagnosed psychiatric illness in an adult ER population using computer assessment.

Methods: 272 patients presenting with low acuity, non-psychiatric complaints were screened using a version of PRIME-MD administered by laptop computer. Excluded were patients who did not speak or read English, were critically ill, intoxicated, or physically unable to participate.

Results: 272 of 307 invited patients consented to participate (88.6%). Two-thirds had one or more psychiatric diagnoses. Anxiety disorders were the most common (52%), with 38% having an affective disorder. 10% indicated suicidal ideation within the past 2 weeks, and 6 of these patients received acute crisis intervention. One, with chief complaint of cough, was acutely suicidal and admitted. Three others were started on antidepressants. Alcohol abuse/dependence was confirmed in 18%, and eating disorders in 5%. Only 10% reported a previous psychiatric diagnosis or current

psychiatric medications. Mean completion time was 5.1 minutes (SD=3.8). In a subset of 50 patients asked, 84% felt comfortable being interviewed by computer, 96% understood the questions, and 46% preferred the computer, 10% a person, and 44% had no preference.

Conclusions: Incidence of psychiatric disorders in ER patients is high. Computer assessment is useful and well accepted by ED patients. Computers provide a time and cost-efficient means for increasing psychiatric disorder detection rates.

NR405 Wednesday, May 22, 12:00 p.m.-2:00 p.m.

Correlates of Psychiatric Morbidity Among Low-Income Women in Aleppo, Syria

Nael Kilzieh, M.D., *VAPSHCS, American Lake Division 116-M, Tacoma, WA 98493*; Wasim Maziak, M.D., Taghrid Asfar, M.D., Fawaz Mzayek, M.D., M. Fouad, M.D.

Summary:

Objective: We examined socio-demographic correlates of psychiatric morbidity among low-income women in Aleppo, Syria. We hypothesized that women who are physically abused will have a higher level of psychiatric morbidity.

Method: A sample of 412 women was recruited from 8 randomly selected primary care centers, that serve low income families in Aleppo, Syria. Self Report Questionnaire (SRQ-20), with psychotic items excluded, was used to measure psychiatric morbidity. SRQ's validity, including Arabic translated-version, has been established. A special questionnaire was prepared to obtain relevant socio-demographic factors. These included age, race, religion, residence, education, work, economic status, polygamy, age of marriage, number of children, as well as physical abuse.

Results: Response rate was 97%. Married women constituted 88%. Rural residence accounted for 17%. The prevalence of psychiatric morbidity (SRQ $\geq$ 8) was 56%. Prevalence of physical abuse was 26%, illiteracy 26%, and polygamy 8%. Predictors of women's higher psychiatric morbidity in a logistic regression model were physical abuse, illiteracy, polygamy, and rural residence.

Conclusion: Social factors are important predictors of psychiatric morbidity among low-income women in Aleppo, Syria. Poor education and physical abuse are prevalent, and are strong predictors of such morbidity. Our findings provide specific foci for interventions.

NR406 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Acute Stress and Depressive Symptoms After an Industrial Disaster

Philippe J.R. Birmes, M.D., *Department of Psychiatry, Chu de Toulouse, Place Baylac, Toulouse 31059, France*; Dominique Coppin, M.D., Nathalie Vinnemann, M.D., Jean-Paul Charlet, M.D., Henri Juchet, M.D., Dominique Lauque, M.D., Laurent J. Schmitt, M.D.

Summary:

Objective: An explosion of a factory caused the death of 30 people and injured 2,500. We studied the relation between acute stress reaction (ASR) and early major depressive symptoms (MDS).

Method: A total of 270 subjects were hospitalized in two emergency departments. One hundred fifty-three of them (57%) agreed to participate. They were given the Stanford Acute Stress Reaction Questionnaire (SASRQ) and the Beck Depression Inventory 13-items (BDI) from five to eight weeks post-trauma.

Results: 57% of the 153 subjects were male. The mean age was 37 years (SD=16). 22% were exposed in the factory, 41% near the factory, and 37% in other places. 31% were secondly hospitalized in surgical units. 24% reported an ASR in the first month post-trauma and 9% reported a BDI total score $\geq$ 16 (MDS subjects). 92% of the MDS subjects have reported an ASR, but only 18% of the non-MDS subjects have reported an ASR (Fisher's exact test: $p<0.00001$). Among ASR subjects mean BDI scores were significantly higher (9.8 ± 7.2) than in those without ASR (3.9 ± 3.8; Mann and Whitney's test: $p<0.00001$).

Conclusion: High levels of acute stress following exposure to an industrial disaster are risk factors for early major depressive symptoms.

NR407 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Acute Stress and Posttraumatic Stress Symptoms After an Industrial Disaster

Philippe J.R. Birmes, M.D., *Department of Psychiatry, Chu de Toulouse, Place Baylac, Toulouse 31059, France*; Dominique Coppin, M.D., Nathalie Vinnemann, M.D., Jean-Paul Charlet, M.D., Henri Juchet, M.D., Dominique Lauque, M.D., Laurent J. Schmitt, M.D.

Summary:

Objective: An explosion of a factory caused the death of 30 people and injured 2,500. We studied the relation between acute stress reaction (ASR) and early posttraumatic stress (PTS) in these victims.

Method: A total of 270 subjects were hospitalized in two emergency departments. One hundred fifty-three of them (57%) agreed to participate. They were given the Stanford Acute Stress Reaction Questionnaire (SASRQ) and the Impact of Event Scale (IES) from five to eight weeks post-trauma.

Results: 57% of the 153 subjects were male. The mean age was 37 years (SD=16). 22% were exposed in the factory, 41% near the factory, and 37% in other places. 31% were secondly hospitalized in surgical units. 24% reported an ASR in the first month post-trauma and 28% reported an IES total score > 42 (PTS subjects). 57% of the PTS subjects have reported an ASR but only 11% of the non-PTS subjects have reported an ASR (Fisher's exact test: $p<0.00001$). Among ASR subjects mean IES cores were significantly higher (48.2 ± 15.2) than in those without ASR (25.9 ± 15; $t = 7.8$ ddl = 148 $p<0.00001$).

Conclusion: High levels of acute stress following exposure to an industrial disaster are risk factors for early posttraumatic stress.

NR408 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Murder-Suicides Involving Children 18 Years and Younger: A Five-Year Florida Study

Donna Cohen, Ph.D., *Aging/Mental Health Department, University of South Florida, 13301 Bruce B. Downs Boulevard, Tampa, FL 33612-3899*; Carl Eisdorfer, M.D.

Summary:

Objective: The purpose of this study was to identify the prevalence and characteristics of homicide-suicides (HSs) over a 5 year period in Florida where victims were 18 yrs. or less.

Method: We reviewed medical examiner files from all districts in Florida from 1997–2001. All completed HSs, where a child 18 and younger was killed by a parent or family member, as well as attempted HSs where a child(ren) survived were tabulated. Main outcome measures were the number of HSs as well as sociodemographic and clinical characteristics.

Results: A total of 48 children were killed in 35 HSs over 5 yrs. Another 14 children recovered from their wounds in 8 attempted HSs. When a parent killed a child(ren), they were equally likely to be the mother or father. When a parent killed a child(ren) and another adult the perpetrator was always the father.

Conclusions: About 10 children a year were killed in a HS. The percentage of women killing children was higher than HSs in

general. Fathers killed children and wives but mothers only murdered children. Clinicians should screen for children at risk where parents have psychiatric problems or there is evidence of domestic conflict or violence.

NR409 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Increased Risk of Accidents and Injuries for Patients with ADHD

Andrine R. Swensen, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Ami J. Claxton, Ph.D., Howard G. Birnbaum, Ph.D., Paul E. Greenburg, M.B.A.

Summary:

Objective: Studies have documented the increased prevalence of accidental injuries for ADHD patients; however, little is known regarding the costs of these accidents or the impact of medication on accident risk.

Methods: A retrospective analysis was performed on a database that included medical, pharmaceutical, and disability claims for employees, spouses, dependents, and retirees (1996 through 1998; n > 100,000). 1,308 ADHD patients (1,204 unique families) were identified. Controls were matched on age, gender, state, and employment status. Analyses were restricted to 1998 claims. Standard statistical methods were utilized.

Results: More ADHD patients suffered an accident than controls in 1998 (32% vs. 20%). ADHD patients were 1.7 times more likely to suffer from an accidental injury requiring medical treatment than controls ($p < 0.001$). The accident-specific costs were greater for ADHD patients ($209 vs. $131) than for controls ($p < 0.05$). However, when analyses were restricted to individuals with an accident, no differences were observed. Stimulant/medication usage (supply + 15 days) was not associated with a decreased risk of accidental injury.

Conclusion: The impulsivity and risk taking behavior associated with ADHD can lead to increased risk of accidental injury. Furthermore, it does not appear that current pharmacotherapies decrease this risk.

NR410 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Increased Risk of Self-Injury for Patients with ADHD

Andrine R. Swensen, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Albert J. Allen, M.D., Markus Kruesi, M.D., Anna Purdum, M.S., George Goldberg, M.D.

Summary:

Objective: Two symptoms of ADHD, hyperactivity and poor impulse control, may increase risk of injury for patients with this disorder.[1] A preponderance of research conducted to date has focused on the association between ADHD and accidental injury.[2] The purpose of this study was to evaluate the risk of the spectrum of intentional injuries, from poisonings to suicides, for ADHD patients.

Methods: Between January 1, 1991 and May 31, 2000, patients with a diagnosis of ADHD (n = 55,760) were retrospectively identified from a U.S. managed care database. Age-, gender-, and index-year-matched controls (n = 167,280) were randomly selected. Key outcome measures were intentional injury (e.g., poisoning), suicide attempts, and completed suicides. Multivariate analyses were used.

Results: ADHD patients were 2.5 times more likely to suffer from an intentional injury (95%CI: 2.1–2.8). Additionally, ADHD patients were 2.9 times more likely to attempt suicide (95% CI: 2.4–3.5); this remained statistically significant after adjusting for depression and substance abuse. ADHD patients were 3 times more likely to complete suicide, however, this was not statistically significant due to small numbers and inadequate power (95% CI: 0.75–12).

Conclusion: ADHD can have serious consequences and may be an important disorder to target with suicide prevention efforts.

NR411 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Ordering Practices and Value of Laboratory Tests for Psychiatric Inpatients

Jeffrey P. Staab, M.D., *Department of Psychiatry, University of Pennsylvania, 3400 Spruce Street, 11 Founders Building, Philadelphia, PA 19104*; Vivianna Van Deerlin, M.D., Donald S. Young, M.D., James L. Stinnett, M.D.

Summary:

Objective: Information about the utility of laboratory tests for psychiatric inpatients is limited. This study examined laboratory results from 205 consecutive psychiatric inpatients to provide empirical data on cost effective laboratory use.

Methods: Laboratory tests and abnormal results were examined from two units in a university hospital (105 adult and 50 geropsychiatry patients) and one unit in a community hospital (50 addictions psychiatry patients). Forty-four (21.5%) randomly selected charts were reviewed by two psychiatrists to determine the number of (a) clinically significant test results, (b) test results that changed patient management, (c) tests that were clearly indicated, and (d) indicated tests that were not ordered.

Results: Geropsychiatry patients had significantly more tests (52.3 tests/patient) and a higher percentage of abnormal results (13.6%) than adult (26.8 tests/patient, 5.8% abnormal) or dual diagnosis (36.6 tests/patient, 7.2% abnormal) patients, because of more repeat lab testing. Only 29% of abnormal results were clinically significant and just 35% of those changed patient management (i.e., only 1/54 tests changed patient care). Serum electrolytes were ordered most often, but were least useful. CBCs and urinalyses produced the greatest number of irrelevant abnormalities. Tests for pregnancy and medication toxicity were omitted most frequently. Only 20.7% of lab orders were clinically indicated.

Conclusions: Psychiatric inpatients received many "screening labs" that were uninformative, while more pertinent tests were underutilized.

NR412 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Construct Validity of the Psychiatric Diagnostic Screening Questionnaire

Thomas Sheeran, Ph.D., *Department of Psychiatry, Brown University, 235 Plain Street, Suite 501, Providence, RI 02905*; Mark Zimmerman, M.D.

Summary:

Objective: The Psychiatric Diagnostic Screening Questionnaire (PDSQ) is a 125 item self-report scale designed to screen for 15 of the most common DSM-IV Axis I disorders encountered in outpatient mental health settings (Zimmerman & Mattia, 2001). Prior research established the measure's reliability and criterion-related validity (Zimmerman & Mattia, 1999). The goal of this project was to evaluate the construct validity of the PDSQ via factor analysis.

Method: A sample of 2,440 adult psychiatric outpatients completed the PDSQ before their intake appointment. Two independent factor analyses were conducted on two, randomly-split subsamples (N=1,220)

Results: Results of the two factor analyses were identical. Thirteen factors were extracted, and ten mapped directly onto the expected DSM-IV diagnoses: Major Depression, Dysthymia, Mania, Alcohol Abuse, Drug Abuse, PTSD, Social Phobia, OCD, Bulimia and GAD. Two of the three remaining factors were com-

posites: Panic/Agoraphobia and Hypochondriasis/Somatization. The last factor was comprised of the six PDSQ items assessing suicidality. Finally, one PDSQ module, Psychosis, was not well-supported by the factor analysis.

Conclusion: Overall, the construct validity of the PDSQ was well-supported. Combined with prior psychometric analyses, results suggest that the PDSQ is a useful measure for detecting many of the most common DSM-IV Axis I Disorders.

NR413 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

ADHD Subtypes Change Dramatically with Gender and Age

Atilla Turgay, M.D., *Department of Psychiatry, Scarborough Hospital, 3050 Lawrence Avenue, East, Scarborough, ON M1P 2V5, Canada*; Rubaba Ansari, M.A., Mansoor Zafar, M.D.

Summary:

This study included 2,298 males and 635 females (N=2933) with ADHD.

Objectives and method: Subjects were systematically studied re: the ADHD subtypes, age, and gender relationships. Evaluations included Gadow-Sprafkin general psychopathology screening scales, DuPaul ADHD scales and semistructured interviews.

Findings: The community-based studies in the same area identified Male:Female (M:F) ratio of 2.5:1. Male:Female (M:F) ratio in this study was 3.6:1, showing the under-identification of females (P<0.0001). As age increased, the M:F ratio decreased. Among children age two to five (N=359), the M:F ratio was 5.18:1; for patients over 19 (N=297) M:F ratio approached the community sample's ratio, showing improved identification of females in adulthood. ADHD subtypes changed dramatically as age increased. In the two to five age group, ADHD combined type: predominantly inattentive type ratio (ADHD:ADD) was 38:1. In the over 19 age group, ADHD:ADD ratio was 0.89. ADHD predominantly inattentive type was more common in females than males (18.59% vs 30.47%). For every age group, ADHD hyperactive-impulsive (HI) type was the least common subtype, 2.08% of males and 1.73% of females with ADHD had HI type.

Conclusions: ADHD-HI type is very rare for every age group and for both genders. Hyperactivity decreases and identification of females improves as age increases.

NR414 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Comorbidity, Gender, and Age Relations in Child and Adolescent OCD

Atilla Turgay, M.D., *Department of Psychiatry, Scarborough Hospital, 3050 Lawrence Avenue, East, Scarborough, ON M1P 2V5, Canada;* Mansoor Zafar, M.D., Hoda Rizkallah, M.D., Borivoje Trifinovic, M.D., Atif Shaikh, M.D., OCD Study Group

Summary:

Objectives: To determine the frequency, nature, age, and gender relations of comorbidity in child and adolescent OCD.

Method: This study involved 25 females and 34 males with the DSM-IV diagnosis of OCD. Yale-Brown Checklist for OCD, Gadow-Sprafkin, and Offord and Boyle parent and teacher questionnaires were used in reviewing comorbidities, and DuPaul ADHD rating scales supported the diagnosis of ADHD and its subtypes.

Results: (1) 42.3% of OCD patients were females and 57.62% were males. Most patients were identified after age 12 (p= 0.02425). Only five males and two females (11.86%) had OCD alone, the others had at least one more comorbid psychiatric disorder. Some minor gender differences in comorbidity did not reach statistical significance (p=0.14451). Most frequent comorbid disorders in males and females were: generalized anxiety disorder (64.70% vs 60%), ADHD (61.76% vs 20%), oppositional defiant disorder (32.35% vs 12%), Tourette's disorder (14.70 vs 12%), major depression (14.70% vs 12%), and dysthymic disorder (11.76 vs 12 %).

Conclusions: OCD in children presents with many other comorbid disorders. Clinicians should explore for the presence of other commonly associated comorbid disorders since the treatment approach may change dramatically according to the nature of these disorders.

NR415 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Evaluation of the Sleep Activity Profile of Pregabalin Compared to Alprazolam in Normal Volunteers

Ian Hindmarch, Ph.D., *H.P.R.U., Surrey University, Egerton Road, Guildford, Surrey GU2 5XP, United Kingdom*; Jean Dawson, Neil Stanley

Summary:

Objective: Pregabalin is a novel centrally acting drug displaying anxiolytic properties, in addition to efficacy in neuropathic pain, that may modulate the BZ-GABAergic complex by its action on an allosterically-linked Ca^{2}♠ channel. The current study was designed to evaluate the effects on sleep and daytime activity levels of pregabalin (PGB) compared with placebo (PBO) and alprazolam (ALP).

Methods: A total of 24 volunteers with normal and stageable sleep were randomized, double-blind, to a three-way crossover study (including a seven-day washout). Wrist actigraphy (WA) and sleep EEG (after adaptation) were performed serially during each treatment condition.

Results: On actigraphy, PGB was associated with modest but significantly greater activation compared with ALP. Both PGB and ALP modestly but significantly reduced time-to-sleep-onset ($p < 0.02$) and improved sleep efficiency compared with PBO (in a normal volunteer sample with no sleep complaints). The most notable differences were that PGB was associated with significantly less increase in REM latency compared with ALP, while PGB significantly ($p < 0.001$) increased slow-wave sleep (stage 3/4: 23% increase) compared with both ALP and PBO.

Conclusion: Pregabalin appears to have an effect on sleep and sleep architecture that distinguishes it from the benzodiazepines. Enhancement of slow-wave sleep is intriguing since reductions have frequently been reported in GAD.

NR416 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

A Placebo-Controlled Trial of Pramipexole for Bipolar Depression

Joseph F. Goldberg, M.D., *Department of Psychiatry, Payne Whitney-NY Presbyterian Hospital, 525 East 68th Street, Box 140, New York, NY 10021*; Katherine E. Burdick, M.A., Carrie J. Endick, C.S.W.

Summary:

Background: The potential antidepressant properties of dopamine agonists have been suggested by a number of recent reports, particularly with respect to anergic depressions as seen in patients with bipolar disorder. We conducted a preliminary, double-blind, placebo-controlled trial of pramipexole added to standard mood stabilizers in severely depressed bipolar outpatients.

Method: 24 DSM-IV adult depressed-phase nonpsychotic bipolar outpatients (mean +/– SD) 31-item Hamilton Depression Scale (HAM-D) score = 33.7 +/– 8.0) underwent a 6-week 1:1 randomized trial of placebo or flexibly-dosed pramipexole (begun at 0.125 mg BID, increased by 0.125–0.25 mg/day every 3 days; mean +/– SD dose 1.7 +/– 1.3 mg/day) added to lithium ([Li♠]≥0.6 mEQ/

L), valproate ([valproate]≥45 mcg/ml) or carbamazepine ([carbamazepine]≥4 mcg/ml), held constant 1 month pre-enrollment.

Results: 1) study completion occurred comparably for subjects on active drug (75%) or placebo (67%); 2) ≥50% reduction from baseline HAM-D occurred in 58% taking pramipexole vs. 17% taking placebo (p=.039) mean +/- SD baseline HAM-D scores yielded greater reductions with pramipexole (12.9 +/- 15.5 points; 95% C.I. = 3.1–22.7) than placebo (8.0 +/- 11.1 points; 95% CI= 0.9–15.1); 4) switches to mania/psychosis occurred in 1 subject (8%) with active drug and none with placebo; 5) nausea and sedation occurred more often with active drug than placebo.

Conclusions: These preliminary findings suggest antidepressant efficacy with good tolerability for pramipexole added to standard mood stabilizers among severe, nonpsychotically depressed bipolar patients.

NR417 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Safety Meta-Analysis of Olanzapine-Fluoxetine Combination Versus Placebo

Sanjay Dube, M.D., *Eli Lilly & Company, Lilly Corporate Center, Indianapolis, IN 46284*; Scott W. Andersen, M.S., David B. Clemow, Ph.D., Todd M. Sanger, Ph.D., Sara A. Corya, M.D., Gary D. Tollefson, M.D.

Summary:

Background: Recent evidence suggests that olanzapine-fluoxetine combination (OFC) has enhanced antidepressant qualities compared with monotherapies and is a promising treatment option for difficult-to-treat depressions. As an index of its tolerability, OFC's acute safety profile was examined against placebo.

Methods: Metanalysis of safety measures were performed from two parallel, 8-week double-blind trials (n=148). Patients with psychotic depression were treated with OFC (5–20 mg/day and 20–80 mg/day) or placebo.

Results: Of events occurring in ≥10% of patients, significantly more OFC patients experienced somnolence (25%, 5%; p=0.001) and peripheral edema (10.4%, 0%; p=0.003). The proportion of patients with >10% increase in weight was significantly higher for OFC patients than placebo (6.7%, 0%; p=0.035) patients. No other significant differences were seen between OFC treatment and placebo for adverse events (including weight gain), extrapyramidal symptoms, abnormal electrocardiograms, or categorical changes in vital signs or laboratory analyses.

Conclusion: Acute OFC treatment was associated with a higher incidence of somnolence, peripheral edema, and potentially significant weight gain compared with placebo. This profile is similar to those of OFC's component monotherapies[1,2], and provides evidence for the acute tolerability of this combination treatment.

NR418 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Does the Pharmacotherapy of ADHD Beget Later Substance Abuse?

Timothy E. Wilens, M.D., *Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114*; Stephen V. Faraone, Ph.D., Samantha C. Gunawardene, B.S., Joseph Biederman, M.D.

Summary:

Objective: Using meta-analytic techniques, we evaluated the literature to determine if stimulant treatment of Attention Deficit Hyperactivity Disorder (ADHD) is related to a heightened risk, no appreciable effect, or a protective effect on later substance use disorders (SUD).

Methods: A systematic search of the literature was conducted. Meta-analytic techniques were applied to the data to evaluate overall risk of SUD in treated vs. untreated ADHD youth, class of substances affected by ADHD treatment, and influencing factors in outcome. Odds ratios depict the protective effect of treatment.

Results: This search revealed five studies of ADHD youth followed at least four years (N=576 treated and 339 untreated subjects). ADHD pharmacotherapy was associated with a reduction in risk for SUD (OR=2.3; CI 1.1–4.6, p=0.02). Similar reductions were found in risk for later drug or alcohol use disorders. In accounting for findings, only severity at baseline was associated with outcome (p<.001). The effect was stronger in older adults compared to young adults.

Conclusions: Despite the limitations of a largely naturalistic sample, the literature suggests that stimulant treatment of ADHD does not increase but actually decreases the risk for SUD. Further evaluation attendant to the baseline severity of illness, adequacy of treatment, and mechanism of risk reduction is warranted.

NR419 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

An Open Study of Bupropion Sustained Release in Adults with ADHD and BPD

Timothy E. Wilens, M.D., *Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114*; Joseph Biederman, M.D., Thomas J. Spencer, M.D., Stephanie L. Van Patten, M.A., Sarah A. Brown, B.A., Robert L. Doyle, M.D., Kristine A. Girard, M.D.

Summary:

Objective: Despite the increasing recognition of comorbid Attention Deficit/Hyperactivity Disorder (ADHD) and BPD, there are no prospective trials of pharmacological agents to treat ADHD in these patients. Given the efficacy of bupropion for ADHD in adults, as well as improvement in depression in BPD adults with minimal manic activation, we studied the tolerability and efficacy of sustained-release bupropion in adults with ADHD plus BPD.

Methods: This was an open, prospective, six-week trial of bupropion SR (up to 200 mg BID) in adults with DSM IV ADHD plus BPD I (10%) or BPD II (90%). Adults receiving adjunct antimanic agents (mood stabilizers and antipsychotics) at baseline were included in the study. We used standardized structured psychiatric instruments for diagnosis. Efficacy was based primarily on CGI, ADHD symptom checklist, and the Young Mania Rating Scale (YMRS).

Results: Thirty (Mean Age = 34 years) of 36 patients completed the protocol (17% attrition). At endpoint (LOCF), compared to baseline, treatment with bupropion SR resulted in reductions in the ADHD symptom checklist (–55%, p<0.001) and clinical global impression (CGI) of severity of ADHD (–40%, p<0.001). There was little evidence of manic activation; conversely, treatment was associated with reductions in ratings of mania (CGI: –30%, p<0.01; YMRS: –58%, p<0.001) and depression (CGI: –39%, p<0.001; BDI: –53%; p<0.001; HAM-D: –57%, p<0.001).

Conclusions: The results from this open study of adults with ADHD plus largely BPD II suggest that bupropion SR may be effective in treating ADHD without significant activation of mania.

NR420 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Duloxetine Versus Paroxetine in the Treatment of Depression

David J. Goldstein, M.D., *Eli Lilly and Company, Lilly Corporate Center, DC2206, Indianapolis, IN 46285*; Yili Lu, Ph.D., Michael J. Detke, M.D., Curtis G. Wiltse, Ph.D., Craig Mallinckrodt, Ph.D., Mark A. Demitrack, M.D.

Summary:

Objective: To compare the clinical efficacy of duloxetine (40 & 80 mg/day administered BID), a potent and balanced dual reuptake inhibitor of serotonin (5-HT) and norepinephrine (NE) (Bymaster

et al., 2001 Pitsikas, 2000), with the SSRI paroxetine (20 mg QD) and placebo in the treatment of major depressive disorder (MDD).

Method: In this 8-week, randomized, double-blind study, efficacy was evaluated using total $HAMD_{17}$ (primary), MADRS, CGI-S, PGI-I, HAMA and visual analogue scales for pain. Safety and tolerability were also assessed.

Results: Duloxetine at both doses was superior to placebo in reduction of $HAMD_{17}$ total scores. Duloxetine 80 mg/day was statistically superior to placebo on most secondary efficacy measures and was statistically superior to paroxetine on $HAMD_{17}$ total score. The remission rate for duloxetine 80 mg/day was 50%, paroxetine 37%, and placebo 30%. Duloxetine 80 mg/day significantly reduced overall pain. Insomnia was the only adverse event reported significantly more frequently for duloxetine 80 mg/day than for the SSRI paroxetine. There was no significant difference between duloxetine and placebo groups in the incidence of hypertension.

Conclusions: Duloxetine is efficacious for patients with MDD. Duloxetine, a dual reuptake inhibitor of both 5-HT and NE, may be more effective than paroxetine, an SSRI, for patients with MDD.

NR421 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Duloxetine Reduces Anxiety Symptom Severity

David J. Goldstein, M.D., *Eli Lilly and Company, Lilly Corporate Center, DC2206, Indianapolis, IN 46285*; Michael J. Detke, M.D., Yili Lu, Ph.D., Mark A. Demitrack, M.D.

Summary:

Objective: To examine the effect of duloxetine, a potent and balanced dual reuptake inhibitor of serotonin (5-HT) and norepinephrine (NE) (Bymaster et al., 2001), on symptoms of anxiety in depressed patients. Anxiety occurs in about 60% of patients with major depressive disorder (Stein et al., 1995).

Methods: Three multi-site, randomized, double-blind, placebo-controlled studies of duloxetine in major depression were evaluated for effects on anxiety. Study 1 assessed duloxetine 120 mg/d administered BID and fluoxetine 20 mg/d. Study 2 assessed duloxetine 40 mg/day and 80 mg/day administered BID and paroxetine 20 mg/d. Study 3 assessed duloxetine at 60 mg/day. All studies used the 17 item Hamilton Depression Rating Scale. Studies 1 and 2 used the Hamilton Anxiety Rating Scale (HAMA). The HAMD anxiety/somatization subfactor and anxiety psychic item (Item 10) and HAMA were evaluated.

Results: Duloxetine was significantly more effective for the HAMD Item 10 and anxiety/somatization subfactor over placebo in studies 1, 2, and 3 and over fluoxetine in study 1. In study 2, duloxetine (80 mg/d) was significantly more effective for the anxiety/somatization subfactor over paroxetine, and duloxetine 80 mg/d significantly reduced HAMA total score compared to placebo.

Conclusion: In these studies it was shown that duloxetine effectively relieves anxiety in depressed patients, and the anxiolytic effect was greater for duloxetine than for SSRIs.

NR422 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Patient and Rater Education About Expectations in Clinical Trials

Daniel L. Zimbroff, *Pacific Clinical Research, 1317 West Foothill Boulevard, Suite 200, Upland, CA 91786*; George Mendez, B.S.

Summary:

Methods: The Patient and Rater Education of Expectations in Clinical Trials ("PREECT"), a 2 component approach has been developed for psychopharmacology clinical trials. PREECT emphasizes the development of a research alliance between the investigating physician and the study subject, rather than the traditional therapeutic alliance. PREECT also includes careful training of study site staff about the potential harmful impact of supportive and encouraging remarks to the subject during study participation. Placebo response and signal detection data from two double-blind, randomized psychopharmacology clinical trials were examined.

Results: In trial One, the PREECT site had the lowest placebo-response rate of the 6 sites that enrolled subjects. 3/19 (15.5%) placebo-treated subjects had sustained 50% HAM-D response, defined as a 50% Ham-D response for ≥2 weeks. The range of sustained placebo response rates for the non-PREECT sites ranged from 25% to 44.4%. The Day 35 endpoint mean difference between active treatment and placebo was −3.07 points on the HAM-D at the PREECT site, and −2.57 points at Day 42. The Day 42 endpoint difference ranged between +1.91 and −8.00 point (SD 6–9 points) at the other 5 sites. In trial Two, the PREECT site had a 55 point LSAS difference between the SSRI test agent group and placebo. Drug-placebo differences ranged from 63.3 to −8.1 at the other sites with comparable numbers of subjects.

Conclusions: Preliminary evidence from two well-controlled psychopharmacology clinical trials indicate that the PREECT approach reduced the placebo-response rate and improved signal detection as compared to sites not using the PREECT approach. This may have important implications for psychotropic drug development, as high trial failure rates, primarily due to high placebo response rates, add time and cost to new drug development, and potentially leads to the discontinuation of useful, innovative therapies from further development.

The authors thank Sanofi-Synthelabo Pharmaceuticals Inc & Solvay Pharmaceuticals for their cooperation in providing the placebo response data from the trial.

NR423 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

The Efficacy of Intramuscular Olanzapine in Acutely Agitated Patients

Stacy R. David, Ph.D., *Lilly Research Labs, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Barry Jones, M.D., Karla Alaka, M.S.C., Padraig Wright, M.D., Cindy C. Taylor, Ph.D., Alan F. Breier, M.D.

Summary:

Objective: In four double-blind clinical trials, the efficacy of intramuscular (IM) olanzapine 2.5–10.0 mg/injection for acute agitation in schizophrenia (fixed-dose, N=311; dose-range, N=270), bipolar mania (N=201), or dementia (N=272) was compared with IM haloperidol 7.5 mg/injection, lorazepam 1.0 or 2.0 mg/injection, and placebo.

Methods: Patients were treated with 1–3 IM injections/24 hours. Efficacy assessments included baseline-to-endpoint changes on the PANSS-Excited Component (PANSS-EC) and additional efficacy scales. Clinical response (≥40% improvement) and onset of action (schizophrenia fixed-dose) were also compared.

Results: In schizophrenic patients, olanzapine reduced agitation significantly more than haloperidol by 15 minutes after the first injection ($p<0.05$) and significantly more than placebo at all time-points ($p<0.001$). Across all studies, olanzapine was similarly superior to placebo on the PANSS-EC at 2 and 24 hours after the first injection for all doses ($p<0.05$) and, in general, was comparable to active comparator. Additional efficacy scales and clinical response generally yielded similar results. ACES scores indicated that the reduced agitation achieved with olanzapine was a direct effect and was not secondary to a general sedative effect.

Conclusions: Four large, double-blind, placebo- and comparator-controlled studies support the efficacy of IM olanzapine in the rapid control of agitation in patients with schizophrenia, bipolar mania, and dementia.

NR424 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Evaluation of Duloxetine in the Treatment of Depression

Pierre V. Tran, M.D., *Lilly Research Labs, Eli Lilly & Company, 639 South Delaware Street, Indianapolis, IN 46285*; Yili Lu, Ph.D., Michael J. Detke, M.D., David J. Goldstein, M.D., Craig Mallinckrodt, Ph.D., Curtis G. Wiltse, Ph.D., Mark A. Demitrack, M.D.

Summary:

Objective: To examine the antidepressant efficacy of duloxetine, a potent and balanced reuptake inhibitor of serotonin and norepinephrine (Bymaster et al., 2001; Pitsikas, 2000).

Method: Data from two 8 week, and one 9 week randomized, double-blind, placebo-controlled studies of depressed outpatients were examined. Depression was measured by $HAMD_{17}$ total score (primary), MADRS, CGI, and PGI scales. Duloxetine was studied in doses ranging from 40 mg—120 mg/day.

Results: In all studies, duloxetine (40–120 mg/day) was superior to placebo in change on $HAMD_{17}$ total score. In the first study, the remission rates were 43% for duloxetine 120 mg/d given BID, 30% for fluoxetine 20 mg/d, and 27% for placebo. In the second study, duloxetine 80 mg/day given BID resulted in a significantly greater reduction in $HAMD_{17}$ total score compared to paroxetine. The remission rate for duloxetine (80 mg/day) was 50% compared to 37% for paroxetine 20 mg/d, and 30% for placebo. In the third study, the odds ratio for remission for duloxetine (60 mg QD) was 2.6 relative to placebo.

Conclusion: These data demonstrate that duloxetine is efficacious in the treatment of depression.

NR425 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Safety and Tolerability of the Antidepressant Duloxetine

Pierre V. Tran, M.D., *Lilly Research Labs, Eli Lilly & Company, 639 South Delaware Street, Indianapolis, IN 46285*; Michael J. Detke, M.D., David J. Goldstein, M.D., Craig Mallinckrodt, Ph.D., Mark A. Demitrack, M.D.

Summary:

Objective: To examine the safety and tolerability of the antidepressant duloxetine, a potent and balanced dual reuptake inhibitor of serotonin and norepinephrine (Bymaster et al., 2001; Pitsikas, 2000), across multiple clinical trials.

Method: Data from 7 double-blind placebo-controlled trials were pooled for analyses (duloxetine at 40–120 mg/d n=1032, placebo n=723). Patients were treated for up to 12 weeks.

Results: Discontinuation due to adverse events was 14.6% and 5.0% for the duloxetine and placebo groups, respectively. Treatment-emergent adverse events with an incidence for duloxetine of ≥5.0% and twice the rate of placebo were nausea, dry mouth, fatigue, dizziness, constipation, somnolence, decreased appetite, and sweating. The incidence of diastolic hypertension (elevated BP for 3 consecutive visits) for duloxetine was 0.3%. There were no clinically relevant effects on corrected QT interval or body weight. No significant differences existed between duloxetine and placebo in the incidence of treatment-emergent abnormal laboratory values at endpoint. The difference in mean change from baseline to endpoint in ASEX total score was not significantly different between duloxetine and placebo.

Conclusion: Duloxetine is safe and well tolerated.

NR426 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Long-Term Safety Upon Switching from Daily SSRIs to Fluoxetine Once Weekly

Cherri M. Miner, M.D., *Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, DC 2423, Indianapolis, IN 46285*; Eileen Brown, Ph.D., Jill S. Gonzales, Chad Stroud

Summary:

Objective: Fluoxetine once-weekly was found to be effective for maintenance of response for up to 3 months in subjects whose depressive symptoms had responded to daily dosing with SSRIs. Whether once-weekly enteric-coated fluoxetine 90mg will continue to be safe for longer term treatment was examined.

Methods: Entry criteria: Historical diagnosis of major depression for current episode, treatment with citalopram (20–40 mg/day, n=83), paroxetine (20 mg/day, n=77), or sertraline (50–100 mg/day, n=86) for 6–52 weeks immediately prior to entry into initial 12-week study, and positive response to that antidepressant (HAMD ≤10). Subjects were switched to open label, enteric-coated fluoxetine 90mg taken weekly for 12 weeks. Subjects (n=168) who were successfully maintained for 12 weeks on once-weekly fluoxetine were allowed to continue receiving it in an open-label extension to evaluate long-term safety. Safety measures included adverse events, vital signs, and clinical laboratory tests. Efficacy measure was change from baseline-to-endpoint for CGI-Severity. Compliance with weekly dosing was also evaluated.

Results: Fifty-nine percent (n=99) of subjects completed 2 to 12 months extension phase treatment with 90mg fluoxetine. No clinically meaningful changes from baseline-to-endpoint were noted in vital signs or clinical laboratory tests. Adverse event reports were similar at baseline and endpoint. No significant increases were found in CGI-Severity within or between prior SSRI therapy groups.

Conclusion: Enteric-coated fluoxetine taken once-weekly was well-tolerated and efficacious when taken for up to 15 months in subjects who responded to acute therapy with other SSRIs and were subsequently switched to fluoxetine once-weekly for continuation/maintenance therapy.

NR427 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Body Handlers' Response to Terrorism in Oklahoma City

Phebe M. Tucker, M.D., *Department of Psychiatry, University of Oklahoma, 920 Stanton Young Boulevard, WP 3440 Box 26901, Oklahoma City, OK 73190*; Betty Pfefferbaum, M.D., Debby E. Doughty, Ph.D., Dan E. Jones, Ph.D., Fred B. Jordan, M.D., Robert D. Vincent, Sara Jo. Nixon, Ph.D.

Summary:

Objective: Posttraumatic stress symptoms and depression were assessed in 51 body handlers 2 years after working with human remains in Oklahoma City's 1995 bombing.

Method: 135 surveys were mailed to volunteer body handlers (38% response) to measure demographics, previous disaster experience and training, physical and interpersonal blast exposure, problems and coping techniques, and PTSD and depressive symptoms at the time of body handling an one year later.

Results: Most respondants (67%) had no medical experience before the disaster, and many had a friend (12%) or acquaintance (45%) killed. After the disaster, 14% sought mental health treatment, and 9% increased alcohol use. However, retrospectively reported posttraumatic stress and depressive symptoms were low at the time of the disaster, and decreased significantly one year later ($p<.0001$). Neither gender, age, physical blast exposure, knowing someone killed or injured, or personal or professional disaster experience predicted posttraumatic stress symptoms. Individuals who increased alcohol use, who sought mental health

treatment, and who reported new onset of physical problems were more likely to have emotional sequelae. Coping techniques included using social support, positive reframing, distractions, and rituals (visiting the bomb site or memorial services), but none predicted emotional outcomes.

Conclusion: Unexpected resilience was found in relatively inexperienced Oklahoma City body handlers identifying human remains that included victims known to them. Possible reasons are explored, and may involve strong social support, positive management style, and higher socioeconomic and educational level.

NR428 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Paroxetine Treatment of PTSD: Effects on Emotional Symptoms, Autonomic and Diurnal Cortisol Secretion

Phebe M. Tucker, M.D., *Department of Psychiatry, University of Oklahoma, 920 Stanton Young Boulevard, WP3440 Box 26901, Oklahoma City, OK 73190*; Katherine L. Beebe, Ph.D., Akm Hossain, M.D., Richard P. Trautman, M.D., Dan E. Jones, Ph.D., Dorothy B. Wyatt, R.N.

Summary:

Objective: Effects of paroxetine treatment of PTSD on subjective symptoms, physiological reactivity and diurnal cortisol secretion were assessed.

Method: 30 PTSD patients (CAPS-1>50), 27 depressed, and 20 asymptomatic, traumatized controls were recruited by advertisement. All were outpatients, free of medical illness, other primary Axis I disorders (SCID) and psychotropic and cardiovascular medications. Baseline psychometric and physiological assessments (heart rate and blood pressure responses to 4-minute trauma scripts) and AM and PM cortisols were measured for all. 24 PTSD patients received open-label paroxetine (20–50) mg/day) for 10 weeks, with assessments repeated.

Results: Discriminant analysis comparing PTSD and non-PTSD subjects showed combined autonomic measures had 65% sensitivity and 85% specificity, with heart rate best distinguishing PTSD patients. PTSD patients had higher baseline autonomic reactivity than depressed and control patients in all measures ($P<0.05$) except diastolic blood pressure in controls ($p=0.06$). PTSD patients' baseline cortisols differed from non-PTSD subjects only in lacking a significant difference between AM and PM cortisols, indicating a flattened diurnal pattern.

After medication, PTSD symptoms significantly improved (CAPS, TOP-8, CGI), as well as sleep time and quality, depression (BDI) and anxiety (BAI). Treated PTSD patients decreased all autonomic reactivity measures significantly ($p<0.05$). Paroxetine treatment resulted in significant AM and PM cortisol differences ($p=0.037$).

Conclusion: Paroxetine treatment of PTSD resulted in improved subjective symptoms, dampening of autonomic reactivity, and enhancement of diurnal cortisol secretion. Pharmacotherapy may change some H PA-axis alterations in PTSD, helping us better understand this disorder's complex pathophysiology.

NR429 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Safety Meta-Analysis of Olanzapine-Fluoxetine Combination Versus Fluoxetine

Sara A. Corya, M.D., *6820 Parkdale Place #115, Indianapolis, IN 46254*; Scott W. Andersen, M.S., Sofia Paul, Ph.D., Sanjay Dube, M.D., Ahmed Deldar, Ph.D., Todd M. Sanger, Ph.D., Gary D. Tollefson, M.D.

Summary:

Background: Recent evidence suggests that olanzapine-fluoxetine combination (OFC) enhances antidepressant effects in treatment-resistant depression (TRD). An investigation was undertaken to determine if OFC yields new adverse effects not associated with fluoxetine monotherapy.

Methods: Metanalysis of safety data from four 6- to 8-week, double-blind studies (n=688) was performed. OFC was compared with fluoxetine for treating TRD patients (three studies) or for ameliorating sexual dysfunction reported with fluoxetine (one study). Adverse events, vital signs, electrocardiograms (ECGs), laboratory analytes, extrapyramidal symptoms (EPS) and sexual dysfunction (ASEX scale; n=564) were analyzed.

Results: Of events occurring in ≥10% of OFC or fluoxetine patients, significantly more OFC patients experienced weight gain, somnolence, increased appetite, and asthenia, and significantly less OFC patients experienced headache, diarrhea, nausea, and insomnia compared with fluoxetine patients. The proportion of patients with >10% weight gain was significantly higher for OFC patients than fluoxetine (16.3%, 0.4%) patients. There were no significant categorical changes in laboratory analytes, ECG, heart rate, and EPS measures, or significant mean differences for ASEX between OFC and fluoxetine patients.

Conclusion: No unexpected changes were seen in adverse effects commonly reported with fluoxetine monotherapy[1], and the observed differences between OFC and fluoxetine are consistent with the olanzapine component[2]. These results support the acute safety and tolerability of OFC.

NR430 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Long-Term Olanzapine-Fluoxetine Use in MDD: Interim Data

Sara A. Corya, M.D., *6820 Parkdale Place #115, Indianapolis, IN 46254*; Scott W. Andersen, M.S., Sanjay Dube, M.D., Linda S. Kelly, B.S.N., Todd M. Sanger, Ph.D., Douglas J. Williamson, M.D., Gary D. Tollefson, M.D.

Summary:

Background: Olanzapine-fluoxetine combination (OFC) has demonstrated treatment effects in treatment resistant depression (TRD), likely reflecting elevated norepinephrine, dopamine, and serotonin levels in prefrontal cortex. Long-term (76 weeks) safety and efficacy was investigated in a broader group of patients with major depressive disorder (MDD) with or without TRD.

Method: Interim data were analyzed for 560 enrolled patients over 52 weeks of open-label OFC treatment. Safety was assessed via adverse events, laboratory analytes, vital signs, electrocardiography and extrapyramidal symptom measures. MADRS was the primary efficacy measure.

Results: The five most frequently reported adverse events were somnolence, weight gain, dry mouth, increased appetite, and headache. MADRS mean total scores decreased 6 points from baseline (31.6) after 2 to 5 days of treatment, 17 points after 8 weeks, and 18 points after 52 weeks. For patients with physician-defined TRD, MADRS mean total scores decreased 7 points from baseline (32.6) after 2 to 5 days, 15 points after 8 weeks, and 17 points after 52 weeks. Response and remission rates were high (63%, 55%) and the relapse rate was low (12%).

Conclusions: The OFC safety profile is similar to that of the component monotherapies[1,2]. OFC showed rapid, sustained improvement in depressive symptoms in patients with MDD, with or without TRD.

NR431 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Evaluating Prescriber Nonadherence to Neuroleptic Treatment Guidelines

Michael J. Sernyak, M.D., *Department of Psychiatry, VACT HCS, 950 Campbell Avenue, #116A, West Haven, CT 06516*;

David Dausey, M.P.H., Rani Desai, Ph.D., Robert A. Rosenheck, M.D.

Summary:

Objective: While many guidelines have been proposed for the use of medications in the treatment of schizophrenia, actual treatment often appears to be at odds with expert recommendations. This study was designed to determine prospectively reasons for this apparent non-concordance.

Methods: Patients with schizophrenia or schizophreniform disorder and treated with neuroleptic medication (except clozapine) were identified and their prescribing psychiatrists were interviewed using a semi-structured form that used treatment guidelines previously endorsed by the prescribers to indicate the need for medication change and documented whether the indicated changes would be implemented.

Results: 27 psychiatrists were interviewed who treated the 47 patients enrolled in the study. 22 of the 47 patients (47%) were rated by their psychiatrist as needing a medication change. For 21/22 (95%) of the patients, the psychiatrist indicated that a medication change, though indicated, would not be attempted. In 15/22 (68%) of these cases the psychiatrist attributed this decision to either patient non-compliance or refusal.

Conclusions: In 95% of the patients meeting operationalized criteria for a medication change, the psychiatrist indicated that a change would not be attempted—usually citing patient-centered reasons. These results suggest that evaluating the "real world" outcomes of treatment guidelines must include the role of patient agreement with treatment guideline suggestions and the degree to which clinicians successfully advocate for a course of treatment that they think is indicated.

NR432 Wednesday, May 22, 03:00 p.m.-05:00 p.m.

Undiagnosed Hyperglycemia in Clozapine-Treated Patients with Schizophrenia

Michael J. Sernyak, M.D., *Department of Psychiatry, VACT HCS, 950 Campbell Avenue, #116A, West Haven, CT 06516*; Barbara Gulanski, M.D., Douglas Leslie, Ph.D., Robert A. Rosenheck, M.D.

Summary:

Objective: Clozapine has been associated with hyperglycemia and diabetes mellitus. We examined the rate of undiagnosed impaired fasting glucose and diabetes mellitus in patients prescribed clozapine at 8 Department of Veterans Affairs (VA) medical centers.

Methods: For all patients diagnosed with schizophrenia and treated with clozapine by the VA in New England, an attempt was made to obtain a fasting plasma glucose (FPG) test. Among the group not previously diagnosed as diabetic, patients were divided into normal FPG (<110mg/dl) or elevated FPG (≥110mg/dl). Clinical and socio-demographic characteristics of the two groups were compared using chi-square and t-tests.

Results: Overall 121 patients were not previously diagnosed as diabetic and received an FPG. Ninety-three (77%) had a normal FPG, and 28 (23%) had an elevated plasma glucose—including 17% with impaired fasting glucose and 6% with diabetes. Patients with hyperglycemia were significantly older and more commonly co-diagnosed with bipolar disorder.

Conclusions: Hyperglycemia was common in patients receiving clozapine who had not been previously diagnosed as diabetic. These patients should be considered a group at high-risk to develop diabetes mellitus and deserve both close monitoring and early intervention at the first sign of the onset of either diabetes or impaired glucose tolerance.

NR433 Wednesday, May 22, 03:00 p.m.-05:00 p.m.

T4 Augmentation in Partial Responders with Major Depression

Anita H. Clayton, M.D., *Department of Psychiatry, University of Virginia, 2955 Ivy Road, Northridge Suite 210, Charlottesville, VA 22903*; Caroline Shen, M.D.

Summary:

Background: Of patients treated for major depression, up to 45% show partial or no response to pharmacotherapy. Two strategies to increase response are to change agents or to augment the initial antidepressant with a second medication, with a 50–60% response rate with either strategy. Most clinical data on thyroid augmentation involves the use of triiodothyronine (T3) to augment tricyclic antidepressants, with few studies examining thyroid augmentation of newer antidepressants, such as serotonin reuptake inhibitors (SRIs). This study reports on the efficacy of augmenting partial responder unipolar and bipolar depressed patients treated with SRIs with thyroxine (T4).

Methods: 16 patients who were considered partial responders to treatment with antidepressants were augmented with T4. T4 was started at 50 ug/d and increased to subjective improvement in mood, TSH<1.0 uIU/ml, T4 at the upper limit of the normal range, or intolerable side effects. Thyroid profiles were monitored prior to augmentation and every 4–8 weeks after dose change.

Results: 80% of the patients were female. Two patients had bipolar affective disorder, type II (BPAD). Four patients had comorbid hypothyroidism, and 4 were ≥50 years old. Nine patients (6 females, 3 males) noted subjective improvement in mood, and were considered full responders. Eight of the 9 had suppression of TSH to <1.0 uIU/ml. Six of the 9 subjects had sustained improvement in mood for at least 12 months. Depressed patients who improved with thyroxine augmentation (60%) were younger ($p<0.05$), received a higher T4 dose ($p<0.05$), had a greater serum T4 level ($p<0.05$), demonstrated a suppressed TSH ($p=0.72$), and were diagnosed with BPAD (2/2 responded).

Conclusions: Thyroxine is an effective augmentation strategy for partial responder depressed patients. It is most useful when doses are pushed such that serum T4 levels rise to slightly above the upper limit of normal, and TSH is suppressed to <1.0 uIU/ml.

NR434 Wednesday, May 22, 03:00 p.m.-05:00 p.m.

Oxcarbazepine in the Treatment of Mood Disorders

Suhayl J. Nasr, M.D., *NASR Psychiatric Services PC, 2814 South Franklin Street, Michigan City, IN 46360-1843*; Michelle Casper, B.S.

Summary:

Objective: This study is a retrospective review of the use of Oxcarbazepine, a newly approved antiepileptic Drug (AED), in a general psychiatric practice.

Methods: The records of eighty-eight Caucasian outpatients with mood disorder who were given at least 4 weeks of Oxcarbazepine over a 9 months period were reviewed. There were 64 females and 24 males. Their mean age was 41 years (+/–15). 58 (66%) had failed to improve or tolerate at least one other AED. 50 (57%) patients had Unipolar Depression, 29 (33%) had Bipolar Disorder, and 9 (10%) had other diagnoses. Outcome measures included the SCL90, Visual Analog Scale (VAS), Carroll Depression (self) Rating Scale (CDRS), and CGI-C, and CGI-S pre and post treatment.

Results: There was significant improvement ($p<0.0001$) in the CGI-S from 5.6 (+/–0.96) down to 3.2 (+/–1.5). Unipolar patients reported significantly more improvement in their VAS than bipolar patients ($p<0.04$). A similar trend was noted on the CDRS ($p<0.06$). Oxcarbazepine was well tolerated at a mean dose of 799mg/day (+/–358mg).

Conclusions: These findings suggest that there is a potential for using Oxcarbazepine in the treatment of mood disorders, especially those who fail to respond to or tolerate other AED's.

NR435 Wednesday, May 22, 03:00 p.m.-05:00 p.m.

Effects of Conventional and Atypical Antipsychotics on Neurogenesis in Rats

Sahebarao Mahadik, M.D., *Medical Research, VA Medical Center, One Freedom Way, Augusta, GA 30904*; Chandramohang Wakade, M.B.B.S., Fung-Chow Chiu, M.D.

Summary:

Objective: To investigate the possible mechanisms of the neuroprotective actions of atypical antipsychotic.

Method: Adult rats received rispendone 2.5 mg/kg, or haloperidol 2 mg/kg ad lib in drinking water. Control animals received vehicle only. After 20 days of treatment, rats were injected 1P 50 mg/kg bromo-deoxyuridine (BrdU) to label newly divided cells. After sacrifice, brains were embedded for frozen sectioning and immunostained for BrdU cells.

Results: BrdU+ cells were found in subependymal zone and dentate gyrus in hippocampus. Compared with haloperidol and control, atypical antipsychoric stimulated a 300% to 400% increase of BrdU cells in the subependymal zone. Significant thickening of the subependymal layer was observed with atypical antipsychotic. In hippocampus, compared with haloperidol Risperidone induced a significant increase of BrdU cells. With atypical antipsychoric, BrdU cells were found in correx, septum, and corpus callosum, suggesting migration of newly divided cells.

Conclusions: Chronic treatment with atypical antipsychotics may increase neurogenesis in adult rat brain. The neuroprotective effects of atypical antipsychotics might offset the recently observed progressive decline in hippocampal volumes after onset of schizophrenia and lead to improved cognition and functional outcome. The induction of neurogenesis in hippocampus by risperidone may parallel the cognitive improvements.

NR436 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Significant Ethnic Differences in Middle-Aged Women Receiving Psychotropics

Ruby C. Castilla-Puentes, M.D., *Department of Epidemiology, University of Pittsburgh, 3811 O'Hara Street, SWAN-Study, Pittsburgh, PA 15213*; Joyce T. Bromberger, Ph.D., James Perel, Ph.D., Karen Matthews, Ph.D.

Summary:

Objective: To compare the prevalence of psychotropic medication use in a premenopausal multi-ethnic cohort.

Method: We use the baseline data from the Study of Women's Health Across the Nation. Women (n=3,304), being of the following ethnic backgrounds, 250 Chinese, 281 Japanese, 286 Hispanic, 935 Black, and 1550 White, aged 42–52, provided self-report data on medication use. We compared prevalence of psychotropic medication use among the five ethnic groups. We examined the differences of self-report data with ethnicity. For unadjusted comparisons, CIs were calculated using the method of Cornfield and *P* values were derived from the Pearson $[chi]^2$ test or Fisher exact test if any cell contained ≤5 observations.

Results: A total of 328 (9.9%) women, mean age 45.85 (SD ± 2.69) reported the use of psychotropic medications. 56.9% of them reported current use of antidepressants (mainly SSRIs 40.2%). Rates of psychotropic medication use differ significantly across groups. Current use rates: Whites, 13.1%; Hispanics, 9.9%; Blacks, 7.8%; Japaneses 4.6% and Chineses 4.0%. Significant ethnic differences, p<0.001 were associated with the current use of psychotropic medication and SSRIs; use of mood stabilizers and benzodiazepines, ps<0.01.

Conclusions: Data suggest that rate of Mood Stabilizers, Benzodiazepines and SSRIs use is widely different among ethnic groups in midlife women. This data underline the importance of considering ethnic and racial factors in psychiatric research.

NR437 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Therapeutic Response to Sertraline in Medically Depressed Elderly

Javaid I. Sheikh, M.D., *Department Of Psychiatry, Stanford University School of Medicine, 795 Willow Road, 116A/MPD, Menlo Park, CA 94025*; Erin K. Cassidy, M.D., P. Murali Doraiswamy, M.D., Peter Holland, M.D., Tal Burt, M.D., Cathryn M. Clary, M.D.

Summary:

Introduction: This study evaluates the impact of medical comorbidity on therapeutic response to sertraline in late-life depression.

Methods: Patients aged 60 years or older with DSM-IV major depression and a 17-item HAM-D total score greater than 18 were enrolled in an 8-week, double-blind, placebo-controlled, sertraline treatment study. Medical comorbidity was defined as the presence of one or more of the following three categories of illnesses: vascular morbidity (cardiovascular, cerebrovascular, or peripheral vascular), diabetes, or arthritis. In the current analysis, patients with vs. without significant medical comorbidity were compared on baseline clinical variables, including HAM-D, CGI, SF-36, and Q-LES-Q and on overall clinical response including time-to-response.

Results: At baseline, medical comorbidity was associated with greater overall impairment in QOL. A total of 728 patients (mean age, 69.8 years; mean HAM-D, 21.4) were randomized to either sertraline or placebo. Treatment with sertraline was associated with significantly greater improvements in the HAM-D total score than treatment with placebo regardless of comorbidity status.

Conclusions: Comorbidity appeared to have no significant effect on antidepressant treatment response. Sertraline was effective in reducing depressive symptomatology, regardless of the presence of comorbid medical illness, was safe, and well tolerated by patients with or without medical illness.

NR438 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Effects of Fluoxetine on Oxytocin, Vasopressin, and Nitric Oxide Synthase

Do-Hyung Kim, *Department of Psychiatry, Kyunghee University Hospital, 1 Hoegi-Dong, Congdaemun-Ku, Seoul 130-702, Korea*; Jin-Kyung Park, M.D., Tae M. Kim, M.D., Hwan-Il Chang, M.D., Ji-Young Song, M.D., Joo-Ho Chung, M.D., Geon-Ho Bahn, M.D.

Summary:

Objective: This study was aimed to determine the effects of maternal separation and fluoxetine treatment on the oxytocin, vasopressin, and NADPH-d positive neurons in rat hypothalamus.

Method: The tissues were stained by the immunohistochemical and histochemical methods.

Results: The expression of oxytocin and vasopressin showed no differences between each experimental group. The maternal separation with normal saline treatment group showed significant decrease in the density of NADPH-d positive neurons in comparison with continuous maternal care group in paraventricular nucleus. In the maternal separation with fluoxetine treatment group, the density of NADPH-d positive neurons was significantly increased in PVN compared with that of the group of maternal separation with normal saline treatment.

Conclusion: These results suggest the role of NOS in the biological mechanism of maternal separation and the action of fluoxetine. We expect these results will provide a clue for evaluation of pathophysiology of stress or maternal deprivation-related disorders in clinical aspect.

NR439 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Economic Analysis of Sildenafil Citrate Add-On to Treat Erectile Dysfunction Associated with SSRI Use

Sandeep Duttagupta, Ph.D., *Pfizer Incorporated, 235 East 42nd Street, New York, NY 10017*; H. George Nurnberg, M.D.

Summary:

Objective: To compare the economic cost of adding sildenafil to treat selective serotonin reuptake inhibitor (SSRI)-induced erectile dysfunction (ED) with the cost of switching patients to another SSRI or discontinuing all depression pharmacotherapy.

Method: Based on our "real world" experience at an academic medical center, we performed an economic analysis on a hypothetical cohort of 1000 patients taking SSRIs. In our model, patients received SSRIs for an acute period of 60 days followed by continuation treatment for 120 days. We employed several evidence-based assumptions and used standard costs of antidepressants, sildenafil, and unit costs for physician visits within a managed care environment and cost-of-illness methodology to calculate the annualized cost of depression in the SSRI discontinuation group.

Results: In our model, after 6 months of SSRI treatment, the sildenafil add-on group had the lowest cost estimates ($112/patient/month) compared with the group that switched to another SSRI ($169/patient/month) and the group that discontinued SSRIs ($335/patient/month). Sensitivity analyses demonstrated that the physician (specialist) visit was the single most important cost component (range, $100–$760) in this hypothetical population.

Conclusion: Sildenafil can be a cost-effective add-on therapy to control SSRI-induced ED. Health care payers should consider this when developing optimum treatment strategies for men with depression.

NR440 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Risperidone in the Treatment of Patients with Delirium: A Multicenter Observational Trial

Eduard Parellada, M.D., *Department of Psychiatry, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain*; Inmaculada Baeza, M.D., Joan De Pablo, M.D., Ajnhoa Garibi, M.D.

Summary:

Objectives: The purpose of this study was to evaluate the efficacy and tolerability of risperidone in the treatment of patients with delirium.

Patients and method: We conducted an uncontrolled multicenter observational trial in 64 hospitalized patients with delirium due to a general medical condition (DSM-IV criteria). Efficacy and side effects associated with the treatment were assessed with the Trzepacz Delirium Rating Scale (DRS), Positive subscale of the PANSS, Mini Mental State Examination (MMSE), Clinical Global Impression (CGI), and the extrapiramidal subscale of the UKU Side Effect Rating Scale. All patients were treated with risperidone when delirium was diagnosed and followed until they were discharged.

Results: Patients were 62.3% male, mean age of 67.3 ± 11.4 years, with delirium due to a presumed general medical condition (72%) and 28% due to an unspecified etiology. Treatment with a mean risperidone doses of 2.6 ± 1.70 mg/day (day 3) and 1.5 ± 0.80 mg/day (day 7) resulted in significant improvement ($p<0.001$; Wilcoxon test) in the symptoms measured from the inclusion to day 7: DRS (22.5 ± 4.6 to 6.8 ± 7.0); PANSS-P (21.5 ± 8.7 to 10.1 ± 7.2;); MMSE (13.1 ± 10.9 to 26.4 ± 8.9) and CGI (4.5 ± 0.9 to 1.9 ± 1.1). None of patients showed extrapiramidal symptoms. Two patients (3.1%) experienced an adverse reaction.

Conclusions: Symptoms of delirium in medically hospitalized patients may be treated efficaciously and safely by using low-dose of risperidone.

NR441 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Minimal Effect of the Antidepressant Duloxetine on Body Weight

Craig Mallinckrodt, Ph.D., *Eli Lilly and Co, Lilly Corporate Center, DC 2206, Indianapolis, IN 46285*; Pierre V. Tran, M.D., Michael J. Detke, M.D., David J. Goldstein, M.D., Mark A. Demitrak

Summary:

Objective: To examine the effect of duloxetine, a potent and balanced inhibitor of serotonin and norepinephrine (Bymaster et al., 2001; Pitsikas, 2000), on body weight in depressed patients.

Method: Data from 7 double-blind placebo-controlled trials were pooled for analyses (duloxetine 40–120 mg/d n = 1032, placebo n = 723). Patients were treated for up to 12 weeks. Data from a 12-month open-label, single-arm study (n=1282) were analyzed separately.

Results: In the placebo-controlled trials, duloxetine-treated patients lost approximately 0.5 kg compared with a 0.2 kg gain for placebo treated patients ($p<.001$). The incidence of decreased appetite and decreased body weight were significantly greater for duloxetine-treated patients compared to placebo-treated patients (6.5% vs. 2.1% and 1.7% vs 0.6%, respectively). The incidence of increased body weight was significantly lower for duloxetine-treated patients (0.3% vs 1.2%) and the incidence of increased appetite was (nonsignificantly) lower for duloxetine-treated patients (1.2% vs 1.5%). In the open-label study, mean change to endpoint for duloxetine-treated patients was 1.12 kg ($p<.001$).

Conclusion: The antidepressant duloxetine has no clinically meaningful effects on body weight in this patient population.

NR442 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Olanzapine Versus Risperidone: A Comparison of Hospital Length of Stay in Adult Impatients with Schizophrenia

Martin Marciniak, Ph.D., *Lilly Research Labs, Lilly Corporate Center, Indianapolis, IN 46285*; William S. Edell, Ph.D., Madhav Namjoshi, Ph.D., Bryan E. Adams, Ph.D.

Summary:

Objective: To determine the hospital length of stay (LOS) associated with olanzapine and risperidone in adult inpatients with Schizophrenia.

Method: Data were obtained from the CQI+^{SM} Outcomes Measurement System, which tracked patients admitted to adult psychiatric inpatient programs across the United States between January 1, 1997 and September 30, 2000. Severity of illness at admission was determined using the Global Assessment of Functioning (GAF) Scale, the Behavior and Symptom Identification Scale (BASIS-32)©, and the Brief Psychiatric Rating Scale (BPRS). Patients taking olanzapine (n=93) and risperidone (n=71) monotherapy at discharge were compared on LOS.

Results: BPRS, GAF, and BASIS-32© admission scores were statistically indistinguishable across medication groups. Risperidone users were in the hospital longer than olanzapine users (10.9 days vs. 8.7 days, $p<.02$).

Conclusion: In this study olanzapine was associated with a significantly shorter length of stay than risperidone among inpatients with schizophrenia.

NR443 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Hormone Effects in Female SSRI Sexual Dysfunction

Paula L. Hensley, M.D., *Department of Psychiatry, University of New Mexico, 2600 Marble Avenue NE, Albuquerque, NM 87131*; H. George Numberg, M.D., Michael P. Bogenschutz, M.D., Susan Paine, M.D.

Summary:

Objective: Central serotonergic pathways are known to regulate endocrine function and are sensitive to stress, anxiety, and depression. Antidepressants such as serotonergic reuptake inhibitors (SRI) are often associated with sexual dysfunction (SD). One possible mechanism of SRI-associated SD may be changes in serotonin and prolactin levels. We present endocrine data from the pituitary, adrenal, gonadal, and thyroid axes in women with remitted major depressive disorder (MDD) taking SRIs and experiencing SRI-associated SD.

Methods: Serum levels of prolactin, cortisol, progesterone, estradiol, FSH, LH, TSH, T-4 total/free testosterone, and sex hormone binding globulin were evaluated in 21 women. Patients were premenopausal, in good health, without preexisting SD, taking a stable dose of SRI for ≥8 weeks, had HAM-D&A scores <10, and had significant SD by sexual function inventories.

Results: Mean serum cortisol (13.2±δ.9 μU/dL), prolactin (12.0±6.1 ng/mL), total testosterone (35.3±41.2 ng/dL), free testosterone (1.2±1.1 pg/mL), TSH (2.9±4.8 ng/mL), T-4 (7.8±1.4 μU/dL), LH (6.5±6.7 μU/L), free androgen index (0.02±0.03), and sex hormone binding globulin (83.0±56.8 nmol/L) were within normal limits. Progesterone (0.48±0.81 ng/mL), FSH (9.6±10.8 μU/mL), and estradiol (64.6±49.7 pg/mL) were elevated. The samples were characterized by nonspecific interindividual variability.

Conclusion: Female patients with MDD in remission and SRI-associated SD did not have the elevated prolactin levels often assumed to characterize SRI-associated SD. These data do not support a unimodal explanation of SRI-SD (eg, SRI hyperprolactinemia).

NR444 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Smooth and Safe Transition from Intramuscular to Oral Olanzapine in Acutely Agitated Patients with Schizophrenia

Padraig Wright, M.D., *Lilly Research Center, Erl Wood Manor, Sunning Hill Road, Windelsham GU206PH, United Kingdom*; Karena Meehan, M.D., Martin Birkett, B.S.C., Stacy R. David, Ph.D., Cindy C. Taylor, Ph.D., Philip Morris, Ph.D., Alan F. Breier, M.D.

Summary:

Objective: This study compared the efficacy and safety of transitioning patients from IM to oral olanzapine and haloperidol.

Methods: Acutely agitated inpatients with schizophrenia were treated with one to three IM injections of olanzapine (10.0 mg/injection) or haloperidol (7.5 mg/injection) for 24 hours followed by the oral formulations of the same medication (5–20 mg/day) for four days.

Results: IM olanzapine reduced agitation (PANSS excited component [PANSS-EC]), significantly more than IM haloperidol 15, 30, and 45 minutes after the first injection. Mean PANSS-EC changes for olanzapine- (n=122) and haloperidol-treated (n=116) patients, respectively, were –7.1 and –6.7 at the 24-hour IM endpoint, with further changes of –0.6 and –1.3 during oral therapy (not significantly different). Significantly more haloperidol- than olanzapine-treated patients spontaneously reported acute dystonia (4.3% vs. 0%, p=0.03), extrapyramidal syndrome (6.9% vs. 0.8%, p=0.02), and akathisia (5.2% vs. 0%, p=0.01) and met criteria for treatment-emergent akathisia (18.5% vs. 6.5%, p= 0.02).

Conclusion: Olanzapine reduced agitation more rapidly than and as effectively as haloperidol during the IM period. This reduced agitation was maintained by both agents during the transition from IM to oral therapy; however, haloperidol-treated patients experienced significantly more EPS-related adverse events.

NR445 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Bupropion Sustained Release Versus Placebo Comparison of Depressive Symptoms and Weight Loss in Obese Patients with a History of Major Depression

Paul S. Bradley, M.D., *Candler Medical, 340 Eisenhower Drive, Suite 1200, Savannah, GA 31405*; Barbara Haight, Pharm. D., Brenda Jamerson, Pharm.D., Vicki Foster, M.P.S.H., Natalie Richard, M.S., Alan Metz, M.D.

Summary:

Objective: To compare the efficacy of bupropion SR versus placebo in the treatment of depressive symptoms and in the facilitation of weight loss in obese adults with current depressive symptoms and a history of major depression.

Methods: Obese adults with depressive symptoms (but not meeting DSM-IV criteria for a current depressive disorder) were randomized to receive bupropion SR (300–400mg/day) or placebo in combination with a 500-calorie deficit diet for 26 weeks. At each visit, weight and Beck Depression Inventory (BDI) scores were obtained. A prospective analysis of patients with a self-reported history of major depression was conducted.

Results: Ninety-two of the 422 randomized patients reported a history of major depression (50 bupropion SR; 42 placebo). Significantly more bupropion SR patients (52%) than placebo patients (28%) achieved ≥50% reduction in BDI at Week 26, a trend which began at Week 4 and continued throughout the study ($p<0.05$). Mean weight loss was also significantly greater for bupropion SR-versus placebo-treated patients from Week 2 through Week 26 (4.8kg vs 1.6kg, respectively) ($p<0.001$).

Conclusions: Bupropion SR was significantly more effective than placebo in reducing depressive symptoms and facilitating weight loss in obese patients with a history of major depression and current depressive symptoms.

NR446 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

A Ratio to Estimate the Propensity of Antipsychotics to Stimulate Appetite

Serge Beaulieu, M.D., *Douglas Hospital Research Ctr, 6875 LaSalle Blvd, Verdun, PQ H4H IR3, Canada*; Nmk Ng Ying Kin, Ph.D., Trino J. Baptista, M.D.

Summary:

Introduction: Increased appetite is involved in excessive bodyweight gain (BWG) observed during antipsychotic treatment (AP), but may play a role in carbohydrate and lipid metabolism abnormalities even without overt BWG. We hypothesized that appetite stimulation may be related to the interaction of AP with classic neurotransmitters involved in feeding regulation.

Methods: A ratio was constructed for commonly used APs by using their absolute affinities for neurotransmitter receptors as follows: Ratio = (α_1 + H_1 + muscarinic + $5HT_{2A\text{-}2C}$ / (α_2 + D_2 + $5HT_{1A}$). Location of a particular receptor in the ratio was based on clinical and preclinical data regarding the orexigenic (numera-

tor) or anorectic (denominator) effect of the neurotransmitter. The ratio of nine APs was correlated with the BW gain observed after short-term treatment (< 10 weeks).

Results: A significant positive correlation was obtained: r = 0.673, p = 0.047.

Discussion: This ratio may indirectly reflect the relative propensity of a given AP to increase appetite. Clozapine and olanzapine displayed the highest ratios; haloperidol, primozide, and ziprasidone the lowest values; and quetiapine, risperidone, zotepin, and sertindole showed intermediate ratios. Results of this theoretical study may aid clinicians in drug selection for specific patients.

NR447 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Effectiveness of Paroxetine in the Treatment of Unexplained Chest Pain

P. Murali Doraiswamy, M.D., *Department of Psychiatry, Duke University, Box 3018, Durham, NC 27710*; Greg L. Clary, M.D., Indu Varia, Cammie Helleger, Ryan Wagner, Christopher O'Connor, M.D., Katherine L. Beebe, Ph.D.

Summary:

Objective: A significant proportion of patients with angina-like symptoms are diagnosed with noncardiac chest pain when cardiac catheterization or a cardiac stress tests reveal no apparent cardiac cause for the pain. A previous study showed that the TCA, imipramine (Cannon et al, 1994) produced significant improvement in noncardiac chest pain compared to placebo. This study evaluated the efficacy of an SSRI, paroxetine, in reducing this unexplained chest pain.

Methods: A single site, double-blind, placebo-controlled 9-week study of 50 outpatients with normal coronary angiograms or stress tests. Outcome measures were CGI and pain ratings.

Results: CGI ratings of pain at endpoint showed that subjects treated with paroxetine had significantly greater improvement than those treated with placebo ($p<0.05$). The improvement from baseline in self-rated pain on the McGill Visual Analogue Scale also favored paroxetine over placebo. The pain dairy and quality of life measures showed trends to improvement, but the differences between paroxetine and placebo failed to reach significance due to baseline differences and relative short duration. One serious adverse event was reported, which was unrelated to study medication.

Conclusions: Paroxetine appears to be relatively well tolerated and a promising agent for the treatment of unexplained chest pain in patients who have had normal cardiac work ups. The mechanisms underlying this effect are not yet fully known but may involve both serotoninergic and noradrenergic actions of paroxetine. Methodological issues in the conduct of such studies and collection of self-rated pain ratings will also be discussed. The successful treatment of noncardiac chest pain has tremendous potential for reducing health care utilization.

NR448 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Sildenafil for Selective Reuptake Inhibitor Associated Female Dysfunction

H. George Nurnberg, M.D., *Health Science Center, University of New Mexico, 2600 Marble Avenue, NE, Albuquerque, NM 87131*; Paula L. Hensley, M.D., Alan J. Gelenberg, M.D., Maurizio Fava, M.D., Julia K. Warnock, M.D., Harry A. Croft, M.D., Ridwan Shabsigh, M.D.

Summary:

Objective: This report presents preliminary efficacy results from the single-blind, open-label (OL) portion of a double-blind (DB), placebo-controlled study of sildenafil citrate treatment for SRI-associated sexual dysfunction (SD) in women.

Methods: 150 women with clinically recovered major depressive disorder (MDD) and SRI-associated SD were randomly assigned to DB sildenafil (50 mg; flexible) or placebo for 8 weeks, followed by 8 weeks OL sildenafil independent of DB response. Patients were without preexisting SD, taking a stable dose of SRI for ≥8 weks, had HAM-D&A scores <10, and significant SD by FSQ, ASEX, and UNM-SFI inventories. Efficacy was determined using the CGI-SF questionnaire. DB completers continued OL sildenafil for 8 weeks, remaining blind to their DB treatment. After ≥24 weeks of SRI treatment and up to 16 weeks of sildenafil, patients were interviewed by phone to assess SD (CGI-SF), MDD remission (HAM-D), and SRI dose.

Results: At end point, women receiving OL sildenafil demonstrated a 70% improvement in SD on CGI-SF (mean score ≤2= "much/very much improved"). HAM-D scores remained <10 among all patients (n=21). SRI dose remained stable.

Conclusion: Sildenafil effectively reversed SRI-associated SD in women, allowing them to continue with effective SRI treatment for depression. These results confirm earlier reports of the efficacy of sildenafil to treat SRI-associated SD.

NR449 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Sildenafil For SRI-Induced Sexual Dysfunction: A Placebo-Controlled Trial

David L. Ginsberg, M.D., *Department of Psychiatry, NYU School of Medicine, 530 First Avenue, #7D, New York, NY 10016*; Lenard A. Adler, M.D., Andrew McCullough, M.D., Patrick Ying, M.D., Ken Wu, Ph.D., John P. Rotrosen, M.D.

Summary:

Objective: The purpose of the current study was to evaluate the efficacy of sildenafil in reversing SRI-induced sexual dysfunction (SD) in men.

Methods: Twenty-three male outpatients, ages 30–64 years, with clinically recovered mood or anxiety disorder (HAM-D score < 17) and SRI associated SD were randomly assigned to matching placebo (n=12) or sildenafil, 50–100mg, (n=11) for 8 weeks of double-blind treatment. Subjects were evaluated at baseline and at weeks 2, 4 and 8 of treatment. SD was assessed by the International Index of Erectile Function (IIEF), the Arizona Sexual Experience Scale (ASEX) and Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS); in addition, SD was confirmed by RigiScan at baseline.

Results: The patients receiving sildenafil had a statistically significant improvement in SD at 8 weeks as compared to those receiving placebo, as measured by the IIEF, ASEX, and EDITS ($p<0.05$, wilcoxson rank-sum test). The sildenafil group showed statistically significant improvement in the erectile function, intercourse satisfaction, and overall satisfaction domains of the IIEF. The presence of SD, as defined by ASEX, at the end of treatment was significantly reduced in the sildenafil group but not significantly in the placebo group.

Conclusions: Sildenafil was a safe and effective treatment for SRI-induced SD in men. This confirms prior reports of efficacy of sildenafil for this condition.

NR450 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Pharmacokinetic/Dynamic Relationship of Atomoxetine Exposure and Efficacy

Jennifer W. Witcher, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Darcie L. Kurtz, John-Michael Sauer, Ph.D., David Michelson, M.D., Brian P. Smith, Ph.D., Dustin D. Ruff, Ph.D.

Summary:

Purpose: To evaluate the relationship between exposure and efficacy of atomoxetine.

Methods: This was a randomized, double-blind, placebo-controlled study of outpatients between 8 and 18 years of age with ADHD. Patients were randomized to a target dose of atomoxetine (placebo, 0.5 mg/kg/day, 1.2 mg/kg/day, 1.8 mg/kg/day). Blood samples were drawn from each patient at 4 visits for measurement of atomoxetine, and a population pharmacokinetic analysis was performed. Empirical Bayesian clearance estimates were used to calculate $AUC_{0-\tau}$ values as a measure of atomoxetine exposure. The relationship between $AUC_{0-\tau}$ and change from baseline in ADHDRS-IV-Parent: Inv total score was explored.

Results: Pharmacokinetic/pharmacodynamic analysis suggests a maximum expected improvement of −17.4 in ADHDRS-IV-Parent:Inv total score. At the median $AUC_{0-\tau}$ values for the atomoxetine 0.5 mg/kg/day, 1.2 mg/kg/day and 1.8 mg/kg/day groups, 62%, 78%, and 85% of the maximum improvement over baseline would be expected.

Conclusions: At the median $AUC_{0-\tau}$ for the 1.2 mg/kg/day dose, expected improvement approaches its maximum value, and higher $AUC_{0-\tau}$ values would likely result in minimal additional symptom reduction. This finding is consistent with analyses based on dose. In child and adolescent patients, the relationship between systemic exposure and efficacy appears similar to the relationship between dose and efficacy.

NR451 Wednesday, May 22, 03:00 p.m.-05:00 p.m.

How Long Should Patients with Psychotic Depression Stay on an Antipsychotic?

Anthony J. Rothschild, M.D., *Department of Psychiatry, University of Masachusetts Medical Center, 361 Plantation Street, Worcester, MA 01605*; Suzanne Duval, M.D.

Summary:

Introduction: Patients with Major depression with psychotic features (MDpsy) have greater morbidity and mortality than patients with nonpsychotic major depression. In particular, relapse or recurrence has been reported to occur more frequently in patients with psychotic depression than nonpsychotic depression. Despite the frequent relapse and recurrence in MDpsy there are few controlled studies of the efficacy of continuation and maintenance treatments.

Methods: Thirty patients with the diagnoses of unipolar major depression with psychotic features who responded to the combination of fluoxetine and perphenazine were studied after granting written informed consent. If the patient was stable for 4 months, we then tapered the patient gradually off the perphenazine. The perphenazine dose was reduced by 25% of the total dose a week for 4 weeks. Patients remained on their current dose of fluoxetine. Patients were administered the HRSD and BPRS on a weekly basis for the next two months. Impending relapse was defined as any of the following: 1) symptoms meeting DSM-IV criteria for major depression (with or without psychotic features); or 2) a total score of ≥ 17 on the HRSD; or 3) the presence of any psychotic symptoms.

Results: After taper of the perphenazine after four months of treatment with fluoxetine and perphenazine, twenty-two of the 30 patients (73%) did not exhibit signs of relapse over the next 11 months. Eight of the 30 patients (27%) exhibited signs of an impending a relapse over the next 2 months. These 8 patients were placed back on perphenazine (added to the fluoxetine) for a minimum of an additional 2 months of combined treatment. All 8 patients had a remission of their symptoms with reinstitution of the perphenazine. At the 8 month time point, 5 of these 8 patients were able to taper off the perphenazine without signs or symptoms of impending relapse.

Conclusions: The data from this study suggest that a majority of patients with unipolar MDpsy do not require treatment with antipsychotic medication for more than four months. Seventy-three percent of patients with MDpsy treated with the combination of fluoxetine and perphenazine for four months were tapered off the perphenazine at four months without relapse over the next 11 months. Patients who relapsed after antipsychotic taper were more likely to have had a longer duration of the current episode, a history of more frequent past episodes, and were more likely to be younger (under the age of 30).

NR452 Wednesday, May 22, 03:00 p.m.-05:00 p.m.

A Youth/Adult Comparison of Weight Gain Due to Olanzapine and Risperidone

Daniel J. Safer, M.D., *Johns Hopkins, 7702 Dunmanway, Dundalk, MD 21222-5436*;

Summary:

Objective: To report the extent of weight gain induced by olanzepine (OLZ) and risperidone (RIS) in youths as compared to adults.

Method: A Medline search from 1996–2001 identified double-blind and case series studies of OLZ- and RIS-induced weight gain. This review included studies with the following data: age, drug dose, weight gain, duration of treatment and, if available, baseline weight, body mass index (BMI) and percent of subjects with a substantial weight gain. The drug-induced weight gain for youths was defined as the total weight gain minus the estimated age-expected weight gain.

Results: Basic criteria were met by 29 studies in youths and 31 studies in adults. The major findings were: 1) youths received a significantly smaller average daily dose and lower mg/kg dose of RIS than adults 2) preadolescent youths received a consistently lower average daily dose of OLZ than adults 3) the weight gain induced by OLZ and RIS in youths was similar to that in adults and tended to persist for longer periods 4) RIS resulted in greater percent BMI increases for youths than for adults.

Conclusion: Available data suggest that youths are more sensitive than adults to the induction of weight gain by the two most utilized second generation neuroleptics.

NR453 Wednesday, May 22, 03:00 p.m.-05:00 p.m.

Phenomenological and Clinical Aspects of Impulsivity and Compulsivity

Ygor A. Ferrao, M.S.C., *Department of Psychiatry, HMIPV-FFFCMPA, Padre Chagas, 66-801, Porto Algre, RS 90570-080, Brazil*; Ellis D. Busnello, M.D., Vanessa Almeida, M.D., Nadia Bedin, M.D., Rafael Rosa, M.D.

Summary:

Objective: To compare impulsivity and compulsivity.

Method: this is a pilot-study comparing 20 obsessive-compulsive disorder outpatients to 20 outpatients with skin picking and/or trichotillomania. Patients were selected non-probabilistically from two outpatients psychiatric services. The instruments used were SCID-I, Y-BOCS, Schalling Impulsivity Scale, Hamilton Anxiety and Depression Inventories, and a Multidimensional Impulsive-Compulsive Spectrum Assessment Instrument (MICSAI), designed to this particular study.

Results: The Y-BOCS showed statistical differences, with higher scores to OCD patients (F=90,29; p<0,001). Hamilton Inventories and Schalling Impulsivity Scale revealed no significant differences. The MICSAI allowed us to find six statistically significant differences between groups and five other characteristics have shown a tendency to be significant, and 10 of them did not reveal any statistical differences.

Conclusion: Impulsive patients have less intense thoughts related to their actions, as measured by Y-BOCS. We found the following descriptive differences of impulsivity and compulsivity: the ability or inability to delay an impulse; quick response, or act planning; feelings of pleasure or guilt during or after an act; ritualization; and whether patient believes he/she has losses or benefits if prevented from acting. Skin picking and trichotillomania should receive further attention as to their classification on future versions of diagnostic manuals.

NR454 Wednesday, May 22, 03:00 p.m.-05:00 p.m.

Psychiatric Diagnosis in a Deaf Sample Using an American Sign Language Version of the DIS-IV

Annie G. Steinberg, M.D., *Children's Hospital of Philadelphia, 34th Street Civic Center Boulevard, Philadelphia, PA 19104*; Elizabeth A. Eckhardt, C.S.W., Majorie F. Goldstein, Ph.D., Louise Montoya, M.A.

Summary:

Objective: Individuals who are deaf face unique difficulties obtaining accurate diagnoses of their mental health problems and receiving appropriate treatment. This article reports on the development of a computerized version of the DIS-IVin ASL for use with individuals who are deaf.

Method: Seven diagnostic sections of the DIS-IV were translated into ASL, videotaped and incorporated in the computerized version. Sixty Deaf subjects over 18 were recruited from treatment facilities in NY, NJ, PA, and MD. Each subject was tested twice, order randomly assigned, once using a computerized self-administered version and once by a signing clinician using the developed version of the DDIS-IV. The two versions were compared.

Results: The various diagnostic sections demonstrated different degrees of agreement between raters, sensitivities and specificities; concordance between versions varied according to diagnostic section, with percent agreement ranging from 54% to 100%, and kappa statistic ranging from –.08 to 1.0. The Alcohol Abuse diagnostic section had the highest percent agreement between the two versions.

Conclusions: After further field testing, several sections of the Deaf-DIS are likely to be useful diagnostic instruments for deaf individuals. Further validation studies on larger samples of deaf individuals are needed before the complete instrument is ready for use as psychiatric assessment tool with deaf individuals. (This research was funded by National institute of Mental Health, Small Business Innovations Research Grant number: MH55943-01.)

NR455 Wednesday, May 22, 03:00 p.m.-05:00 p.m.

PTSD and ADHD: Comorbidity, Symptom Overlap, and Significance of Age at First Trauma

Irene Powch, Ph.D., *Department of Psychiatry, Portland VA Medical Center, 3710 SW US Veterans Hospital Road, Portland, OR 97207*;

Summary:

The child literature reports significantly higher rates of Attention-deficit/Hyperactivity Disorder in traumatized populations than in controls. There are no published studies on trauma history or posttraumatic stress disorder (PTSD) comorbidity with ADHD in adults.

Objective: To answer the following questions: (1) Do adult veterans with PTSD have higher rates of ADHD (currently and since childhood) than those without PTSD? (2) Of the PTSD group, do those who reported first trauma at age 9 or younger have significantly higher rates of ADHD than those who reported first trauma after age 9?

Methods: Subjects were 42 male veterans recruited from outpatient orientation to skills groups and the dom. PTSD was diagnosed with the Clinician Administered PTSD Scale (CAPS); ADHD was diagnosed with a structured clinical interview created to assess DSM-IV ADHD symptoms in early childhood (to 3rd grade) and currently. Subjects also completed five other measures of trauma history, PTSD, and ADHD.

Results: As predicted, of the PTSD group (N=24), those with early trauma reported twice as many ADHD symptoms since childhood as those with later trauma ($p < .05$). This difference was found for both hyperactivity and inattention, although only the hyperactivity difference was statistically significant ($p < 05$). An ADHD diagnosis current and since childhood was met by 40% of those with early trauma compared to less than 15% of those with later trauma. Multiple regression revealed childhood sexual abuse history and not childhood physical abuse history to predict hyperactivity. The difference in ADHD between the PTSD and no PTSD groups was in the predicted direction but failed to reach statistical significance.

Conclusion: Taken together these results suggest that psychological trauma during a critical period in development may trigger expression of hyperactivity and ADHD in vulnerable populations.

NR456 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Exploring Why Clinicians Choose Hospitalization After Suicide Attempts

Jose de Leon, M.D., *Department of Psychiatry, University of Kentucky, 627 West 4th Street, MHRC 627, Lexington, KY 40508-1207*; Enrique Baca-Garcia, M.D., Carmen Diaz Sastre, M.D., Dolores Braqueais, M.D., Antonio Ramirez, M.D., Luis Jimenez Trevino, M.D., Mercedes Navio

Summary:

Objective: Suicidal behavior is one of the leading causes of visits to the emergency department and mortality. Several guidelines have recently been written for the assessment of suicide, but none are accepted universally. The aim of this article is to find out what main variables emergency room clinicians use to decide patient discharge/hospitalization after a suicidal attempt, in an environment not affected by managed care.

Method: During 1996–98, 563 suicide attempts were studied in a general hospital in Madrid (Spain), which triages all the emergencies for a catchment area of 500,000 persons. On-call psychiatrists judged appropriateness of hospitalization, if it was not previously decided by on-call internists. A research psychiatrist assessed patients using the Beck's Suicidal Intent Scale (SIS).

Results: A high score in 16 of the 20 SIS items was associated with hospitalization versus discharge. The highest odd ratio, 8.9 (95% confidence intervals 5.6–14.2) corresponded to item 13, attitude toward living. A logistic regression model including significant SIS items and demographic variables was performed.

Conclusions: In order to develop appropriate guidelines to treat suicide, real-world studies such as this are needed to explore what clinicians usually use to determine if a suicidal patient needs hospitalization.

NR457 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Do Psychotropics Alter Suicide Risk?

Arifulla Khan, M.D., *Northwest Clinical Research Center, 10126 NE 132nd Street, Kirkland, WA 98034-9043*; Shirin R. Khan, Ross J. Baldessarini, M.D., Walter A. Brown, M.D.

Summary:

Objective: The widely held assumption that psychotropics reduce suicide risk is largely bereft of data. To address this, we reviewed the FDA Summary Basis of Approval reports, via the

Freedom of Information Act, from psychotropic clinical trial data submitted to the FDA during the past 15 years.

Methods: The FDA reports included 73,794 participants in clinical trials evaluating 29 psychotropics; 10 antidepressants, 5 anti-OCD agents, 4 antipsychotics, 4 anti-panic agents, 3 anxiolytics, 1 mood stabilizer, 1 Social Anxiety Disorder (SAD) agent, and 1 PTSD agent. In order to estimate suicide risk, we calculated Patient Exposure Years (PEY) for completed suicide and suicide attempts.

Results: Given the US general population annual suicide risk of 11/100,000, risk was high among clinical trial participants; 725/100,000 in antipsychotic trials, 718/100,000 in antidepressant trials, 524/100,000 in trials for OCD with or without concomitant depression, 425/100,000 in SAD trials, 136/100,000 in anti-panic trials, and zero among those in PTSD trials. Specific information was not available for mood stabilizer trials. Suicide attempt rates were also high. The US general population annual suicide attempt risk is 0.08%. The annual risk is 5.05% in antipsychotic trials, 3.71% in antidepressant trials, 1.57% in trials for OCD 0.67% in anti-PTSD trials, zero in anti-SAD trials, and was not available for mood stabilizer trials.

Conclusion: Interestingly, the suicide and suicide attempt rates were similar for those assigned to active medications and those assigned to placebo. The implications of these findings and their relationship to other data will be presented.

NR458 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

A Game Theory Model of Suicide Behavior Improving Prediction and Prevention

Laurence V. Amsel, M.D., *Child Psychiatry, Columbia University, 245 W. 107th Street, New York, NY 10026*; Avital Pilpel, M.A.

Summary:

Objective: Despite extensive research programs, predicting suicidal behavior, a prerequisite for prevention, has been an elusive goal, perhaps because of the lack of a formal behavioral model. This study aimed at developing and testing a model of suicidal behavior based on John Nash's belief that Game Theory can expose and elucidate the underlying dynamics of complex human interactions.

Method: Using mathematical principals, we are the first to represent ambivalent suicide attempts in a Game-Theory model whose "solution" is a Mixed Nash Equilibrium. We then compared the model's parameters and predictions to the phenomenology described in the established, empirical suicide literature.

Results: 1. Based on the subject's perceived relative value (utility) of the status quo, of dying, and of surviving an attempt (with the resulting interpersonal responses), our model predicts a multiplicity of subtypes of suicidal behavior in a fashion that is both consistent with the published literature and counter-intuitive. 2. It predicts the variability in the degree of lethality of attempts, as well as the dependence of an attempt on the availability of a method with a specified lethality range. 3. It predicts that prevention strategies, such as Kernbergian suicide contracting, will only work with the correctly matched suicidal subtype.

Conclusion: Game Theoretic models of suicidal behavior are highly homoeomorphic to the published body of suicide phenomenon, and may improve the prediction and prevention of suicidal behaviors.

NR459 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Suicide Associated with Pregnancy Outcome: A Record Linkage Study

David C. Reardon, Ph.D., *Elliot Institute, P O Box 7348, Springfield, IL 62791-7348*; Philip G. Ney, M.D., Jesse R. Cougle, M.S., Fritz Schevren, Ph.D., Priscilla Coleman, Ph.D.

Summary:

Introduction: Researchers have found that in the year following a pregnancy outcome, Finnish women who aborted were 6.5 times more likely to die of suicide compared to those who delivered. A British study revealed that higher rates of suicide attempts following abortion were not associated with higher rates of suicide attempts prior to pregnancy. Our objective was to examine this association over a longer period of time and with a control for prior psychiatric history.

Methods: California medicaid records for 63,592 women who had an induced abortion or delivery in 1989, and no subsequent pregnancies were linked to death certificates for 1989 to 1997.

Results: Compared to women who delivered, those who aborted had a significantly higher age adjusted relative risk of dying from suicide (RR=2.54) and accidents (RR=1.82). Controlling for at least one year of prior psychiatric admissions revealed a higher relative risk of suicide for aborting women (RR=3.12). Stratification by time and age revealed that higher rates were most pronounced in the first four years after pregnancy outcome and among younger women.

Conclusions: Higher suicide rates associated with abortion may not be completely explained by prior psychiatric illness and persist beyond one year.

NR460 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Black and White Differences in Risks for Suicidality Among Substance Abuse Patients

Joyce H. Chen, Psychiatry, *Yale University, One Church Street, 7th Floor POS, New Haven, CT 06510*; Holly G. Prigerson, Ph.D., Thomas Gill, M.D., M. Carrington Reid, M.D., Ismene L. Petrakis, M.D., Selby C. Jacobs, M.D., Yeates Conwell, M.D.

Summary:

Objective: The Yale Evaluation of Suicidality (YES) scale is a new instrument recently developed to detect a wider range of suicidal thoughts and behaviors than those identified by previous suicide scales. Using this scale, we examine the differences between Blacks and Whites with a past or current substance abuse diagnosis in risk factors for suicidality.

Method: Patients with a past or current substance abuse diagnosis receiving treatment at the Connecticut Mental Health Center or the West Haven Veterans Affairs Connecticut Healthcare System are participants in an ongoing suicide study. Data on recent and past life events, suicidal behaviors, quality of life, chronic conditions, social support, health service utilization, addictions, and psychiatric evaluation were obtained.

Results: To date, 114 subjects (62 White, 52 Black) have been interviewed. Preliminary analyses indicate that the YES has a high degree of internal consistency amongst Whites (alpha=.90) and Blacks (alpha=.84). The YES is a significant predictor of *past* suicide attempts for Whites (O.R.=3.172, p<.0001) and Blacks (O.R.=1.796, p<.0001), and of *planned* suicide attempts for Whites (O.R.=2.792, p<.0001) and Blacks (O.R.=2.06, p<.0001); suggesting the YES' strong criterion and predictive validity for both groups. Significant (p<.05) risks for suicidality (YES scores) and suicide attempts among Whites were global mental health, social support, and depression; among Blacks, risks were severely disrupting life events and self-destructive behavior. After controlling for these risk factors and for age, the YES remained a significant predictor of past ($O.R._{4}$= 5.217, p<.01) and planned ($O.R._{4}$= 2.789, p<.001) suicide attempts for Whites and of past ($O.R._{44}$=1.662, p<.01) and planned ($O.R._{44}$= 1.904, p<.01) suicide attempts for Blacks. Hopelessness was a risk factor for suicidality for both Whites (β=.39, SE=.03, p<.0001) and Blacks (β=.30, SE=.05, p<.0001)

Conclusion: The YES scale's high internal consistency and criterion validity amongst both Blacks and Whites suggest that it is

well-suited for clinician use in suicidality detection. Results demonstrated that Black and White substance abuse patients have different risk factors for suicidality, and extended prior work indicating that hopelessness is a risk factor for suicidality (Fawcett et al. 1987, Beck et al. 1985).

[4]Adjusted for global mental health, social support, and depression.

[44]Adjusted for positive and negative life events and self-destructive behavior.

NR461 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Suicidal Behavior and Serotonin in Depression and BPD: A Large-Scale Study

Ingrid Kemperman, M.D., *Psychiatry, NYSPI/Columbia University, 1051 Riverside Drive, Unit 42, New York, NY 10032*; Ronald Winchel, M.D., Michael Stanley, Ph.D., J. John Mann, M.D., Barbara Stanley, Ph.D.

Summary:

Suicide and suicide attempts have been associated with altered cerebrospinal fluid 8-hydroxyindoleacetic acid (CSF 5-HIAA) in major depression (MD). More recent findings indicate that the relationship may not be as straightforward as originally thought. Studies have found that high lethality attempts, less planned attempts, or more impulsive attempts are associated with lower CSF 5-HIAA rather than suicidal behavior generally. A problem with most studies is that sample sizes are relatively small and, therefore, may not have adequate power to detect differences between attempters and non-attempters. Furthermore, as a consequence of small samples, studies are usually unable to analyze findings separately for individuals with and without Axis II disorders. We present new unpublished research that demonstrates: 1. that CSF 5-HIAA is substantially lower in depressed attempters irrespective of the lethality or impulsivity of the attempt; and 2, that an Axis II diagnosis, particularly borderline personality disorder (BPD) weakens the relationship between CSF 6-HIAA and suicidal behavior.

The present study is a very large sample study of CSF 5-HIAA in a multidiagnostic group comparing suicide attempters (N=157) with psychiatric controls (N=131). In this study, we had large enough samples to separately study individuals with MD without an Axis II diagnosis and those with the co-morbid diagnosis of MD and Axis II BPD diagnosis, the most common Axis II diagnosis associated with suicidal behavior. We found that CSF 5-HIAA was significantly lower in both the co-morbid group and the depressed group without co-morbid. However, the lowest levels of CSF 5-HIAA were found in the depressed suicide attempters who did not have co-morbid BPD. These findings suggest that suicidality in major depression may be more biologically driven than in co-morbid MD and BPD.

NR462 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Cocaine Consumption in Military Recruits

Pilar A. Saiz, Ph.D., *Department of Psychiatry, University of Oviedo, Julian Claveria No 6-30, Oviedo 33006, Spain*; Maria P. G-Portilla, Ph.D., Begona Paredes, M.D., Sara Martinez, M.D., Teresa Bascaran, M.D., Julio B. Bobes, Ph.D.

Summary:

Objectives: To describe the prevalence of cocaine consumption and the toxicological and psychological profile of a sample of military recruits.

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 cocaine use.- lifetime: 12.4%, previous year: 7.9%, previous month: 4.6%. Cocaine ranking fourth among the illicit drugs ever used. When individuals used cocaine for the first time, they were likely to use it again (64% of individuals who had ever used cocaine had used it in the past year, 37% the last month). Mean age first use of cocaine was 17.14 (2.62). Cocaine is the sixth drug with higher polyconsumption index [mean number of consumption of other drugs: 6.09 (2.57)]. The drugs most commonly used by cocaine consumers are: alcohol (98.2%), cannabis (94.0%), tobacco (93.8%), hallucinogens (67.5%), amphetamines (58.4%), and MDMA (54.9%). Recruits who had ever used cocaine had significantly higher scores on the EPQ-Psychoticism and reported higher levels of sensation seeking (p=.000).

Conclusions: Cocaine users are polyconsumers of other drugs. Cocaine consumers have a different psychological profile characterized by high sensation seeking and high levels of psychoticism.

NR463 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Impact of Trauma on Individuals Diagnosed with Anxiety and Depression

Chris Kladopoulos, M.A., *Department of Adult Psychiatry, North Shore University Hospital, 400 Community Drive, Manhasset, NY 11030*; Juliana R. Lachenmeyer, Ph.D., Laura Bastiani, B.A., Chris Wainman, B.A.

Summary:

Objective: The present study investigated the impact of the events of September 11 on the functioning of patients in treatment in the Anxiety Treatment Program at North Shore Hospital, Long Island, New York. Functioning was assessed using the Global Assessment of Functioning Scale (GAF), (e.g., Kennedy, et al., 1999).

Method: Fifty patients, twenty-four with Obsessive-Compulsive Disorder (OCD), seventeen with Panic Disorder (PD), and nine with Major Depression (MD) with GAF scores ranging from 50–85 were administered a questionnaire designed to examine the impact of the events of September 11.

Results: Results indicated that for the group as a whole, lower GAF scores were associated with a greater likelihood to avoid work and decreased ability to concentrate as well as increased severity in personal symptomatology and poorer overall mood. Analysis by diagnosis indicated that these findings were explained primarily by the PD and MD groups. In contrast, the OCD group regardless of level of functioning reported little impact of these events on their lives.

Conclusions: These findings suggest that individuals with OCD compared to those with PD or MD are relatively unresponsive to even extreme environmental events probably due to their own obsessive thoughts and related high levels of anxiety.

NR464 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

PTSD and Dementia

Deirdre M. Johnston, M.B., *Department of Psychiatry 8th Fl CSB, Wake Forest U Baptist Medial Center, Winston Salem, NC 27157-1087*; Beverly N. Jones, M.D.

Summary:

Background: Severe aggressive outbursts towards caregivers have been reported in combat veterans with dementia. This pilot study is the first to examine the relationship between a history of combat exposure (a risk factor for PTSD) and non-cognitive symptoms in dementia, using caregiver and subject reports.

Methods: Caregivers completed the CERAD Behavioral Rating Scale for Dementia. Descriptive statistics are reported and an analysis of covariance conducted to compare the BRSD total weighted score (TWS) between combat and non-combat veterans.

Results: Preliminary analysis of the data collected to date (N = 50; 36 combat veterans and 14 non-combat) indicates higher total weighted score (TWS) on the CERAD BRSD, i.e., more frequent and severe behavioral disturbance, in combat versus non-combat veterans (39.72 v 33.57). Combat veterans scored higher on BRSD subscales of irritability/aggression (7.86 v 4.71), depression, (6.92 v 5.29), psychosis (3.94 v 3.79), and behavioral dysregulation (4.58 v 4.21). Of the subscales, the irritability/aggression subscale difference emerges as significant, with a p-value of 0.05.

Discussion: Combat exposure may be a risk factor for behavioral problems in dementia, particularly irritability/aggression. A trend towards increased overall symptomatology in the combat group may reach statistical significance with a larger sample size.

NR465 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Lifetime Rates of Intermittent Explosive Disorder in a Community Sample

Emil F. Coccaro, M.D., *Department of Psychiatry, University of Chicago, 5841 South Maryland Avenue, MC#3077, Chicago, IL 60615*; Catherine A. Schimdt, Ph.D., Jack F. Samuels, Ph.D., William W. Eaton, Ph.D., Gerald Nestadt, M.D

Summary:

Objective: The objective of this study was to assess the lifetime prevalence of Intermittent Explosive Disorder (IED) in a community sample.

Methods: A semi-structured interview assessment was added to a more comprehensive diagnostic follow-up study of the Baltimore ECA sample. Diagnosis of IED was made according to both DSM-IV and Research Criteria (RC) and allowed for a "Narrow (IED N)" and a "Broad (IED B)" diagnoses. Final diagnosis of IED by DSM-IV excluded any subject with a life history of Schizophrenia, Mania, or Borderline (BPD) and/or Antisocial Personality Disorder (AsPD); IED by RC did not exclude BPD or AsPD.

Results: Among 252 subjects, the lifetime prevalence of DSM-IV IED ranged from 2.4% (IED N) to 6.0% (IED N+B); the rates with RC ranged from 5.2% (IED N) to 8.4% (IED N+B). The rates of IED by RC in BPD and AsPD patients were four-fold higher, ranging from 22.9% (IED N) to 31.4% (IED N+B).

Conclusions: This pilot study suggests that the lifetime prevalence of IED may be at least 2.4% using DSM-IV Criteria and may be as high as 5.2% to 8.4% using Research Criteria. If so, 6.6 to 14.3 million Americans could have IED at sometime in their lives.

NR466 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

The Contribution of Childhood Trauma to Psychopathy, Risk, and Other Psychopathology in a Severely Mentally Ill Substance-Using, Jail-Diversion Population

Nahama Broner, Ph.D. *Institute Against Violence, New York University, 838 Broadway 3rd Floor, New York, NY 10003*; David P. Bernstein, Ph.D., Damon Maryl

Summary:

Increasingly, there is research, program and policy attention to issues of jail diversion, due to the steady rise in the number of mentally ill individuals arrested and incarcerated, with a federal mandate to fund diversion programs as a vehicle to address their documented many needs. However, in order to adequately establish diversion programs with the right mix of services, it is useful to better understand the kinds of populations one is dealing with for mental health diversion. Notably, one finds homelessness, substance abuse or dependence, serious health problems, and antisocial, criminal and violent behavior histories in this population. It is also now recognized that many of these people have histories of both childhood and adult trauma.

Objective: To determine the contribution of specific types of childhood trauma as risk factors for a broad range of psychopathologies and for recidivism prevalent in jail diversion populations in large urban regions.

Methods: In the context of a completed comparison group 12-month outcome study of the New York City Department of Mental Health's LINK Diversion Program, this presentation focuses on baseline characteristics of 119 male and 93 female diversion-eligible jail detainees. Participants were administered a series of standardized instruments at baseline, three, and 12 months while in jail or the community to assess psychiatric diagnosis and symptoms, substance use, risk for violence, trauma, and health.

Results: Indicate that, while childhood trauma is a distal variable, its prevalence in this population is extensive and it is associated with risk for violence, recidivism, drug use, and various forms of psychopathology explaining 5.5% (e.g. PCL-SV) to 19.6% (e.g., HCR-20) of the variance in psychiatric symptoms and problems, while controlling for the effects of gender.

Conclusions: A discussion of how different types of childhood trauma may serve as specific risk factors for the kinds of psychopathologies that make it difficult to work with this population and that makes this population prone to recidivism will assist in tailoring assessment and diversion interventions.

NR467 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Increased Cortisol Reactivity to Trauma Cues in PTSD

Bernet M. Elzinga, M.S.C., *Department of Psychology, University of Amsterdam, Roetersstraat 15, Amsterdam 1018 WB, Netherlands*; Christian G. Schmahl, M.D., Eric Vermetten, M.D., Richard Van Dyck, M.D., J. Douglas Bremner, M.D.

Summary:

Animal studies have found that prior stressful events can result in increased reactivity in the hypothalamic-pituitary-adrenal (HPA) axis. Findings related to baseline function of the HPA-axis have typically shown normal to decreased function of the HPA-axis in posttraumatic stress disorder (PTSD), however. The purpose of this study was to assess cortisol responsivity to traumatic reminders in patients with PTSD related to childhood abuse. Salivary cortisol levels were measured before, during, and after exposure to personalized trauma scripts in abused women with (N=12) and without PTSD (N=12). PTSD patients had 122% higher group mean cortisol levels during script exposure, 69% higher cortisol levels during recovery, and 60% higher levels in the period leading up to the trauma script exposure compared with controls. PTSD symptoms during the last two weeks were highly predictive of cortisol responses during script exposure (r=.70), but not during baseline and recovery. These results are in line with animal studies showing that early stress is associated with increases in HPA-axis functioning and increased glucocorticoid responsivity to stressors, and suggest that the increased responsivity is associated with PTSD symptomatology.

NR468 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Childhood Trauma and Alterations in Adult Corticotropin Releasing Factor in Personality-Disordered Subjects

Royce J. Lee, *University of Chicago, 5841 South Maryland Avenue, Chicago, IL 60637*; Emil F. Coccaro, M.D., John W. Kasckow, M.D.

Summary:

Objective: Early life stress and persistent stress hormone abnormalities are associated with adult major depression and PTSD. The objective of this study was to test the hypothesis that in

personality disordered subjects, the amount early life stress as measured by the Childhood Trauma Questionnaire (CTQ) is correlated with CSF corticotropin releasing factor (CRF).

Method: Participants were 20 physically healthy, non-psychotic men meeting DSM-IV (APA 1994) criteria for personality disorder (PD). CTQ total and subscales were obtained. CSF CRF was obtained by spinal tap and correlated with CTQ total and the four CTQ subscales scores. Statistical analysis employed Spearman Correlations. Probability levels were set at a two-tailed alpha value of .05.

Results: CSF CRF was correlated with CTQ total (r_s=.468, p= .037). An analysis of the subscales revealed that CSF CRF was correlated with CTQ Emotional Neglect (r_s=.490, p=.028) and CTQ Physical Neglect Abuse (r_s=.454, p=.044) but not CTQ Physical Abuse (r_s=.344, p=.137) or CTQ Sex Abuse (r_s=.315, p=.176).

Conclusions: Consistent with the hypothesis that the severity of early life stress is correlated with stress hormone abnormalities in adulthood. CTQ total and CTQ Emotional Neglect were significantly correlated to CSF CRF in personality disordered subjects.

NR469 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Somatoform Dissociation Conversion in French Psychiatric Outpatients

Jean-Michel Darves-Bornoz, M.D., *Department of Psychiatry, Clinique Psychiatrique University, Hospital Universitaire, Tours 37044, France*; Wissam El Hage

Summary:

Objective: Somatoform dissociation phenomena (conversion) highlighted by Pierre Janet more than one century ago, are often thought in France to be infrequent now. This study aimed at screening, quantifying, and setting these symptoms in context while validating our French version of Nijenhuis's *Somatoform Dissociation Questionnaire (SDQ-20).*

Methods: One hundred and forty psychiatric outpatients (mean age 41, range 17–76; women 56%) consecutively consulting in the University Hospital in Tours, France, completed a battery of tests (SDQ-20, DES, CAPS) related to trauma and dissociation (whether somatoform or psychoform).

Results: Reliability of the SDQ-20 assessed through computing Cronbach's α coefficient for all items (0.83) was good. A principal component analysis of the SDQ-20 ratings yielded a solution with three factors that we named: *"sensory neglect," "subjective reactions to perceptive distortions,"* and *"vigilance modulation disturbance"*. The SDQ-20 scores (mean 27.1, range 20–76) were higher in women (28.9 vs 24.7, p<0.01) but independent from age. Only a quarter of the patients had absolutely no somatoform dissociation manifestation. Seventy-one percent of the patients had experienced one or several events (in mean 4.9 events) listed in the potentially traumatic event inventory within the CAPS. The SDQ-20 mean score was higher (29.5 vs 21.0, p<0.001) in subjects with a history of overwhelming events. SDQ-20 and DES scores were highly correlated (r .644, p<.001) as well as those of SDQ-20 and CAPS (r .642, p<.001) in patients with PTSD (44%).

Conclusions: The study shed light on the high frequency of somatoform dissociation phenomena when looked for, and its strong association with psychotraumatic syndromes. The elements of validity found in the study of our French version of the SDQ-20 allow its use in screening for postraumatic dissociation.

NR470 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Psychobiological Model of Personality Disorders

Jose L. Besteiro, Ph.D., *Department of Psychiatry, Oviedo University, Julian Claveria 6, #3, Oviedo 33006, Spain*; Serafin Lemos, Ph.D., Jose Muniz, Ph.D., Eduardo Garcia, Ph.D., Maria P. G-Portilla, Ph.D., Pilar A. Saiz, Ph.D., Julio B. Bobes, Ph.D.

Summary:

Objectives: To analyze whether the factor structure of personality, neuropsychological, and physiological measures of DSM-IV clusters could correspond to coherent dimensions.

Subjects / Method: The MCMI-II and BFQ were administered to 138 subjects (mean age: 32,5,46,6% males) who met DSM-IV criteria for some personality disorder. The psychophysiological measures were obtained in response to experimental stress, and three STIM computerised tasks (Wisconsin Card Sorting Test, Conditional Continuous Performance Test, and Stroop test) were also administered.

Results: A factor analysis was performed to determine whether subjects' performance on all tests clustered into factors with face validity, which produced five factors (52% total variance / 70% estimated shared variance). Meaningful dimensions were discovered in three factors: *cognitive/perceptive* (17.17% var.), *impulsiveness/aggressiveness* (13.34% var.), and *affective instability* (8.18% var.), that are largely in keeping with Siever and Davis' psychobiological dimensions. Another factor show relationship to Eysenck's psychoticism dimension (7.65% var.), whereas the last one gave no relevant information.

Conclusions: The results reported here provide evidence that three main factors are more consistent with Siever and Davis' psychobiological model of personality disorders than with DSM-IV cluster groupings.

NR471 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Olanzapine in the Treatment of Adult Developmental Stuttering

Gerald A. Maguire, M.D., *Department of Psychiatry, University of CA at Irvine Medical Center, 51 Whitman Court, Irvine, CA 92612*; David L. Franklin, Tony Ortiz, B.S., Gerald E. Maguire, M.D., Charles Tuan-Tu S. Nguyen, M.D., Benjamin P. Yu, M.D., Michael E. Maguire, M.A.

Summary:

Stuttering is classified in DSM-IV as an Axis I disorder and is characterized by frequent prolongations, repetitions or blocks of spoken sounds and/or syllables. Stuttering affects one percent of the adult population and can significantly impact social, academic or occupational functioning. Dopamine antagonists such as haloperidal and risperidone have shown to improve the symptoms of stuttering but are associated with dysphoric side-effects and elevations in prolactin leading to sexual dysfunction. Olanzapine is a novel dopamine antagonist that spares prolactin and has been shown in preliminary studies to improve the symptoms of stuttering. Twenty-four adults who stutter (ages 18–55) participated in this three month, double-blind, placebo-controlled trial comparing the efficacy of olanzapine (2.5mg–5mg/day) in stuttering. Subjects were rated on multiple objective and subjective measures including the SSI-3 (Stuttering Severity Instrument) and the CGI (Clinician's Global Impression). Olanzapine was found to improve stuttering symptoms significantly better than placebo on both the SSI-3 (p<.044) and CGI (p<.028). Olanzapine was very well-tolerated with all subjects on active medication completing the trial and electing to enter the long-term open-label extension. This study suggests that olanzapine is a well-tolerated and useful medication for the treatment of stuttering and further research and clinical experience is warranted.

NR472 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Personality and Pathological Gambling: A Sibling Pair Analysis

Daniela S. Lobo, M.D., *Department of Psychiatry, University of S. Paulo, Martim Francisco No. 204 AP101, Sao Paulo, SP 01226-000, Brazil*; Silvia S. Martins, M.D., Hermano Tavares, Ph.D., Ana Maria Galleti, M.D., Valentim Gentil, M.D.

Summary:

Objective: To compare personality characteristics of pathological gamblers (PG) and a non-pathological gambler sibling, focusing on personality factors related to impulsivity.

Method: Forty gamblers (20 male, 20 female) admitted in 2001 to an outpatient treatment program at University of Sao Paulo Medical School—Institute of Psychiatry, selected by South Oaks Gambling Screen and DSM IV criteria and whose siblings where available for an interview (at most 5 years older or younger than the PG, 16 males and 24 females). All subjects answered a sociodemographic questionnaire, the Temperament and Character Inventory and were compared regarding demographic differences and scores on TCI.

Results: No difference was found regarding age, financial status and years of education. PG scored higher than siblings on Novelty seeking (NS) (p=7.09 E – 12) and on Harm avoidance (p= 0.0068), which is confirmed by previous reports on high levels of NS among PG. Siblings scored higher than PG on Self-directedness (SD) (p= 1.06 E – 10), which has not been previously reported.

Conclusion: These findings raise the question about the role of other personality factors, such as SD, on pathological gambling. Low scores on SD may be related to the concept of impulsivity as difficulty in long-term planning.

NR473 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Zonisamide in Obesity: A 16-Week Randomized Trial

Kishore M. Gadde, M.D., *Duke University Medical Ctr, Box 3812, Durham, NC 27710*; Deborah M. Franciscy, R.D., Ryan Wagner

Summary:

Objective: Based on the finding that zonisamide has serotonergic and dopaminergic effects and the observation that this novel anticonvulsant is associated with weight loss in epilepsy trials, we evaluated its short-term efficacy and safety in the treatment of obesity.

Method: 60 subjects were assigned to receive zonisamide or placebo (1:1 ratio) in a randomized, double-blind fashion for 16 weeks in addition to a slightly hypocaloric (500 kcal/day deficit) diet. Zonisamide dosing was flexible with a maximum of 600 mg/day.

Results: Using the available data for all randomized subjects with the last observation carried forward, the zonisamide group lost, on average, more bodyweight than the placebo group (5.98% vs. 1.09%; p<0.0001) during the 16-week period. 17/30 subjects in the zonisamide group and 3/30 in the placebo group lost ≥5% weight (p<0.0003). A random coefficient regression for weight change, with effects for age, race, gender, BMI, and percent body fat, estimated that zonisamide treatment over the 16-week study duration was associated with a 4.99 kg greater weight loss over placebo treatment (p<0.0001). Zonisamide was tolerated well with minimal side effects.

Conclusion: Zonisamide was significantly more effective than placebo as an adjunct to hypocaloric diet in the treatment of obesity.

NR474 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Topiramate in the Treatment of Bulimia Nervosa: Additional Efficacy

Frederick W. Reimherr, M.D., *Department of Psychiatry, Mood Disorders Clinic, 30 North 1900 East Room 5R218, Salt Lake City, UT 84132*; Scott P. Hoopes, M.D., Debra Karvois, M.S., Rezaul Karim, Ph.D., Marc Kamin, M.D., Normal E. Rosenthal, M.D.

Summary:

Introduction: We conducted an 11-week, randomized, double-blind, placebo-controlled trial to look at the efficacy of topiramate in 68 outpatients with a DSM-IV diagnosis of bulimia nervosa (BN). Primary efficacy analysis showed that topiramate significantly reduced the frequency of bingeing and/or purging.

Methods: Further analyses of secondary endpoints were assessed, including the Eating Disorder Inventory (EDI) Scale, the Eating Attitudes Test (EAT), the Hamilton Anxiety (HAM-A) and Depression (HAM-D) scales, and Patient Clinical Global Assessment scores.

Results: Percent change from baseline in several subscales of the EDI was significantly better for the topiramate group, including Bulimia (*P*=.004), Body Dissatisfaction (*P*=.004), and Drive for Thinness (*P*=.023). The rate of change was also positive for these subscales and for the Ineffectiveness subscale (*P*=.042). Percent change and rate of change in the Bulimia/Food Preoccupation subscale of the EAT was significant for the topiramate group (*P*=.04). Percent improvement (*P*=.054) in HAM-A scores was marginally significant, while improvement in HAM-D scores was not. Patient Clinical Global Assessment was significantly better for the topiramate group (*P*=.004).

Conclusion: These results further support the finding that topiramate is effective for the treatment of BN.

NR475 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Therapeutic Community Yields Abstinence

Chester P. Swett, Jr., M.D., *Department of Psychiatry, Brockton Veterans Adminitration Hospital, 940 Belmont Street, Brockton, MA 02301*; Antone D. Taveira, M.S.

Summary:

Introduction: A therapeutic community (TC) and behavioral approach to treatment of polysubstance abuse have received little attention in recent times in comparison to the use of medication. A survey was carried out to determine the rates of abstinence among 56 discharges from a TC.

Methods: 38 graduates and 18 non-graduates from a TC for male polysubstance abusers (with personality disorders) were carefully followed for 1–2 years to determine if they were abstinent.

Results: Over 71% of the graduates and only 6% of the non-graduates remained abstinent for one year [chi square = 4.8 (df = 1), p<.03]. Twenty-six graduates and 9 non-graduates were followed for two years with 62% and 11% remaining abstinent, respectively Longer mean LOS, attendance at confrontational groups, and part-time work were important factors in achieving abstinence. Graduates were placed in various types of transitional residences at graduation, followed with substance abuse counseling, and returned to alumni groups. Patients were treated strictly with behaviorally oriented groups, and didn't receive psychotropic medication.

Discussion: A sustained, long-term behavioral treatment, TC, and a longer term sheltered living environment without use of medication can be a powerful approach to achieving abstinence from polysubstance abuse.

NR476 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Prevalence of Hepatitis-C Virus in Substance Abuse Outpatients

Jorge F. Perez-Cruet, M.D., *Department of Psychiatry, Oklahoma City VAMC, 3304 Rosewood Lane, Oklahoma City, OK 73120-5604*; Graham Roberts, M.D.

Summary:

Introduction: Hepatitis C virus has become a common cause of chronic liver disease of infectious etiology in the US. The aim of this study was to determine the prevalence of confirmed HCV in opioid, alcohol, and cocaine dependence patients attending an OPD substance abuse program.

Methods: 291 outpatients fulfilling the DSM-IV criteria for opioid, alcohol and cocaine dependence were selected. For each diagnosis the number of patients included: 92 opioids, 108 alcoholics, and 91 cocaine addicts. VA standard tests for HCV antigen and confirmation techniques were used.

Results: The results in confirmed HCV among opioid dependence patients was the highest with 67 (93%) positive and 5 (7%) negative; in 20 no tests were ordered. In alcoholics, 20 (36%) were positive and 36 (64%) were negative; in 52 patients, no tests were done. In cocaine addicts, 15 (35%) positive and 28 (65%) negative; in 48 patients, no tests were ordered. The Fisher probability test showed significant statistical differences between the opioid versus alcohol or cocaine ($p<0.001$) and no statistical difference between alcohol and cocaine. Percent of negatives for HCV was higher in the alcohol and cocaine drug users.

Conclusions: We found a very high percentage of opioid patients with confirmed HCV (93%), confirming that this group to be at a high risk. An unexpected high incidence of HCV (35%) was found in alcoholic and cocaine patients. If a larger number of tests for HCV would have been ordered for alcoholic and cocaine patients, it would have been likely that the number of confirmed HCV would have been even higher. Since HCV prevalence appears to be so high in substance abuse outpatients, the economic restrictions of testing, will be overridden by the potential for treatment prevention of the disease in others, eventual cure of this chronic liver infection, prevention of end stage liver disease, cancer of the liver and a reduction on liver transplantations.

NR477 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Polyunsaturated Fatty Acids and Relapse Vulnerability in Cocaine Addicts

Laure B. Buydens-Branchey, M.D., *Department of Research, VA New York Harbor, 800 Poly Place, Brooklyn, NY 11209*; Marc H. Branchey, M.D., Dana McMakin, M.S., Joseph R. Hibbeln, M.D.

Summary:

Introduction: There is mounting evidence that low plasma levels of some polyunsaturated fatty acids (PUFAs) are associated with several psychiatric disorders, including affective disorders. PUFA status could also influence the risk of relapse to the abuse of substances through actions on central serotonergic and dopaminergic systems, known to play a role in reward mechanisms.

Methods: PUFA status was assessed among 38 cocaine dependent subjects only at baseline, 2 weeks after admission to an inpatient unit. Resumption of substance use was assessed 3, 6 and 12 months following discharge.

Results: Of the 32 patients who remained available for follow-up after 12 months, 12 had relapsed. Subjects relapsing at 3 months had significantly lower baseline levels of total n-6 PUFAs, total n-3 PUFAs and arachidonic acid (AA, 20:4n6) when compared to non-relapsers by ANCOVAs with age and weight as covariates. Lower baseline total n-6 PUFAs and AA were still predictive of relapse 6 and 12 months following discharge. Baseline PUFA levels were better predictors of relapse than patients' age, marital status, educational level, cocaine use parameters or psychopathology that were not significantly different when patient groups were compared.

Conclusions: Low levels of n-6 and n-3 PUFAs measured in cocaine addicts during inpatient admission predicted relapse after their discharge. These data suggest, but do not prove, a causal relationship between n-6 or n-3 status and relapse vulnerability but provide a rationale to explore relationships between addictive disorders and PUFA status in observational and interventional trials.

NR478 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Personality Impairment in Methadone Maintained and Detoxified Opiate Addicts

Enid C. Gertmenian-King, B.A., *Department of Psychiatry, Beth Israel Medical Center, 16th Street at 1st Avenue Room 6K42, New York, NY 10003*; Lisa J. Cohen, Ph.D., Carrie Weaver, M.A., Denise Dunovant, M.A., James Quick, Igor I. Galynker, M.D.

Summary:

Objective: As part of a comprehensive assessment of opiate dependence, we investigated predictors of treatment outcome in a substance abuse population. This study assesses personality impairment in two groups of abstinent opiate dependent, those on Methadone Maintenance Therapy (MMTP) and those who have detoxified from Methadone.

Method: MCM-II scores for 13 axis II disorders and 4 related axis I disorders were compared in 53 subjects, 13 methadone maintained (MM), 15 detoxified opiate abusers (DO) and 25 healthy controls (C). Subjects were recruited from SuCasa, a residential treatment facility which offers both MMTP and Methadone To Abstinence Treatment (MTAR). All subjects were given 3–4 random urine toxicologies to confirm the absence of secondary drug use. Subjects were also screened for psychiatric illnesses, HIV infection, and CNS disorders. MANOVA analyses were used.

Results: By MANOVA, the three groups significantly differed on Cluster A and Cluster B but not Cluster C scales, although 3 out of 5 Cluster C disorders differed on univariate f-tests. Methadone maintained subjects differed from controls on 9 individual scales (schizotypal, thought disorder, antisocial, borderline, passive aggressive, self defeating, avoidant, anxiety and dysthymic disorders), whereas detoxified subjects only differed on 2 (borderline and delusional disorders). MM subjects had marginally higher anxiety and dysthymia scores than DO subjects.

Conclusions: These results suggest either that DO subjects have pre morbid personality strengths, perhaps contributing to success in methadone withdrawal, or that methadone withdrawal improves personality functioning. Consequently, treatment strategies addressing anxiety and Cluster A traits might be helpful. Future studies could assess the personality profiles of pre- and post-withdrawal individuals and compare those who successfully withdraw from those who do not.

NR479 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Oxcarbazepine for the Treatment of Bipolar Disorder

Rodrigo A. Munoz, M.D., *University of California at San Diego, 3130 5th Avenue, San Diego, CA 92103*; Tasha Glenn

Summary:

Objective: An open-label, 12-week prospective study investigated the mood stabilizing effects of oxcarbazepine (OXC) as adjunctive therapy in patients with a DSM-IV diagnosis of bipolar disorder.

Method: This was an open-label study of male or female patients ages 18 to 65 years who had been diagnosed with bipolar mood disorder I or II, and were either currently manic or depressed. Patients were titrated onto doses ranging from 300mg/day up to a maximum of 2400mg/day, in addition to their current treatment regimen. Efficacy in mania was assessed using the Young Mania Rating Scale (YMRS) and in depression using the Hamilton Rating Scale for Depression (HAMD). Additional efficacy measures included the Scale for Affective Disorders and Schizophrenia - mania and depression scales (SADS) and the Global Assessment Schedule (GAS). Patients were tapered off prior treatments when clinically able.

Results: 30 adults were enrolled, 22 patients were manic and 8 were depressed at the time of enrollment. Of the 22 patients who were manic at the start of study drug 68.2% (N=15) responded to OXC with ≥ 50% improvement in YMRS within 3 weeks of starting treatment. Of these 15 patients, 9 remained euthymic throughout the remaining 9 weeks of the study, 3 patients relapsed into mania, 3 became depressed, and 1 patient discontinued from the study. Of the 8 patients that were initially depressed, 87.5% responded with ≥ 50% improvement within 3 weeks of starting treatment and remained euthymic throughout the study, with 1 patient discontinuing from the study. Of the 28 patients who completed the study, the mean weight change was 1.4%. Adverse events were predominantly mild to moderate in intensity with eleven patients reporting at least one serum [Na] below 134mEq/L.

Conclusion: OXC appears to have both acute antimanic and antidepressant effects as an adjunctive treatment. Additionally, oxcarbazepine does not appear to cause weight gain. Low sodium levels were frequently found in the study. Prospective double-blind studies are indicated.

NR480 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

CSF Corticotropin Releasing Factor and Perceived Early Life Stress in Depressed Patients and Healthy Controls

Linda Carpenter, M.D., *Department of Psychiatry, Brown University, 345 Blackstone Blvd., Providence, RI 02906*; Gregory Pelton, M.D., George Heninger, M.D., Christopher McDougle, M.D., Michael J. Owens, Ph.D., Charles B. Nemeroff, M.D.

Summary:

Background: Cerebrospinal fluid (CSF) concentrations of corticotropin releasing factor (CRF) have been found to be elevated in patients with major depression as well in adult animals who were exposed to conditions of stress in the form of brief maternal deprivation or maternal neglect during infancy.

Methods: Twenty-seven adults with major depression and 25 matched controls underwent standard lumbar puncture procedure for collection of a single CSF sample at noon. Subjects provided data about significant adverse early life experiences, and rated their overall perceived level of stress during pre-school years on a 6-point likert scale. CSF CRF values were compared between depressed patients and controls, and the effects of perceived early adversity were statistically explored.

Results: Comparison of the groups showed a trend for depressed patients to have higher levels of CSF CRF than healthy controls. However, when grouped according to "low" (n=36) or "high" (n=15) level of perceived pre-school stress, a significantly higher mean CRF concentration was seen among those with subjective reports of high stress before age 5. In a regression model, perceived level of stress during preschool years was a highly significant linear predictor of CSF CRF concentration, while presence of depression was not.

Conclusions: These preliminary data are limited by the use of a qualitative questionnaire, rather than an established and validated assessment instrument, for the characterization of early life adversity. Nevertheless, the relationship observed between perceived early life stress and adult CSF CRF, closely parallels the findings of recent animal studies. More work is needed to elucidate the critical nature and timing of early events that may be associated with enduring HPA axis changes in humans.

NR481 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Seclusion and Restraint in the Pennsylvania State Hospitals

Robert Davis, M.D., *Associate Medical Director, Office of Mental Health and Substance Abuse Services, Harrisburg State Hospital, First Floor Beechmont Building, Harrisburg, PA 17110*

Summary:

The Commonwealth of Pennsylvania's Office of Mental Health and Substance Abuse Services (OMHSAS) identified seclusion and restraint as practices that are associated with significant risk to the patient and to the staff in the state hospitals. No longer considered acceptable or compatible with best practice, alternatives to the use of these restrictive interventions were encouraged. Strict guidelines for the use of seclusion and restraint were developed to assure patient safety and to assure that neither would be used unless all reasonable alternatives had been exhausted. Additionally, the guidelines required the attending physician to perform an on-site assessment of the patient concurrent with the use of these restrictive measures in order to assure that the patient was not being physically compromised and to assure that alternative measures were being continuously pursued. Prior to the issuance of the guidelines, the incidence and duration of episodes of seclusion and restraint were used as benchmark measures of performance among the State hospitals; this data was used to meet the ORYX requirements of JCAHO. This identification of seclusion and restraint as high-risk interventions and the encouraged use of alternatives caused a decline in the incidence and duration of seclusion and restraint from the initiation of the process in 1997. With adoption of the guidelines in January of 1999, the rate of decline accelerated.

Since 1997, combined incidents of seclusion and restraint have been reduced by 74%, while hours of use have decreased by 96%. One hospital has been virtually seclusion and restraint free for over one year. Several others are approaching zero use. For example, in December 2000, a total of 62.7 hours of both seclusion and restraint were used in nine state hospitals, which include three maximum-security forensic units. The hospitals have an average daily census of 2683 patients. Although skeptics feared that reduction in seclusion and restraint might increase staff and patient injuries, that has not been the experience. Since 1997, the rate of minor assault-related staff injuries showed no increase over the prior four years (0.061/1000 patient-days). Disabling staff injuries have decreased as much as 67% in the hospital using the least seclusion and restraint, with an overall decrease of 0.12/1000 patient-days to 0.10/1000 patient-days since 1997. Patient assault-related injuries have not increased remaining at about 1.5/1000 patient-days. There has been no compensatory increase in the use of use of "as needed" medication. Heightened staff awareness, training in crisis intervention techniques, identification of risk factors, increased use of atypical anitpsychotic medication, and programming tailored to the identified patient needs are all factors that have contributed to the success of this endeavor.

NR482 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Comorbidity Patterns and Correlates in Routine Psychiatric Practice

Joshua E. Wilk, Ph.D., *APIRE, 1400 K Street, NW, Washington, DC 20005*; Joyce C. West, Ph.D., William E.

Narrow, M.d., Darrel Regier, M.D., Steve C. Marcus, Ph.D., Maritza Ribio-Stipec, Sc.D.

Summary:

Objective: To present data on patterns of Axis I comorbidity in a representative sample routine psychiatric practice in the U.S. and the relationship of comorbidity status to specific clinical correlates, patterns of disability, and provision of psychopharmacologic and psychotherapeutic treatment.

Methods: The data were gathered from a sample of 1,843 psychiatrists participating in the American Psychiatric Practice Research Network's *1999 Study of Psychiatric Patients and Treatments.* Data were analyzed to determine the prevalence of Axis I comorbidity rates and the relationship to functional status and treatments.

Results: The most prevalent comorbidity pairing in the sample was depression and anxiety disorders (11.2%). Odds ratios indicated a significantly increased likelihood of substance use disorders given a diagnosis of schizophrenia (1.83, 95% C.I.=1.31–2.55). Specific Axis I comorbid diagnosis pairings were associated with differential rates of disability and psychiatric treatment utilization. For example, those with substance use disorders were significantly less likely to receive psychotherapy if they had comorbid schizophrenia.

Conclusions: Comorbid Axis I disorders have a relatively high prevalence in routine psychiatric practice, with significant implications for patient functioning and treatment. Knowledge of the relationships between comorbid Axis I disorders and functional and treatment characteristics is important for planning effective treatment interventions and research strategies.

NR483 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

No Increase in Sleep-Related Events with Galantamine in Alzheimer's Disease

Stephen Stahl, M.D., *University of California, 8899 University Center Lane, #130, San Diego, CA 92122;* Jeffrey S. Markowitz, D.P.H., Elane Gutterman, Ph.D., Kay Sadik, Ph.D.

Summary:

Objectives: To evaluate the effects of galantamine on rates of sleep-related adverse events (AEs) and concomitant medication (CM) use in patients with alzheimer's disease(AD).

Methods: Data were combined from 3 randomized, double-blind, placebo-controlled galantamine trials (16 and 24 mg/day) in patients with mild-to-moderate AD. Data were analyzed retrospectively to determine whether galantamine use was related to changes in sleep-related AEs and/or the use of DMs (including antidepressants, enxiolytics and antiphychotics) for sleep-related indications.

Results: Data were pooled from 1698 patients, 279 receiving galantamine16 mg/day, 705 receiving galantamine24 mg/day, and 714 receiving placebo. The rates of sleep-related AEs reported in galantamine-treated patients were low and similar to placebo in both groups. These AEs occurred in 2.2% of patients treated with placebo, 1.1 % treated with galantamine 16 mg/day, and 2.6% treated with galantamine24 mg/day ($p > 0.05$). Sleep-related CM rates were also low and similar to placeboe for both galantaminedoses. Sleeprelated CMs were used by 2.7% of placebe patients, 1.1 % of patients receiving galantamine16 mg/day, and 2.8%of patients receiving galantamine 24 mg/day (no significant differences between groups).

Conclusions: Galantamine treatment is not related to increased reates of sleep-related AEs or CM use in patients with AD.

Funding Sources: Research funded by Janssen Pharmaceuticia Products, L.P.

NR484 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Stephen Stahl, M.D., *University of California, 8899 University Center Lane, #130, San Diego, CA 92122;* Jeffrey S. Markowitz, D.P.H., Elane Gutterman, Ph.D., Kay Sadik, Ph.D.

Summary:

Objective: To determine if treatment with donepezil is related to subsequent hypnotic use in patients with AD.

Methods: The study included subjects from a multiwave, consumer-based survey of AD caregivers using a replication strategy (based on study wave). Rates of hypnotic use among users and nonusers of donepezil were compared using chi-square analysis for independent samples and multivariate logistic regression for identification of significant independent correlates of hypnotic use.

Results: A total of 2638 caregivers completed at least 1 study wave. The use of hypnotics was higher in the donepezil subgroup (9.8%) compared to subjects not taking donepezil (3.9%, $p < 0.0001$). Multivariate analysis demonstrated that donepezil use was linked to increased hypnotic use after controlling for disruptive behavior and depressive symptoms (adjusted odds ratio 3.34, $p < 0.0001$). The relationship between donepezil and hypnotic use was similar in each study wave and for the sample as a whole.

Conclusion: In this large community sample, donepezil use was linked to increased hypnotic use. Since sleep quality is an important issue for patients with AD and their caregivers, further evaluation of the potential link between donepezil and sleep-related problems is indicated.

Funding Source: Research funded by Janssen Pharmaceuticia Products, L.P.

NR485 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Escitalopram in the Treatment of Panic Disorder

Stephen M. Stahl, M.D., *Department of Psychiatry, University of California at San Diego, 5857 Owens Avenue, Suite 102, Carlsbad, CA 92009;* Ivan Gergel, M.D., Dayong Li, Ph.D.

Summary:

Background: Escitalopram, the single isomer responsible for the serotonin reuptake inhibition produced by the racemic SSRI citalopram, has been shown to be effective in reducing anxiety symptoms in patients with major depression, social anxiety disorder and generalized anxiety disorder.

Objective: This rendomized, double-blind, placebo-controlled, multicenter trial evaluated escitalopram in male or female patients (aged 18-80) with DSM-IV-defined panic disorder with or without agoraphobia.

Method: A total of 237 patients received double-blind treatment with escitalopram or placebo. Outcome measures included the Modified Sheehan Panic and Anticipatory Anxiety Scale, the Panic and Agoraphobia Scale, the Hamilton Anxiety Scale, Clinical Global Impressions Scale, Patient Global Evaluation, and Quality of Life Questionnaire.

Results: On the basis of these efficacy measures, escitalopram in comparison to placebo significantly reduced panic attack frequency and severity, anticipatory anxiety, and phobic avoidance, and significantly improved overall clinical status and quality of life. Escitalopram treatment was tolerated as well as placebo, with a 6% rate of discontinuation for adverse events.

Conclusion: The results of this study suggest that escitalopram is efficacious and well tolerated in the treatment of panic disorder.

NR486 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Medication Use in Patients with Alzheimer's Disease

Scott Deschene, *Janssen Pharmaceutical Products, 1125 Trenton-Harbourton Road, Titusville, NJ 08560*

Summary:

Objective: To analyze the diagnostic and prescribing habits of US-based physicians caring for patients with AD.

Methods: Physician diagnostic and prescribing habits were analyzed using the NDC Health Patient, IMS, and NDTI databases. All patients diagnosed with AD and/or prescribed acetylcholinesterase inhibitor (AChEI) therapy were included.

Results: Approximately 625,000 patients received AChEI therapy between January and June 2001, with over 57,000 new patients prescribed an AChEI in June 2001. Approximately 14% were new to AChEI therapy, while 5.5 % switched from other drug classes or within the AChEI class. Antidepressants are the most common conjcomitant therapy in AD patients treated with AChEIs, followed by the atypical and conventional antipsychotics. The average duration of AChEI therapy is less htan 6 months, with primary care physicians (60%), neurologists (20%), and psychiatrists (8%) as the main prescribers.

Conclusions: Significant advances have been made in the diagnosis of AD, demonstrated by the number of new patients prescribed AChEIs. These results are consistent with the AAN Practice Parameters (May 2001), which indicated a high incidence of AD diagnosis and follow-up in the first 12 months. Continued efforts must be made to increase the use of approved AD therapies beyond current levels.

Funding Source: Research funded by Janssen Pharmaceuticia Products, L.P.

NR487 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Galantamine Reduces Caregiver Time Assisting Alzheimer's Disease Patients

Mary Sano, Columbia University, P and S Box 16, 630 West 168th Street, New York, NY 10032; Kay Sadik, Ph.D.

Summary:

Objective: To examine the impact of galantamine (Reminyl™) treatment on time spent by caregivers assisting patients with Alzheimer's disease (AD).

Methods: Patients with mild-to-moderate AD received galantamine 24 mg/day or placebo in two 6-month, randomized, double-blind, placebo-controlled trials (n = 824). Daily time spent assisting patients was recorded monthly for 6 months. Categories of change from baseline included: 1) ≥ 30 minute reduction, 2) 15–29 minute reduction, 3) 0–14 minute reduction, 4) 1–15 minute increase, 5) 16–30 minute increase, and 6) > 30 minute increase. Change was compared by treatment group using a Wilcoxon signed rank test (alpha < 0.05, 2-tailed). Stratified analyses were conducted within each severity level (mild AD = MMSE score > 18; moderate AD = MMSE score ≤ 18).

Results: Galantamine significantly reduced caregiver time compared with placebo (p < 0.05) at 6 months. This effect was sigificant for patients with moderate (p < 0.01), but not mild AD.

Conclusions: In addition to providing patient benefits in cognition, activities of daily living, and behavior, galantamine reduces supervision requirements for caregivers. A reduction in caregiver time in more impaired patients where demand is highest has the potential for great economic impact.

Funding Source: Research fundec by Janssen Pharmaceuticia Products, L.P.

NR488 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Employment-Related Impacts Among Caregivers of Alzheimer's Disease Patients

Jeffrey S. Markowitz, D.P.H., Health Data Analyst, 35 Arnold Drive, Princeton Junction, NJ 08550; Elane Gutterman, Ph.D., George Papadopoulos, B.Sc., Kay Sadik, Ph.D.

Summary:

Objective: To determine whether higher-intensity caregiving and more AD symptoms are related to more adverse employment impacts.

Methods: Data were obtained through mail surveys completed by informal
AD caregivers. Impact on employment was defined as changes in employment or lost work days within the past 6 months. Weekly hours of caregiving and a demand scale of caregiving tasks reflected garegiving intensity. AD symptoms were assessed by disruptive behavior and memory impairment subscales.

Results: The work status of the 3,804 respondents was 37.6% full-time, 16.1% part-time, and 46.3% not working. Their median caregiving involvement was 25 hours/week, and almost half reported employment changes. In the employed or recently employed, 39.3% reported work loss of 30+ days. Based on bivariate logistic regression, increments in caregiving intensity were related to more adverse employment outcomes (p < 0.001).Odds of adverse employment impact ranged from 1.86 for those caregiving 10–29 hours (95% CI 1.52–2.27) to 3.39 for those caregiving 70+ hours (95%CI 2.75–4.18). AD symptoms also were sigificant correlates of employment outcomes.

Conclusions: More intensive caregiving was associated with employment changes and missed workdays. Interventions htat reduce time spent providing care and delay progression of impairment may benefit caregivers wanting to maintain their employment.

Funding Source: Research funded by Janssen Pharmaceuticia Products, L.P.

NR489 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Olanzapine in the Treatment of Bipolar Depression

Mauricio Tohen, M.D., *Lilly Research Labs, One Corporate Plaza, Indianapolis, IN 46285;* Richard Risser, M.S., Robert W. Baker, M.D., Angela R. Evans, Ph.D., Gary Tollefson, M.D., Alan Breier, M.D.

Summary:

Objective: Determine the efficacy and safety of olanzapine compared to placebo in the treatment of bipolar depression.

Methods: Patients with bipolar depression and baseline MADRS rating ≥ 20 were randomized for eitht weeks of double-blind treatment with olanzapine (5–20 mg/d, n=270) or placebo (n=377). Additionally, 86 patients were randomized to the combination of olanzapine (6 or 12 mg/d) plus fluoxetine (25 or 50 mg/d).

Results: Starting at week 1 and sustained throughout the study, improvement for both olanzapine and olanzapine-fluoxetine groups was superior to the placebo group. Endpoint mean MADRS change was significantly greater on olanzapine (–12.7) or olanzapine + fluoxetine (–17.1) than on placebo (<9.4, p < .001). Improvement on olanzapine+fluoxetine was significantly greater than on olanzapine alone (p = .002). Induction of mania (baseline YMRS < 15 and ≥ 15 subsequently) did not differ between groups (olanzapine 5.7%, placebo 6.7%, olanzapine+fluoxetine 6.4%). Common (< 10%) and sigificant adverse events reported in the olanzapine group compared to placebo were somnolence, weight gain, increased appetite, and dry mouth, wheras headache and insomnia were common and significant on placebo.

Conclusion: Olanzapine demonstrated superiority to placebo in the treatment of bipolar depression; olanzapine+fluoxetinealso showed superiority compare to placebo and to olanzapine.

Funding Source: This study was funded by Eli Lilly and Company.

NR490 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Escitalopram: A New Treatment for Depression and Anxiety

Sandeep Gupta, , Ph.D., *Department of Pharmacology, Forest Laboratories, 909 Third Avenue, New York, NY 10022; Connie Sanchez, D.Sc.*

Summary:

Background: Escitaqlopram, the S-enantiomer of the antidepressant citalopram, has been shown to be responsible for the inhibition of 5-HT reuptake as well as the antidepressant activity of citalopram

Objective: To further characterize the pharmacological profile of escitalopram.

Method: Radioligand binding and uptake assays were used to assess the potency and selectivity of escitalopram for various monoamine transporters and receptor sites. Activity in a number of animal models of depression and anxiety also was quantified.

Results: Escitalopram is at least twice as potent as citalopram for the inhibition of 5-HT reuptake in vitro and in vivo, wheras the R-enantiomer is several fold less potent. Radioligand binding studies targeting over 140 sites including human monoamine transporters, serotonergic, adrenergic, muscarinic and dopamine receptors and various ion channels indicate that escitalopram is the most selective 5-HT transport inhibitor (SSRI) among antidepressants developed for clinical use, including citalopram. Escitalopram is active in acute and chronic models predictive of antidepressant activity, i.e., mouse forced swim test, resident-intruder paradigm and agonistic behavior, and chronic mild stress-induced "anhedonia" in rats. In the latter rat models, escitalopram shows a faster onset of action than other antidepressants, including citalopram. Escitalopram also shows potent anxiolytic-like effects in a number of rodent models such as footshock- induced ultrasonic vocalization, dorsal peri-aqueductal grey stimulation, and black and white box. In models predictive of antidepressant and anxiolytic activity, escitalopram was more than twice as potent as citalopram, wheras R-citalopram was much less or not active.

Conclusion: These data predict a better clinical efficacy and tolerability of escitalopram than citalopram, and possibly other antidepressants, in the treatment of depression and anxiety disorders.

Funding Source: Forest Laboratories and H. Lundbeck A/S.

NR491 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Escitalopram is Efficacious and Well Tolerated in the Treatment of Social Anziety Disorder

Siegrried Kasper, M.D., *Department of General Psychiatry, University of Vienna, Wahringer Gurtel 18–20, Wien, A-1090, Austria;* Henrik Loft, M.S.C., James R. Smith, Ph.D.

Summary:

Background: Escitalopram is a potent and highly selective SSRI, whose efficacy and safety in the treatment of MDD have recently been established.

Objective: This study compared the eficacy and safety of escitalopram to placebo in the teatment of Social Anxiety Disorder (SAD).

Method: After a 1-week, single-blind placebo period, outpatients (aged 18–65 years) with primary diagnosis of SAD (DSM-IV), who had an LSAS > or = 70 and a CGI-S > or = 4 at baseline, were randomised to 12 weeks of double-blind treatment with escitalopram (n = 181) or placebo (n = 177). Patients on escitalopram started at 10mg/day; if needed, the dose could be doubled after 4, 6, or 8 weeks of treatment, so that the escitalopram-treated patients received 20mg/day.

*Results:*The primary efficacy variable, change in LSAS score from baseline to endpoint, showed a significant improvement for escitalopram relative to placebo. Secondary efficacy analyses also showed a significantly better therapeutic effect at enpoint for escitalopram relative to placebo on: CGI-S, CGI-I, LSAS avoidance and fear/anxiety, and 2 of 3 items on the Sheehan Disability Scale (SDS). Escitalopram was well tolerated in this patient population.

Conclusion: This phase III study dimonstrates that escitalopram 10–20 mg/day is effective and well tolerated in the treatment of Social Anxiety Disorder.

NR492 Wednesday, May 22, 3:00 p.m.-5:00 p.m.

Confirmation of Dementia Subtypes Using Functional Neuroimaging

Michael Mega, M.D., 4238 Reed Building, 710 Westwood Plaze, Los Angeles, CA 90095–17569; Ivo D. Dinov, Ph.D., Jeffrey L. Cummings, Arthur W. Toga

Summary:

Objective: To investigate the value of neuroimaging in aiding the clinical diagnosis of specific dementia subtypes.

Methods: From a database of over 350 patients who underwent resting 99mTc-HMPAO single photon emission computed tomography (SPECT) within one month of clinical evaluation, we selected 10 elderly individuals with stable mild cognitive impairmant (MCI), 10 patients with Alzheimer's disease (AD), 10 patients with dementia with Lewy bodies (DLB), 10 patients with vascular dementia (VaD), and 10 patients with frontotemporal dementia (FTD), all of similar demographics. Sub-Volume Threshholding (SVT) corrected random lobar noise to produce 3D significance maps to explore patterns of hypoperfusion that significantly differentiated these dementia subtypes.

Results: Compared with stable MCI patients, significant regional differences were found in the statistical brain maps of patients with AD, DLB, VaD, and FTD. In addition, a comparison of maps among dementia subtypes suggested regionally unique patterns of cerebral dysfunction.

Conclusion: Neuroimaging is a useful method for confirming the clinical diagnosis of specific dementia sybtypes. This technique may also be useful for differentiating dementia sybtypes early in the disease process.

Funding Source: Research funded by Janssen Pharmaceuticia Products, L.P.

NR493 Presented at 2001 Annual Meeting

Hallucinations and Delusions in Schizophrenia: A 15-Year Follow-UP Study

Martin Harrow, Ph.D., *University of Illinois, Department of Psychiatry, 1601 West Taylor Street, M/C912, Chicago, IL 60612;* Dana J. Sheldon, B.S., Ellen Herbener, Ph.D., Joseph F. Goldberg, M.D., Eileen Martin, Ph.D., Kalman Kaplan, Ph.D.

Summary:

Objective: Multi-year longitudinal data on the course of hallucinations and delusions is rare. The current 15-year follow-up study provides data on whether hallucinations are persistent trait-like phenomena. Further, is this vulnerability to hallucinationsover time limited to schizophrenia patients or do other types of psychotic patients also experience recurrent hallucinations?

Method: We assessed longitudinally 256 patients from the Chicago Follow-up Study. We evaluated patients for psychosis and other major symptoms 6 times over a 15-year period. The sample included 65 schizophrenics. 30 schizoaffectives, 23 bipolar manics, 24 other psychotic, and 114 non-psychotic patients. The SADS was used to evaluate both hallucinations and delusions at each of the 6 assessment over the 15 years. Other standardized measures were employed thought disorder and negative symptoms. Satis-

factory inter-rater reliability was obtained for all positive and negative symptoms (e.g. inter-rater reliability for hallucinations: r = .91).

Results: 1) Patients with hallucinations early in their illness show severe hallucinations years later ($p < .001$). 2) Contrary to expectations, non-schizophrenic patients who show hallucinations early also tend to show recurrent hallucinations years later. 3) Almost all hallucinating patients simultaneously showed delusions)$p <$ .01). 4) The data indicate that recurrent hallucinations are not unique to schizophrenia and bipolar disorders.

Conclusions: In addition to schizophrenics, non-schizophrenic patients with early sign of hallucinations also show a long-term vulnerability to trait-like recurrences of hallucinations years later. The high rate of delusions in halluciating patients suggests that hallucinations in schizophrenics are not just perceptual phenomena. Rather, strange beliefs and unrealistic ideas are important factors in schizophrenic and other psychotic patients hallucinations, and is one of the pathogenic factors involved in their hallucinations.

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