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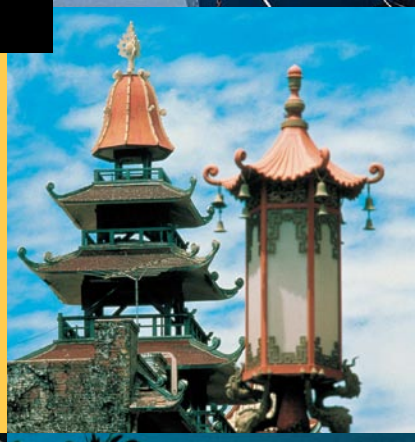

2009 NEW RESEARCH ABSTRACTS

Monday, May 18, 2009

9:00 a.m. - 10:30 a.m.
Hall D, Exhibit Level,
Moscone Convention Center

NEW RESEARCH POSTER SESSION 1: SCHIZOPHRENIA & OTHER PSYCHOTIC DISORDERS

» NR1-001

SUBJECTS WITH SCHIZOPHRENIA OR SCHIZOAFFECTIVE DISORDER & HEPATIC ILLNESS: BASELINE CHARACTERISTICS FROM A TRIAL OF PALIPERIDONE ER

Joan Amatniek M.D., Carla M. Canuso, M.D., Stephen Rodriguez, M.S., Lian Mao, Ph.D., Eriene A. Youssef, Pharm.D., David C. Henderson, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be aware of the demography, clinical characteristics and etiology of liver impairment in a population of patients with schizophrenia who present with hepatic illness.

SUMMARY:

Background: Cormorbid hepatic illness (HI) in patients with schizophrenia or schizoaffective disorder (SCH/SCA) is relatively common but poorly characterized. Baseline interim data from SCH/SCA patients with HI participating in an ongoing study evaluating the effects of paliperidone ER, which undergoes limited hepatic metabolism, are presented.
Methods: Data from 9-week, open-label, single-arm study of outpatients with stable SCH/SCA and HI was reviewed to assess psychosocial characteristics, and etiology and stage of HI. Inclusion criteria: Child-Pugh scores of well-compensated (Class A) to functionally compromised (Class B) HI and liver tests (LTs) =3x upper limits of normal (ULN). Subjects received antipsychotic treatment as usual for 4 weeks, 1-week cross-titration and paliperidone ER for 4 weeks. Study endpoints: AEs (primary), laboratory tests, movement disorder scales, PANSS, quality of life and alcohol use. Study ID: CR014341.
Results: 69 US subjects enrolled; 57 (82.6%) with SCH and 12 (17.4%) with SCA. Mean (SD) age: 48.2 (7.5) years. Most subjects were male (70.6%), black (64.7%), with =high school education (73.6%), unemployed (89.7%); 44.9% lived in supported housing. Most common etiology of liver disease: viral hepatitis (95.7%). Most had a Child-Pugh rating of A (85.1%). Of subjects with viral hepatitis who required laboratory testing (n=58), 89.9% had hepatitis type C. Mean LTs (alanine and aspartate aminotransferase) were just above ULN (44.7 ± 23.9 U/L and 39.2 ± 17.1 U/L, respectively). Mean (SD) PANSS total score: 73.8 (12.6). Most subjects had used tobacco (95.7%), alcohol (84.1%), marijuana (62.3%) and cocaine (60.9%); 36.2% had used heroin.
Conclusion: Subjects included had significant psychosocial impairment. Their HI tended to be mild and due to viral hepatitis possibly related to prior substance abuse. Safety and efficacy of paliperidone ER in these patients are currently under study.
Supported by Ortho-McNeil Janssen Scientific Affairs, LLC

REFERENCES:

1) Rosenberg SD, Goodman LA, Osher FC, Swartz MS, Essock SM, Butterfield MI, Constantine NT, Wolford GL, Salyers MP: Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness. Am J Public Health 2001; 91(1):31-37

2) Drake RE, Brunette MF: Complications of severe mental illness related to alcohol and drug use disorders. Recent Dev Alcohol 1998; 14:285-299

» NR1-002

PATIENT-REPORTED PREVALENCE, SEVERITY, AND BOTHERSOMENESS OF MEDICATION-EMERGENT ADVERSE EVENTS AMONG INPATIENTS TREATED FOR SCHIZOPHRENIA

Anthony H. Lawson, M.A., Haya Ascher-Svanum, Ph.D., Michael D. Stensland Ph.D., Virginia Stauffer Pharm.D., Robert R. Conley M.D., Xianchen Liu M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participants should be able to recognize the most prevalent, most severe, and most bothersome medication-related adverse events reported by inpatients treated with antipsychotics for schizophrenia.

SUMMARY:

Objective: To assess patient-reported prevalence, severity, and bothersomeness of medication-emergent adverse events (AE) among inpatients treated for schizophrenia.
Methods: Data were drawn from a prospective, multi-site, naturalistic, non-interventional observational study of individuals who were initiated on olanzapine or ziprasidone during their psychiatric hospitalization. The analytic sample included study participants whose primary diagnosis was schizophrenia (N=99). During a structured interview, patients rated the severity and how bothersome they found 33 potential treatment-emergent AEs associated with antipsychotic therapy. Ratings pertained to AEs experienced in the week prior to initiating olanzapine or ziprasidone. The most prevalent, severe, and bothersome patient-reported medication-related AEs were identified.
Results: Most (75%) patients reported experiencing insomnia, making it the most prevalent AE, followed by somnolence (65%), akathisia (59%), asthenia (59%), and akinesia (42%). In terms of severity, insomnia was the most severe AE among patients who reported this symptom followed by changes in sexual performance, tremors, akinesia, and rhinitis. Insomnia was also rated as the most bothersome AE among those experiencing it, followed by tremor, asthenia, dyskinesia, and joint pain. Prior weight gain was reported by 26% of the patients who rated severity as the 21st most prevalent of 33 events and bothersomeness as the 25th most prevalent of 33 events. Weight loss was reported by 13% of the patients who reported it as relatively severe (11th of 33) but less bothersome (29th of 33).
Conclusions: Among inpatients treated for schizophrenia, insomnia was found to be the most common, most severe, and most bothersome treatment-emergent AE for the patients. Other less prevalent but highly bothersome AEs included tremor, asthenia, dyskinesia, and joint pain. This study was funded by Eli Lilly and Company.

REFERENCES:

1) Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, Keefe RS, Davis SM, Davis CE, Lebowitz BD, Severe J, Hsiao JK: Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. New England Journal of Medicine 2005; 353: 1209-1223

2) Kahn RS, Fleischhacker WW, Boter H, Davidson M, Vergouwe Y, Keet IP, Gheorghe MD, Rybakowski JK, Galderisi S, Libiger J, Hummer M, Dollfus S, López-Ibor JJ, Hranov LG, Gaebel W, Peuskens J, Lindefors N, Riecher-Rössler A, Grobbee DE: Effectiveness of antipsychotic drugs in first-episode schizophrenia and schizophreniform disorder: an open randomised clinical trial. The Lancet 2008; 371: 1085-1097

» NR1-003

METABOLIC SYNDROME AND GLUCOSA DISTURBANCES IN A SPANISH SAMPLE OF ELDERLY CHRONIC SCHIZOPHRENIC INPATIENTS

Manuel Arrojo-Romero, Ramón Ramos-Ríos, M.D., Eduardo Paz-Silva, M.D., Fernando Carballal-Calvo, M.D., Alicia Crespí-Armenteros, M.D., Ramón Fernández- Pérez, M.D., José Luís Bouzón-Barreiro, M.D., Jorge Seoane-Prado, M.D., Rosario Codesido-Barcala, M.D., Javier D. López-Moríñigo, Ignacio Tortajada-Bonaselt, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participants should be able to recognize the high risk of obesity, glucose disturbances and lypodystrophies in elderly schizophrenic patients treated with antipsychotics.

SUMMARY:
Objectives: To determine the prevalence of metabolic syndrome (MS) and glucose disturbances in a sample of elderly schizophrenic patients and analyze the related risk factors
Methods: We carried out an analysis of metabolic parameters in 82 Caucasian schizophrenic inpatients (52.4 % females) older than 60 years old with a mean age of 70 years (SD 6.9) of a psychiatric hospital (Hospital Psiquiátrico de Conxo, Santiago de Compostela, Spain). We estimated the prevalence of the MS using the revised National Cholesterol Educative Program-Adult Treatment Panel III definition (ATP-III, 2005) based on the presence of 3 of the following abnormalities; elevated waist circumference (male = 102 cm; female = 88 cm) for Caucasians, elevated triglycerides =150 mg/dL or receiving drug treatment, decreased high-density lipoprotein cholesterol male <40 mg/dL, female <50 mg/dL or receiving drug treatment, elevated blood pressure =130/=85 mm Hg =130/=85 mm Hg or receiving drug treatment, elevated fasting plasma glucose =100 mg/dL or on drug treatment. Insulin-resistance (IR) was evaluated by the HOMA method. (IR = (insulin x glucose) /22.5; insulinemia expressed in µU/ml and glucaemia in mmol/L)
Results: Prevalence of MS was 54.9%. 26.8% of the sample had the diagnosis of diabetes, 58.5% presented hyperglycemia (fasting glucose =100mg/dL) and 8.5% hyperinsulinaemia. Significant correlations ($p< 0.05$) were found between insulin-resistance and BMI and all the parameters that define the MS with the exception of blood pressure. Patients with MS show higher mean values of IR (3.47 vs. 1.23, $p<0.01$) and BMI (31.2 vs. 25.5, $p<0.01$).
Conclusion: Metabolic syndrome and glucose disturbances are highly prevalent among elderly patients with schizophrenia. Assessment and monitoring of glucose disturbances and the other associated risk factors of the metabolic syndrome should be part of the clinical management of these patients.

REFERENCES:
1) Suvisaari JM, Saarni SI, Perälä J, Suvisaari JV, Härkänen T, Lönnqvist J, Reunanen A. Metabolic syndrome among persons with schizophrenia and other psychotic disorders in a general population survey. J Clin Psychiatry 2007; 68(7):1045-55.

2) Henderson DC. Schizophrenia and comorbid metabolic disorders. J Clin Psychiatry 2005; 66 Suppl 6: 11-20.

» NR1-004

ORAL SUPPLEMENTATION AND CONCOMITANT MEDICATION IN THE TREATMENT OF SCHIZOPHRENIA WITH LONG-ACTING ATYPICAL ANTIPSYCHOTICS

Haya Ascher-Svanum Ph.D., Xiaomei Peng, M.D., M.S., William Montgomery, B.Pharm.,Douglas E. Faries, Ph.D., Anthony H. Lawson, M.S., Michael Witte, Ph.D., Diego Novick, M.D., Nadia Jemiai, M.S., Elena Perrin, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should recognize that atypical antipsychotics (risperidone, olanzapine) in long-acting injection formulations appear to differ on supplementation with oral antipsychotics and several other oral medications. The differences may have important ramifications because depot is often chosen for schizophrenia patients previously nonadherent to oral medications. Current preliminary findings highlight the need for comparative studies in usual care.

SUMMARY:
Objective: To assess the use of oral antipsychotics and other concomitant oral medications – psychotropics and the anticholinergic benztropine - during the 1-year open-label treatment of schizophrenia with olanzapine long-acting injection (OLAI), and to compare with previously published rates for risperidone long-acting injection (RLAI).
Method: One-year rates of concomitant oral medication use were drawn from 2 comparable open-label, single-arm extension studies of patients with schizophrenia treated with long-acting atypical antipsychotic medications: one for OLAI (n=931), with extension of 3 OLAI clinical trials (1), and one for RLAI (n=371), with extension of 2 RLAI clinical trials (based on published 1-year data) (2).
Results: Supplementation with oral olanzapine occurred in 21% of OLAI-treated patients (median duration 10 days). Oral risperidone was supplemented – beyond the first 3 weeks of treatment in 45%-83% of RLAI-treated patients (median duration not reported). Use of the anticholinergic benztropine was low among OLAI-treated patients (3%, median duration 14 days) and higher among RLAI-treated patients (31%-44%) (median duration not reported). Lorazepam was used by 11% of OLAI compared to 24%-55% of RLAI-treated patients. Zolpidem was used by 4% of OLAI and 11%-12% of RLAI-treated patients.
Conclusions: Atypical antipsychotic therapies in long-acting injection formulations were found in this preliminary analysis to differ on concomitant use of oral atypical antipsychotic and other oral medications. OLAI therapy may require less oral supplementation compared to RLAI, thus offering a simpler treatment regimen. Though limited by cross study comparisons and the need for replication, the current findings may have important clinical and economic ramifications as depot formulations are often chosen for persons previously nonadherent to oral medication regimens.
Funded by Eli Lilly and Company.

REFERENCES:
1) McDonnell DP, Andersen S, Detke H, Watson S: 160-week interim results from an open-label extension trial of olanzapine long-acting injection. [Abstract] Schizophr Res 2008; 102(Suppl 2):269

2) Lindenmayer JP, Khan A, Eerdekens M, Van Hove I, Kushner S: Long-term safety and tolerability of long-acting injectable risperidone in patients with schizophrenia or schizoaffective disorder. Eur Neuropsychopharmacol. 2007; 17(2):138-144

» NR1-005

COST-EFFECTIVENESS OF OLANZAPINE LONG-ACTING INJECTION IN THE TREATMENT OF NONADHERENT PATIENTS WITH SCHIZOPHRENIA IN THE UNITED STATES

Haya Ascher-Svanum Ph.D., Nicholas M. Furiak, M.S., Robert W. Klein, M.S., William Montgomery, B.Pharm., Lee J. Smolen, B.S., Anthony H. Lawson, M.S., Robert R. Conley, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should recognize that olanzapine pamoate for injection, a long-acting depot preparation of olanzapine, is an effective, well tolerated, and potentially cost-effective treatment option that is specifically tailored for a costly, complex, and challenging group of schizophrenia patients – those who are non-adherent with their oral antipsychotic regimens.

SUMMARY:
Objective: This study examines, from a U.S. health care perspective, the cost-effectiveness of olanzapine long-acting injection (OLAI) compared to risperidone long-acting injection, haloperidol decanoate, and oral olanzapine in the treatment of schizophrenia patients who are nonadherent with oral antipsychotics (1,2).
Methods: A 1-year microsimulation economic decision model was developed to simulate the dynamic usual care of schizophrenia patients who may switch, continue, discontinue, and restart medications. The model captures clinical and cost parameters including adherence levels, relapse with and without hospitalization, quality

adjusted life years (QALYs), treatment discontinuation by reason, treatment-emergent adverse events, suicide, health care resource utilization, and direct medical care costs. Published medical literature, unpublished data, and a clinical expert panel were used to develop baseline model assumptions. Key model outcomes included annual total direct cost per treatment, cost per stable patient, and incremental cost-effectiveness values per 1 QALY gained.
Results: OLAI was found to have an incremental cost of $60,273/QALY over haloperidol decanoate. OLAI dominated all other comparators by producing more QALYs and fewer inpatient relapses (dominant over RLAI) or by producing more QALYs and fewer inpatient relapses with a lower incremental cost-effectiveness ratio (extended dominance over oral olanzapine). The base case and multiple sensitivity analyses found OLAI to be a cost-effective option in terms of incremental cost/QALY gained. Results were most sensitive to change in the cost of relapse.
Conclusions: OLAI is projected in this microsimulation model to be a cost-effective treatment option for a costly, complex, and challenging group of patients - nonadherent schizophrenia patients - by yielding more QALYs and fewer inpatient relapses than each comparator and providing a cost-effective option in terms of incremental cost per QALY gained.

REFERENCES:

1) Lauriello J, Lambert T, Andersen S, Lin D, Taylor CC, McDonnell D: An 8-week, double-blind, randomized, placebo-controlled study of olanzapine long-acting injection in acutely ill patients with schizophrenia. J Clin Psychiatry 2008; 69(5):790-799

2) Citrome L. Olanzapine pamoate: a stick in time? Int J Clin Pract. 2008 Oct 1. [Epub ahead of print]

» NR1-006

RECURRENCE PATTERN OF THE PATIENTS WHO HAD BEEN DIAGNOSED WITH BRIEF PSYCHOTIC DISORDER: 2 YEARS OF FOLLOW UP BY RETROSPECTIVE CHART REVIEW

Won-Myong Bahk, M.D., Young-Eun Jung, M.D., Ho-Jun Seo, M.D., Tae-Youn Jun, M.D., Jeong-Ho Chae, M.D.Department of Psychiatry, College of Medicine, The Catholic University of Korea, Seoul, Korea

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the incidence and patterns of recurrence in patients with brief psychotic disorder for 2 year

SUMMARY:

The brief psychotic disorder is characterized by sudden onset of psychotic symptoms which may include delusion and hallucination, last at least a day, but not more than a month. The aim of current study was to evaluate the incidence and patterns of recurrence in patients with brief psychotic disorder for 2 years and find the predictor related to outcome.
We recruited the inpatients who were diagnosed with brief psychotic disorder from January 2001 to December 2005 and could be followed up for 2 years after discharge. During this period, recurrence of psychotic symptoms and other psychiatric disorders were assessed and relations between these recurrence and various clinical characteristics were evaluated. Twenty eight patients were included in this study with fulfillment of inclusion criteria. During 2 years of follow up periods, psychiatric disorders were recurred in 9 cases. 5 cases (17.8%) were re-diagnosed with schizophrenia, brief psychotic disorder recurred in 2 cases (7.1%), with full recovery of their functioning. 2 cases (7.1%) were re-diagnosed with bipolar I disorder with psychotic features.
In comparison between the patients with recurrence and not, no significant difference was detected in demographic and clinical variables. In comparison among the patients with three different diagnoses of recurrences, all patients with brief psychotic disorder and bipolar disorder had their first onset before forties. Patients recurred with schizophrenia had non-significant trend of longer periods of untreated psychosis. Patients with bipolar disorder had more confusion during the psychotic periods and patients with schizophrenia showed affective flattening more frequently. In the future, prospective studies which have large sample size would be needed.

REFERENCES:

1) Yung AR, Phillips LJ, Yuen HP, Francey SM, McFarlane CA, Hallgren M, McGorry PD. Psychosis prediction: 12-month follow up of a high-risk ("prodromal") group.Schizophr Res 2003;60:21-32.

2) Yung AR, Phillips LJ, Yuen HP, McGorry PD. Risk factors for psychosis in an ultra high-risk group: psychopathology and clinical features. Schizophr Res 2004;67:131-142.

» NR1-007

EFFECT OF ARIPIPRAZOLE VS. HALOPERIDOL IN PANSS PROSOCIAL ITEMS IN EARLY EPISODE PATIENTS WITH SCHIZOPHRENIA

Ross Baker Ph.D., John P Docherty, M.D., Edward Kim, M.D., M.B.A., Andrei Pikalov, M.D., Ph.D., James Eudicone, M.S., Suja Mathew, B.S., Raymond Mankoski, M.D., Ph.D., Robert D McQuade, Ph.D., Ronald N Marcus, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the audience will be able to describe the relative effectiveness of aripiprazole and haloperidol on residual "barrier" negative symptoms after antipsychotic treatment of early-episode schizophrenia, as measured by two PANSS prosocial subscales.

SUMMARY:

Background: Negative symptoms have been reported to show little change after antipsychotic treatment. Relatively small improvements in these symptoms appear correlated with larger change in functional recovery (1). Clinical reports have suggested a specific benefit from aripiprazole in some patients with these "barrier symptoms".
Objective: Compare the effect of aripiprazole (arip) vs. haloperidol (hal) in early-episode patients with schizophrenia using two PANSS scales of relevant items: the Prosocial Scale and a modified Prosocial Scale.
Methods: "Early episode" was defined as ?40 years of age, and ?5 years since first diagnosis. The PANSS Prosocial Subscale consists of six PANSS items broadly related to social engagement (2). The modified Prosocial Subscale consists of four PANSS items, including difficulty with abstract thinking - an item not contained within the prosocial subscale but empirically demonstrated as a prominent residual symptom. Measurements were taken at approximately monthly intervals for up to 1 year. Mean changes from baseline in both drug groups were compared for each subscale using an ANOVA model with last observation carried forward.
Results: Arip demonstrated significant improvements vs. hal as early as Week 18 on both the prosocial subscale (-4.75 arip n=237 vs. -3.78 hal, n=123, $p<0.05$) and on the modified prosocial subscale (-3.16 arip, -2.27 hal, $p<0.05$). Patients showed similar significant improvements at each time tested through Week 52 with the modified subscale, but less consistent improvement over time with the prosocial subscale. Similar significant improvements were observed at Weeks 46 and 52 (endpoint) with both subscales.
Conclusions: In patients with early episode schizophrenia, aripiprazole demonstrates greater improvements in prosocial PANSS items than haloperidol. The cognitive and functional implications of these findings remain to be clarified.

REFERENCES:

1) Leucht S, Lasser R: The concepts of remission and recovery in schizophrenia. Pharmacopsychiatry. 2006; 39:161-170

2) Purnine DM, Carey KB, Maisto SA, Carey MP: Assessing positive and negative symptoms in outpatients with schizophrenia and mood disorders.

J Nerv Ment Dis 2000;188:653-661

» NR1-008

CARDIOVASCULAR AND RESPIRATORY COMORBIDITIES IN PATIENTS WITH BIPOLAR DISORDER: A SYSTEMATIC REVIEW

Julio Bobes M.D., José M. Montes, M.D., José Mostaza, M.D., Fernando Rico-Villademoros, M.D., Eduard Vieta, M.D., Jerónimo Saiz-Ruiz, M.D., on behalf of the Spanish Consensus Group of Experts on Physical Health in Patients with Bipolar Disorders.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize the prevalence of cardiovascular and respiratory comorbidities among patients with bipolar disorder.

SUMMARY:

Objective: To synthesize the available knowledge on cardiovascular and respiratory comorbidities in patients with bipolar disorder (BD).
Methods: Relevant studies were identified by a MEDLINE search from 1966 to January 2008, and supplemented by a manual review of reference lists of the articles identified and previous review articles. When available, priority was given to comparative studies.
Results: We identified 21 studies, 15 (71%) comparative. As compared to the general population, two studies reported higher point-prevalence rates of hypertension (28-60.8% vs 11.9-43%), two studies lower point-prevalence rates (10.4-34.8% vs 14.9-36.8%), one study a higher lifetime-prevalence rate (28.7% vs 14.8%), and one study a significantly increased incidence rate ratio (1.24 females and 1.34 for males). In addition, two studies reported higher point-prevalence rates of hypertension than in medical samples (4.6-18.1% vs 2.2-9.2%) and one study reported a higher risk than in patients with schizophrenia (OR 1.13, 95%CI 1.01-1.26). Point-prevalence rate of stroke was not different than in the general population (n=1, 1.7 vs 2.1, p=0.063); four studies evaluating the risk of stroke as compared to clinical samples provide contradictory results. Point-prevalence rates (n=2, 15.9-17% vs 8.3-10%) and lifetime-prevalence rate (n=1, 16.7% vs 9.7%) of asthma were higher than in the general population. Point-prevalence rates of COPD were also higher than in the general population (n=1, 10.6% vs 9.4%) and in clinical samples (n=3, 1-12.9% vs 0.6-3.6%).
Conclusion: BD seems to be associated with an increased frequency of hypertension, asthma and Chronic Obstructive Pulmonary Disease (COPD). Available data do not support an association between BD and stroke.

REFERENCES:

1) Kupfer DJ.: The increasing medical burden in bipolar disorder. JAMA. 2005;293:2528-30.

2) McIntyre RS, Soczynska JK, Beyer JL, Woldeyohannes HO, Law CW, Miranda A, Konarski JZ, Kennedy SH: Medical comorbidity in bipolar disorder: re-prioritizing unmet needs. Curr Opin Psychiatry. 2007;20:406-16.

» NR1-009

FACTORS ASSOCIATED WITH METABOLIC SYNDROME IN PATIENTS WITH SCHIZOPHRENIA - RESULTS FROM A GERMAN OBSERVATIONAL STUDY

Frank Boess, Anette Minarzyk, M.S., Catherine Beal, M.S., Hans-Peter Hundemer, M.D., Thomas Forst, M.D., Daniel Kopf, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should have learned something about the association of schizophrenia, metabolic syndrome and antipsychotic therapy.

SUMMARY:

Introduction: Increased prevalence of cardiovascular risk factors in patients on antipsychotics was seen in several studies. In this observational study we assessed the presence of metabolic syndrome (MetS) in differently treated patients with schizophrenia at baseline and 3 months to identify prognostic factors associated with MetS.
Methods: Enrollment criteria of the study were to initiate/switch treatment-naive or previously treated adult patients with schizophrenia to new antipsychotic medication. Physical and laboratory parameters were evaluated to assess the presence of MetS (NCEP definition). Patients with complete data for MetS-diagnosis at both visits (476 of 642) were analyzed descriptively, prevalence of MetS and 95% CI were calculated by post-baseline treatment cohorts: olanzapine (Olz, N=206, risperidone (Risp, N=69), quetiapine (Quet, N=33), other atypical monotherapy (Atyp, N=72), typical therapy (Typ, N=16), any combination (Comb, N=80). Multivariable forward selection logistic regressions were used to explore factors associated with MetS, providing p-values and odds ratios (OR)
Results: The prevalence of MetS was 40.3% [CI 35.90; 44.90] at baseline and 42.7% [CI 38.16;47.23] after 3 months. In the cohorts it ranged between 30.4% [CI 19.92;42.69] (Risp), and 68.8% [CI 41.34;88.98] (Typ) at baseline, and between 38.4% [CI 31.68;45.36] (Olz) and 68.8% [CI 41.34;88.98] (Typ) after 3 months. Factors significantly associated with MetS at baseline were: presence of concomitant non-psychiatric disease (p<0.001, OR 4.09), smoking status (p=0.0098 OR 0.53); at 3 months: female vs. male (p<=0.0185, OR 0.56), smoking status (p<=0.049, OR 0.60) and increased C-reactive protein, (p<=0.062, OR 2.00).
Conclusion: Overall, no significant difference in prevalence of MetS at baseline and after 3 months was observed. Factors significantly associated with MetS included somatic comorbidity, smoking status, sex, and increased C-reactive protein.

REFERENCES:

1) Correll CU, Frederickson AM, Kane JM, Manu P.: Equally increased risk for metabolic syndrome in patients with bipolar disorder and schizophrenia treated with second-generation antipsychotics.Bipolar Disord. 2008 Nov;10(7):788-97.

2) Moebus S, Hanisch JU, Aidelsburger P, Bramlage P, Wasem J, Jöckel KH.: Impact of 4 different definitions used for the assessment of the prevalence of the Metabolic Syndrome in primary healthcare: The German Metabolic and Cardiovascular Risk Project (GEMCAS). Cardiovasc Diabetol. 2007 Sep 6;6:22.

» NR1-010

TREATMENT PATTERNS AMONG A NATIONWIDE COMMUNITY SAMPLE OF PEOPLE WITH SCHIZOPHRENIA USING ATYPICAL ANTIPSYCHOTICS

Susan Bolge Ph.D., Jessica Panish, M.H.S., Riad Dirani, Ph.D., Debbie Kenworthy, Deborah Freedman, M.B.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, participants should be able to describe the overall treatment patterns of community-based patients with schizophrenia treated with atypical antipsychotic therapy. Participants should gain an understanding of concomitant use of psychotropic medications, perception of treatment efficacy and side effects, use of inpatient and outpatient health care resources and health insurance status.

SUMMARY:

Purpose: To describe treatment patterns of adults with schizophrenia using atypical antipsychotics.
Methods: Data were taken from a nationwide survey of adults (>=18 years old) self-reporting a diagnosis of schizophrenia, collected from December 2007 to February 2008. Data were obtained through self-reported questionnaires on the Internet and through 43 interview facilities across the US. Analyses are descriptive in nature.
Results: 1,083 patients, including 747 (69%) atypical users, par-

ticipated. Mean age was 43; 52% were female and 38% were non-white. In the past year, 9% were newly diagnosed with schizophrenia; 37% diagnosed 1-5 years ago, 21% diagnosed 6-10 years ago and 33% diagnosed 11+ years ago. Atypical users reported using a mean (SD) of 1.4 (0.6) atypical agents and 3.0 (1.7) psychotropic medications in total. There was 8% concomitant use of traditional antipsychotics, 46% use of antidepressants, 31% use of anxiolytics and 33% use of non-antipsychotic mood stabilizers. 58% of atypical users reported that medication controlled symptoms quite a bit or eliminated all symptoms. Patients reported experiencing a mean (SD) of 3.7 (3.4) AEs, most commonly difficulty thinking/concentrating (50%), restlessness (48%), difficulty sleeping (44%), sleepiness (44%) and weight gain (43%). In the past 6 months, 30% of atypical users were hospitalized and 39% visited the emergency room. Mean (SD) days hospitalized for mental health: 3.6 (14.3). Mental health care was most commonly received from community mental health centers (CMHCs) (50%) and psychiatrist offices (49%). Health insurance was most commonly through Medicare (40%) or Medicaid (40%).
Conclusion: Polypharmacy is a common practice among schizophrenia patients receiving atypical antipsychotic therapy, with nearly half of the patients taking an antidepressant. Treatment for this population is often provided through CMHCs and private psychiatrists' offices.
Supported by Ortho-McNeil Janssen Scientific Affairs, LLC

REFERENCES:

1) Morrato EH, Dodd S, Oderda G, Haxby DG, Allen R, Valuck RJ. Prevalence, utilization patterns, and predictors of antipsychotic polypharmacy: experience in a multistate Medicaid population, 1998-2003. Clin Ther 2007; 29(1):183-195

2) Stahl SM, Grady MM. A critical review of atypical antipsychotic utilization: comparing monotherapy with polypharmacy and augmentation. Curr Med Chem 2004; 11(3):313-327

» NR1-011

POST-INJECTION DELIRIUM/SEDATION SYNDROME OBSERVED WITH OLANZAPINE LONG-ACTING INJECTION

Elizabeth Brunner M.D., David P. McDonnell, M.B.B.Ch., M.R.C.Psych., Sebastian Sorsaburu, M.D., Holland C. Detke, Ph.D., Scott W. Andersen, M.S., Richard F. Bergstrom, Ph.D., Malcolm Mitchell, M.B.B.S., M.F.P.M., Kristen Ogle, Ph.D., Angela Gulliver, Pharm.D., Susan B. Watson, Ph.D., Sara A. Corya, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the incidence of post injection delirium/sedation syndrome observed with olanzapine long-acting injection and to understand its recommended risk management and medical management procedures.

SUMMARY:

Objective: A recognized potential risk of intramuscular products is accidental intravascular injection, the signs and symptoms of which are dependent on the formulation and safety profile of the injected medication. During clinical trials of olanzapine long-acting injection (LAI), cases were identified in which a cluster of adverse events characterized by post-injection delirium and/or excessive sedation were observed. This post-injection delirium/sedation syndrome (PDSS) appeared to be potentially related to inadvertent intravascular injection of a portion of the olanzapine LAI dose.
Methods: Safety data were pooled from all completed and ongoing olanzapine LAI clinical trials through the last database lock in 2007 (cutoff date: 30 Sep 2007), and adverse event data through 31 May 2008 were also reviewed for occurrence of potential PDSS cases. Incidence of post-injection delirium/sedation was estimated by dividing number of events by number of injections or number of patients. Results. As of 31 May 2008, incidence of post-injection delirium/sedation syndrome following administration of olanzapine LAI was 0.07% per injection and 1.4% per patient. Affected patients presented with symptoms consistent with excessive systemic levels of olanzapine (e.g., sedation, dizziness, confusion, slurred speech, altered gait, weakness, muscle spasms, and/or unconsciousness). No clinically significant decreases in vital signs were observed. All patients recovered completely from signs and symptoms of post-injection delirium/sedation syndrome after 1.5 to 72 hours. Conclusion. The incidence of PDSS with olanzapine LAI was similar to a reported rate of a similar syndrome observed with intramuscular procaine penicillin G. Special precautions when using olanzapine LAI include proper injection technique and implementation of a post-injection observation period. Post-injection delirium/sedation signs and symptoms should be managed as medically appropriate. Research supported by Lilly.

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» NR1-012

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF FLEXIBLE-DOSE PALIPERIDONE ER IN THE TREATMENT OF PATIENTS WITH SCHIZOAFFECTIVE DISORDER

Carla Canuso M.D., Nina Schooler, Ph.D., Colette Kosik-Gonzalez, M.A., Jennifer Carothers, M.B.A., Sc.D., Ibrahim Turkoz, M.S., Jean-Pierre Lindenmayer, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant will be familiar with the clinical characteristics of patients with schizoaffective disorder and understand the role that paliperidone extended-release (ER) may play in treating the range of symptoms experienced by this patient population.

SUMMARY:

Background: Antipsychotics are the core treatment for schizoaffective disorder (SCA), but they have not been systematically studied either alone or in combination with other psychotropic agents. Data are from a trial of paliperidone extended-release (pali ER).
Methods: A 6-week, international, double-blind, placebo-controlled study enrolled SCA subjects with an acute exacerbation. Inclusion criteria: SCID-confirmed DSM-IV diagnosis of SCA; PANSS total score >=60; score >=4 on >=2 PANSS items: hostility, excitement, tension, uncooperativeness or poor impulse control and prominent mood symptoms (>=16 YMRS and/or HAM-D-21). Stably dosed antidepressants/mood stabilizers were permitted. Randomization was stratified by the use or absence of antidepressants/mood stabilizers. Subjects were randomized to 6 mg/day pali ER or placebo. Doses could be adjusted (3-12 mg/day) up to day 15. Endpoints: PANSS (primary), YMRS, HAM-D-21 and AEs. Study ID: CR013099.
Results: Subjects were randomized to pali ER (n=216) or placebo (n=95); 52.1% received antidepressants/mood stabilizers. Mean (SD) modal dose of pali ER: 8.6 (2.5) mg/day. Greater improvement was noted with pali ER vs placebo on mean [SE] PANSS total score (–22.3 [1.6] vs –13.0 [2.2]; P<0.001). This effect was consistent in both strata. In patients with prominent manic or depressive symptoms, pali ER showed improvement vs placebo on mean [SE] YMRS (–11.4 [1.1] vs –6.5 [1.4]; P=0.001) and HAM-D-21 (–11.7 [1.0] vs –7.6 [1.2]; P<0.001), respectively. Most common AEs (pali ER vs placebo): headache (15.0% vs 12.6%), akathisia (6.1% vs 1.1%), dizziness (8.4% vs 5.3%), insomnia (6.5% vs 5.3%) and dyspepsia (5.6% vs 5.3%).
Conclusion: This study demonstrated the efficacy and tolerability of pali ER in SCA. Pali ER improved the full range of psychotic and affective symptoms, and provided benefit as monotherapy and

in combination with antidepressants/mood stabilizers.
Supported by Ortho-McNeil Janssen Scientific Affairs, LLC

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» NR1-013

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF TWO DOSE RANGES OF PALIPERIDONE ER IN THE TREATMENT OF SUBJECTS WITH SCHIZOAFFECTIVE DISORDER

Jennifer Carothers, Carla M. Canuso, M.D.,Jean-Pierre Lindenmayer, M.D., Colette Kosik-Gonzalez, M.A., Ibrahim Turkoz, M.S., Nina Schooler, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the clinical characteristics of patients with schizoaffective disorder and understand the role that paliperidone extended-release (ER) may play in treating this understudied patient population.

SUMMARY:

Background: Although antipsychotics are widely used in patients with schizoaffective disorder (SCA), they have not been systematically studied in this population. Data are presented from a placebo-controlled trial of two dose ranges of paliperidone extended-release (ER) in patients with SCA.
Methods: A 6-week, international, double-blind, placebo-controlled study enrolled SCA subjects with an acute exacerbation. Inclusion criteria: SCID-confirmed DSM-IV diagnosis of SCA; PANSS total score >=60; score >=4 on two or more PANSS items: hostility, excitement, tension, uncooperativeness or poor impulse control and prominent mood symptoms (>=16 YMRS and/or HAM-D-21). Stably dosed antidepressants/mood stabilizers were permitted. Patients were randomized to placebo, paliperidone ER 6 mg/d (lower dose) or 12 mg/d (higher dose). Doses could be reduced to 3 mg/d and 9 mg/d in the two dose groups, respectively, with optional increases to initially assigned dose; no adjustments after day 15. Primary endpoint was PANSS total score change at endpoint. Study ID: CR010498.
Results: Subjects were randomized to 6 mg/d paliperidone ER (n=109), 12 mg/d paliperidone ER (n=100) or placebo (n=107). Mean (SD) modal daily doses in lower- and higher-dose groups were 5.7 (0.9) and 11.6 (1.0) mg/d, respectively. Mean [SE] PANSS total score significantly improved with higher dose vs placebo (LOCF: –32.4 [2.1] vs –24.1 [2.1]; P=0.003); change with lower dose (–27.7 [2.1]) was similar to placebo (P=0.187). These LOCF results were consistent with MMRM analyses (P=0.032 and P=0.286, respectively). Most common AEs were headache (placebo 16.8%, lower dose 13.9%, higher dose 13.3%) and tremor (3.7%, 12.0%, 11.2%, respectively).
Conclusion: This study demonstrated the efficacy, safety and effective dosing of paliperidone ER in patients with SCA. Improvement was consistently observed for higher-dose paliperidone ER vs placebo. Supported by Ortho-McNeil Janssen Scientific Affairs, LLC

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6-week, placebo-controlled studies. J Clin Psychiatry 2008; 69(5):817-829

» NR1-014

ANALYSIS OF NINE ARIPIPRAZOLE TRIALS TO EVALUATE STRATEGIES FOR SWITCHING PATIENTS WITH SCHIZOPHRENIA TO ARIPIPRAZOLE

Christina Cognata- Smith Pharm.D., Ross A Baker, Ph.D., M.B.A., Andrei Pikalov, M.D., Ph.D., Suja Mathew, B.S., Stephen Kaplita, M.S., William H Carson, M.D. Randall Owen, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to describe the different methods for switching patients with schizophrenia to aripiprazole.

SUMMARY:

Objective: Assess whether patients switched to aripiprazole more commonly experience exacerbation of psychosis compared with patients switched to other antipsychotic drugs or who remained on current treatment.
Methods: Nine studies including 4,687 patients with schizophrenia were identified for analysis. Studies were grouped by switch strategy - switch to aripiprazole with prior therapy control, adjunctive therapy with prior therapy control and switch to other antipsychotic medications as active control. The incidence and 95% CI were calculated for PRAEs within 28 days after starting aripiprazole therapy. The Medical Dictionary for Regulatory Activities (MeDRA) search terms related to positive symptoms were used to define PRAEs.
Results: In one study (Study 215) (1), cross-titration over 30 days was associated with a low incidence of PRAEs in the first 28 days of treatment: 6.9% (n=102, 95% CI: 2.8, 13.6). Higher rates were seen after abrupt 12.6% (n=103, 95% CI: 6.9, 20.6) and tapered titrations 18.3% (n=104, 95% CI: 11.4, 27.1). Another study (Study 169) showed comparably low rates of PRAEs for cross titrations 2% (n=200, 95% CI: 0.5, 5) and tapered titrations 1.5% (n=199, 95% CI: 0.3, 4.3). Similar rates of PRAEs were observed in three studies where patients remained on stable doses of prior antipsychotic therapy (Studies 122, 170 and 397). Rates of PRAEs in the two adjunctive aripiprazole studies were similar to rates in patients who remained on stable doses of prior therapy. Switch studies (087, 100, 152 and 034) with active control showed abrupt switches, resulting in somewhat higher rates of PRAEs.
Conclusion: Patients maintained on stable doses of antipsychotic therapy experience exacerbation of psychosis (2). Patients switched to aripiprazole do not more commonly experience exacerbation of psychosis, especially when using cross-titration methodology.

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2) Essock SM. Effectiveness of switching antipsychotic medications: Am J Psychiatry. 2006; 163:2090-2095

» NR1-015

TREATMENT EFFECTIVENESS IN SCHIZOPHRENIA & SCHIZOAFFECTIVE DISORDERS: PRELIMINARY VALIDATION OF THE PATIENT ASSESSMENT QUESTIONNAIRE (PAQ)

Lisa Cohen Ph.D., Ramin Mojtabai, M.D., Ph.D., Patricia Corey-Lisle, Ph.D., Edward Ip, Ph.D.,Sophia Haeri, B.A.,Sally Shumaker, Ph.D.

EDUCATIONAL OBJECTIVES:

By the conclusion of this presentation, participants will be able to distinguish between medication efficacy and effectiveness, and understand the preliminary psychometric properties of the Patient Assessment Questionnaire (PAQ).

SUMMARY:

Objectives: Recent multi-site comparative trials of antipsychotic

therapy effectiveness have failed to demonstrate meaningful differences in effectiveness between these treatments second-generation antipsychotic therapy as compared to older first-generation agents (1, 2). Understanding benefit of these therapies may be enhanced by assessing the patient's perspective of both the efficacy and tolerability of treatment in real-world use. The PAQ was developed to assess the subjective impact of treatment.
Methods: The PAQ was developed using accepted methods for new patient-reported outcomes, included review of literature, patient focus groups and expert panel review. The proposed PAQ items were tested using an Automated Computer Assisted Survey Instrument (ACASI) on psychiatric outpatients.
Results: Preliminary data gathered from 111 psychiatric outpatients (68 male, 43 female; Age range 24-69, Mean Age=45.5; Ethnicity: 37% African-American, 26% Latino, 23% Caucasian, 4% Asian, 10% Other) showed good internal reliability for the scale as a whole (initial Cronbach's alpha: .92). Initial factor analysis suggested two factors. Items were then examined individually, and 11 items that showed ceiling effects and/or factor loadings on either factor of <.4 were discarded (no items showed floor effects). Exploratory Factor Analysis (Varimax Rotation) was re-run, and two factors again emerged: Factor 1 (Eigenvalue 13.7, accounted for 30% of variance) is a nonspecific depression factor which may reflect general health-related quality of life. Factor 2 (Eigenvalue 3.1, accounted for 7% of variance) appears to capture information related to psychosis and side effects, and may reflect more illness-specific symptoms.
Conclusions The PAQ may prove to be a useful tool for assessing health-related quality of life and illness-specific symptoms in schizophrenia spectrum patients. Commercial Support was provided by Bristol-Meyers Squibb.

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» NR1-016

EARLY RESPONSE PREDICTS FUTURE TREATMENT SUCCESS DURING ARIPIPRAZOLE TREATMENT OF ADOLESCENTS WITH SCHIZOPHRENIA

Christoph Correll M.D., Robert D. McQuade, PhD, William H. Carson, MD, Margaretta Nyilas, MD, Robert A. Forbes, PhD, Taro Iwamoto, PhD, Ray Mankoski, MD, PhD, Suja J. Mathew, Andrei Pikalov, MD, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the predictive value of early response during aripiprazole treatment of adolescents with schizophrenia.

SUMMARY:

Purpose: To evaluate the predictive value of early response/early remission in adolescents with schizophrenia treated with aripiprazole (ARI) in a randomized, placebo-controlled trial.
Methods: Post-hoc analysis of data from a 6-week, randomized, double-blind, placebo-controlled trial of ARI (10 or 30 mg/day) in adolescents (13 -17 years) with schizophrenia. Early Improvement (EI) defined as =20% reduction from baseline in PANSS (Positive and Negative Syndrome Scale™) Total score as calculated at Week 2. Response defined as =20% reduction in PANSS Total at endpoint (Week 6, LOCF). Remission defined as <3 (mild or less) on 8 PANSS items at Week 6 (LOCF): delusions, conceptual disorganization, hallucinatory behaviour, unusual thought content, mannerisms/posturing, blunted affect, social withdrawal, lack of spontaneity/flow of conversation. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated, as was percent by week of PANSS Total reduction in all patients on ARI and on placebo.
Results: 294 patients were included in the analysis (ARI n=196; placebo n=98). For ARI patients, in predicting Response, EI at Week 2 demonstrated: sensitivity=48%, specificity=98%, PPV=98%, NPV=41%. For Remission, EI at Week 2 demonstrated: sensitivity=49%, specificity=89%, PPV=88%, NPV=52%. Corresponding placebo values (Response, Remission): sensitivity=30%, 32%; specificity= 85%, 82%; PPV=71%, 52%; NPV= 49%, 67%. For ARI patients, nearly 50% of the PANNS Total reduction was achieved by Week 2; up to 75% by week 3; a similar pattern was observed with placebo.
Conclusions: This is the first confirmation that, like in adults, the majority of response occurs early in adolescents with schizophrenia. Moreover, those who respond or remit early are likely to maintain that status at 6 weeks. Further analysis is warranted to better characterize patients with later onset response or remission.Support: Otsuka America Pharmaceutical, Inc.

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» NR1-017

CLINICAL AND FUNCTIONAL OUTCOMES IN SCHIZOPHRENIA AFTER INITIATION OF RISPERIDONE LONG-ACTING THERAPY: RESULTS FROM US, SPAIN, AUSTRALIA AND BELGIUM

Concetta Crivera, Pharm.D., M.P.H., Chris M. Kozma, Ph.D., An Jacobs, Riad G. Dirani, Ph.D., Kasem S. Akhras, Pharm.D., Lian Mao, Ph.D., Stephen C. Rodriguez, M.S., Wayne Macfadden, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to study clinical and functioning outcomes in patients with schizophrenia after initiation of risperidone long-acting therapy (RLAT) in four countries.

SUMMARY:

Introduction: Two 2-year prospective studies were conducted in patients with schizophrenia who were initiated on risperidone long-acting therapy (RLAT) by their health care providers. This analysis describes clinical and functioning outcomes in patients from the US who participated in the Schizophrenia Outcomes Utilization Relapse and Clinical Evaluation (SOURCE) study and from the multinational electronic Schizophrenia Treatment Adherence Registry (eSTAR) for Spain, Belgium and Australia.
Methods: Data were collected at baseline and at 3-month intervals up to 24 months for clinical effectiveness outcomes with the Clinical Global Impression of Illness Severity (CGI-S) and for patient functioning outcomes with the Global Assessment of Functioning (GAF). Patient characteristics and clinical and functional outcomes were evaluated by country. Paired t tests were used to test if post-baseline values were significantly different from the baseline value.
Results: The numbers of patients enrolled in each country were 532 (US), 1345 (Spain), 784 (Australia), and 408 (Belgium). Baseline CGI-S scores ranged from 4.4 to 4.6 and baseline GAF scores ranged from 42.9 to 47.3, indicating that patients were moderately to markedly ill with moderate-to-severe impairment of function. Significant improvement in both measures compared with baseline were observed within each country (P<0.001 at all post-baseline visits). Patients completing the 2-year studies showed approximately a 1-point reduction in CGI-S and approximately 15 points of improvement in GAF.

Conclusion: Significant improvements in clinical and functional outcomes in patients with schizophrenia over 24 months after the initiation of RLAT were seen across countries in these 2-year, prospective, observational studies. Supported by Ortho-McNeil Janssen Scientific Affairs, LLC

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» NR1-018

INITIATION OF RISPERIDONE LONG-ACTING THERAPY IN PATIENTS WITH SCHIZOPHRENIA IN THE VA: EFFECTS OF COMORBID CONDITIONS ON HEALTH CARE UTILIZATION

Concetta Crivera Pharm.D.,Xinhua S. Ren, Ph.D. M.P.H.,Mirko Sikirica, Pharm.D.,Wayne Macfadden, M.D.,Riad Dirani, Ph.D.,Shirley Qian, M.S., Lewis E. Kazis, Sc.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the effects of risperidone long-acting therapy (RLAT) on health care utilization in patients with schizophrenia with varying numbers of comorbid medical and psychiatric conditions.

SUMMARY:

Objective: To assess health care utilization following initiation of RLAT in schizophrenia patients with comorbid conditions in the Veterans Health Administration (VA).
Methods: The study identified all VA patients with schizophrenia who initiated RLAT between 10/1/2005 and 9/30/2006 and had at least four (total) injections. Paired t tests for means/proportions were used within each comorbidiity frequency category to compare changes in health services use between 12 months prior to and 12 months post initiation of RLAT.
Results: Among 924 patients who met the study criteria, 10.3% (N=95) had zero, 28.9% (N=267) had 1-2, 29.1% (N=269) had 3-4, and 31.7% (N=293) had 5 or more comorbid medical and/or psychiatric conditions. The mean injection interval between RLAT treatments was 14 days across all comorbid frequency categories. Between the pre- and post-RLAT initiation periods, the mean number of psychiatric hospitalizations and length of stay decreased across all patients and within each comorbid frequency category whereas the mean number of psychiatric-related outpatient visits increased. These differences were statistically significant in patients with 3-4 or 5+ comorbid conditions.
Conclusion: Patients with schizophrenia in the VA system with varying numbers of comorbid conditions had a decrease in number and length of psychiatric hospitalizations, and an increase in psychiatric-related outpatient visits after the initiation of RLAT.
Supported by funding from Ortho-McNeil Janssen Scientific Affairs, LLC and Center for the Assessment of Pharmaceutical Practices, Boston University School of Public Health, Center for Health Quality, Outcomes, and Economic Research, Veterans Health Administration was the research entity.

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» NR1-019

EFFECT OF NICOTINE REPLACEMENT ON AGITATION AND AGGRESSION IN SMOKERS WITH SCHIZOPHRENIA: A DOUBLE BLIND, RANDOMIZED PLACEBO CONTROLLED PILOT STUDY

Cristian Damsa, M. D., Coralie Lazignac, M.D., Eric Adam, MSc., Salvatore Virgillito MSc., Michael H. Allen, M. D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the potential benefits of nicotine replacement for alleviating agitation in smokers with schizophrenia confined in nonsmoking environments.

SUMMARY:

Background: Despite high rates of tobacco use among patients with schizophrenia, little is known about their reaction to nicotine withdrawal, especially during emergency care. Studies suggest that smoking bans may increase aggressive behaviors and that nicotine replacement may help alleviate this. This study was designed to test if nicotine reduces agitation and aggression in a susceptible population of smokers with schizophrenia.
Methods: The study population consisted of patients admitted to a Psychiatric Emergency Unit with a diagnosis of schizophrenia (DSM IV). The hospital is “smoke free” so nicotine abstinence was routine and monitored by staff. Patients were assessed with the PANSS-Excited Component (PEC), Agitated Behavior Scale, Overt Aggression Scale and the Fagerstrom Test for Nicotine Dependence. Subjects with a score less than 14 on the PEC, or a Fagerstrom Test score less than 6 were excluded. The subjects were randomized into nicotine replacement and placebo groups. The nicotine group received a 21 mg/day transdermal patch. Subjects were reassessed at 4 hours and 24 hours after placement of the nicotine or placebo patch.
Results: Placebo and nicotine groups did not differ significantly in age, sex, nicotine dependence and initial agitation levels (Student t-test). Patients receiving nicotine had significantly lower levels of agitation according to the PEC (p=0.00052) after 4 hours of treatment than those receiving placebo. This difference persisted after 24 hours of observation (p=0.03015).
Discussion: This study suggests that, although patients may have no intention to quit smoking and may not request nicotine replacement, nicotine reduces agitation in smokers with schizophrenia. Larger studies should determine the prevalence and contribution of nicotine withdrawal in these settings and confirm the benefits of nicotine replacement. It is possible that treatment for nicotine withdrawal may help avoid physical and chemical restraint in some cases.

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» NR1-020

DOSE SELECTION OF ASENAPINE: APPLICATION OF MATHEMATICAL MODELS BASED ON D2 RECEPTOR OCCUPANCY

Rik DeGreef, Alan Maloney, Per Olsson-Gisleskog, Klaas Prins, Joep Schoemaker, John Panagides

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: Describe the development of mathematical models across a series of antipsychotics that describe the relationships between pharma-

cokinetics, D2 receptor occupancy and efficacy or the occurrence of extrapyramidal symptoms.
Describe how these models were used to predict an effective and well-tolerated dosing regimen for asenapine in patients with schizophrenia.

SUMMARY:

Objective: Asenapine is being developed for schizophrenia and bipolar disorder. We report on the development and application of mathematical models, based on dopamine D2 receptor occupancy, that were employed in dose selection for Phase III studies of asenapine in schizophrenia.
Methods: Clinical data for antipsychotic drugs were collected from public sources; in-house data were used for asenapine. D2 occupancy data originated from published positron emission tomography (PET) studies that included blood sampling for pharmacokinetics. Clinical efficacy data (group mean change in Positive and Negative Syndrome Scale [PANSS] total score) were taken from placebo-controlled trials (4–8 weeks); when evaluating extrapyramidal symptoms (EPS), measured using the Simpson-Angus Scale (SAS), additional non–placebo-controlled trials were included. A generally applicable model connecting antipsychotic dose, pharmacokinetics, D2 occupancy, PANSS response, and SAS response was developed and used to simulate the effects of asenapine at doses of 5–20 mg BID.
Results: Initial simulations indicated that clinically relevant decreases in PANSS total score (>/=8 points vs placebo) occurred with asenapine dosages of 5 mg BID and higher. This prediction was confirmed in clinical trials, demonstrating significant efficacy vs placebo with 5 mg BID, but not at lower doses. The final model simulations, updated with the newly obtained data on asenapine, indicated that 5–10 mg BID would result in a mean PANSS decrease vs placebo of 8–10 points and a mean SAS response vs placebo of <0.2 points.
Conclusion: The results from simulations using this model framework based on D2 occupancy indicate that asenapine 5–10 mg BID provides antipsychotic efficacy with limited risk of EPS. This dose range has been tested in Phase III clinical trials in which the safety and efficacy of asenapine in schizophrenia was established.
This research was supported by Schering-Plough.

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» NR1-021

VALIDATION OF A LONG-TERM SURVEILLANCE TOOL FOR USE BY PSYCHIATRIC NURSES EVALUATING PATIENTS SUFFERING FROM A PSYCHOSIS, PARTICULARLY SCHIZOPHRENIA

Antonio Delgado, Yves Lecrubier

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that – since relapses in schizophrenic patients should be detected as early as possible - the nurse/patient relationship established during regular contacts for long-acting injectable treatment may play a crucial role in detecting relapses, and the 4D Questionnaire seems to be a relevant tool to detect prodromes of relapses and forewarn the psychiatrist.

SUMMARY:

Introduction:The main reasons for relapses in schizophrenia are well known. Nevertheless, despite of the use of injectable antipsychotics, relapses occur and should be detected ideally as early as possible. The regular contacts between patient and care team for injectable treatments facilitate the long-term surveillance and the detection of prodromes of relapse.
Objective: The objective of this study was to validate a standardized questionnaire for the long-term surveillance of psychotic patients for use by nurses, as well as to measure its agreement with the clinical evaluation by psychiatrists.
Results: This was an open, non-comparative 12-week study in 902 patients. The inclusion criteria were diagnosis of schizophrenia, follow-up at least 6 months, stable for at least 4 weeks, and treated with risperidone long-acting injectable (RLAI).
Assessment of the patients was carried out by nurses (Questionnaire 4D: Delusions, Disorganization, Deficit, Depression) and by psychiatrists (BPRS, CGI-Severity and –Improvement) at baseline, 6 and 12 weeks. The medical ratings were: no change, insignificant change, prodrome of relapse or relapse. The nurse-rated items were: psychiatrist consultation not necessary, optional, justified or required.Overall agreement in the ratings of the necessity for a consultation (not always related to a relapse) for the 3 evaluations was 28%. However, nurse and psychiatrist agreement was 72.9% regarding Improvement of Clinical Global Impression. The diagnosis of relapse expressed by the physicians corresponded to the observations of the nurses with a sensitivity of 60% and a specificity of 86%.
Conclusion: The nurse/patient relationship established during regular contacts for long-acting injectable treatment may play a crucial role in detecting relapses. The 4D Questionnaire seems to be a relevant early warning tool for psychiatrists to spot prodromes.Supported by Janssen Cilag France

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» NR1-022

IMPAIRMENT IN VERBAL FLUENCY IN SCHIZOPHRENIA: A PREFRONTAL DEFICIT?

Ofelia Delgado Ph.D., Antonieta Nieto, Ph.D., Dr. José Barroso, Ph.D., Daniel Ferreira, Ph.D., Josefa Ramos, Ph.D., Mercedes de la Varga, M.D., Fernández, Silvia, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the diversity of verbal fluency tasks and their potential use for neuropsychological assessment in schizophrenia. In addition, participants should be able to estimate the impairment on phonetic and semantic fluency and its association with the schizophrenic symptoms.

SUMMARY:

Introduction: Prefrontal functions have been reported to be impaired in patients with schizophrenia. Verbal fluency tasks are amongst the most widely used for prefrontal dysfunction assessment. Performance on verbal fluency has been found to be diminished in schizophrenia, but the interpretation of this alteration is still controversial. Recent functional imaging studies suggest that semantic and phonemic fluency are related to relatively different neural system with phonemic fluency (PF) specially linked to prefrontal system and semantic fluency (SF) more dependent of temporal regions. We studied whether patients with schizophrenia show a differential impairment on fluency tasks and the association of performance with clinical symptoms.
Methods: 25 patients diagnosed with schizophrenia (CIE-10/OMS), age range 26-55, were assessed with Phonemic (FAS) and Semantic (animals) fluency tasks. MMSE was used to examine general cognitive state. Positive and Negative Syndrome Scale (PANSS) was used for symptoms evaluation.

Results: 32% of patients show a poor performance on PF, whereas SF is altered in 80% of patients. Performance is not related with MMSE scores. We found a negative correlation between PF performance and the severity of "emotional withdrawal", "poor rapport", "lack of spontaneity" and a positive correlation with "unusual thought content". SF correlates negatively with "conceptual disorganization" and "difficulty in abstract thinking". Both fluency tasks correlate negatively with "lack of judgment and insight".
Conclusions: Impairment in verbal fluency in schizophrenic patients is not a homogeneous deficit: Semantic fluency is disproportionately affected. Phonemic Fluency performance is mainly associated with negative symptoms whereas Semantic Fluency is related to disorganization. Our results suggest that verbal fluency impairment in schizophrenia may not only reflect a prefrontal deficit but, specially, a temporal lobe deficit.

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» NR1-023

COMPARISON OF OLANZAPINE LONG-ACTING INJECTION SWITCHING METHODS: AN 8-MONTH ANALYSIS OF PATIENTS WITH SCHIZOPHRENIA AT RISK OF RELAPSE

Holland Detke Ph.D., Fangyi Zhao, Ph.D., Scott W. Andersen, M.S.,Susan B. Watson, Ph.D., David P. McDonnell, M.B., M.R.C.Psych.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe any differences in efficacy or safety/tolerability parameters for patients who are switched directly to olanzapine LAI versus those who simultaneously tapered off their previous medication.

SUMMARY:

OBJECTIVE: To compare the safety and efficacy of direct switch versus taper of previous antipsychotic medication when changing to olanzapine long-acting injection (LAI). Analyses were based on 8-month data from an ongoing 2-year open-label study of olanzapine LAI in adults with schizophrenia. METHODS: Outpatients considered at risk for relapse (N=264) received olanzapine LAI every 4 weeks with a starting dose of 405 mg and flexible dosing thereafter. Investigators, at their discretion, could either directly switch patients or taper their previous antipsychotic medication during the first 2 weeks of treatment.
RESULTS: At time of study entry, 62 patients were receiving typical antipsychotics, 188 were receiving atypical antipsychotics (76 receiving oral olanzapine), and 34 were not receiving any antipsychotic; a total of 16 were on injectable antipsychotic medication. Some patients were taking more than one antipsychotic at baseline. Of 264 total patients, 150 (56.8%) were switched directly and the rest were tapered. The 2 groups did not significantly differ in discontinuation rate (direct: 29.3%, taper: 28.9%, p~1.0) and there was no significant difference between the groups on PANSS total score mean change at any visit up to 8 months (direct: -1.5, taper: -3.4, p=.785, from a mean baseline of 56.7 [SD=9.8]).
Treatment-emergent adverse events in >=5% of patients were: increased weight (10.2%), insomnia (8.3%), anxiety (6.8%), somnolence (6.8%), and increased appetite (5.7%). The switch groups did not significantly differ in mean weight change (p=.419), with an average weight gain of 2.0 kg, nor did they significantly differ in terms of laboratory analytes or other safety parameters.
CONCLUSIONS: Based on this 8-month analysis of efficacy and tolerability/safety data, there did not appear to be clinically significant differences for those who were directly switched to olanzapine LAI versus those who were tapered.
Research supported by Eli Lilly and Company.

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» NR1-024

ASENAPINE PHARMACOKINETICS: INFLUENCE OF CYTOCHROME P450 MODULATORS AND UDP-GLUCURONYLTRANSFERASE INHIBITION

Peter Dogterom, Ellen Hulskotte, Mireille Gerrits,Cees Timmer, Ad Sitsen, Rik de Greef, Edwin Spaans, Pierre Peeters

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: Describe the effects of interaction with cytochrome P450 modulators and a UDP-glucuronyltransferase inhibitor on the pharmacokinetics of asenapine.Discuss the clinical consequences of pharmacokinetic interactions between asenapine and various drugs commonly used in psychiatry.

SUMMARY:

Introduction: Asenapine is a novel psychopharmacologic agent in development for the treatment of bipolar disorder and schizophrenia. We assessed the pharmacokinetic interactions between asenapine and several commonly used drugs that are substrates, inhibitors, or inducers of CYP450 isoenzymes, and one UDP-glucuronyltransferase (UGT) inhibitor.
Methods: In separate studies, healthy volunteers took single sublingual doses of asenapine 5 mg before and at steady-state exposure to cimetidine (a nonspecific CYP450 inhibitor), fluvoxamine (CYP1A2 inhibitor), paroxetine (CYP2D6 inhibitor and substrate), carbamazepine (CYP3A4 inducer), or valproate (UGT inhibitor). In another study, single sublingual doses of asenapine 5 mg and single oral doses of the CYP2D6 substrate imipramine 75 mg were given separately and simultaneously. Exposure to asenapine, paroxetine, and imipramine and its metabolite desipramide was assessed.
Results: Asenapine exposure was minimally affected by interactions with standard CYP450 modulators (Table); the greatest increase (29%) was due to CYP1A2 inhibition with fluvoxamine. UGT inhibition by valproate did not affect asenapine pharmacokinetics. Regarding CYP2D6 involvement, asenapine coadministration approximately doubled single-dose paroxetine concentrations but did not alter exposure to imipramine or desipramine.
Effects of Pharmacokinetic Interactions on Asenapine Exposure

Asenapine	Cmax	AUC0–inf
Modulator		
Cimetidine	–13%	1%
Fluvoxamine	13%	29%
Paroxetine	–13%	–9%
Carbamazepine	–16%	–16%
Imipramine	17%	10%
Valproate	2%	–1%

Conclusions: Except for coadministration with fluvoxamine, for which a decrease in asenapine dose may be considered, no dose adjustment of asenapine is routinely needed when coadministered with the agents tested. Some caution is advised when coadministering asenapine with drugs that are predominantly metabolized by CYP2D6. Research supported by Schering-Plough.

REFERENCES:

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» NR1-025

IMPACT OF MARIJUANA USE ON SYMPTOM SEVERITY AND OUTCOME IN FIRST EPISODE PSYCHOSIS

Kia Faridi M.D., Ashok K. Malla, M.B.B.S., FRCPC(C)

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the frequency of marijuana use among patients with a first episode of psychosis and describe the impact of baseline use and persistant use on psychotic symptoms.

SUMMARY:

Marijuana use is a frequent co-morbidity among people with a first episode of psychosis (FEP), and some reports have shown more severe symptoms or worse outcome among marijuana-using FEP patients. The objective of this study was to examine the impact of marijuana use at baseline on the severity of psychotic symptoms and outcome over the first year of treatment, and to examine whether symptom severity differed between those patients who continued to use marijuana and those who ceased using over the course of treatment. The study was conducted at PEPP-Montreal, a specialized integrated treatment service for all incident FEP cases within a defined area. Subjects were 192 consecutive admissions, age 14 to 30, suffering from at least one week of psychotic symptoms meeting DSM-IV criteria and with no past antipsychotic treatment. Diagnoses, including co-morbid substance use disorders, were determined using the SCID-IV administered shortly after admission and again at one year. Symptoms were evaluated at Baseline and Months 3, 6, 9, and 12 by the Positive and Negative Symptom Scale (PANSS), and PANSS scores were analyzed by repeated measures ANOVA. 62 subjects (33.3%) had a current cannabis use disorder at baseline. There was no difference in positive, negative, or general symptom severity over the first 12 months of treatment between users and non-users. Likewise, there was no difference in time to remission nor in likelihood of relapse in 12 months, but there was a trend towards THC users suffering from more continuous illness compared with non-users (60.8% vs 44.6%, chi=3.57, p=0.059). 20 of 48 marijuana users (41.7%) ceased consumption during the first year in treatment. These subjects did not differ in symptom severity, time to remission, or relapse compared to persistent marijuana users over the first 12 months.

REFERENCES:

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» NR1-026

THE COMPARATIVE EFFICACY OF ILOPERIDONE AND HALOPERIDOL ACROSS FOUR SHORT-TERM CONTROLLED TRIALS

John Feeney M.D., Curt Wolfgang, Ph.D., Mihael Polymeropoulos, M.D., Paolo Baroldi, M.D., Ph.D., Jennifer Hamilton, M.S.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: 1)Recognize the elements of trial design that make estimating effect size and relative effect size difficult;
2)Recognize that the differences in dropout rates between short-term placebo-controlled trials (PCTs) and active-control trials (ACTs), previously reported in the literature, will contribute to these difficulties; and 3)Become familiar with the data bearing on the comparative efficacy of iloperidone and haloperidol.

SUMMARY:

Objective: The performance of iloperidone, a new atypical antipsychotic, relative to haloperidol in the treatment of schizophrenia was examined across 4 short-term controlled trials.
Methods: Placebo-controlled trials (PCTs) conducted to support registration often include a positive control as an internal measure of assay sensitivity. In a 6-week PCT conducted with iloperidone, haloperidol served as the positive control. Because the validity and reliability of active comparisons in PCTs has been questioned, other sources of comparative data were also examined. Three active-controlled trials (ACTs) were conducted comparing iloperidone and haloperidol. While data from these trials were intended to be pooled and formally compared to show non-inferiority with long-term treatment, the short-term (6 week) data from these 3 trials provide another source of information bearing on the relative short-term efficacy.
Results: In the PCT, the change from baseline on the PANSS-T differed by 4 points between the iloperidone group and the haloperidol group (intent-to-treat, last-observation-carried-forward (LOCF) analysis). In all 3 ACTs, the effect sizes were numerically similar for iloperidone (mean dose 12 mg/day) and haloperidol (mean dose 12 mg/day), with differences of 0.4, 0.7, and 1.7 points. The dropout rate in the PCT (63%) was twice that observed in each of the 3 ACTs (14-29%). This difference in retention rates between short-term PCTs and ACTs in schizophrenia/schizoaffective patients has been previously observed. Conclusions: Because higher dropout rates force more assumptions about missing data in LOCF analyses, lower dropout rates in the ACTs may allow for a more valid and reliable comparison between drugs. In these perhaps more reproducible and clinically meaningful comparisons, similar effect sizes were observed for iloperidone 12 mg/day and haloperidol 12 mg/day in the treatment of the symptoms of schizophrenia. Vanda Pharmaceuticals sponsored this analysis.

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2) Lieberman JA, Stroup TS, McEvoy JP, et al. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med 2005; 353:1209-1223

» NR1-027

OPTIMIZATION OF DOSING STRATEGY FOR PALIPERIDONE PALMITATE IN SCHIZOPHRENIA: RESULTS OF DOUBLE-BLIND STUDIES AND POPULATION PHARMACOKINETIC SIMULATIONS

W. Wolfgang Fleischhacker M.D., Srihari Gopal, M.D., M.H.S., Mahesh N. Samtani, Ph.D., Jorge A. Quiroz, M.D., Gahan Pandina, Ph.D., An Vermeulen, Ph.D., Virginie Herben, Ph.D., Cristiana Gassmann-Mayer, Ph.D., Pilar Lim, Ph.D., Vivek Kusumakar, M.D., Joseph Palumbo, M.D.

EDUCATIONAL OBJECTIVES:

The reader will learn that paliperidone palmitate (PP), a new investigational long-acting psychotropic, is initiated with a deltoid 150mg eq. dose delivered intramuscularly (IM). When administered with a needle length optimized to assure IM delivery, PP will rapidly achieve plasma levels within its therapeutic range. Subsequent once-monthly IM dosing (deltoid or gluteal) maintains a clinically and statistically significant response across the full range of tested doses (25–150mg eq).

SUMMARY:
Aim: Establish an optimized dose-initiation strategy for paliperidone palmitate (PP) using schizophrenia clinical studies and population (pop) PK simulation.
Methods: Trial A (53wk DB): pts with acute exacerbation of schizophrenia randomized to (1) flexibly dosed risperidone LAI (25, 37.5 or 50mg)+oral risperidone supplementation (RLAI+RIS; placebo [PB] injection Day1, 25mg RLAI [Day8, 22], followed by flexibly dosed RLAI injection); or (2) PP arm (initial 50mg eq. gluteal dose on Days1 and 8, plus oral PB, followed by flexibly dosed gluteal PP (25, 50, 75 or 100mg eq.) every 4wks, and PB IM every other 2wks to correspond to matched RLAI dosing. Pop PK: a nonlinear mixed-effects model using pooled data was developed and simulations conducted. Trial B (13wk DB): pts with acute exacerbation of schizophrenia randomized to (1) PP25, 100 or 150mg eq. intramuscular (IM; Day1 PP150mg eq. IM deltoid muscle, then fixed IM dose of PP in deltoid or gluteal from Day8 and then every 4wks); or (2) PB IM on Day1 onwards.
Results: Trial A (n=570): PP50 gluteal injection resulted in lower plasma levels in 8-day initiation vs active moiety conc for RLAI+RIS. PP+PB and RLAI+RIS improved mean change PANSS score, but RLAI+RIS vs PP+PB noninferiority was not met (by 0.84 points; primary endpoint). Rates of AEs were similar for both groups. Pop PK: deltoid injection with higher dose of PP (150mg eq.) on Day1 and optimized needle length resulted in faster initial release. Trial B (ITT=636): differences observed in mean change±SD PANSS score, PP25=–8±19.9; PP100=–12±17.6; PP150=–13±18.5 vs PB=–3±19.3 ($p<0.04$), thus validating PK modeling. Safety was similar to earlier studies.
Discussion: Initiated as 150mg eq. IM deltoid injection, with optimized needle length, PP rapidly achieved plasma conc associated with effective symptom control. Subsequent monthly dosing (deltoid or gluteal) maintained clinically and statistically effective response across 25–150mg eq. Funded by J&J PRD.

REFERENCES:

1) Meltzer HY, Bobo WV, Nuamah IF, Lane R, Hough D, Kramer M, Eerdekens M: Efficacy and tolerability of oral paliperidone extended-release tablets in the treatment of acute schizophrenia: pooled data from three 6-wk, placebo-controlled studies. J Clin Psychiatry 2008; 69(5):817-829.

2) Kramer M, Simpson G, Maciulis V, Kushner S, Vijapurkar U, Lim P, Eerdekens M: Paliperidone extended-release tablets for prevention of symptom recurrence in patients with schizophrenia: a randomized, double-blind, placebo-controlled study. J Clin Psychopharmacol 2007; 27(1):6-14.

» NR1-028

THOUGHT DISORDER – A NEW PERSPECTIVE

Cherrie Galletly Ph.D., Jonathan Crichton, B.A, M.A., Ph.D.

EDUCATIONAL OBJECTIVES:
The established literature tends to regard thought disordered persons as incapable of meaningful communication. This poster offers a new perspective on thought disorder. After reading this poster, the participant will be aware of the interactional achievements of many people with thought disorder. The participant will also have an appreciation of the skills utilised by psychiatrists when they talk with people with thought disorder.

SUMMARY:
This paper examines the discursive construction of people with thought disorder – a common symptom in psychotic illnesses such as schizophrenia. The paper draws on an ongoing interdisciplinary collaboration between an applied linguist and a psychiatrist which explores the language used by people with severe thought disorder in interactions with their psychiatrists.
The research and clinical literature on thought disorder constructs the thought disordered person as incapable of meaningful social interaction. This is a model that views thought disorder exclusively as a brain dysfunction which is evidenced by dysfunctions in speech (Docherty 2005, McKenna & Oh 2005). We argue that this model draws attention away from 1) what thought disordered people can actually accomplish in interaction, and 2) how thought disordered people and their psychiatrists routinely communicate on matters consequential for treatment.
The study seeks to address this "discourse of deficit" by investigating the interactional accomplishments of thought disordered people in clinical interviews. Informed by the work of Goffman and Grice, the paper explores and takes issue with the deficit construction using examples of analysed data.

REFERENCES:

1) Docherty N. M.(2005). Cognitive impairments and disordered speech in schizophrenia: Thought disorder, disorganization, and communication failure perspectives. J Abnorm Psychol. 2005 May; 114(2):269-78.

2) McKenna, P. J. & Oh, T. M. (2005). Schizophrenic Speech: Making Sense of Bathroots and Ponds that Fall in Doorways. Cambridge: Cambridge University Press.

» NR1-029

CONVICTION AND DOUBT IN DELUSIONS

Icelini Garcia-Sosa M.D., Michael Garrett, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to 1)Recognize approaches to assess conviction and doubt in patients with delusions, 2)Identify possible areas of treatment interventions 3)Discuss the implications of doubt and conviction in multiple dimensions of psychosis.

SUMMARY:
Delusions have traditionally been regarded as fixed, false beliefs, held with absolute conviction and not amenable to reason. However, research has shown that delusions are multidimensional, varying independently in measures of conviction, preoccupation, distress and relation to action. The objective of this study is to further understand conviction and doubt in the presence of delusions, and to elucidate the main reasons why patients doubt them. It was hypothesized that some degree of doubt is held in delusional belief and its formation, it is elicited with some ease using this specific approach and that doubt may be correlated with other dimensions of psychosis.
Method: A cross-sectional investigation was conducted on 25 individuals with delusions. A detailed assessment using an open interview and standardized instruments to measure conviction and doubt as well as psychotic illness severity.
Results: Most patients (23/25) had Reasons for Doubt (RFD). The degree of conviction was evenly distributed in 3 groups, absolute, high and medium-low conviction. The most common RFD was a family member, significant other or doctor kindling doubt. Less doubt has a trend to correlate with higher scores in negative symptoms.
Conclusions: Individuals with delusions commonly experience some pre-existing doubt or continue to doubt them. There are implications for cognitive interventions for psychosis.

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2) Douglas Turkington, David Kingdon, and Peter j. Weiden Cognitive Behavior Therapy for Schizophrenia Am J Psychiatry, Mar 2006; 163:365-373

» NR1-030

SWITCHING FROM RISPERIDONE TO PALIPERIDONE ER IN STABLE BUT SYMPTOMATIC OUTPATIENTS WITH SCHIZOPHRENIA – INTERIM ANALYSIS

Wagner Gattaz M.D., Marcio Versiani, Ph.D., Rodrigo A. Bressan, Ph.D.,

Sandra Ruschel, Ph.D., Mário Louzã, Ph.D., Elaine Henna, M.D., Acioly L. T. Lacerda, Ph.D., Fábio Rocha, Ph.D., Irismar R. Oliveira, Ph.D., Ernindo Sacomani, Ph.D., Hamilton M. Grabowski, Ph.D., Hélio Elkis, Ph.D., João A. Campos, M.D., João Quevedo, Ph.D., André Brasil, Ph.D., José C.B. Appolinário, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the results of the switching from risperidone to paliperidone ER.

SUMMARY:

Objectives: To explore the effectiveness of flexible doses of paliperidone ER in subjects with schizophrenia who presented an insufficient response to a previous treatment with risperidone, as measured by the Positive and Negative Syndrome Scale (PANSS) scores.

Methods: This is a 2-month interim analysis of a non-randomized, multicenter, single arm, open label study. Subjects were directly switched from their previous risperidone regimen to a paliperidone ER dose range of 3 to 12 mg/day. Patients were assessed with: Positive and Negative Syndrome Scale (PANSS), Short Form 36-item Health Survey (SF-36), Pittsburgh Sleep Quality Index (PSQI), Personal and Social Performance (PSP), Clinical Global Impression (CGI), Extrapyramidal Symptom Rating Scale (ESRS) and patient' satisfaction. Tolerability was also assessed with adverse events report. In the present analysis efficacy was based on the PANSS scores.

Results: Forty one patients were included in this interim analysis. The switch occurred immediately for all subjects due to lack of effectiveness of previous treatment. Statistically significant improvements at endpoint were seen in PANSS total score (-15.3, p< 0.0001) and in positive, negative and the general psychopathology subscales scores. There were a better patient' satisfaction with the antipsychotic treatment at 2-month of study when compared to Visit 1 (p= 0.0065). Gastrointestinal disorders (10.6%), weight gain (8.5%), and anxiety (10.6%) were the most frequently reported adverse events.

Conclusions: The switch from risperidone to paliperidone ER in stable but symptomatic outpatients with schizophrenia was associated with a significant reduction of the severity of symptoms, as observed in PANSS scores, as well as a better patients' satisfaction to their treatment. Paliperidone ER was also well-tolerated.This study was supported by Janssen-Cilag Brazil.

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1) Marino J, Caballero J. Paliperidone extended-release for the treatment of schizophrenia. Pharmacotherapy. 2008;28(10):1283-98.

2) Canuso CM, Youssef EA, Bossie CA, Turkoz I, Schreiner A, Simpson GM. Paliperidone extended-release tablets in schizophrenia patients previously treated with risperidone. Int Clin Psychopharmacol. 2008;23(4):209-15.

» NR1-031

LONG-TERM EFFICACY, SAFETY AND TOLERABILITY OF PALIPERIDONE PALMITATE IN PATIENTS WITH SCHIZOPHRENIA

Sri Gopal M.D., Ujjwala Vijapurkar, Ph.D., Pilar Lim, Ph.D., Margarita Morozova, M.D., Ph.D., Mariëlle Eerdekens, M.D., M.B.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the efficacy and tolerability of the investigational, injectable atypical antipsychotic paliperidone palmitate during long-term treatment of patients with schizophrenia.

SUMMARY:

Introduction: Efficacy and safety results from a long-term 52-week open-label (OL) extension study of paliperidone palmitate (PP) are presented. Methods: Patients who either successfully completed the randomized placebo-controlled recurrence prevention (RP) part of the preceding phase (median duration 105 and 171 days in the placebo and PP groups, respectively) or who were in the transition/maintenance phase of the trial when the RP phase was terminated, but had received more than 1 dose of PP, could enter the OL 52-week flexible-dose phase.

Results: 388 patients were included in the 52-week OL phase; mean duration was 303 days and 73% of patients received 12 PP injections. Mode dose of PP was 100mg for 56%, 50mg for 34%, 75mg for 9% and 25mg for 1% of patients during the OL phase. During the OL phase, maintenance of previous symptom (PANSS total score) and functional (Personal and Social Performance scale score) improvement on PP treatment were observed. Patients previously treated with PB in the RP phase demonstrated symptom improvement (–8.4±19.43 change from OL baseline to end point) and improvement in function (6.0±13.20 change from OL baseline to end point). During the OL phase, the most frequent (>=5%) AEs were insomnia (7%) and schizophrenia, nasopharyngitis, headache and weight increase (6% each). Serious AEs (mainly schizophrenia related) were reported at 6%. Weight change during the OL was 0.9±4.3kg (total PP group). The low incidence of EPS-related AEs (comparable with placebo in the RP phase) continued in the OL phase. Local injection site tolerability was good.

Discussion: Once-monthly (once every 4-wks) PP was effective and well tolerated with schizophrenia patients demonstrating maintenance of symptom improvements during the long term. Funded by J&J PRD.

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» NR1-032

MEDICATION SATISFACTION IN SUBJECTS WITH SCHIZOPHRENIA TREATED WITH PALIPERIDONE ER AFTER SUBOPTIMAL RESPONSE TO ORAL RISPERIDONE

Augusto Grinspan M.D., Carla M. Canuso, M.D., Ursula Merriman, B.S., C.V. Damaraju, Ph.D., Larry Alphs, M.D., Ph.D., Amir Kalali, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant will be aware of changes in medication satisfaction in patients with schizophrenia when an antipsychotic is changed due to a suboptimal response.

SUMMARY:

Background: Patient satisfaction with medication may be related to efficacy and long-term adherence in schizophrenia. This study evaluated medication satisfaction after treatment with paliperidone ER in subjects with a current suboptimal response to oral risperidone.

Methods: A 6-week international study. Inclusion criteria: schizophrenia per DSM-IV, treated with oral risperidone (4 or 6 mg/day) at least 4 weeks prior to entry, PANSS score >=4 on >=3 items (tension, unusual thought content, delusions, hallucinatory behavior, excitement, grandiosity or suspiciousness/persecution) and dissatisfaction with current medication (Treatment Satisfaction Questionnaire for Medication =3). Subjects randomized (1:1) in a blinded fashion to paliperidone ER 6 mg (optional increase to 12 mg) either immediately (6 weeks total) or delayed (continued risperidone for 2 weeks followed by paliperidone ER for 4 weeks). Primary endpoint for the overall group: change in Medication Satisfaction Questionnaire (MSQ) (1=extremely dissatisfied to 7=extremely satisfied) at week 6 endpoint (LOCF).

Study ID: CR014347.
Results: For the overall group, mean (SD) MSQ score improved significantly from 2.7 (0.8) at baseline to 5.1 (1.2) at endpoint (P<0.001). 82.7% of subjects were satisfied with their medication at endpoint vs 3.7% at baseline. Mean (SD) PANSS total score improved from baseline to endpoint (–12.9 [13.1]; P<0.001). At week 2, a higher percentage of subjects receiving paliperidone ER (immediate-initiation group) were satisfied with their medication compared with those still receiving risperidone (delayed-initiation group) (67.7% vs 45.3%; P=0.002). Most common AEs for overall group: insomnia (9.1%), constipation (7.6%), headache (7.6%) and somnolence (6.6%).
Conclusion: Schizophrenia subjects suboptimally responsive to risperidone reported improved medication satisfaction after 4 or 6 weeks of paliperidone ER. Supported by Ortho-McNeil Janssen Scientific Affairs, LLC

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» NR1-033

EFFICACY OF ILOPERIDONE IS COMPARABLE TO RISPERIDONE IN A META-ANALYSIS OF A PLACEBO- AND RISPERIDONE-CONTROLLED CLINICAL TRIAL FOR SCHIZOPHRENIA

Jennifer Hamilton M.S., Mihael Polymeropoulos, MD, John Feeney, MD, Paolo Baroldi, MD, PhD and Curt Wolfgang, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to (1) understand the impact of early drop-outs in relative efficacy estimates; (2) understand that differences in titration schedules between two active treatments can lead to bias in efficacy estimates; and (3) the “length of stay” covariate is a simplistic but valid pattern mixture model approach as an alternative to last observation carried forward.

SUMMARY:

Objective: In trials to establish the efficacy of antipsychotics, patients are prone to drop out early if they experience unsatisfactory results in the initial days of the study. Although statisticians generally acknowledge that results from LOCF are biased, its use in regulatory settings has persisted for various reasons. As an alternative to LOCF, we implemented a simplified pattern mixture model approach to examine the efficacy of iloperidone and risperidone in a placebo-controlled Phase 3 study. Methods: The efficacy of iloperidone at a dose range of 12-24 mg/d was evaluated in a 6-week, double-blind, placebo- and active-controlled (risperidone 6-8 mg/d) trial of acute exacerbation of schizophrenia. Dropout cohort data was analyzed to determine what effect dropouts had on efficacy measures. Based on the longer titration period for iloperidone, an analysis was conducted implementing length of stay into the model and a subgroup analysis using LOCF of patients that received =14 days of treatment. Results: The length of stay covariate was significant (p<0.001) and when adjusting for length of stay, both dose groups of iloperidone, 12-16 mg/d and 20-24 mg/d showed significantly greater improvement than placebo on the PANSS-T (-12.6; p=0.021 and -15.4; p=0.001, respectively) and BRPS (-8.1; p=0.0.018 and -9.4; p=0.001, respectively) and both iloperidone treatments are similar to risperidone on PANSS-T (-15.6; p=<0.001) and BPRS (-9.6; p=0.001). An LOCF analysis of patients with =14 days of treatment confirms the comparable efficacy of iloperidone to risperidone, supported from the overlapping 95% confidence intervals and by the observed cases data at Week 6. Conclusion: In this Phase 3 schizophrenia trial, a meta-analysis which adjusts for drug titration differences, showed that iloperidone was more effective than placebo and comparable to risperidone for the treatment of acute psychotic exacerbation. Vanda Pharmaceuticals sponsored this study.

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» NR1-034

INSULIN SENSITIVITY IN PATIENTS WITH SCHIZOPHRENIA OR SCHIZOAFFECTIVE DISORDER TREATED WITH OLANZAPINE OR RISPERIDONE

Thomas Hardy M.D., Robert R. Henry, M.D., Tammy D. Forrester, M.S., Ludmila A. Kryzhanovskaya, M.D., Ph.D.,Susan B. Watson, Ph.D.,David M. Marks, M.D., Sunder Mudaliar, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describedescribe changes in insulin sensitivity and other metabolic parameters in patients with schizophrenia or schizoaffective disorder treated for 12 weeks with olanzapine or risperidone.

SUMMARY:

OBJECTIVE: To assess whether treatment with olanzapine (OLZ) or risperidone (RIS) is associated with changes in insulin sensitivity (IS) in nondiabetic adults with schizophrenia or schizoaffective disorder. METHODS: Patients (N=130) were randomly assigned to OLZ or RIS for 12 weeks of double-blind treatment. IS was measured by a 2-step, hyperinsulinemic, euglycemic clamp procedure. Whole body adiposity was measured by DEXA. The primary endpoint was the within-group change from baseline in the normalized IS index (Mffm/I) at the low insulin phase of the clamp, using an ANCOVA model including weight change as a covariate. RESULTS: 41 OLZ- and 33 RIS-treated patients completed both baseline and endpoint clamp measurements. Mean Mffm/I at low insulin phase declined 9.0% (p=.226) in the OLZ group and 16.9% (p=.030) in the RIS group (between-groups p=.204). At high insulin phase, Mffm/I declined 10.4% (p=.036) in the OLZ group and 3.5% (p=.529) in the RIS group (between-groups p=.809). Results were similar when weight change was removed from the model. Mean weight change was +3.9 kg for OLZ (p<.001) and +2.2 kg for RIS (p=.013), b/t groups p=.076. OLZ (1.73 kg, p=.001) but not RIS patients (1.08 kg, p=.057) experienced significant increase in fat mass, b/t groups p=.306. A significant increase in fasting glucose (0.30 mmol/L, p=.007) was observed in OLZ patients (b/t groups p=.132). HbA1c did not change significantly in either group, and the change in fasting glucose observed during OLZ treatment was not correlated with changes in Mffm/I.
CONCLUSIONS: Small, but statistically significant decrements in insulin sensitivity were observed with both treatments; however, neither group demonstrated statistically significant changes at both insulin doses tested. There were no significant between-group differences in IS at either insulin dose. The current results do not suggest a differential, pharmacological effect of OLZ or RIS on peripheral IS. Research supported by Lilly.

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» NR1-035

A DOUBLE-BLIND COMPARISON OF LURASIDONE AND ZIPRASIDONE ON COGNITIVE FUNCTION IN OUTPATIENTS WITH SCHIZOPHRENIA OR SCHIZOAFFECTIVE DISORDER

Philip D. Harvey Ph.D., Masaaki Ogasa,MD, Josephine Cucchiaro,PhD, Antony Loebel, MD, Richard SE Keefe, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the measurement of cogntive functioning with performance and interview based measures.
They should also be able to evaluate the differential usefulness of performance-based and interview based assessments.

SUMMARY:

The FDA has asked for the use of a co-primary measure to demonstrate clinical relevance of any detected changes in cognitive enhancement trials. There are few data available regarding whether these co-primary measures are sensitive to treatment-related changes and whether these changes are comparable to potential improvements in performance-based measures of cognition.
Adult outpatients, ages 18-70 years who met DSM-IV criteria for chronic stable schizophrenia or schizoaffective disorder were recruited. Eligible patients were randomized to 21 days of treatment with a fixed dose of lurasidone (a new atypical antipsychotic with high affinity for D2 and 5-HT2A receptors, as well as for serotonin receptor subtypes implicated in cognition, including 5-HT7 and 5-HT1A) 120 mg once daily or ziprasidone 80 mg BID. The intent-to-treat sample consisted of 150 patients on lurasidone and 151 patients on ziprasidone A similar proportion of patients completed the study on lurasidone and ziprasidone [67.5% (n=123) vs. 69.3% (n=111)]. Study participants were tested at baseline and endpoint with the MATRICS consensus cognitive battery (MCCB) and an interview-based co-primary assessment of cognitive functioning the Schizophrenia Cognition Rating Scale (SCoRS). The SCoRS ratings were based on the interviewer's best judgment, after interviews with the patient and a caregiver.
There were no baseline differences at in MCCB or SCoRS ratings, although at week 3 lurasidone was superior on the SCoRS at a trend level (p=0.058). There was no significant within-group improvement from baseline on the SCoRS for the ziprasidone patients (p=0.185), although lurasidone patients improved significantly (p<0.001).On the MCCB, at week 3 lurasidone (p=0.026) but not ziprasidone (p=0.254) was associated with significant within group-improvement. Effect size for improvement on the SCoRS (0.43) was over twice as large as the improvement on the MCCB (0.157) for the lurasidone patients.
These data indicate that interview-based, "co-primary" measures of cognitive improvements (e.g., the SCoRS) may be more sensitive to change compared to the MCCB. Ratings on the SCoRS are not performance-based, meaning that practice effects are not a viable explanation for any improvements detected.
Lurasidone showed general trends toward improvement on the MCCB, as well as the SCoRS, and is being assessed in ongoing trials. Supported by DSPA.

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» NR1-036

MAINTENANCE DOSING OF ONCE-MONTHLY (4-WEEKLY) PALIPERIDONE PALMITATE IN SCHIZOPHRENIA: PHARMACOKINETIC RATIONALE BASED ON POPULATION BASED SIMULATIONS

J. Thomas Haskins Ph.D., Mahesh N. Samtani, Ph.D., Larry Alphs, M.D., Jennifer Kern Sliwa, PharmD., B.C.P.P., Kim Stuyckens, M.Sc., Virginie Herben, Ph.D., An Vermeulen, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to explain why population pharmacokinetic simulations support a proposed monthly (4-weekly) maintenance dose of paliperidone palmitate being 75mg eq. in the majority of patients, with a dosing range of 25–150mg eq.

SUMMARY:

Introduction: The maintenance dosing regimen for the investigational product paliperidone palmitate (PP) is currently being explored using population PK simulations. The choice of dosing strengths for once-monthly (4-weekly) PP maintenance therapy was supported by comparing steady state (SS) exposure at low-, mid- and high-dose levels to those attained with approved once-daily dose strengths of paliperidone (pali) extended-release (ER) tablets.
Methods: A 2-compartment model involving sequential zero/1st order absorption with lag-time best described pali ER PK. A 1-compartment model with parallel zero/1st order absorption best captured pali PK after PP administration. PK profiles (n=5000) over 53wks were simulated based on population PK models for both pali products. Pop median and 90% prediction interval of simulated PK profiles were superimposed for the 2 pali products.
Results: Simulations indicate monthly maintenance dosing of PP 25, 75, 100, 150mg eq. provided sustained SS pali plasma concentrations within the exposure window for 2, 6, 8 and 12mg doses of pali ER, respectively. At all doses, SS peaks and troughs for PP were completely encompassed within pali ER exposure window (which displayed a flat profile at SS due to ER properties). Proposed monthly maintenance dosing range for PP is 25–150mg eq. as, in terms of SS exposure, this is contained within dose strengths approved for pali ER (3–12mg). The recommended daily dose of pali ER for schizophrenia is 6mg; therefore, proposed recommended monthly maintenance dose for PP is 75mg eq. Recommended dose ranges of pali ER (3–12mg) and PP (25–150mg eq.) were well tolerated in clinical trials.
Conclusion: PK simulations suggest that the plasma concentrations with the monthly maintenance dose of PP 75mg eq. (25–150mg eq.) will be encompassed within the same exposure window as observed with the approved pali ER doses (3–12mg). Funded by J&J PRD.

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» NR1-037

INCREASE OF SYMPTOM REMISSION IN PSYCHOSIS – INTEGRATING SCIENCE AND SERVICE IN THE SWEDISH CLIPS STUDY

Lars Helldin, Fredrik Hjärthag, M.Sc., Ulla Karilampi, M.Sc.,

Anna-Karin Olsson, M.Sc., Torsten Norlander, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize the presented Swedish CLIPS-study, as an example of how the integration of science and service could lead to positive health outcomes for the patients, indicated by an enhanced percentage of patients in symptom remission. The CLIPS-study should also be recognized as an important source of knowledge regarding many different aspects of the psychotic illnesses, also including longitudinal perspectives.

SUMMARY:
Background: The Clinical Long term Investigation of Psychosis in Sweden (CLIPS), started year 2000 in the NU Health Care region as a naturalistic study, aiming at enhancing general and specific knowledge about psychosis, as well as applying the findings in clinical practise.
Methods: Initially, the CLIPS was a single-centre study and included in total 264 patients (1). Since 2005, the CLIPS has expanded into a longitudinal, multi-centre study that targets all patients with a psychosis diagnosis, after informed consent. The patients are evaluated once a year by their case manager for physical status, psychiatric symptoms, side effects, social functioning, satisfaction with care, and quality of life. Relatives are questioned about their perceived care burden. The patients are also investigated by an occupational therapist for functional performance. Every fourth year the patients meet a psychologist for a cognitive evaluation. Beside being a guideline for treatment, the information is also used for scientific research.
Results and Discussion: About 300 patients are currently taking part in the CLIPS study. As a likely consequence of the annual assessments with a structured focus on the patients' illnesses and treatments, the percentage of patients in remission, according to the Andreasen criterias (2), has raised in the last three years from 35 % to about 50 %. Also, scientific articles have been published, and manuscripts have been submitted, on symptom remission, cognition, family burden, and functional performance, within the frame of the CLIPS.
Conclusion: The CLIPS study proves that science can be successfully integrated with clinical practise for better evidence base health care, including a higher percentage of patients in remission.
This study was supported by unrestricted grants from Janssen-Cilag AB, Sweden.

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» NR1-038

ALGORITHMS INCLUDING AMANTADINE, METFORMIN AND ZONISAMIDE FOR MITIGATION OF WEIGHT GAIN DURING OLANZAPINE TREATMENT IN OUTPATIENTS WITH SCHIZOPHRENIA

Vicki Hoffmann Pharm.D., Michael Case, MS, Jennie Jacobson, PhD

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should understand the relative risks and benefits of adjunctive pharmacotherapy treatment algorithms using amantadine, metformin and zonisamide for mitigation of weight gain during olanzapine treatment for schizophrenia or schizoaffective disorder.

SUMMARY:
Objective: To determine if weight gain during olanzapine treatment can be mitigated with treatment algorithms including amantadine, metformin and zonisamide.
Methods: In this 22-week study of open-label olanzapine for patients aged 18-65 with schizophrenia or schizoaffective disorder, all patients received weight management information at baseline. Patients were randomized to Algorithm A (N=76) or B (N=73) or no adjunctive therapy (OLZ; N=50). Algorithm A: 100 mg amantadine twice/day, with possible switches first to metformin 1000-1500 mg/day and then zonisamide 100-400 mg/day, dependent on patient weight gain. Algorithm B: metformin 1000-1500 mg/day, with possible switches to amantadine 100 mg twice/day and then to zonisamide 100-400 mg/day.
Results: Mean baseline weight ranged from 77.0 kg to 79.1 kg. Mean modal olanzapine dose ranged from 12.9 mg/day to 13.5 mg/day. Mean weight gain was OLZ: 2.8 kg ± 0.8, A: 2.4 kg ± 0.7 and B: 0.7 kg ± 0.6, with p-values of 0.11 for OLZ vs. A, 0.04 for OLZ vs. B and 0.07 for OLZ vs. pooled A and B. In the OLZ, A and B groups respectively, 27.7%, 18.3% and 22.2% of patients experienced weight gain =7% of baseline weight. In Group A, 30 patients (42.3%) switched to metformin during the study period; 7 (9.9%) later switched to zonisamide. In Group B, 25 patients (34.7%) switched to amantadine; 9 (12.5%) switched to zonisamide. Improvements in BPRS and CGI-S were similar across groups. Mean improvement in MADRS score was less for Groups A and B than for OLZ (p=0.04). Group A did not differ significantly from either Group B or OLZ in frequency of adverse events. Diarrhea was more common in Group B than the OLZ group (p=.005). Insomnia was more common in the OLZ group than Group B (p=.040).
Conclusion: Adjunctive treatment with metformin, with potential progression to amantadine and then zonisamide, resulted in significantly less weight gain over 22 weeks, compared to olanzapine alone. Funded by Eli Lilly and Company

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» NR1-039

REASONS FOR ADHERENCE TO ANTIPSYCHOTIC TREATMENT: THE PATIENT'S PERSPECTIVE

Liu-Seifert Hong Ph.D., Olawale O. Osuntokun, M.D., Jenna L. Godfrey, M.S., Peter D. Feldman, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to gain a better understanding of what subjective benefits are reported by patients with schizophrenia during successful treatment with antipsychotic medications, and how these feelings may be associated with clinical outcomes and adherence to treatment.

SUMMARY:
Objective: To examine patient-reported attitudes toward antipsychotic medication and their relationship with clinical outcomes and adherence to pharmacotherapy.
Methods: The clinical development archive for olanzapine was examined for all studies with >=50 patients and involving use of the Positive and Negative Syndrome Scale (PANSS) and Drug Attitude Inventory (DAI-10). Four randomized, double-blind studies were identified, which included adult patients (18–65 years) with DSM-IV schizophrenia, schizoaffective disorder, or schizophreniform disorder who were receiving randomly assigned treatment with olanzapine (5–20 mg/day), another antipsychotic (haloperidol, 2–20 mg/day; risperidone, 2–10 mg/day; ziprasidone, 80–160 mg/day), or placebo.
Results: Patient-reported improvements (DAI-10) were signifi-

cantly greater for olanzapine (n = 712) than for the other treatments (haloperidol, n = 145; risperidone, n = 158; ziprasidone, n = 271; placebo, n = 102) on most of the DAI-10 items. For example, significantly fewer patients felt "weird" during olanzapine treatment than with haloperidol (P = .025) or ziprasidone (P = .037), significantly more reported feeling relaxed with olanzapine than with haloperidol (P = .008) or risperidone (P = .046), and significantly more patients receiving olanzapine considered their medication's benefits to outweigh its risks than was the case for risperidone (P = .036). Positive attitude toward medication reported by patients was associated with greater clinical improvement on the PANSS, as well as with lower discontinuation rates.

Conclusions: Patients' perceptions of treatment benefits can be associated with corresponding differences in objective clinical measures, including reduction of symptom severity and lower discontinuation rates. These findings may contribute to a better understanding of reasons for treatment adherence from patients' own perspectives.

REFERENCES:

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» NR1-040

EFFECTS OF WATER INTAKE AND SMOKING ON THE ABSORPTION OF SUBLINGUALLY ADMINISTERED ASENAPINE

Ellen Hulskotte, Edwin Spaans, Cees Timmer, Andreas Schrödter, Christel Machielsen, Peter Schnabel, Michiel Van Den Heuvel, Rik De Greef, Pierre Peeters

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to:Summarize the effects of water intake and smoking on the absorption and bioavailability of sublingually administered asenapine.State the possible clinical consequences of drinking water less than 10 minutes after sublingual dosing of asenapine.

SUMMARY:

Objective: Asenapine is being developed for treatment of schizophrenia and bipolar disorder. We studied the effects of water intake and concomitant smoking on the absorption of sublingual (SL) asenapine.

Methods: A 28-day trial assessed the effects of water intake following asenapine (10 mg QD) in 15 healthy men. In a 4-period 4-sequence crossover design, subjects drank 150 mL of water 2, 5, 10, or 30 minutes (reference) after taking asenapine. A single-dose 2-way crossover trial assessed the effects of smoking (from 5 min before to 10 min after 5 mg asenapine) in 24 healthy men (reference regimen: no smoking >/=30 min before and >/=10 min after dosing). In both studies, effects on asenapine exposure (AUC and Cmax) were assessed using bioequivalence criteria.

Results: Mean asenapine Cmax and AUC0–24 values for water at 10 min vs 30 min postdose were within 2% of each other. Based on bioequivalence criteria, no effect was present for AUC0–24, but this could not be concluded for Cmax owing to 40% within-subject variation. Mean asenapine Cmax and AUC0–24 were decreased by 12% and 10%, respectively, for water at 5 min postdose and by 21% and 19% for water at 2 min. For smoking vs non-smoking, no effect was seen on Cmax or AUC0–inf (Table).

Conclusion: Absorption and bioavailability of SL asenapine are not affected by concomitant smoking or by water taken 10 min or later after dosing. Research supported by Schering-Plough.

Water Intake and Smoking Effects on Asenapine PK [Mean (SD)]

		Test	Ref*	Test/Ref
Water intake				
Cmax (ng/mL)	2 min	4.15 (2.09)	4.99 (2.05)	0.79
	5 min	4.38 (1.91)		0.88
	10 min	4.69 (2.22)		0.98
AUC0–24 (ng h/mL)	2 min	29.8 (10.2)	36.3 (11.3)	0.81
	5 min	32.5 (11.1)		0.90
	10 min	35.9 (15.6)		0.99
Smoking				
Cmax		3.16 (1.73)	3.00 (1.51)	1.02
AUC0–inf		25.6 (11.2)	24.3 (10.1)	1.06

*Reference: water 30 min postdose; nonsmoking

REFERENCES:

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» NR1-041

ATTENTIONAL MODULATION OF EXTERNAL SPEECH ATTRIBUTION IN PATIENTS WITH PARANOID SCHIZOPHRENIA

Lana Marija Ilankovic M.S.C., Rolf Engel,Prof., Joseph Kambeitz, Hans-Juergen Moeller,Prof., Kristina Hennig-Fast,Prof.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand how different atentional mechanisams are involved in appraisal of speech in patients with paranoid schizophrenia.

SUMMARY:

A range of psychological theories have been proposed to account for the experience of auditory hallucinations and delusions in schizophrenic patients. Most influential theories are those implicating the defective monitoring of inner speech. However, there are other studies that measured response bias independently of self-monitoring and found the results inconsistent with defective self-monitoring model, but explained by an externalizing response bias. The aim of the present study was to identify the role of attentional biases in external misattribution of source by modulating participant's endogenous expectancies.23 paranoid schizophrenic patients and 23 healthy controls participated in 2 versions of the audio-visual task, which differed based upon level of the cue predictivness. Participants passively listened to recordings of single adjectives spoken in their own and another person's voice (alien) preceded by their own or another person's (alien) face and made self/nonself judgments about the source. The acoustic quality of recorded speech was experimentally manipulated by altering the pitch. In both versions of the task, patients showed increased error rates when listening to the distorted words spoken by themselves, misidentifying their own speech as spoken by someone else comparing to controls. However, patients made significantly more errors across all the conditions in which the cue was invalid(not predictive), but were particularly prone to misidentify their own speech (original/distorted) as alien, when preceded by an alien face.We confirmed the presence of the externalizing bias in patients with paranoid schizophrenia listening to their own voice, that was moreover amplified when they were cued with the alien face. This may reflect the dominance of top-down attentional mechanism in paranoid schizoprenic patients, responsible for the misattribution of the ambiguous sensory material.

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» NR1-042

DIFFERENTIAL BRAIN VOLUME CORRELATES OF TRAIT ANHEDONIA IN SCHIZOPHRENIA: A VOXEL-BASED MORPHOMETRIC STUDY

Jung Suk Lee, M.D. Department of Psychiatry, Yonsei University College of Medicine, 134 Shinchon-dong, Seodaemun-gu, Seoul 120-752, Korea, Ji Won Chun, M.A., Jeong-Ho Seok, M.D., Ph.D., Hae-Jeong Park, Ph.D., Jae-Jin Kim, M.D., Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to discuss the changes in gray matter volume that are associated with trait anhedonia in schizophrenia.

SUMMARY:

Objectives: The aim of this study was to characterize the association between trait anhedonia and regional gray matter volumes in patients with schizophrenia.
Methods: Forty-six patients with schizophrenia and fifty-six age-, sex- matched healthy controls underwent magnetic resonance imaging for the high resolution T1-weighted images. Trait anhedonia was measured using the Chapman Revised Physical Anhedonia Scale. Voxel-based morphometry was performed to investigate brain volume correlates of trait anhedonia.
Results: Compared to the patient group, more significant correlations between the degree of trait anhedonia and regional gray matter volumes in the control group were shown mainly in the limbic and paralimbic regions including the right hippocampus, the left ventromedial prefrontal cortex, the right anterior cingulate, the right posterior cingulate, and the right insula. On the other hand, compared to the control group, those in the patient group were shown in the anterior temporal regions such as the bilateral temporal poles and the right uncus and the somatosensory areas such as the premotor cortex and the left postcentral gyrus.
Conclusion: The results in the control group suggest that variation in trait anhedonia in healthy people may be related to the degree of paralimbic development. However, the results in the patient group may be related to psychopathology. The involvement of the temporal pole in the patient group is consistent to the previous finding of the close relationship between the temporal pole morphology and psychotic symptoms in schizophrenia. The involvement of the somatosensory areas may occur because antipsychotic medication affected on assessing trait anxiety. In conclusion, normal brain volume correlates of trait anhedonia are distorted in patients with schizophrenia.

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» NR1-043

EUFEST: THE EFFECTS OF FIRST AND SECOND GENERATION ANTIPSYCHOTICS ON METABOLIC AND CARDIOVASCULAR RISK FACTORS

Rene Kahn M.D., W Wolfgang Fleischhacker, M.D., Onur Karayal,M.D., Cynthia Siu, Ph.D., Elizabeth Pappadopulos, Ph.D. and the EUFEST Study Group

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to have better understanding of the effects of first and second generation antipsychotics on metabolic and cardiovascular risk factors in first-episode schizophrenia

SUMMARY:

Objectives: Available data on antipsychotic-induced metabolic disturbances and cardiovascular risk factors in first-episode schizophrenia patients are limited. The EUFEST study offers a unique opportunity to compare the long-term effects of first and second generation antipsychotics on metabolic syndrome (MS) and CHD risk factors.
Methods: In an open-label randomized trial of haloperidol (HAL, N=103) vs. amisulpride (AMP, N=104), olanzapine (OLZ, N=105), quetiapine (QUET, N=104), and ziprasidone (ZIP, N=82), body weight (WT), waist circumference (WC), and laboratory data were assessed at baseline, 3 (WT/WC only), 6, 9 (WT/WC only) and 12 months. Mixed effects models were applied in the analysis.
Results: Using baseline data to identify subjects with MS1, elevations in metabolic risks were found: 17 of 422 subjects (4.5%) had MS (>= 3 risk components), 233 (55%) had one or more elevated risks at baseline, 37% for 1 risk factor and 13% for 2. Thirty-six patients (8%) demonstrated abdominal obesity and 18 (24%) hypertension. Tobacco use was reported in 266 (53%) patients at baseline. Compared to HAL, the ZIP group showed a significantly smaller increase in WC over time ($p<0.05$), while no differences were found between HAL and the other atypicals (AMP, OLZ, QUET, all $p>0.05$). Median percent changes in triglycerides and HDL were: 34% and -12% for AMP, 7% and 0% for HAL, 9% and -9% for OLZ, 11% and 5% for QUET, and -31% and -3% for ZIP, respectively. Week 52 mean/SE use of tobacco (per week) was significantly higher in the HAL group (92/24) compared to OLZ (40/8, $p<0.05$) and QUET (42/11, $p<0.05$). Similar results were seen in the AMP (46/9, $p=0.27$) and ZIP (42/11, $p=0.06$) groups, but the differences were not statistically significant.
Conclusions:Our findings suggest there are differences among first and second generation antipsychotics concerning their effects on metabolic or cardiovascular risks in first-episode schizophrenia.
Supported by funding from Pfizer Inc.

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» NR1-044

ZIPRASIDONE WITH ADJUNCTIVE MOOD STABILIZER IN MAINTENANCE TREATMENT OF BIPOLAR DISORDER: METABOLIC AND WEIGHT EFFECT PROFILES

Onur Karayal M.D., Kathleen S. Ice,Ph.D., Cynthia Siu, Ph.D., Elizabeth Pappadopulos, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to have a better understanding of the time course and maintenance treatment of bipolar disorder with ziprasidone.

SUMMARY:

Objectives: In a randomized, double-blind, placebo-controlled, study, ziprasidone combined with a mood stabilizer (lithium or valproic acid) showed efficacy in bipolar disorder maintenance treatment. Here, we report the weight and metabolic profiles of ziprasidone in the stabilization and randomization phases. Methods: In the open-label stabilization phase, 584 patients with bipolar I disorder (DSM-IV) received up to 4 months of ziprasidone (80-160 mg/d) combined with lithium or valproic acid (ZIP+MS). Patients who achieved at least 8 weeks of clinical stability were subsequently randomized to double-blind treatment (up to 6 months) of ziprasidone + MS (ZIP+Li, N=57; ZIP+VAL, N=70) vs. placebo + MS (PBO+Li, N=49; PBO+VAL, N=63).
Results: During the stabilization phase, overall mean change in body weight was 0.3 (SD 5.3) kg. Week 16 mean changes (and

SD) for other metabolic parameters were: waist circumference 0.7 (8.5) cm, fasting glucose -1.6 (22.6) mg/dL, triglycerides 4.1 (78.1) mg/dL, and HDL 0.1 (8.0) mg/dL. During the double-blind, placebo-controlled, adjunctive maintenance phase, the week 24 mean changes (and SD) from baseline in body weight for the 4 study groups were: ZIP+Li = -0.4 (4.2) kg, PBO+Li = -1.4 (SD 4.3) kg, ZIP+VAL = -1.1 (5.2) kg, and PBO+VAL = 1.5 (5.0) kg. Similar week 24 mean changes (and SD) in related metabolic parameters for the ZIP+MS vs. PBO+MS groups were: waist circumference -1.0 (5.6) vs. -0.2 (4.5) cm, fasting levels of glucose 0.3 (22.9) vs. 2.6 (22.9) mg/dL, HDL -0.7 (7.6) vs. -0.8 (9.5) mg/dL, and triglycerides 5.2 (61.0) vs. -0.8 (82.8) mg/dL respectively. Conclusions: Efficacy of ziprasidone combined with mood stabilizers was established in the maintenance treatment of bipolar disorder in this 6-month, placebo-controlled study. With favorable weight effect and metabolic profiles, ziprasidone adjunctive therapy is an important option for long-term maintenance treatment of bipolar disorder. Supported by funding from Pfizer Inc.

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» NR1-045

SCHIZOTAXIA AS A SYNDROME

Ersin Hatice Karslioglu M.D., Nevzat Yuksel, M.D., Belma Bekci, Ph.D., Sirel Karakas, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the concept of schizotaxia as a clinically recognizable syndrome.

SUMMARY:

The term of schizotaxia, which was firstly used by Paul Meehl in 1962, has been reformulated by Tsuang et al. and defined as a syndrome composed of neuropsychologic deficits and negative symptoms which are seen among the non-psychotic first-degree relatives of schizophrenic patients.
In this study we aimed to investigate the differences among the first-degree relatives of schizophrenic patients, the ones who has been determined as schizotaxic among them, and the healthy individuals.
Thirty schizophrenic patients, 36 first-degree relatives and 30 healthy controls were evaluated according to DSM-IV diagnoses (Axis I and II), Global Assessment of Functioning Scale, Symptom Check List 90-R, Scale for the Assessment of Positive and Negative Symptoms, and Hamilton Anxiety and Depression Scales.
The first degree relatives of schizophrenic patients showed some deficits in attention, verbal memory and executive functions similar to schizophrenic patients and showed differences from control group. Seven of 36 relatives (19.4 %) were met the criteria of schizotaxia. The schizotaxic individuals had lower functioning and higher anxiety levels than non-schizotaxic relatives and control group. Although there are two studies about the treatment of schizotaxic persons, this is the first independent study supporting the idea which claims that schizotaxia is a separate syndrome to our knowlegde. Because of the limited numbers of subjects in our study, extended evaluations on larger series are needed to challenge these results.

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» NR1-046

INITIATION DOSING OF DELTOID INTRAMUSCULAR PALIPERIDONE PALMITATE IN SCHIZOPHRENIA: PHARMACOKINETIC RATIONALE BASED ON MODELING AND SIMULATION

Jennifer Kern Sliwa Pharm.D., Mahesh N. Samtani, Ph.D., J. Thomas Haskins, Ph.D., Larry Alphs, M.D., Kim Stuyckens, M.Sc., Virginie Herben, Ph.D., An Vermeulen, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand that the results of a population pharmacokinetic simulation model support the initiation of long-acting injectable paliperidone palmitate in the deltoid muscle at a dose of 150mg eq. on Day 1, followed by 100mg eq. paliperidone palmitate on Day 8.

SUMMARY:

Introduction: This analysis compared the dosing strategy for paliperidone palmitate (PP) treatment initiation in schizophrenia as a deltoid injection of 150mg eq. then 100mg eq. (150/100) vs 100mg eq. then 100mg eq. (100/100), on Days 1 and 8, using a population pharmacokinetic (PK) simulation model.
Methods: A 1-compartment disposition model with zero/1st order absorption best described the PK of PP. The following were identified as important predictors of PP PK: injection site/volume, needle length, renal function and BMI. Paliperidone (pali) plasma concentrations over 53 wks were simulated based on final estimates of the population PK model. PK profiles for n=5000 pts were simulated after injections on Days 1, 8 and 36, and every 4 wks thereafter. Population median and 90% prediction intervals of simulated plasma concentration (conc) vs time profiles after multiple doses were graphically displayed. Trough plasma target conc of 7.5ng/mL pali (central D2-receptor occupancy of ~60%) was used to compare strategies.
Results: Simulations predict that 1 wk post 1st dose, 73% of pts on 100/100 will achieve target pali plasma conc >7.5ng/mL, while 84% will achieve this with 150/100. Initial exposure during the 1st mnth following 150/100 regimen overlapped with exposure observed with 75mg eq. steady state exposure at 1 yr. The higher initial dose resulted in faster attainment of steady state. Comparison of pre-dose exposure on Days 8 and 36 showed that the 150/100 regimen resulted in pts remaining within an efficacious conc window (3.5–50ng/mL), even at trough. The suggested initiation regimen (150/100) has been studied in a Phase III trial (n=76) and was well tolerated and efficacious after 1 wk.
Conclusion: Using the 150/100 deltoid regimen is predicted to result in a greater percentage of pts with schizophrenia who will achieve target plasma conc by the end of the 1st wk of treatment as compared to those receiving the 100/100 deltoid regimen. Funded by J&J PRD.

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» NR1-047

COMPARISON OF SWITCHING STRATEGIES TO ARIPIPRAZOLE TREATMENT IN PATIENTS WITH SCHIZOPHRENIA

Chul Eung Kim M.D., Tae Yeon Suh M.D., Min Hee Kang M.D., Jung Seop Lee M.D., Jae Nam Bae. M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand switching strategies when treated with aripiprazole. And also, participant should be able to recognize and manage the

new developing adverse events after switching to aripiprazole.

SUMMARY:
Background: In clinical practice, changing antipsychotics is common despite of the lack of information on risks and benefits associated with medication changes. It is important to find optimal switching strategy for the patients to produce best possible outcomes. Objective : This paper assesses the clinical outcomes of three switching strategies(cross tapering, abrupt switching, tapering switch) in naturalistic real clinical settings. Method : This was a retrospective cohort analysis of patients with a diagnosis of schizophrenia and schizoaffective disorder according to DSM-IV TR criteria , and treated in a University hospital in Korea between March 2005 and February 2007. Patients were evaluated for one year after switching to aripiprazole. Results : The study enrolled 48 patients from in- and outpatient department. All patients were grouped as cross tapering group(41.6%), abrupt switching group(47.9%), and tapering switch group(10.4%). The rate of aripiprazole retention for one year was 50%, 30.4%, 20% respectively. The rate of development of all kinds of adverse events was 70%, 60.9% and 80% respectively. There was no clinical significance both the rate of retention and development of adverse events among three switching strategies groups. Conclusion : Any of the three strategies evaluated in this study was safe and showed similar clinical outcomes for one year. Key Words : Aripiprazole. Switching Strategy. Schizophrenia.

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» NR1-048

SWITCHING FROM ATYPICAL ANTIPSYCHOTICS TO ARIPIPRAZOLE IMPROVES COGNITIVE FUNCTION, ATTITUDE TOWARD MEDICATION, AND METABOLIC ABNORMALITIES

Sung-Wan Kim, M.D., Il-Seon Shin, M.D., Jae-Min Kim, M.D., Jeong-Hoon Lee, M.D., Yo-Han Lee, M.D., Su-Jin Yang, M.D., Kyung-Yeol Bae, M.D., Seon-Young Kim, M.D., Jin-Sang Yoon, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand the effectiveness of switching to aripiprazole from atypical antipsychotics in patients with schizophrenia.

SUMMARY:
Objectives: To examine changes in cognitive function and clinical features following a switch from atypical antipsychotics to aripiprazole in patients with schizophrenia.
Method: Sixty-one patients with schizophrenia treated with atypical antipsychotics participated in this open-label, 26-week study. Antipsychotics were switched to aripiprazole and neurocognitive functions were measured at 12 and 26 weeks using the computerized battery. The secondary outcome measures were the Positive and Negative Syndrome Scale (PANSS), Social and Occupational Functioning Assessment Scale (SOFAS), Calgary Depression Scale for Schizophrenia, Subjective Wellbeing under Neuroleptics Scale, and Drug Attitude Inventory (DAI). Safety measures included metabolic parameters, the Simpson–Angus Scale (SAS), Barnes Akathisia Scale, and Abnormal Involuntary Movement Scale (AIMS).
Results: Significant improvements in cognitive function were observed in Verbal Learning Test (VLT), Wisconsin Card Sorting Test, and Trail Making Test type-A following a switch to aripiprazole. Scores on the PANSS, SOFAS, DAI, SARS and AIMS were significantly improved. Metabolic parameters, including serum cholesterol levels, were also improved. The changes in cognitive measures were not correlated with the changes in positive symptoms or movements scales. The improvement of the scores on the DAI and delayed recall of VLT were significantly greater in the patients treated with antipsychotics for less than 1 year than in those treated for more than 1 year, in whom the improvement in metabolic parameters was significantly greater.
Conclusion: Patients with schizophrenia who were switched from their prior antipsychotic to aripirazole demonstrated improvements in cognitive function, psychotic symptoms, social function, attitude toward medication, and metabolic abnormalities.

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» NR1-049

THE EFFICACY AND TOLERABILITY OF CARIPRAZINE IN ACUTE MANIA ASSOCIATED WITH BIPOLAR I DISORDER: A PHASE II TRIAL

Mary Ann Knesevich M.D., Kelly Papadakis, MD; Anjana Bose, PhD; Qing Wang, PhD; Andrew Korotzer, PhD; Istvan Laszlovszky, PharmD

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to compare the tolerability and efficacy of cariprazine and placebo in patients with acute mania associated with bipolar I disorder.

SUMMARY:
Introduction: Cariprazine (RGH-188) is a dopamine D3/D2 receptor functional antagonist.
Methods: This was a randomized, double-blind, placebo-controlled, flexible-dose study of cariprazine (3-12 mg/day) in patients (male or female, 18-65 years) with DSM-IV-defined acute mania associated with bipolar I disorder. There was a 4-day no-drug washout period, followed by 3 weeks of double-blind treatment. The primary efficacy parameter was change from baseline to Week 3 in Young Mania Rating Scale (YMRS) score using the last-observation-carried-forward (LOCF) approach.
Results: In both groups, 118 patients received at least one dose of double-blind study drug. A total of 61.9% placebo and 63.6% cariprazine patients completed the study. Baseline YMRS scores were 30.2 (placebo) and 30.6 (cariprazine). Cariprazine significantly reduced YMRS scores vs. placebo at Week 3 (adjusted mean difference (95%CI) = -6.12(-8.91,-3.32); P<0.0001; LOCF). Significant difference for change in YMRS was also seen based on Observed Cases and MMRM analyses (adjusted mean differences (95%CI) were -5.50 (-7.92, -3.09) and -7.01(-9.97, -4.04), respectively, P<0.0001). Serious adverse events (AEs) were reported for 5 (4%) placebo and 4 (3%) cariprazine patients. AEs led to the discontinuation of 12 (10%) placebo and 17 (14%) cariprazine patients. The most common AEs (>10% for cariprazine) were extrapyramidal disorder, headache, akathisia, constipation, nausea, and dyspepsia.
Conclusion: This Phase II study demonstrates the efficacy of cariprazine in acute mania associated with bipolar I disorder.
Supported by funding from Forest Laboratories, Inc. and Gedeon Richter.

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NR1-050

EARLY RESPONSE TO ANTIPSYCHOTIC DRUG THERAPY AS A PREDICTOR OF SUBSEQUENT RESPONSE IN THE TREATMENT OF PATIENTS WITH FIRST EPISODE PSYCHOSIS

Sara Kollack-Walker Ph.D., Virginia Stauffer, PharmD, Michael Case, MS, Robert Conley, MD, Haya Ascher-Svanum, PhD, Bruce J Kinon, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to distinguish after 2 weeks of treatment those patients with a first episode psychosis who are and are not likely to respond after 2 months of treatment with the same antipsychotic.

SUMMARY:

Objective: Assess whether early response to antipsychotic therapy accurately predicts later response in treatment of patients with first episode psychosis.
Method: We used data from a randomized, double-blind trial of olanzapine vs. haloperidol for the treatment of 225 moderately ill patients with a first episode of a psychotic disorder. Patients were categorized as Early Responders (ER) or Early Non-responders (ENR), based on a Classification and Regression Tree-derived threshold of =26.2% improvement in Positive and Negative Syndrome Scale (PANSS) Total score at Week 2. Conditional probabilities for predicting response at Week 12 were calculated for 3 different thresholds: =40% and =50% improvement in PANSS Total score, and remission, per modified Andreason remission criteria. The ER and ENR groups were also compared on visitwise changes in PANSS scores.
Results: Following 2 weeks of treatment, 43% (97/225) of patients were identified as ER. Early response most strongly predicted later response when later response was defined as =50% improvement in PANSS Total score. At this level, 73.9% of later non-responders had been correctly identified as ENR (high specificity), and the likelihood of correctly predicting later non-response based on early non-response was 79.7% (high negative predictive value). ER showed significantly more improvement than ENR in all PANSS measurements (e.g., Total score, Positive, Negative and General Psychopathology) at all time points from Week 1 to Week 12 (p<.001).
Conclusion: Patients with first episode psychosis who fail to respond in first 2 weeks of therapy appear less likely to respond to the same medication in the following 10 weeks; those who do respond early tend to show persistently greater improvement in psychopathology at all subsequent visits. Current findings are consistent with previous research in the antipsychotic treatment of patients with schizophrenia who are chronically ill.
Funded by Eli Lilly & Company

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NR1-051

A CLINICAL RESEARCH PROGRAM FOR THE TREATMENT OF SCHIZOAFFECTIVE DISORDER

Colette Kosik-Gonzalez, Carla M. Canuso, M.D., Jennifer Carothers, M.B.A., Sc.D., Amir Kalali, M.D., Jean-Pierre Lindenmayer, M.D., Ibrahim Turkoz, M.S., Nina Schooler, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the clinical and psychopathological characteristics that are distinctive to schizoaffective disorder, and describe the elements of a registration program for this population.

SUMMARY:

Background: Although schizophrenia and bipolar disorder have been the focus of extensive clinical research, schizoaffective disorder (SCA) remains understudied. Key design elements and demographic and clinical characteristics are presented from the first registration program in SCA.
Methods: Two international, double-blind, placebo-controlled studies assessing paliperidone ER in patients with SCA. Subjects met SCID-confirmed DSM-IV criteria for SCA; PANSS total score >=60, a score of >=4 on >=2 PANSS items of hostility, excitement, tension, uncooperativeness and poor impulse control and prominent mood symptoms (>=16 YMRS and/or HAM-D-21). Stable doses of antidepressants/mood stabilizers permitted. Endpoints: PANSS (primary), the novel CGI-Severity for Schizoaffective Disorder (CGI-S-SCA), YMRS and HAM-D-21.
Results: 614 patients were in the ITT population; 40.4% US and 59.6% ex-US. Mean age: 37.4 years (range 18-61). 60.4% were male and 48.9% Caucasian. Mean ages at first psychiatric and SCA diagnosis were 25.2 (range 4-56) and 31.7 (range 3-61) years, respectively. Approximately 45% of patients were taking concomitant antidepressants and/or mood stabilizers. 31.4% of patients had attempted suicide in their lifetime. Mean (SD) baseline PANSS total score: 92.8 (12.9). Mean (SD) baseline CGI-S-SCA score: 4.6 (0.6). Percentages of patients with YMRS>=16 or HAM-D-21>=16: 79.5% and 66.9%, respectively; 46.4% had both scores >=16. In subjects with prominent manic or depressive symptoms, mean (SD) baseline YMRS and HAM-D-21 scores were 28.1 (7.5) and 25.0 (6.3), respectively.
Conclusions: This population presented with the full range of psychotic and affective symptoms characteristic of SCA. Findings suggest that a schizoaffective diagnosis is often preceded by an earlier diagnosis of another psychiatric disorder. Further, data suggest these patients often experience repeated hospitalizations and carry a high suicide risk.
Supported by Ortho-McNeil Janssen Scientific Affairs, LLC

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NR1-052

A LONGITUDINAL ANALYSIS OF CHANGES IN TOTAL CHOLESTEROL AND FASTING GLUCOSE IN ADULTS TREATED WITH OLANZAPINE

Ludmila Kryzhanovskaya M.D,Brian Millen, PhD;Olawale Osuntokun, MD, Carol Robertson-Plouch, DVM;Janice Carlson,PhD; Nayan Acharya, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the patterns of changes in fasting glucose and cholesterol in patients treated with olanzapine over time.

SUMMARY:

Objective: To characterize the changes in total cholesterol and glucose over time in adult patients treated with olanzapine for up to 12 months.
Methods: Long-term changes in total cholesterol and glucose were pooled from 86 olanzapine clinical trials for all patients (N=12,425), regardless of exposure, and in subsets of patients who had minimum exposures of 12, 24, or 48 weeks. Longitudinal analyses of changes in these parameters in groups of patients who had

completed minimum treatment periods were analyzed to elucidate patterns of change over time. Kaplan-Meier survival analyses of time to shifting from normal-to-high or borderline-to-high NCEP and ADA categories were also conducted.
Results: The mean changes in nonfasting total cholesterol (N=729) showed increases until approximately 4 6 months. In Kaplan-Meier survival analyses of time to change from normal-to-high (N=1581) or borderline-to-high total cholesterol (N=777), increases appeared gradually over time; the time to event was earlier for patients who had borderline cholesterol levels at baseline. Mean changes in fasting (N=208) and nonfasting (N=674) glucose increased over time; however, the rate of increase slowed after approximately 6 months. In Kaplan-Meier survival analyses (N=2782) of time to change from the normal-to-high or borderline-to-high fasting glucose categories, the majority of shifts from borderline-to-high appeared to happen within the first year of treatment, while shifts from normal-to-high appeared to happen at a relatively constant rate over the first 2 years of treatment. The same pattern was noted for total cholesterol and nonfasting glucose.
Conclusions: Mean change in glucose levels increased over time; however, the rate of increase slowed after approximately 6 months. Mean total cholesterol increased for up to approximately 4 6 months. Clinicians should monitor their patients for clinically significant changes in these parameters.
Research supported by Eli Lilly and Company.

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» NR1-053

THE IMPACT OF SYMPTOMATOLOGY ON RESPONSE TO A HEALTH PROMOTING INTERVENTION AMONG OLDER ADULTS WITH SCHIZOPHRENIA

Heather Leutwyler, MSN, FNP, CNS, Margaret Wallhagen, PhD, GNP-BC, Christine McKibbin, PhD

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to describe the impact of schizophrenia symptoms on diabetes knowledge and confidence for diabetes management in response to a health promoting intervention among older adults with schizophrenia and comorbid type 2 diabetes mellitus.

SUMMARY:
Background: The portion of older adults with schizophrenia is growing but their health status is poor. To evolve best practices that facilitate health, factors that influence responses to interventions, such as symptoms of schizophrenia, must be understood (1).
Purpose: To explore the relationship between the symptoms of schizophrenia experienced by older persons diagnosed with schizophrenia and type 2 diabetes mellitus (DM) and their response to a health promoting intervention.
Method: Secondary data analysis of a lifestyle intervention program for persons over age 40 with schizophrenia or schizoaffective disorder and DM recruited from board-and-care facilities and day treatment programs (2). Participants were randomly assigned to a 24-week Diabetes Awareness and Rehabilitation Training (DART; n=32) or Usual Care plus Information (UCI; n=32) comparison group. Baseline and 6-month assessments included a diabetes knowledge test (DKT), confidence for diabetes management (CDM), and symptomatology defined by the Positive and Negative Syndrome Scale (PANSS). Hierarchical regression models were used to analyze the data.
Results: A significant condition by symptom interaction was found for DKT. The difference between change in knowledge for DART and UCI groups depends on prevalence and severity of total, negative, and general symptoms. There was no significant condition by positive symptom interaction for DKT. A significant main effect was found between total, negative, positive, and general symptoms in the total sample for improvement in CDM. Higher prevalence and severity of symptoms was negatively associated with improvement in CDM.
Conclusion: Research is needed on larger samples of older adults with schizophrenia, those with greater severity of symptoms, and using measures that more completely capture the individual experience of symptoms. Researchers need to consider the impact of schizophrenia symptoms on response to health promoting interventions.

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» NR1-054

LURASIDONE FOR SCHIZOPHRENIA: SYMPTOMATIC REMISSION DURING SHORT-TERM TREATMENT

Anthony Loebel Ph.D., Josephine Cucchiaro, Ph.D., Masaaki Ogasa, M.S., Robert Silva, Ph.D., Cynthia Siu, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant will have a better understanding of the importance of remission as the optimal treatment outcome in schizophrenia. The participant will also have a better understanding of the time course and probability of achieving remission after short-term treatment with lurasidone.

SUMMARY:
Background: Lurasidone is a novel psychotropic agent with high affinity for D2 and 5-HT2A receptors, as well as for receptors implicated in the enhancement of mood and cognition (5-HT7, 5-HT1a and a2c). We investigated remission rates in this analysis of data from a double-blind, placebo-controlled, 6-week trial of lurasidone in hospitalized patients with schizophrenia.
Methods: Patients hospitalized for an acute exacerbation of schizophrenia were randomized to 6 weeks of double-blind, fixed-dose treatment with lurasidone 40 mg (N=50; baseline PANSS total, 89.6), lurasidone 120 mg (N=49; PANSS total, 92.8), or placebo (N=50; PANSS total, 93.3). Symptomatic remission was defined, using consensus criteria, as an LOCF-endpoint score <=3(mild or less) on 8 core PANSS items (P1-3, G5, G9, N1, N4, N6).
Results: Treatment with lurasidone (40 mg and 120 mg, respectively) was associated with significantly greater LOCF-endpoint improvement than placebo on the PANSS total score (-12.9 and -16.1 vs. -5.7; $p<0.05$ for both comparisons to placebo). Treatment with lurasidone 120 mg or 40 mg was also associated with a significantly higher remission rate at endpoint compared to placebo (31% and 34% vs. 6.1%; $p<0.01$). Number needed to treat rates (NNT [95%CI]) for achieving remission were similar for lurasidone 40 mg (NNT=4.0 [3, 10]), and lurasidone 120 mg (NNT=3.6 [2, 8]). A significantly higher proportion of patients treated with lurasidone 120 mg completed the 6-week study and met criteria for remission compared to placebo ($p=.02$), while a numeric trend favoring LUR 40 vs. placebo was found ($p=0.08$).
Conclusion: In this short-term, placebo-controlled, phase 2 trial, the novel psychotropic lurasidone was associated with higher symptomatic remission rates than placebo in patients with schizophrenia. Further studies are underway to fully characterize lurasidone's clinical profile and dose-response characteristics.

Supported by funding from Dainippon Sumitomo Pharma America, Inc.

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» NR1-055

BEYOND THE METABOLIC SYNDROME: CHRONIC MEDICAL COMORBIDITY IN INSTITUCIONALIZED SCHIZOPHRENIC PATIENTS

Javier López-Moríñigo, Fernando Carballal-Calvo, M.D., Manuel Arrojo-Romero, M.D., Eduardo Paz-Silva, M.D., Ramón Ramos-Ríos, M.D., Rosario Codesido-Barcala, M.D., Alicia Crespí-Armenteros, M.D., Ramón Fernández-Pérez, M.D., José Luís Bouzón-Barreiro, M.D., Jorge Seoane-Prado, M.D., Ignacio Tortajada-Bonaselt, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session the participant should be able to recognise the most frequent chronic illnesses presented in schizophrenic inpatients.

SUMMARY:

OBJETIVE: To assess the prevalence of chronic medical comorbidity in institucionalized schizophrenic patients
METHODS: We designed a specific protocol for the study of chronic medical illnesses. Sociodemographic and clinical variables were obtained from medical histories. All information was revised by a specialist in internal medicine of our long-term psychiatric hospital and all participants signed an informed consent.
RESULTS: We recruited 191 patients (71.8% men) with a mean age of 58.3 years (SD 14.6). 78.5% of the sample had at least one chronic disease. Cardiovascular diseases (35.6%) were the most prevalent in our sample. For the different systems studied hyperlipemia (20.4%), chronic obstructive pulmonary disease - COPD (17.3%), cerebrovascular disease (2.1%), chronic renal failure (4.2%), hepatitis B (21.5%), chronic anaemia (7.3%), benign prostatic hyperplasia (5.93% of men), uterine prolapse and uterine polyps (2.1% of women), arthrosis (13.1%), cataracts (3.7%), psoriasis (3.1%) and thyroid disturbances (4.2%) were the main conditions related. Five patients (2.6%) had neoplasia and no cases of rheumatoid arthritis were reported.
CONCLUSION: The significant increased medical comorbidity is consistent with the previous studies. Improved detection and treatment of medical illness could result in significant benefits in the psychosocial functioning and quality of life of schizophrenic patients.

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» NR1-056

AN OPEN LABEL STUDY OF SWITCHING FROM ORAL ANTIPSYCHOTICS TO RISPERIDONE LONG ACTING IN SCHIZOPHRENIC SUBJECTS WITH NON-ADHERENCE TO THE TREATMENT

Mário Louzã M.D., Hélio Elkis, Ph.D., Sandra I. Ruschel, Ph.D., Eduarodo P. Sena, Ph.D., Rodrigo Bressan, Ph.D., Paulo B. Abreu, Ph.D., Hamilton Grabowski, Ph.D., José C.B. Appolinário, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to known the effects of long-acting risperidone in improving the adherence of patients with schizophrenia.

SUMMARY:

Background: It is known that one of the greatest challenges of schizophrenia long- term treatment is to maintain the subject's adherence to the treatment. Several evidences suggest that long-acting risperidone may play an important role in improving the adherence of patients with schizophrenia.
Objectives: To assess the effectiveness of the switching to long-acting risperidone in patients with schizophrenia non-compliants with typical or atypical oral antipsychotics, and to evaluate the subject's perception of the medication.
Methods: After a 2-week run-in period, patients with schizophrenia (DSM-IV) received a flexible dose regimen of long-acting risperidone (doses of 25 mg, 37,5 mg, or 50 mg were used according to clinician's judgement) every 2 weeks for 12 months. Effectiveness was assessed by the Positive and Negative Syndrome Scale (PANSS) and CGI (Clinical Global Impression). The subject's perception of the medication was measured by the Drug Attitude Inventory (DAI-10). Tolerability was assessed by adverse events report. An ITT approach using mixed-effects model was performed.
Results: Fifty three patients were included in this analysis. Improvement was observed from week 2 through the 12-month treatment period with significant reduction in total PANSS scores (-9.08, p<.0001). CGI-S scores improved from 3.55 to 3.19 (p=.01). DAI-10 improved over the course of treatment (-2.29, p=.0062). Long-acting risperidone was well tolerated. Of the 53 patients who were included in this analysis, the most frequently reported adverse events were insomnia (22,6%), weight gain (13,2%) and acute dystonia (3,8%).
Conclusions: Switching from oral antipsychotics to long-acting risperidone in non-compliant patients was associated with a significant reduction of the severity of symptoms and a better patient's attitude to treatment. Long-acting risperidone was also well-tolerated. This study was supported by Janssen-Cilag Brazil.

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» NR1-057

LONG-ACTING RISPERIDONE ADJUNCTIVE TO STANDARD CARE IN PATIENTS WITH BIPOLAR DISORDER WHO ARE EXPERIENCING MOOD SYMPTOMS

Wayne Macfadden M.D., Caleb M. Adler, M.D., Norris Turner, Pharm.D., Ph.D., Ibrahim Turkoz, M.S., J. Thomas Haskins, Ph.D., Larry Alphs, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the role of risperidone long-acting therapy adjunctive to treatment as usual in treating patients with bipolar disorder who are experiencing mood symptoms.

SUMMARY:

Background: Treatment of bipolar patients with multiple relapses remains challenging. This analysis examined the efficacy of risperidone long-acting therapy (RLAT) plus treatment as usual (TAU) in bipolar disorder patients with acute mood symptoms.
Methods: Post-hoc analysis was performed from the open-label (OL) phase of an international study (United States and India) of RLAT for patients with bipolar disorder who relapsed at least 4 times in the previous 12 months. During the 16-week OL phase, RLAT was administered (25–50 mg every 2 weeks) adjunctively with any combination of TAU (mood stabilizers, antidepressants

and anxiolytics). Patients with baseline symptoms of depression (MADRS >16), mania (YMRS >16) or mixed symptoms (both >16) were analyzed. Week 16 (last observation carried forward) endpoints: change from baseline, remission rates (MADRS <=10, YMRS <=10 and CGI <=3 at endpoint of the OL phase) and adverse events (AEs). Statistical significance was determined using paired t tests. Study ID: CR004693.
Results: Of 275 enrolled patients, 148 (53.8%) were symptomatic at OL baseline. Mean (SD) baseline YMRS, MADRS and CGI-BP-S scores of symptomatic patients were 19.5 (12.4), 15.5 (11.8) and 4.3 (0.8), respectively; 73.7% of symptomatic patients at baseline completed the 16-week OL phase. Significant improvements were noted from OL baseline to week 16 endpoint in mean [SD] YMRS (–13.9 [13.3]; P<0.001), MADRS (–5.8 [13.0]; P<0.001) and CGI-BP-S
(–1.8 [1.5]; P<0.001) total scores. Over half (55.6%) achieved remission at endpoint. Most common AEs (>=10%): tremor (22.3%), muscle rigidity (14.9%), weight increase (14.9%) and headache (12.2%).
Conclusion: Improvements were observed when OL RLAT adjunctive with TAU was used to treat patients with bipolar disorder who were experiencing mood symptoms, with no unexpected safety or tolerability trends.
Supported by Ortho-McNeil Janssen Scientific Affairs, LLC

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» NR1-058

EFFECT OF POLYMORPHISMS IN THE DOPAMINE RECEPTOR 2 GENE ON ILOPERIDONE EFFICACY FOR THE TREATMENT OF PATIENTS WITH SCHIZOPHRENIA

Kendra Mack M.S., Louis Licamele, M.S., Andrew Thompson B.S., Christian Lavedan Ph.D., Simona Volpi, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to Understand how the Taq1A polymorphism in the dopamine receptor 2 gene may contribute to the early inter-individual differences in the therapeutic efficacy of iloperidone.

SUMMARY:

Objective: It has been proposed that single nucleotide polymorphisms (SNPs) in the dopamine receptor 2 gene (DRD2) play a role in the presentation of schizophrenia symptoms and their treatment, and may explain some inter-individual differences observed in antipsychotic response. Iloperidone is a novel mixed D2/5-HT2 antagonist with high affinity for DRD2. In clinical trials, iloperidone has demonstrated efficacy for a broad range of schizophrenia symptoms, with a favorable profile on key metabolic parameters and on movement disorders (extrapyramidal symptoms and akathisia). A pharmacogenetic analysis of DRD2 was conducted in a phase III clinical trial to identify DNA polymorphisms predictive of iloperidone response. Method: A mixed-effects model repeated measures analysis was performed by genotype, for several DRD2 SNPs, on improvement of symptoms assessed by the Positive and Negative Syndrome Scale Total (PANSS-T) score. Results: SNP allele frequencies varied across populations. Genotype differences were statistically significant between Blacks, Whites and Asians. In the overall population, and in Whites alone, one SNP (Taq1A, rs1800497), located in the 3' untranslated region of DRD2, was significantly associated (p=0.05) with iloperidone efficacy at days 7, 10, 14 and 21, but not at day 28. The same trend was observed in Blacks, but did not reach statistical significance. Conclusions: These results suggest that rs1800497 may contribute to the early inter-individual differences in the therapeutic efficacy of iloperidone. To explain these findings, the functional effect of rs1800497 on the expression and/or function of DRD2 remains to be investigated. This study provides new insights into the response to iloperidone, developed with the ultimate goal of directing therapy to patients with the highest benefit-to-risk ratio. Vanda Pharmaceuticals sponsored this study.

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» NR1-059

PREDICTORS OF REMISSION IN SCHIZOPHRENIA

Prakash Masand M.D., Cedric O'Gorman, M.D., Francine Mandel, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to consider the potential relationship between a patient's early response to an antipsychotic, as measured by the PANSS and BPRS, and the probability of later remission.

SUMMARY:

Background: The first consensus-based definition of remission provided a conceptual model incorporating criteria for schizophrenia that could be conveniently assessed in different phases of the disorder.(1,2) This definition linked remission to symptoms as defined in the DSM-IV and used established rating scales to measure these symptoms. The objective of these analyses was to determine whether remission could be predicted by improvement defined by rating scales such as the PANSS or BPRS at early time points during treatment.
Methods: A search of the ziprasidone clinical trials database identified10 ziprasidone studies, all >= 1 year, including acute core studies and their open-label extensions, as well as 1-year trials. As many as 600 subjects were included in analyses that identified potential symptomatic, syndromal, and functional predictors of functional remission in schizophrenia. Several criteria for response were examined as predictors of remission, and CGI-I of 1, PANSS and BPRS scores at weeks 1, 3, and 4 were used to predict remission at end point. Remission was also defined using the working group definition: PANSS (P1, P2, P3, N1, N4, N6, G5, and G9) <= 3 for >= 6 consecutive months and BPRS (items 4, 7, 8, 11, 12, 15, and 16) <= 3 for >= 6 consecutive months. ROC curves were generated for each of these predictors (at each time point) for each of these definitions at end point, and area under the ROC curve (AUC) was calculated.
Results: In the combined ziprasidone arms, BPRS scores at weeks 1, 3, and 4 successfully predicted PANSS remission ($p < 0.01$); and BPRS remission ($p < 0.0001$) at study end point (44–196 weeks). PANSS scores (at weeks 1, 3, and 4) successfully predicted PANSS remission ($p < 0.01$); and BPRS remission ($p = 0.02$ at week 3 only) at study end point. AUC ranged from 0.59 to 0.93.
Conclusion: BPRS and PANSS remission criteria at study end points were accurately predicted by BPRS or PANSS total scores at weeks 1, 3, and 4. Supported by funding by Pfizer Inc.

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NR1-060

LONG-TERM OPEN-LABEL SAFETY OF OLANZAPINE LONG-ACTING INJECTION: 190-WEEK INTERIM RESULTS

David McDonnell M.B., Scott W. Andersen, M.S., Holland C. Detke, Ph.D., Fangyi Zhao, Ph.D., Susan B. Watson, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe findings related to the long-term safety and tolerability of olanzapine long-acting injection.

SUMMARY:

OBJECTIVE: The primary objective of this ongoing open-label study is to examine the long-term safety and tolerability of olanzapine long-acting injection (LAI). Current results are from an interim analysis, with a maximum treatment duration of 190 weeks. METHODS: Patients were 18-75 years of age with schizophrenia or schizoaffective disorder (N=931), enrolled in an open-label extension study following 1 of 3 randomized, controlled studies of olanzapine LAI, in which patients had been randomly assigned to oral olanzapine, olanzapine LAI, or placebo. During the open-label extension, all patients received flexibly-dosed olanzapine LAI at injection intervals of approximately 2-4 weeks. RESULTS: At time of analysis, rate of study discontinuation was 46.3%. Discontinuation rate at 18 months was 34.3%. The most common reasons for discontinuation were: subject decision (23.4%), adverse event (6.7%), and lost to follow-up (5.7%). Adverse events in >=5% of patients were increased weight, insomnia, anxiety, somnolence, headache, and nasopharyngitis. There were 26 occurrences of temporary post-injection syndrome, characterized by sedation- and/or delirium-related symptoms following possible accidental intravascular injection of a portion of the dose; all of these patients fully recovered within 72 hours. Mean weight change was +1.88 kg, with 32.1% of patients experiencing >=7% weight gain. Percentages of patients who increased from normal to high on fasting glucose, random total cholesterol, or random triglycerides were 5.5%, 5.2%, and 14.3%, respectively. Mean Clinical Global Impressions-Severity scores remained stable throughout (2.9 at baseline to 2.8 at endpoint). CONCLUSIONS: Olanzapine LAI discontinuation rates have been low compared with studies of other depot antipsychotics. Safety findings were consistent with those observed with oral olanzapine treatment, with the exception of those specific to intramuscular injection. Research supported by Eli Lilly and Company.

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NR1-061

THE RELATIONSHIPS BETWEEN SYMPTOMS OF SCHIZOPHRENIA AND THE COGNITIVE DOMAINS OF MATRICS COGNITIVE BATTERY

Shin Min-Sup Ph.D., Choong-Wan, Woo, M.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to identify the specific relationships between cognitive domains of MCCB and symptoms of schizophrenia and to recognize that the verbal learning domain in MATRICS Cognitive Battery (MCCB) is highly associated with symptoms of schizophrenia, especially disorganized symptoms.

SUMMARY:

Objective: This study aims to examine the relationships between symptoms of schizophrenia and cognitive domains of the MATRICS Cognitive Battery (MCCB).
Method: Thirty stable schizophrenic patients, whose diagnoses were confirmed using the Schedule for Affective Disorders and Schizophrenia (SADS), were evaluated using the Positive and Negative Syndrome Scale (PANSS) and the MCCB. Three symptom dimensions of schizophrenia were rated using selected items of the PANSS according to the findings of previous factor analytic studies. Correlation and multivariate regression analyses were conducted on the obtained data after controlling for age, gender, general intelligence (IQ), and depression.
Results: While severity of positive and negative symptoms showed no significant correlations with any cognitive domain scores of the MCCB, severity of disorganized symptoms showed strong negative correlation with verbal learning domain score. When examining the relationships between cognitive domains of the MCCB and the specific symptom scores of the PANSS, we found that attention/vigilance score negatively correlated with difficulty in abstract thinking and that verbal learning score showed negative correlations with motor retardation, conceptual disorganization, and difficulty in abstract thinking scores. In addition, impaired social cognition was associated with delusion, suspiciousness, active social avoidance, and conceptual disorganization scores. Multivariate analysis showed that verbal learning score was the most significant predictor of the three symptom dimension scores.
Conclusions: The present study suggested that certain cognitive domains (attention/vigilance, verbal learning, and social cognition) have specific relationships with some of schizophrenic symptoms. Notably, verbal learning seems to be highly associated with symptoms of schizophrenia, especially disorganized symptoms.
This study is supported by SNU Research Fund.

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NR1-062

DIAGNOSTIC VALIDITY OF MMPI-2 FOR PATIENTS WITH SCHIZOPHRENIA AND DEPRESSIVE DISORDER

Shin Min-Sup Ph.D., Soon-Ho Seol, M.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the effectiveness and validity of content scales and reconstructive clinical (RC) scales of MMPI-2 to assist in the differential diagnosis for patients with schizophrenia and depressive disorder.

SUMMARY:

Purpose. This study was conducted to evaluate the capacity of content scales and reconstructed clinical (RC) scales of MMPI-2 to assist in the differential diagnosis for patients with schizophrenia and depressive disorder.
Methods. Sixty-one patients with schizophrenia (31 paranoid schizophrenia; 30 non-paranoid schizophrenia) and 28 patients with depressive disorder performed MMPI-2. MANOVA and post-hoc ANOVA (with Bonferroni correction) were performed on MMPI-2 clinical, content, and RC scales. Secondly, discriminant analyses were performed to examine whether scales of MMPI-2 could differentiate the diagnosis.
Results. The depressive group showed MMPI-2 profiles characterized by a significant elevation in the clinical scale of D compared with the schizophrenia group. Higher Anxiety (ANX) and Depres-

sion (DEP) scores in content scales and higher Demoralization (RCd) and Cynicism (RC3) scores in RC scales are likely to be associated with a diagnosis of depressive disorder, whereas higher Bizarre Mentation (BIZ) scores in content scales tended to be associated with a diagnosis of schizophrenia. A discriminant function using these variables was highly reliable. Patients with paranoid schizophrenia reported significantly less depressive symptoms (D and DEP) and showed a tendency to be less anxious (ANX), to be less uncomfortable (RCd) than the depressive group. Patients with non-paranoid schizophrenia, in contrast, showed scores between those of the other two groups, and no significant difference from them.
Conclusions. The findings of the present study are important in terms of indicating that MMPI-2 RC scales have considerable potential in terms of supplementing clinical and content scales for the differentiation of psychiatric disorders. And the current study is worth of the first research to identify the differences of MMPI-2 profile between schizophrenia subtypes- paranoid schizophrenia and non-paranoid schizophrenia.

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» NR1-063

EVALUATION OF TREATMENT ADHERENCE AND THERAPEUTIC ALLIANCE IN PSYCHOTIC PATIENTS IN TRANSITION FROM ORAL TO LONG ACTING INJECTABLE RISPERIDONE

David Misdrahi, Antonio Delgado, Denis Comet, Jean-François Chiariny

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand that the treatment adherence and therapeutic alliance determined by the degree of insight and of disease severity can be easily assessed by the self-questionnaires MAQ and 4 PAS.

SUMMARY:

Objective: Evaluation of treatment adherence and therapeutic alliance in patients treated with oral risperidone for an acute psychotic episode and for whom the psychiatrist decided to switch to risperidone long acting injectable.
Methods: In a cross-sectional study performed under real-life conditions, treatment adherence was assessed by a self-questionnaire using MAQ (Medication Adherence Questionnaire) and MARS (Medication Adherence Rating Scale) scales and therapeutic alliance by the 4 PAS scale. The level of treatment acceptance, insight (G12 PANSS) and the disease severity (CGI-S) were assessed by a psychiatrist.
Results: A population of 1887 patients (age 36.8±11.9y) was treated by 399 psychiatrists for a recent acute episode of psychosis (13.0% first episode, 61.6% with schizophrenia). Hospitalization was necessary in 57.8% of patients. The psychiatrists observed reluctance or total/partial refusal of treatment in 41.6% and a passive, moderately active or active acceptance in 58.4% of the patients. The therapeutic alliance (4 PAS) (evaluated in 1530 patients) was 35.8±5.9 points (median 36, maximum 44). Therapeutic adherence (MAQ) was low in 53.0%, medium in 29.6% and high in17.4% of the patients. A strong correlation was observed between good adherence and good treatment acceptance as evaluated by the physician ($p<0.001$) and a high therapeutic alliance score ($p<0.001$). Low adherence was significantly associated with a diagnosis of schizophrenia ($p<0.001$), with CGI-S ($p<0.001$), and with severe insight ($P<0.001$). These last parameters were significantly associated with a low therapeutic alliance score (4 PAS).
Conclusion: The self-questionnaires MAQ and 4 PAS allow evaluation of treatment adherence and therapeutic alliance determined by the degree of insight and of disease severity. These tools are easy to use and can help the clinician to better assess and improve patient adherence to treatment.Supported by Janssen Cilag France.

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» NR1-064

PERSONALITY DISORDER IN FIRST ADMITTED SCHIZOPHRENIC PATIENTS: PREVALENCE AND DIAGNOSTIC STABILITY

Javad Moamai M.D., Jacques Seguin,MD,FRCPC.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:1)Recognize the prevalence rate of personality disorder in inpatient schizophrenic populations.2)Appraise the diagnostic stability of comorbid personality disorder in schizophrenia.

SUMMARY:

Background: While the relationship between Personality Disorder (PD) and Schizophrenia (SZ) has long been discussed, little is known about the predictive validity of these diagnoses coexisting. The aim of this naturalistic study was to determine the prevalence and Longitudinal Diagnostic Stability (LDS) of PD in an inpatient SZ population.
Methods: Data were taken from separation sheets (ICD-9 format) of all 1331 first admitted adult SZ patients (18-64 years) to a Quebec regional psychiatric hospital, from 1980 to 2007. A subgroup of 534 multi-admission cases provided data on LDS. Clinical patterns of PD were evaluated using predictive values analysis and prevalence-odd ratio statistics.
Results: Over the study period, the observed prevalence rate of PD was 10.6% among first admission subjects suffering from schizophrenic spectrum disorders. This rate was equally distributed among the three clusters of PD. The presence of PD was correlated with younger age and readmission rate but not to gender, drug abuse, involuntary hospitalization and length of stay. Over a median period of seven years, the crude LDS of PD was 61% (clusters A = 33%, B = 58% and C = 63%). The borderline PD with a LDS of 71% was the most stable type.
Conclusions: Our study found that PD in SZ had a fair to good stability rate over time. However, stability values of subtypes were mixed. Interestingly, the first admission SZ subjects had a somewhat lower rate of PD than the general population, possibly due to the more florid psychotic symptoms of their illness.

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» NR1-065

EVALUATION OF COGNITIVE FUNCTION IN PATIENTS SWITCHED FROM RISPERIDONE TO ARIPIPRAZOLE USING DIFFERENT TITRATION STRATEGIES: AN OPEN-LABEL STUDY

Reza Moghadam Pharm.D., Jean-Pierre Kahn, M.D., Ph.D.; Anne Dillenschneider, M.D., Sieglinde Modell, M.D.; Christian Werner, M.D.; Wendy Kerselaers, M.S.; Jean-Yves Loze, M.D.; Robert D. McQuade, Ph.D.;

William H. Carson, M.D.; Jurgen Lissens, M.Sc.; Vincent Rykmans, M.D.; Raymond Sanchez, M.D.

EDUCATIONAL OBJECTIVES:

Describe the effects on cognitive function of 12 weeks of open-label aripiprazole to which patients have been switched from risperidone.

SUMMARY:

Background: Aripiprazole is effective in treatment of schizophrenia (1). Less well studied are the cognitive effects of aripiprazole in schizophrenia.
Objective: Evaluate cognition using the Group Espanol para la Optimizacion y Tratamiento de la Esquizofrenia (GEOPTE) scale for social cognition and the PANSS Cognition subscale after changing from risperidone to aripiprazole using either fixed- or variable-dose switching strategies.
Methods: Analyses of secondary endpoints related to cognitive function were performed on data from a 12-week, open-label aripiprazole study among 400 patients with schizophrenia who had efficacy and/or safety issues with risperidone therapy. Patients were randomized to two switching strategies - a titrated dose (5 mg/day to 15 mg/day by Week 4) or a fixed dose (initiated at 15 mg/day). Mean changes in GEOPTE and PANSS Cognition subscale scores were summarized using descriptive statistics with 95% confidence intervals.
Results: The GEOPTE scale (2) is a 15-item scale that measures both the patient's and caregiver's subjective perception of the patient's deficits. A negative change score signifies improvement. GEOPTE summary scores and PANSS Cognition subscale scores had decreased at Weeks 4 and 12 (LOCF) regardless of switching strategies; Week 12 GEOPTE patient summary score change was -5.27 (n=194) and -6.12 (n=191), and GEOPTE caregiver summary change was -4.17 (n=98) in the titrated dose and -7.19 (n=95) in the fixed dose, respectively. Aripiprazole was well tolerated, with the most common adverse event reported being insomnia (8.5%, n=34/399).
Conclusions: Non-optimally treated schizophrenia patients on risperidone who were switched to aripiprazole showed reductions in GEOPTE patient and caregiver summary scores and PANSS Cognition subscale. Additional research is warranted to evaluate the potential impact of aripiprazole on cognition.

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» NR1-066

FEASIBILITY AND ACCEPTABILITY OF AN AUDIO COMPUTER-ASSISTED SELF-INTERVIEW INSTRUMENT (ACASI) TO ASSESS SYMPTOMS AND SIDE-EFFECTS IN OUTPATIENTS

Ramin Mojtabai M.D., Sophia Haeri, BA; Eda Inan, BA; Jamie Johnson, BA.; Lisa Cohen, PhD; Igor Galynker,PhD; Patricia K. Corey-Lisle,PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, participants will gain new understanding of the advantages of using the Audio Computer-Assisted Self-Interview (ACASI) when administering self-report questionnaires in schizophrenia spectrum patients.

SUMMARY:

Background: With rare exceptions, there are few self-report measures of symptoms and medication side-effects in schizophrenia. This may reflect cognitive difficulties with attention and working memory. Here, we report on feasibility and acceptability of the ACASI, specifically designed to administer self report measures of symptoms and side effects to patients with schizophrenia.
Method: Adult outpatients with clinical diagnoses of schizophrenia or schizoaffective disorder completed the ACASI battery. The battery included 7 self-report questionnaires measuring symptoms, quality of life, health status, medication adherence, substance abuse, subjective experience of cognitive deficits, and demographic variables. Questions were presented simultaneously on a computer touch screen and by audio recording. Research staff was nearby to answer questions. After completing the battery, patients were asked questions about their experience of using the ACASI.
Results: Of 185 patients who consented to the study, all but 2 completed the battery. Of these, 180 also responded to post interview questions. The large majority (N=176, 95%) had a positive attitude towards the ACASI interview. They found the interview "interesting" and "easy". Others expressed a sense of accomplishment at having completed the computer interview. Only 2 patients had a negative reaction, one towards the computer. Others found the audio presentation of questions confusing. Of note, there were no skipped questions or missing data.
Conclusions:The ACASI methodology provides a feasible and convenient way to obtain self-report data from schizophrenic patients. The overwhelming majority of these patients had a positive attitude towards this format and preferred it to paper and pencil questionnaires. This assessment may represent an efficient supplement to clinical interviews in routine clinical setting in future as well as a valuable research technique.
Commercial support provided by Bristol-Meyers Squibb.

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» NR1-067

NEUROLOGICAL COMORBIDITIES IN PATIENTS WITH BIPOLAR DISORDER: A SYSTEMATIC REVIEW

José Manuel Montes M.D., Jerónimo Saiz-Ruiz, M.D., Julio Bobes, M.D., José Mostaza, M.D., Eduard Vieta, M.D., Fernado Rico-Villademoros, M.D., on behalf of the Spanish Consensus Group of Experts on Physical Health in Patients with Bipolar Disorders.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize the prevalence of neurological comorbidities among patients with bipolar disorder.

SUMMARY:

Objective: to synthesize the available knowledge on neurological comorbid disorders in patients with bipolar disorder (BD).
Methods: relevant studies were identified by a MEDLINE search from 1966 to January 2008, and supplemented by a manual review of reference lists of the articles identified and previous review articles. We included studies with any design, in patients with BD as diagnosed by any criteria, with sample size =30 patients, and reporting any measure of frequency or association about comorbidities. Priority was given to comparative studies.
Results: We identified 21 studies: 11(52.4%) were comparative; 10 (47.6%) were cross-sectional and 11 (52.4%) were retrospective cohort studies; 2 (9.5%) were a population-based studies; and 2 (9.5%) used a probabilistic sampling. An increased point-prevalence of migraine in patients with BD, compared with the general population, was reported in two studies (24-24.8% vs 10.3-11%). One study also reported a higher lifetime-prevalence of migraine in patients with BD than in the general population (15.2% vs 7%). Two studies reported a higher point-prevalence of dementia in patients with BD as compared with that of the general popula-

tion (1.8% vs 1%) or with that of patients with arthrosis/diabetes (1.9% vs 1.1/1%), respectively. However, in one study the point-prevalence of Alzheimer disease did not differ between patients with BD and the general population (0.7% vs 0.6%). Data on other neurological comorbidities such as epilepsy, Parkinson disease or multiple sclerosis, are very limited.
Conclusion: BD seems to be associated with an increased frequency of migraine. The possible association between BD and dementia should be further investigated.

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» NR1-068

REMISSION IN SCHIZOPHRENIA – COURSE AND CORRELATES

Leena Naughton M.D., Olivia Gibbons MD, Aideen Lynch MSc, Paul O'Connell MD, Harry G Kennedy MD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify and compare the differences in characteristics of persons suffering from schizophrenia in remission, and non remission, and they relate to treatment. This can be used to improve management practices and protocols, and to guide future studies.

SUMMARY:

Aims: Criteria for remission in schizophrenia were recently defined (Andreason et al 2005). We hypothesised that those in remission would differ from those not in remission according to aspects of the natural history of their illness. We expected to find clinical associations of remission such as use of clozapine.
Methods: We identified 69 patients in a forensic psychiatric hospital who met ICD-10 criteria for schizophrenia or schizoaffective disorder using SCAN and I-SHELL, for whom we had PANSS assessments repeated over a six month period. We used review of case notes (mean 10.2 years available in the hospital) supplemented by interview to rate the lifetime course of the illness according to ICD-10 and DSM-IV-TR criteria. Data was entered and analysed in SPSS-15. Remission status based on serial PANSS assessments was arrived at, by the clinicians independently of the clinicians assessing diagnosis and clinical course.
Results: Of 69 patients, 26 had a remission and 43 did not. Whether using ICD-10 or DSM-IV categories for course of illness, remission was more common in those with and episodic course with full remissions between episodes, while lack of remission was more common in those with a continuous course, or those with residual negative symptoms (X2=13.5, df=4, p=0.009). Those in remission were more likely to be further along the pathway through care (linear association r=4.76, df=1, p=0.03). Use of clozapine was unrelated to remission status. Those with schizoaffective disorder were more likely to be in remission than those with schizophrenia (X2=4.2, df=1, p=0.040).
Conclusion: Remission status is related to positive outcome, but is as much related to course and diagnosis (schizoaffective or not) as to specific treatments such as clozapine.

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» NR1-069

CHANGES IN ADIPOSITY, INSULIN SENSITIVITY AND LIPID METABOLISM DURING RANDOMIZED ANTIPSYCHOTIC TREATMENT IN SCHIZOPHRENIA

John W. Newcomer, M.D.; Dan W. Haupt, M.D.; Peter A. Fahnestock, M.D.; Karen S. Flavin, R.N., C.C.R.C.; Ginger E. Nicol, M.D.; Julia A. Schweiger, C.C.R.C.; Elizabeth T. Westerhaus, M.A.; Angela M. Stevens, B.S.; Michael D. Yingling, B.S.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the utility of certain clinically available markers of cardiometabolic risk in monitoring patients taking antipsychotic medications. Differential risk across treatment groups, and the role of pretreatment condition upon switching medications in determining outcomes will be discussed.

SUMMARY:

Background: Treatment with antipsychotic medications can contribute to increases or decreases in body weight, as a function of individual medication effects and pretreatment conditions. Increases in adiposity are relevant to risk for cardiovascular disease (CVD) and diabetes mellitus, common causes of morbidity and mortality in patients with schizophrenia (1). Pre-treatment conditions have important effects on treatment response (2). However, no studies to date have aimed to stratify such pre-treatment conditions across prospective, randomized treatment groups.
Methods: Schizophrenia patients (n=81) were randomized to 12 weeks of treatment with olanzapine, quetiapine, risperidone, or ziprasidone, balancing prior treatment conditions and baseline age and adiposity across treatment groups. Detailed metabolic measurements, including dual energy X-ray absorptiometry (DEXA), hyperinsulinemic, euglycemic clamps with stable isotopomer tracers, and fasting plasma lipid measurements were used to quantify whole-body and regional adiposity, whole-body and tissue-specific insulin sensitivity, as well as plasma lipid levels, at baseline and after 12 weeks of treatment.
Results: Results of this study indicate significant differential treatment-related changes in DEXA-measured adiposity (F[3,71]=6.23, p=0.001), fasting plasma triglyceride (F[3,71]=4.18, p=0.009), fasting cholesterol (F[3,71]=3.9, p=0.01), fasting HDL (F[3.71]=3.24, p=0.03), and fasting LDL (F[3,70]=2.75, p=0.05). In addition, pretreatment conditions play an important role in determining current treatment-related changes.
Discussion: Antipsychotic medications produce differential effects on direct measures of adiposity and insulin sensitivity, as well as on related and clinically-available measurements relevant to the prediction of cardiometabolic risk. Previous treatment with high-risk agents is associated with greater decreases in adiposity, insulin sensitivity and adverse lipid levels when switching to a lower-risk agent. These results are relevant to understanding opportunities to reduce cardiometabolic risk in persons treated with antipsychotic medications.

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» NR1-070

STRATEGIES FOR THE MANAGEMENT OF ANTIPSYCHOTIC-INDUCED SEXUAL DYSFUNCTION

Luciana Nunes M.D., Márcio Gerhardt Soeiro de Souza, M.D., Luiz Henrique Junqueira Dieckmann, M.D., Fernando Sargo Lacaz, M.D., Mariane Nunes, M.D., Sandra Nunes, Ph.D., Rodrigo Bressan, Ph.D, Jair de Jesus Mari, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session the participant should be able to recognize the importance of evaluating sexual complains of psychotic patients, since they usually are adverse effects from antipsychotic drugs and are strongly associated with compliance issues. Therefore participants should be able to learn about pharmacological and psychological strategies to treat sexual symptoms secondary to antipsychotic use.

SUMMARY:
INTRODUCTION: Sexual dysfunctions are common in psychiatric patients. While it occurs in 30% of men in general population, it can be found in more than 60% of schizophrenic patients. The combination of counseling, antipsychotic's dose reduction, the change of first generation to second generation antipsychotic can be useful to reduce sexual function deterioration. A systematic review about sexual dysfunction clinical management demonstrates that the most used medications are: bromocriptine, carbegoline, ciproheptadine, amantadine, shakuyaku-kanzo-to, sildenafil, vardenafil and selegiline. However, the majority of recent studies were realized in short periods of time, had small sample of patients and few were randomized and placebo controlled. CASE REPORT:DS, 27 years old Caucasian male presented with a recent history of social isolation, apathy, fear, vague discourse, decreased work performance. After four months, he developed persecutory delusions and auditory hallucinations. Once given the diagnostic of Paranoid Schizophrenia it was prescribed Risperidone 4 mg/day with remission of symptoms. However, after 3 months, the patient discontinued treatment because severe erection dysfunction. He had a relapse of positive symptoms and after the reintroduction of medications and stabilization of disease, he was prescribed tadalafil 20 mg. Therefore the patient had better treatment compliance since his sexual performance improved. CONCLUSION: This case report reinforces the importance of being aware of our patient's sexual complains, since it can lead to a worse adherence. The phosphodiesterase V inhibitors are well tolerated, they don't have neurological side effects and they don't interfere with neuroleptic's pharmacodynamics. Prospective longitudinal studies are necessary to improve the treatment of antipsychotic sexual dysfunction.

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» NR1-071

REASONS FOR DISCONTINUATION AND CONTINUATION OF ANTIPSYCHOTIC THERAPY FROM PATIENT AND CLINICIAN PERSPECTIVES

Allen Nyhuis M.S., Haya Ascher-Svanum, Ph.D., Virginia L. Stauffer, Pharm.D.,Bruce J. Kinon, M.D., Douglas E. Faries, Ph.D., Glenn A. Phillips, Ph.D., Diana O. Perkins, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should recognize that medication efficacy appears to be the core driver of medication continuation and of medication discontinuation, especially with regard to improvement on positive symptoms. Reasons for medication discontinuation differ somewhat from reasons for continuation, with a high level of concordance between patients' and clinicians' perspectives.

SUMMARY:
Objective: To assess the reasons for discontinuation and for continuation of antipsychotic medication in the treatment of schizophrenia from patient and clinician perspectives (1,2).
Methods: Two measures were developed to assess the Reasons for Antipsychotic Discontinuation/Continuation (RAD), one from patient's perspective (RAD-I), and the other from clinician's perspective (RAD-Q). These measures were administered to patients enrolled in a 12-week study of antipsychotic medication in the treatment of schizophrenia (N=630). Reasons for discontinuation and reasons for continuation with the assigned antipsychotic during the study were assessed. Reported reasons were rated as being a primary reason, very important, somewhat important, or of minor importance. The top primary reasons for medication discontinuation and continuation were identified from patient and clinician perspectives, and level of concordance between patients' and clinicians' reasons was assessed.
Results: The top primary reasons for medication discontinuation differed from the top primary reasons for continuation on the medication, with a high level of concordance between patients' and clinicians' perspectives. The top 3 primary reasons for medication discontinuation were insufficient improvement or worsening of positive symptoms, medication-related adverse events, and insufficient improvement or worsening of mood symptoms. The top 3 primary reasons for medication continuation were improvement in positive symptoms, subjective perception of improvement, and improvement in level of functioning.
Conclusions: Medication efficacy appears to be the core driver of medication continuation and discontinuation, especially with regard to positive symptoms. Reasons for medication discontinuation differ somewhat from reasons for continuation, with a high level of concordance between patients' and clinicians' perspectives. Funded by Eli Lilly and Company.

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» NR1-072

PREDICTIVE POWER OF EARLY IMPROVEMENT WITH ATYPICAL ANTIPSYCHOTICS FOR LATER TREATMENT RESPONSE IN PATIENTS WITH SCHIZOPHRENIA

Cedric O'Gorman M.D., John Kane, M.D., Shitij Kapur, M.D., Ph.D., Sheela Kolluri, Ph.D., Elizabeth Pappadopulos, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to demonstrate the predictive power of week 1 and week 2 improvement to later treatment response, as measured by changes from baseline CGI-I and BPRS scores.

SUMMARY:
Background: Prediction of antipsychotic treatment response based on patient outcomes within the first 2 weeks of treatment would facilitate the decision to continue treatment or switch to an alternative agent.
Methods: Data were pooled from 2 similarly designed, 6-week (ziprasidone vs olanzapine, mean doses: 129 and 11.3 mg/d, respectively) or 8-week (ziprasidone vs risperidone, mean doses: 114.2 and 7.4 mg/d, respectively), flexible-dose, randomized, comparative trials of inpatients with an acute exacerbation of schizophrenia or schizoaffective disorder. Improvement at week 1 and week 2 was defined as >= 10% and >= 20% reductions from baseline BPRS scores, respectively, or a measurement of either 1, 2, or 3 for CGI-I. Response at week 6 was defined as a >= 40% reduction from baseline BPRS score or a measurement of either 1 or 2 for CGI-I. Sensitivity (SENS) and specificity (SPEC), posi-

tive predictive value (PPV), negative predictive value (NPV), and predictive power (PP) were calculated.
Results: Using BPRS scores, week 1 improvement identified 71/107 (66.4%, SENS) week 6 responders; week 1 nonimprovement identified 159/262 (60.7%, SPEC) week 6 nonresponders. Of 174 week 1 improvers, 71 (40.8%, PPV) were week 6 responders. Of 195 week 1 nonimprovers, 159 (81.5%, NPV) were week 6 nonresponders. The PP was 65.4%. Using week 2/week 6 BPRS scores yielded: SENS 80.4%, SPEC 69.2%, PPV 52.9%, NPV 89.2%, and PP 72.5%. Using week 1/ week 6 CGI-I scores yielded: SENS 68.9%, SPEC 51.1%, PPV 71.9%, NPV 47.5%, and PP 62.6%. Using week 2/week 6 CGI-I scores yielded: SENS 96.3%, SPEC 25.6%, PPV 76.3%, NPV 61.1%, and PP 74.5%.
Conclusion: Early nonimprovement was highly predictive of later nonresponse for BPRS, but not for CGI-I. The difference between BPRS and CGI-I in predicting later nonresponse suggests further research is needed to compare the predictive capabilities of clinical vs research tools for outcomes in schizophrenia.
This study was supported by Pfizer Inc.

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» NR1-073

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RESPONSE EFFICACY/SAFETY STUDY OF PALIPERIDONE PALMITATE IN ADULTS WITH SCHIZOPHRENIA

Gahan Pandina Ph.D., Jean-Pierre Lindenmayer, M.D., Julia Lull, M.A., Pilar Lim, Ph.D., Cristiana Gassmann-Mayer, Ph.D, Srihari Gopal, M.D., M.H.S., Eric Yuen, M.D., Joseph Palumbo, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the efficacy and tolerability of paliperidone palmitate when initiated at 150mg eq. (deltoid muscle), followed by 25–150mg eq. doses monthly, beginning on Day 8 (deltoid or gluteal muscle).

SUMMARY:

Introduction: Efficacy and safety of 3 fixed doses of paliperidone palmitate (PP) vs placebo (PB) were investigated in a 13-week, double-blind, multicenter study in subjects with DSM-IV schizophrenia.
Methods: Adults with acute exacerbation of schizophrenia were randomized 1:1:1:1 to fixed-dose PP 25, 100, 150mg eq. or PB. PP groups received an initiation dose of 150mg eq. (deltoid muscle) on Day 1, followed by the randomly assigned fixed dose (deltoid or gluteal muscle) on Day 8, and every 4 wks thereafter. PB pts received PB on Days 1 and 8, and every 4 wks thereafter.
Results: ITT analysis set (n=636): 67% men, 54% white (30% black). Mean±SD changes from baseline to endpoint in PANSS total score (primary outcome) showed dose-related significant reductions (p<=0.034) for PP vs PB: 25mg eq.=–8.0±19.90; 100mg eq.=–11.6±17.63; 150mg eq.=–13.2±18.48 vs PB=–2.9±19.26. Statistically significant improvement in PANSS total score began at Day 8 for PP 25 and 150mg eq., and at Day 22 for all PP groups vs PB. Dose-related improvement in mean Personal and Social Performance (PSP) scale scores was seen with PP (100mg eq.=6.1 [p=0.007]; 150mg eq.=8.3 [p<0.001]) vs PB=1.7. TEAEs occurred at similar rates with PP (60.0–63.2%) and PB (65.2%). TEAEs occurring >=2% more frequently with PB than PP (total group) included insomnia (16.5 vs 11.5%) and schizophrenia (11.6 vs 8%). Serious TEAEs were more common with PB (14.0%) than PP (8.0-13.3%). EPS-related TEAEs were infrequent; akathisia was most frequently reported (PB=4.9%; 25mg eq.=1.3%, 100mg eq.=4.8%, 150mg eq.=5.5%). Weight increase (>=7%) was dose related with PP (6-13%) vs PB (5%).
Conclusion: PP was effective and generally safe and well tolerated when initiated at 150mg eq. (deltoid muscle) on Day 1, followed by 25–150mg eq. monthly doses, beginning on Day 8 (deltoid or gluteal muscle). There was a dose response in primary and secondary endpoints (PANSS and PSP). There were no unexpected AEs. Funded by J&J PRD.

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» NR1-074

PSYCHIATRIC-RELATED UTILIZATION AND COSTS ASSOCIATED WITH PALIPERIDONE ER COMPARED WITH OTHER ATYPICAL ANTIPSYCHOTICS IN A COMMERCIAL HEALTH PLAN

Jessica Panish,Riad Dirani, Ph.D.,Rachel Halpern, Ph.D., Feng Cao,Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to understand the psychiatric-related health care resource utilization and costs associated with atypical antipsychotics used in the treatment of schizophrenia in a commercial health plan population.

SUMMARY:

Background: The burden of schizophrenia is substantial, but steps can be taken to manage the disease. This study examined psychiatric-related health care resource utilization and costs among patients initiated on paliperidone (pali) ER compared with risperidone (ris), aripiprazole (ari), olanzapine (olan), ziprasidone (zip) or quetiapine (que).
Methods: Patients were assigned to initial cohorts based on index antipsychotic and matched via propensity score analysis on age, gender, census division, race, income, baseline antipsychotic use, baseline comorbid conditions and baseline psychiatric-related utilization. Follow-up psychiatric-related health care resource utilization and costs were based on medical claims with primary ICD9 diagnosis codes 290.xx-319.xx; or outpatient pharmacy claims for atypical antipsychotics; or CPT codes for psychiatric drug management, medical encounters for therapy and evaluation. Descriptive analyses compared outcomes between the pali ER and other cohorts.
Results: The sample comprised 562 patients with at least one pharmacy claim: pali ER (n=95), ris (n=94), ari (n=94), olan (n=89), zip (n=95) or que (n=95). There were no significant differences among cohorts in any of the follow-up psychiatric-related health care resource utilization outcomes, such as ER visits and inpatient facility admissions. Patients on pali ER had significantly lower mean psychiatric-related medical costs ($753) compared with olan ($2,019, P=0.014), que ($1,832, P=0.026), ris ($1,656, P=0.058), and zip ($1,817, P=0.011). Mean psychiatric-related health care costs (medical + pharmacy) were lower for pali ER ($3,510) compared with zip ($4,559, P=0.030) and olan ($4,800, P=0.027).
Conclusion: This analysis suggests that patients from this sample of commercial health plan members who received pali ER may have lower psychiatric-related costs than those using other atypical antipsychotics.

Supported by Ortho-McNeil Janssen Scientific Affairs, LLC

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» NR1-075

SUICIDE PREDICTORS IN A LARGE SIMPLE TRIAL OF PATIENTS WITH SCHIZOPHRENIA

Elizabeth Pappadopulos Ph.D., Wolfgang Fleischhacker, M.D., John Kane, M.D., Sybil Eng, Ph.D., Jamie Geier, Ph.D., Charlotte Kremer, M.D., Yikang Xu, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to understand the relationship between baseline patient characteristics, including duration of illness, and the risk of suicide among patients with schizophrenia treated with ziprasidone or olanzapine in this large simple trial.

SUMMARY:

Background: In patients with schizophrenia, suicide is of particular concern, and several risk factors have been identified (1). Elucidation of such characteristics is critical to the development of suicide primary prevention efforts among patients with schizophrenia. We sought to determine baseline factors associated with completed suicide in patients with schizophrenia receiving treatment with ziprasidone or olanzapine in a randomized, open-label, post-approval large simple trial conducted in 18 countries.

Methods: 18,154 patients were followed for 1 year. Demographic data, medical/psychiatric history, and concomitant medication use were recorded using a baseline questionnaire; hospitalization, vital status, randomized study medication status, and concomitant antipsychotic medication(s) data were recorded using follow-up questionnaires. A blinded endpoint committee adjudicated the secondary endpoint of completed suicide according to a prespecified algorithm.

Results: There were no significant differences in demographic characteristics between patients who completed suicide (n = 35; 0.19%) and those who did not. Univariate analyses showed that patients who completed suicide were more likely to have had a shorter duration of schizophrenia illness, diagnosis during adulthood, higher CGI score indicative of more severe disease, more psychiatric hospitalizations, and a greater number of past suicide attempts. Patients who completed suicide also showed greater baseline use of concomitant antipsychotics, antidepressants, and hypnotics, sedatives, or anxiolytics in univariate analyses. Multivariate logistic regression modeling identified history of suicide attempts and baseline use of hypnotics, sedatives, or anxiolytics as significant risk factors for completed suicide.

Conclusion: In this real world cohort of 18,154 people with schizophrenia, one-year incidence of completed suicide was 1.9 per 1000 patients. These findings are consistent with previous evaluations (2) that associate completed suicide with shorter duration of illness, a history of suicide attempts, and comorbid mood/anxiety symptoms. Supported by funding by Pfizer Inc.

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» NR1-076

LONG TERM MAINTENANCE OF WEIGHT LOSS IN PATIENTS WITH SERIOUS MENTAL ILLNESS (SMI) THROUGH A BEHAVIOURAL PROGRAMME IN UK. RESULTS AT 8 YEARS

John Pendlebury, Holt R, Wildgust H, Bushe CJ

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to be recognize that self-referral to weight management programmes is successful in achieving weight loss in SMI patients. It can be hypothesized that longer term weight management clinics may function in addition as group therapy. Methods to retain subjects for longer need developing.

SUMMARY:

The prevalence of obesity is approximately two fold higher in people with serious mental illness than the general population. Furthermore antipsychotic treatment is associated with significant weight gain. Obesity is linked with various adverse outcomes and is challenging to manage.

A weight management clinic started 8 years ago and accepts self-referred patients only. The clinic is staffed by a community mental health nurse and an occupational therapist. The programme runs an 8-week rotational topic cycle with weekly 1-hour group sessions. Since May 2000, 113 patients (46 men, 67 women) have enrolled providing total of 142 patient episodes with mean baseline weight 90.1 kg ± 1.6 kg ((BMI 32.2 ± 0.5 kg/m2). Sessions attended range 1-315 (mean 61, median 48). 80% patients attended continuously > 8 weeks, and 56% > 6 months. There was a progressive statistically significant reduction in mean weight and BMI throughout the attendance at the clinic with no suggestion of a plateau. Weight loss occurred in 91% of patients, weight maintenance 4.5%, and weight increase 4.5% at final visit. Subjects leaving the programme had gained 11.7 ± 1.8 kg on return. Mean weight loss at final visit was 7.2 ± 0.6 kg. Weight loss was correlated only with number of sessions attended ($r=0.42$, $p<0.0001$). Of the 35patients attending > 2 year, 80 % had lost >7% body weight. The obesity (=30 kg/m2) prevalence fell from 61% at baseline to 40% at the final visit. The sole significant predictor of weight loss was number of sessions attended. Patients continuing to attend a weight clinic over 8 years lose weight incrementally with clinically significant shifts in BMI. Interpretation is limited to naturalistic data from a well-motivated cohort.

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» NR1-077

EVALUATION OF THE EFFECTIVENESS, THE EFFECT ON COGNITIVE FUNCTIONING AND WEIGHT CHANGE IN SCHIZOPHRENIA: AN OPEN-LABEL STUDY (CN138-166)

Joseph Peuskens, M.D., Ph.D., Eric Constant, M.D., Ph.D., Chris Bervoets, M.D., André De Nayer, M.D., Haitham Mourad, M.D., Bart Roussard, M.D., Stefaan Geerts, M.D., Wendy Kerselaers, M.S., Annick de Patoul, M.D., William H Carson, M.D., Robert D. McQuade, Ph.D., Véronique Halkin, M.D., M.P.H, M.P.A

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the audience will be able to evaluate the effectiveness and describe the secondary outcomes related to verbal cognitive function and weight of patients with schizophrenia after 12 weeks of open-label aripiprazole in a naturalistic setting.

SUMMARY:
To evaluate the effectiveness and effect on cognitive functioning and weight of a 12-week treatment with aripiprazole in a broad range of patients with schizophrenia.
Methods: In an open-label naturalistic setting in multiple sites, aripiprazole was started at 15 mg/day in 361 patients; dosing adjustments were allowed as per clinical judgment to a range of 10-30 mg/day.
Effectiveness was measured by the Clinical Global Impression - Improvement (CGI-I). The following scale was used for secondary outcome measures: Patient Global Impression - Improvement (PGI-I) scale. Cognitive functioning was measured by the California Verbal Learning Test (CVLT) indices and the letter and category Verbal Fluency (VF) tests. Mean change in cognitive test scores and in body weight from baseline to Week 12 were calculated (LOCF) using descriptive statistics with 95% confidence intervals.
Results: At study endpoint, the mean CGI-I score was 3.0 (95% CI: 2.8, 3.2; LOCF), demonstrating the effectiveness of aripiprazole as the upper bound of the 95% CI was less than 4 (the score of "no change"). Both patient and caregiver PGI-I scores (LOCF: 2.9, 95% CI: 2.79, 3.09 and, 3, 95% CI: 2.74, 3.17, respectively) corroborate this finding. Verbal fluency, (letter fluency and category fluency), showed an increase from baseline to Week 12, on average 3.0 (SE: 0.5; OC) and 2,9 (SE: 0.4; LOCF) more letters and 1.8 (SE: 0.5; OC) and 1.7 (SE: 1.4; LOCF) category words were produced at Week 12. Patients showed an increase on all CVLT indices at Weeks 4 and 12. For total recall the increase was 9.4 (SE: 0.6; LOCF) words and for semantic clustering the increase was 0.3 (SE: 0.1, LOCF). For the discriminability index the improvement was 3.3 (SE: 0.5; LOCF). The mean change in baseline body weight at Week 12 (LOCF) was -1.5 kg (95% CI: -1.94, -0.97) n=328.Aripiprazole was well tolerated, with the most common treatment-related adverse event reported being insomnia (51 patients [14.13%]).
Conclusions: The study demonstrates the effectiveness of 12-week therapy with ariprazole in the treatment of patients with schizophrenia and confirms the positive effect of aripiprazole on weight. More rigorous, controlled trials are needed to determine the nature and extent of potential cognitive improvement with aripiprazole.

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» NR1-078

COLLECTING TRACES OF ACTIVITY IN OROFACIAL MUSCLES DURING AUDITORY VERBAL HALLUCINATIONS IN SCHIZOPHRENIC PATIENTS

Lucile Rapin, Polosan M., M.D., Dohen M.,Ph.D., Bougerol T., M.D., Ph.D., Loevenbruck H., Ph. D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session,the participants will have a better understanding of auditory hallucinations physiopathological mechanisms in schizophrenic psychosis.

SUMMARY:
Background: Auditory verbal hallucinations (AVH) are affecting 50% to 80% of the schizophrenic patients and they have a stressful impact on the patient's daily life. AVH are defined as speech percept in the absence of an external auditory stimulus. One appealing hypothesis is that the production of inner speech is disturbed in a way that the own verbal thoughts of the patient are considered as external voices. One way to establish a relationship between AVH and inner speech is to measure orofacial muscle activity, using electromyography (sEMG). Few previous studies discussed the association between AVH and the activity of the speech musculature.
Objective: Testing the hypothesis that AVH are associated with a dysfunction of inner speech production by recording orofacial sEMG and electroglottography (EGG) signals during the occurrence of AVH in schizophrenic patients.
Method: Six paranoid schizophrenic patients and three control healthy subjects have been examined by sEMG of mean speech muscles and EGG during 4 conditions: reading in overt speech, reading in whispered speech, silent condition and hallucinating state. For healthy subjects, the hallucinating state was replaced by reading in inner speech. The whole experiment was video monitored to track visible facial movements
Results: The orbicularis oris inferior showed the most important activation in all conditions. In five patients out of six, sEMG activity for this muscle was lower in the hallucinatory condition than in the overt and whispered speech conditions, but higher than in the baseline condition. The overt speech condition was associated with higher sEMG levels than the whispered speech in three patients.
Conclusion: This study suggests that AVH in schizophrenia are related to some specific speech muscles activity supporting the physiopathological hypothesis of a misattributed inner speech.

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» NR1-079

SOMNOLENCE AND SEDATION IN ADOLESCENT PATIENTS WITH SCHIZOPHRENIA TREATED WITH ARIPIPRAZOLE IN AN ACUTE STUDY WITH LONG TERM FOLLOW-UP

Adelaide Robb M.D., Robert D. McQuade, PhD, William H. Carson, MD, Margaretta Nyilas, MD, Robert A. Forbes, PhD, Taro Iwamoto, PhD, Ray Mankoski, MD, PhD, Suja J. Mathew, Andrei Pikalov, MD, PhD

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to demonstrate increased knowledge about somnolence and sedation occurring in adolescent patients with schizophrenia treated with aripiprazole.

SUMMARY:
Background: Somnolence/sedation are relatively common side effects of antipsychotics to which adolescents may be more sensitive. The purpose of this post hoc analysis was to evaluate characteristics of somnolence/sedation in adolescents with schizophrenia treated with aripiprazole.
Methods: Data are derived from a 6-week, double-blind, placebo controlled, randomized clinical trial comparing two fixed doses of aripiprazole (10 and 30mg, N=302) and a 26-week, open-label, follow-up study with flexible dosing (5-30mg, N=239). Somnolence/sedation were evaluated with respect to time of onset, severity, dose at onset, dose-reduction/ discontinuation rates, age, gender, and ethnicity.
Results: In both the short- (ST) and long-term (LT) studies, almost all reported cases of somnolence/sedation were classified as mild (ST: n=25, 12%; LT: n=24, 10%) or moderate (ST: n=8, 4%; LT: n=9, 4%), and only one patient was discontinued due to somnolence. Most events (76%) started early (within 2 and 4 weeks) and resolved within the study period. A possible dose-dependence was seen, with more events reported at the 30mg dose. In the short-term trial, African Americans reported substantially higher rates (35% in the 10mg arm and 55% in the 30mg arm) than the overall population (12% in the 10mg arm and 22% in the 30mg arm). No

differences were noted in incidence stratified by age or gender.
In the LT open-label study, the overall incidence of somnolence/sedation was low (14%) and was similar between groups switched from aripiprazole 10mg, 30mg or placebo. When sedation or somnolence occurred, most investigators took either no action or reduced dose.
Conclusions: Somnolence/sedation in adolescents with schizophrenia treated with aripiprazole, if experienced, is typically mild, transient and manageable. In general, higher doses lead to an increased incidence in younger patients. Ethnicity may be a modifying factor and should be evaluated further.
Support: Otsuka America Pharmaceutical, Inc.

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» NR1-080

SCHIZOPHRENIA COLLABORATIVE RESOURCE (SCORE) TOOL: TRACKING PATIENT PROGRESS

Stephen Rodriguez M.S., Cynthia Bossie, Ph.D., Wayne Macfadden, M.D., J. Thomas Haskins, Ph.D., John Docherty, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant will be aware of the Schizophrenia Collaborative Resource (SCoRe) physician tool, a new interactive, user-friendly software program designed to assist and guide clinicians in identifying a patient's current stage of illness, create a personalized patient profile and track patient progress over time. This tool was designed to support the long-term management of patients with schizophrenia.

SUMMARY:

Background: Unlike many other chronic disorders, stages of illness and disease progression for patients with schizophrenia are not well characterized. We describe software entitled the Schizophrenia Collaborative Resource (SCoRe) tool that identifies the stage of illness, creates a personalized patient profile and tracks patient progress over time.
Methods: A group of clinicians who are experts in the treatment of patients with schizophrenia were involved in development. Literature reviews were conducted and data from clinical trials were analyzed to guide the clinicians in describing stages of illness, associated symptom severity and level of functioning.
Results: Interactive software has been designed for use in clinical practice to capture information (from both clinicians and patients) about the status of patients with schizophrenia, including current interventions, symptom severity, social functioning, stress tolerance, cognition and physical health. A patient's illness is staged according to an algorithm that considers the type of clinical intervention needed and the severity of core symptoms of schizophrenia. Four stages of illness are defined based on clinician input and data analysis: 1) acute, 2) stabilization, 3) stable and 4) remission. These stages are reassessed at each subsequent visit. This information can then be used to develop treatment goals and to track patient progress. The program can also provide graphical outputs of a patient's clinical profile over time.
Conclusion: SCoRe may help in the management of patients with schizophrenia by identifying milestones for improvement throughout the course of illness. Additionally, this software provides physicians with a mechanism to record and track patient progress and assist with the development of treatment goals. Supported by funding from Ortho-McNeil Janssen Scientific Affairs, LLC

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» NR1-081

ANTIDEPRESSANT EFFECT OF ANTIPSYCHOTICS IN SCHIZOPHRENIA: COMPARISON OF TYPICAL AND ATYPICAL ANTIPSYCHOTIC DRUGS

Antonio R Sa, M.D., M.Sc., Belquiz Avrichir, M.D., Ph.D., Helio Elkis, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the risks of depressive symptoms in patients with schizophrenia and they should be able to identify advantages of atypical antipsychotics for people with both schizophrenia and depression.

SUMMARY:

Objective: Despite progress in the treatment of schizophrenia the efficacy of atypical antipsychotics on depressive symptoms in schizophrenia is not well established and for clarify this question we examined the effects of atypical versus typical antipsychotics on depressive symptoms in a cohort study in patients with schizophrenia. Methods: The data were drawn from a cohort, naturalistic, observational study with 96 subjects diagnosed as being affected by schizophrenia during a re-exacerbation phase. The patients were taking typical or atypical antipsychotics. All subjects completed the Calgary Depression Scale for Schizophrenia (CDSS) to rate the severity of the depressive symptoms. The severity of schizophrenic symptoms was rated by the Positive and Negative Syndrome Scale (PANSS) and the Clinical Global Impression (CGI) severity and improvement scales. Assessments of scales above were undertaken at baseline, 8 weeks, 16 weeks and 24 weeks. Results: The PANSS total score higher than 70 and female gender were significantly associated with the presence of depressive symptoms. Global improvement of depressive symptoms was associated with use of antipsychotics in general, however atypical antipsychotics showed a statistically significant effect when compared to typical antipsychotics. Conclusion: This observational study provides evidence that atypical antipsychotics are more effective than typical antipsychotics on the depressive symptoms in patients with schizophrenia. Keywords: Schizophrenia; depression; antipsychotics; treatment response; comorbidity.

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» NR1-082

THE EFFECT OF ARIPIPRAZOLE ON AUDITORY EVENT-RELATED POTENTIAL IN SCHIZOPHRENIA

Gabriele Sachs M.D., Oliver Pintsov, M.D., Peter Anderer, Ph.D.,Doz., Gerda Saletu-Zyhlarz, M.D., Prof., Bernd Saletu, M.D., Prof.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that aripiprazole lead to an improvement in distinguishing relevant from irrelevant auditory information in patients with schizophrenia.

SUMMARY:

Background: The amplitude of the P300 component of the auditory event-related brain potential (ERP) is consistently reduced in schizophrenia. Schizophrenia patients have difficulty distinguish-

ing relevant from irrelevant auditory information. During the P2/N2 time interval, opposite patterns of brain activity were found in schizophrenia suggesting attention allocation to task-irrelevant stimuli. So far the effect of atypical antipsychotics on ERPs in patients with schizophrenia is less evaluated.
Objectives: The objective of this study was to examine the effects of aripiprazole on ERPs in a patient with schizophrenia. To investigate the neurophysiological changes that contribute to cognitive impairment in schizophrenia using ERP components N1, P2, P300.
Methods: ERPs were recorded before and after four weeks of treatment from 19 EEG leads in a two-tone oddball paradigm in 5 medication free patients with DSM-IV schizophrenia and were compared with healthy controls (n = 42).
Results: At baseline, non-target P2 and target P300 amplitudes were reduced as compared with healthy controls (z=-2.6 and -2.1 for P2 and P300, respectively). A clinical improvement assessed with the PANSS, CGI-I and BACS (Brief Assessment of Cognition) was noted. Treatment with aripiprazole over 4 weeks was associated with an increase of P300-amplitudes and higher P2/N2 differentiation.
Conclusion: The P300 amplitude reduction indicating an impairment in cognitive recources for the evaluation of relevant information. The lack of P2/N2 differentiation indicates difficulties in distinguishing task stimuli of differing relevance and is in line with previous results in patients with schizophrenia. Our findings showing the first time that aripiprazole lead to an increase of reduced P300 amplitudes and improvements in distinguishing relevant from irrelevant auditory information.

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» NR1-083

SELECTIVE ATTENTION AND SELECTION FOR ACTION AMONG CHRONIC SCHIZOPHRENIA PATIENTS

Ziad Safadi Ph.D., Avishai Henik Ph.D., William B. Lawson, Ph.D., M.D., Ora Kofman. Ph.D., Limor Lichtenstein-Vidne, M.A., Maria Hipolito, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to learn about cognitive abilites of schizophrenia patients.

SUMMARY:

Objective: The goal of the current research is to examine the ability of schizophrenia patients to produce post-conflict adaptation as indication of selection for action in sequential Stroop-Flanker task.
Method: sixteen chronic schizophrenia subjects and sixteen control subjects were tested using Stroop-Flanker paradigm. A central color word was employed as a target flanked by a Stroop stimulus (originally based on Henik et al., 1999). we manipulated the presentation of continuous trials to exclude any repetition, in order to avoid the episodic memory effect (Mayr, 2003).
Results: Within trial analysis demonstrate significant effect of the relevant flanker dimension (word) but not the irrelevant (color) among both patients and control groups. Between trials analysis revealed negative priming among control group, and positive priming among patients in the color dimension. Moreover, patients were able to exhibit post conflict adaptation for color dimension.
Conclusion. The results suggest that at early stages of processing, both groups process the relevant dimension of the distractor but not the irrelevant to task dimension. At late stage of processing Schizophrenia patients show less automatic processing and more strategic compare to control group.

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» NR1-084

MORTALITY IN PATIENTS WITH BIPOLAR DISORDER: A SYSTEMATIC REVIEW

Jerónimo Saiz-Ruiz M.D., Fernando Rico-Villademoros, M.D., José M. Montes, M.D., José Mostaza, M.D., Julio Bobes, M.D.,Eduard Vieta, M.D., on behalf of the Spanish Consensus Group of Experts on Physical Health in Patients with Bipolar Disorders.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should gain increased awareness about the overall and cause-specific mortality rates among patients with bipolar disorder.

SUMMARY:

Objectives: To evaluate the overall and cause-specific mortality rates in patients with bipolar disorder.
Methods: A Medline bibliographic search (up to January 2008) in reference lists of primary articles and relevant review articles. It included articles published in Spanish or English, relating to patients diagnosed with bipolar disorder according to any criteria, reporting mortality data (overall or cause-specific) in the form of the standardized mortality rate (SMR) or data for calculating the SMR. The number of studies reporting a significantly increased mortality and the corresponding range of SMRs are presented.
Results: We identified 11 studies. Eight had been carried out in Europe, 2 in the USA and 1 in Japan. Nine were carried out using registries, 1 was a prospective cohort study and 1 did not have a clear design. The overall mortality rate in bipolar disorder was higher than in the general population in 5 of 7 studies (SMR 1.58-2.62), for both males (in 4 of 6 studies, SMR 1.78-2.50) and females (in 5 of 6 studies, SMR 1.45-3.01). In terms of specific causes, we found an increased mortality rate compared with the general population due to suicide in 6 of 6 studies (SMR 9.77-19.57), due to diseases of the circulatory system in 3 of 5 studies (SMR 1.38-2.18), and due to infections in 2 of 3 studies (SMR 2.49-2.85). Only 1 of 6 studies reported an increased mortality from cancer in patients with bipolar disorder.
Conclusion: The mortality rate in patients with bipolar disorder is higher than in the general population, with mortality due to suicide being particularly significant. Available data do not support an excess of mortality from cancer in patients with bipolar disorder.

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» NR1-085

PROFILES AND THERAPEUTIC STRATEGIES OF ANTIPSYCHOTIC TREATMENT NON-ADHERENCE IN PATIENTS WITH SCHIZOPHRENIA

Luis San, M.D., Ph.D., Antonio Ciudad, M.D., Ph.D., Miguel Bernardo, M.D., Ph.D., José M. Olivares, M.D., Ph.D., Pepa Polavieja, D.Stat., BelenYruretagoyena, Ph.D., Inmaculada Gilaberte, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to identify A) some sociodemographic/clinical features, and B) modifications of treatment strategies (pharmacological and/or non-pharmacological) considered in patients with schizophrenia who are at risk of non-adherence to oral antipsychotic medication.

SUMMARY:
Introduction/Objectives: Given its utmost clinical relevance (1), authors investigated the profiles and therapeutic strategies employed for non-adherence to schizophrenia antipsychotic pharmacotherapy.
Methods: A Spanish cohort of 591 outpatients with schizophrenia whose therapy was modified because of risk of non-adherence to oral antipsychotic (AP) medication was studied to investigate the relapse rate during 12 months. Sociodemographic and clinical data, including validated measures of severity, premorbid adjustment, quality of life, insight, and drug attitudes were collected. Baseline results and the therapies implemented are presented in this poster with appropriate descriptive statistics.
Results: Patients had a mean (SD) age of 40.1 (11.2) years, 377 (63.8%) were males, 285 (48.2%) were receiving permanent disability social benefits, and 458 (77.5%) had to leave duties unattended in the last month. The median (IQR) time-since-diagnosis was 15.3 (10.0) years and were hospitalized for 21 (15) days within the previous 6 months. Patients had a severe condition (CGI-S score =4 in 87.6%) and poor premorbid adjustment (mean total PAS score of 0.56), quality of life (mean EuroQol-5D health-status value of 0.58) and insight (mean global SUMD score of 5.99). Drug attitudes were good in 277 patients (46.9%). Modification of AP medication was recorded in 510 patients (86.3%). These were dose/route changes (43.3%), addition of other AP (24.1%), both combined (14.2%), and switching (20.4%). Other treatment strategies of non-adherence were modification of concomitant medications in 84 (12.2%) and of non-pharmacologic therapies in 190 (32.1%) patients.
Discussion: Patients under oral AP medications whose therapy was modified because of risk of non-adherence showed a severe clinical condition, did not have necessarily a bad attitude toward medication (2), and required more modifications of AP medications than of non-pharmacologic therapies.
Research funded by Eli Lilly and Co.

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» NR1-086

TRANSLATIONAL MODELING OF THE ASENAPINE PLASMA CONCENTRATION–DOPAMINE D2 RECEPTOR OCCUPANCY RELATIONSHIP IN RATS AND HUMANS

Mohammed Shahid, Brian Henry, Marita Prohn, Rik de Greef

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to:
1) Describe the relationship between asenapine plasma concentration and asenapine D2 receptor occupancy, and the correlations in these measures taken in humans and rats.
2) Describe how mathematical models have been used to characterize the in vivo D2 receptor occupancy of asenapine.

SUMMARY:
Objective: Asenapine is under development for the treatment of schizophrenia and bipolar disorder. Optimal efficacy of antipsychotics has been associated with dopamine D2 receptor occupancy levels in the range of 60%–80%. Here, we describe a pooled analysis of in vivo D2 occupancy in rats and humans; from this analysis, we determine the in vivo potency of asenapine using a single pharmacokinetic-pharmacodynamic (PK-PD) model, and then compare the in vivo potency of asenapine with its in vitro receptor affinity.
Methods: Asenapine plasma concentrations and D2 occupancy data were obtained after administration of asenapine to rats (0.003–0.3 mg/kg), healthy human volunteers (0.1 mg QD or 0.3 mg BID), and patients with schizophrenia (2.4–4.8 mg BID). Asenapine plasma concentrations resulting in 60% and 80% D2 occupancy were determined using the parameter estimates of an Emax model.
Results: Asenapine plasma concentrations producing 50% D2 occupancy were 0.58 ng/mL (range, 0.35–0.81 ng/mL) in rats and 0.66 ng/mL (range, 0.38–0.93 ng/mL) in humans (P=NS), which are comparable to the in vitro affinities of asenapine for the rat (pKi, 8.5) and the human (pKi, 8.9) D2 receptor. Exposure-related asenapine plasma concentrations producing 60% and 80% D2 occupancy were 0.87 and 2.32 ng/mL, respectively, in rats, and 0.98 and 2.62 ng/mL in humans.
Conclusion: Asenapine plasma concentrations producing in vivo D2 occupancy in the range of 60%–80% are comparable in rats and humans, suggesting that, for asenapine, in vivo D2 occupancy in rats is a good predictor of D2 occupancy in humans. Further, the results of this analysis indicate that, for asenapine, PK-PD relationships for D2 occupancy can be translated from preclinical models to the clinical setting. This research was supported by Schering-Plough.

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» NR1-087

BASELINE SERUM PROLACTIN IN DRUG NAIVE FIRST EPISODE SCHIZOPHRENIA PREDICTS A POSITIVE CLINICAL AND SOCIAL OUTCOME AT FIVE YEARS POST DISCHARGE FOLLOW

Amresh K. Shrivastava M.D., Manoj Tamhane, M.D., Meghana Thakar, M.A., Yves Bureau, Ph.D., Nilesh Shah, M.D., D.P.M.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand: 1)predictors of outcome; and 2) biological markers for outcome of schizophrenia.

SUMMARY:
Serum prolactin is an indicator of tuberoinfundibular dopamine activity, has been reported to be increased in a wide variety of mental illness and with antipsychotic therapy. However its relationship with psychopathology and outcome is not clear. Serum prolactin levels were measured in 30 male and 30 female drug naive patients of schizophrenia. Subsequently, these patients were treated with antipsychotics. The severity of psychopathology & outcome was measured using a modified brief psychiatric rating scale (BPRS) and using the Global Assessment of Functioning questionnaire (GAF) at baseline, three and six weeks after being admitted. Following drop-out of patients and a few cases with unexplained abnormally high prolactin measures we had 18 male & 22 female patients available for reassessment at five years. Contrary to expectations, prolactin levels in patients were twice as high compared to volunteer controls. This difference was found to be statistically significant for males only. Correlations for BPRS and GAF with prolactin, were not significant for any time point up to six weeks. Significant positive correlations were observed using measures obtained at five years follow-up only. From the present study it seems that baseline serum prolactin levels in drug naive patients of schizophrenia may not be a reliable indicator of psychopathology but it may be an indicator of good prognosis in long term. Further research is necessary to arrive at a definite conclusion.

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» NR1-088

PREVALENCE OF LIVER DISEASE IN VETERANS WITH BIPOLAR DISORDER OR SCHIZOPHRENIA

Mirko Sikirica Pharm.D., Bret E. Fuller, Ph.D.,Veronica Rodriguez, Ph.D., Alex Linke, B.S., Mirko V.Sikirica, Pharm.D.,Riad Dirani, Ph.D., Peter Hauser, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the prevalence of four liver diseases (Hepatitis C Virus [HCV], Nonalcoholic Fatty Liver Disease [NAFLD], chronic and alcohol-induced cirrhosis) among veterans with and without mental health and substance use disorders (SUD).

SUMMARY:

Objective: To assess the prevalence of 4 liver diseases (HCV, NAFLD, chronic and alcohol-induced cirrhosis) in patients (veterans) with and without mental health and substance use disorders (SUD).

Methods: Patients (veterans) in this retrospective electronic chart review were enrolled in VISN 20 facilities from 01/01/01 to 12/31/06 and assigned to 2 groups: schizophrenia and schizoaffective (SZ) disorder with and without comorbid SUD; and bipolar disorder (BPD) with and without SUD. Each veteran in either group was randomly matched with a single veteran without a psychiatric diagnosis. Logistic regression models evaluated risk for overall liver disease (diagnosis of any of the 4 liver diseases).

Results: Patients with SZ (n=6521) had a higher prevalence of overall liver disease than a matched set of patients without SZ (22.4% vs 3.2%; OR=8.73). Prevalence of HCV was higher for SZ patients (16.5% vs 1.9%; OR=10.21), as was alcohol-related cirrhosis (1.6% vs 0.4%; OR=4.09). Patients with BPD (n=5319) had higher prevalence of liver disease than a matched set of patients without BPD (21.5% vs 3.5%; OR=7.58). Rates of HCV (15.5% vs 2.1%; OR=8.60) and alcohol-related cirrhosis (1.6% vs 0.4%; OR=3.82) were higher for BPD patients. Logistic regression showed these risk factors for development of liver disease for the SZ sample (vs matched controls): diabetes (OR=1.29), hypertension (OR=1.27), HIV (OR=3.54), SUD (OR=2.28), alcohol use disorder (OR=3.05), presence of SZ (OR=2.74). The model for BPD patients showed the following risk factors for developing liver disease: diabetes (OR=1.40), HIV (OR=3.66), SUD (OR=2.68), alcohol use disorder (OR=3.22). BPD elevated risk of liver disease (OR=2.27).

Conclusions:This study shows that presence of mental illness in veterans is a significant risk factor for the diagnosis of liver disease, including HCV and alcohol-related cirrhosis.

Supported by Ortho-McNeil Janssen Scientific Affairs, LLC. Portland VA Medical Center (research entity).

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» NR1-089

EFFECT OF RISPERIDONE LONG-ACTING INJECTION ON HOSPITALISATION IN SCHIZOPHRENIA PATIENTS: A MIRROR IMAGE ANALYSIS

Mala Singh

EDUCATIONAL OBJECTIVES:

This study aims to examine the long-term effects of risperidone long-acting injection (RLAI) on hospital admissions using a mirror image analysis.

SUMMARY:

Schizophrenia is a chronic condition often requiring long-term treatment. Frequent relapses are associated with poor long-term outcomes. Compliance with treatment is a major factor in relapse. Long-acting injectable antipsychotics may improve compliance, reduce relapse and thus improve long-term outcomes.

This study aims to examine the long-term effects of risperidone long-acting injection (RLAI) on hospital admissions using a mirror image analysis. All patients with schizophrenia who had been receiving treatment with RLAI for two years or more were eligible to participate in this retrospective case note review. The number of hospital admissions and number of days spent in hospital was assessed for two years prior to treatment with RLAI and for the first two years of treatment with RLAI.

During the two years prior to treatment with RLAI, the mean number of admissions to hospital for a psychotic relapse was 2.6 and the mean number of days spent in hospital during this two-year period was 181.9.

During the first two years of treatment with RLAI the mean number of hospital admissions reduced to 1 and the number of days spent in hospital decreased by 143 days to 38.9.

This long-term, retrospective study clearly demonstrates that treatment with RLAI results in fewer hospital admissions and fewer overall days in hospital compared to previous treatment. Reducing hospital admissions is likely to result in substantial cost savings. Perhaps more importantly, reducing relapse may help to improve long-term outcomes for patients.

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» NR1-090

SWITCHING ANTIPSYCHOTIC DRUGS ENHANCES IMPROVEMENT IN PATIENTS WHO SHOW LACK OF AN EARLY RESPONSE TO THEIR INITIAL ANTIPSYCHOTIC THERAPY

Virginia Stauffer Pharm.D., Lei Chen, MD, Haya Ascher-Svanum, PhD, Sara Kollack-Walker, PhD, Wei Zhou, MS, Shitij Kapur, MD, John Kane, MD, Bruce J Kinon, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to assess, in a prospective manner, how well early response to atypical antipsychotic treatment predicts clinical outcomes at 12 weeks, and the utility of switching to an alternative atypical antipsychotic for those patients who failed to show an early response to the initial drug therapy.

SUMMARY:

Objective: Examine the utility of switching to an alternative antipsychotic drug for patients who fail to show an early response to their initial antipsychotic therapy.

Methods: This randomized, double-blind, flexible-dose, 12-week study enrolled 630 patients diagnosed with schizophrenia or schizoaffective disorder. All patients were initially assigned to risperidone (RIS) therapy (2-6 mg/day) for 2 weeks. Early responders

(=20% improvement PANSS total score from baseline to 2 weeks) continued on RIS (N=144), whereas early non-responders to RIS were randomized at Week 2 (1:1) double-blind to continue on RIS (N=192) or switch to olanzapine (OLZ) (10-20 mg/day; N=186) for 10 additional weeks of therapy. These two early non-responder groups were compared on efficacy and safety parameters.
Results: Early non-response to RIS was observed in 72.4% of patients. Early non-responders had significantly less improvement in PANSS total score throughout the 12-week study (p<.001) compared to early responders. Switching RIS early non-responders to OLZ resulted in significant symptom improvement in PANSS total score (p=.020) and MADRS (p=.020) at endpoint (up to 10 weeks). Among the early non-responders, OLZ-treated patients had numerically greater weight gain (p=.143), significantly greater increase in triglycerides (p=.005), but a greater decrease in prolactin (p<.001). Among early non-responders who were still at least moderately ill at Week 2, OLZ-treated patients experienced significantly greater improvement in PANSS total, positive, negative and general psychopathology scores (p<.05) and in the MADRS (p<.001), with separation between the OLZ and RIS groups evident by 4 weeks after switching.
Conclusion: Switching RIS early non-responders to OLZ at Week 2 is an effective strategy to facilitate further symptom improvement but is also accompanied by changes in safety parameters, thus warranting individual benefit-risk considerations.
Funded by Eli Lilly and Company

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» NR1-091

DISSOCIATIVE SYMPTOMS AND INTERREGIONAL EEG CROSS-CORRELATIONS IN PARANOID SCHIZOPHRENIA

Marek Susta Ph.D., Petr Bob, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to demonstrate that EEG cross-correlations in patients with paranoid schizophrenia are negatively related to dissociative symptoms.

SUMMARY:

Recent findings indicate that binding of synchronized and distributed activity is crucial for the mechanism of consciousness and there is increased evidence that disrupted feature binding produce disintegration of consciousness in schizophrenia (1, 2). These data suggest that the disrupted binding and disintegration of consciousness could be related to dissociation that is historically linked to splitting in schizophrenia. We have examined cross-correlation function with aim to investigate relations among EEG activities of cortical sites and used psychometric measures of positive and negative schizophrenia symptoms (PANSS) and dissociation (DES) in 50 patients with paranoid schizophrenia. The results show statistically significant Spearman correlations of DES with cross-correlation function in 14 (of 28) EEG pairs (r from -0.26 to -0.39, p<0.05). Positive symptoms display significant Spearman correlation with mean of cross-correlation function only in 1 EEG pair (F4-C4, r= -0.34, p<0.05).
Results of Mann-Whitney test between patients with high (DES=30) and low dissociation show statistically significant differences between the groups for cross-correlations in 16 EEG pairs. In summary, these data indicate that EEG cross-correlations in patients with paranoid schizophrenia are negatively related to dissociative symptoms, which could be caused by defective communication between brain sites. Commercial Support:
Funding for this work was provided by the Czech Ministry of Education within the projects MSM0021620849 and Centre for Neuropsychiatric Research of Traumatic Stress (1M06039).

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» NR1-092

SELECTIVE ESTROGEN RECEPTOR MODULATORS SHARE THE ANTIPSYCHOTIC GENE EXPRESSION PROFILE, SUGGESTING THEIR POTENTIAL IN THE TREATMENT OF SCHIZOPHRENIA

Andrew Thompson B.S., Louis Licamele, M.S., Simona Volpi, Ph.D., Shruti N. Mitkus, Ph.D., Kendra Mack, M.S., Mihael H. Polymeropoulos, M.D., Christian Lavedan, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:
1. Appreciate the effect of selective estrogen receptor modulators (SERMs) on specific genes involved in fatty acids and cholesterol biosynthesis, or in phospholipid metabolism.
2. Recognize the similarity of effect of SERMs and antipsychotics on the expression of the human genome.
3. Realize why SERMs may have a potential antipsychotic therapeutic benefit.

SUMMARY:

Objective: A possible protective effect of estrogen has been proposed for schizophrenia based on the observation that, relative to men, women show a delay in disease onset age with a second onset peak after age 44 years. Recently, DNA variants which may contribute to the risk of developing schizophrenia have been identified in the estrogen receptor alpha gene. Several clinical studies have shown that the selective estrogen receptor modulator (SERM) tamoxifen can reduce mania symptoms in patients with bipolar disorder. Symptoms of psychosis and cognitive functioning were also shown to improve in women affected with schizophrenia who were treated with oestradiol or raloxifene. To better understand the effect of SERMs at the molecular level, their impact on the expression of the human genome was evaluated. Methods: The gene expression group profile of tamoxifen, raloxifen and clomiphene was determined in a cell line by analyzing the up- and down-regulation of 12,490 genes. Truncated Kolmogorov-Smirnov (KS) statistics were used to compare the SERM gene signature with that of a library of 463 drugs used to treat a variety of disorders. Results: It was discovered that the gene expression signature of the SERMs was the most similar to that of the antipsychotics, as compared to all other drug group profiles. SERMs affect lipid homeostasis in a manner similar to antipsychotics (KS scores of 0.997 and 0.806 for the top 20 and 100 probe sets, respectively). A number of genes up-regulated by both SERMs and antipsychotics were Sterol Regulatory Element Binding Proteins (SREBP) responsive genes in the cholesterol biosynthetic pathway, which have been shown to be activated by the modulation of the estrogen receptor. Conclusions: These results support an antipsychotic therapeutic effect of SERMs, possibly through the alteration of lipid homeostasis.
Vanda Pharmaceuticals sponsored this study.

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» NR1-093

FACTORS ASSOCIATED WITH WEIGHT GAIN DURING OLANZAPINE TREATMENT IN PATIENTS WITH SCHIZOPHRENIA OR BIPOLAR DISORDER: RESULTS FROM A PROSPECTIVE, SIX-MONTH

Tamas Treuer M.D., Vicki Poole-Hoffmann, Pharm.D., Antony Kuang-Peng Chen, M.D., Victoria Irimia, M.D., Ph.D., Magdalena Ocampo, M.D., Gang Wang, M.D., Pritibha Singh, M.Sc., Susanna Holt, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant 1. will be informed about lifestyle and behavioral factors associated with weight gain during oral olanzapine therapy; and 2. will recognize the importance of weight control intervention for 'at risk' patients prior to initiating olanzapine or during the early stages of therapy.

SUMMARY:

Aim: Further research is needed regarding the main determinants of weight gain during olanzapine therapy in routine clinical practice. The aim of this prospective, six-month, observational study was to examine which clinical, eating- and lifestyle-related factors were associated with weight gain in patients initiating or switching to oral olanzapine for the treatment of schizophrenia or bipolar mania.

Methods: 622 outpatients were enrolled from four countries (China, Romania, Mexico, and Taiwan). Assessments were conducted at monthly intervals for six months and included demographic and clinical factors, and changes in appetite, eating habits and physical activity. Exploratory, mixed model repeated-measures analysis, adjusted for baseline weight, was used to examine which factors were associated with weight gain during six months of olanzapine therapy.

Results: 93% of the patients completed the study and 86% were still taking olanzapine at the end of the study. After 6 months, the LS mean weight change was +4.1 kg and 43.9% of the patients had significant (=7%) weight gain. Consistent with previous studies, substantial inter-individual variation in weight change was observed.1,2 Patients with early significant (=7%) weight gain after 2 months of therapy (23.5%) gained significantly more weight overall. Patients participating in a weight control program at study entry had a lower mean weight gain after 6 months. Ten factors were associated with weight gain during 6 months of olanzapine therapy: country, housing conditions, stronger appetite, excessive amount of food needed to feel full, eating until uncomfortably full, thoughts preoccupied with food, meal location, increased meal frequency, evening snack consumption, and a lower amount of vigorous exercise.

Conclusion: The results show that certain eating- and lifestyle-related factors influenced weight gain during olanzapine therapy and that early weight control intervention can help minimize weight gain.

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2) 2. Kinon BJ, Kaiser CJ, Ahmed S, Rotelli MD, Kollack-Walker S: Association between early and rapid weight gain and change in weight over one year of olanzapine therapy in patients with schizophrenia and related disorders. J Clin Psychopharmacol 2005; 25:255-258.

» NR1-094

RISK OF CANCER AND HIV INFECTION IN PATIENTS WITH BIPOLAR DISORDER: A SYSTEMATIC REVIEW

Eduard Vieta M.D., Julio Bobes, M.D., Fernando Rico-Villademoros, M.D., José Mostaza, M.D., José Manuel Montes, M.D., Jerónimo Saiz-Ruiz, M.D., on behalf of the Spanish Consensus Group of Experts on Physical Health in Patients with Bipolar Disorders.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize the prevalence of cancer and HIV infection among patients with bipolar disorder.

SUMMARY:

Objective: to synthesize the available knowledge on the prevalence of cancer and HIV infection in patients with bipolar disorder (BD).

Methods: relevant studies were identified by a MEDLINE search from 1966 to January 2008, and supplemented by a manual review of reference lists of the articles identified and previous review articles. We included studies with any design, in patients with BD as diagnosed by any criteria, with sample size =30 patients, and reporting any measure of frequency or association about comorbidities. Priority was given to comparative studies.

Results: We identified 3 comparative studies providing information on the risk of malignancies (1 nested case-control study, 1 retrospective cohort study and 1 cross-sectional study) and 4 comparative studies presenting data on the prevalence of HIV infection (2 retrospective cohort studies and 2 cross-sectional studies). The nested case-control study showed that patients with BD had a similar cancer risk as people without either BD or schizophrenia; the other two comparative studies showed that some cancers were less common in patients with BD than in patients without psychiatric disorders (i.e. lymphoma or metastatic cancer) or than in the general population (i.e. prostate and lung cancer). As compared with the general population, two studies reported a higher prevalence of HIV infection among patients with BD (0.8-9.1% vs 0.3-0.5%) and one study reported a similar prevalence (1% vs 0.5%); in another study, the prevalence of HIV infection in patients with BD was higher than in patients without a psychiatric diagnosis (0.1% vs 0%).

Conclusion: Available data do not support that patients with BD have an increased risk of cancer. Although the information is limited, it suggests that BD might be associated with an increased frequency of HIV infection

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» NR1-095

EFFECT OF 6 GENETIC MAKERS ASSOCIATED WITH ILOPERIDONE EFFICACY ON LONG TERM CLINICAL OUTCOME OF PATIENTS WHO SWITCH TO ILOPERIDONE

Simona Volpi Ph.D., Christian Lavedan, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:
1. Understand the genotype effect of 6 specific DNA polymorphisms on iloperidone efficacy.
2. Recognize how these genetic markers may be valuable to patients, even if previously treated with a different antipsychotic.

SUMMARY:

Objective: In a double-blind, placebo- and active-controlled phase III clinical trial, 6 single nucleotide polymorphisms (SNPs) were found to be associated with the efficacy of a novel antipsychotic, iloperidone, during the short-term phase of the study. Patients, who received iloperidone, ziprasidone or placebo for four weeks, were then enrolled in an optional open-label 6-month extension phase where they all received iloperidone. A pharmacogenetic analysis was conducted in the extension phase for the individuals who switched to iloperidone, in an attempt to validate the genotype effect of the 6 SNPs in this independent group of patients.

Method: Analysis of the genotype effect on iloperidone response, as measured by change in the Positive and Negative Syndrome

Scale Total (PANSS-T) score, was performed using a general linear model with baseline value as a covariate. For patients who switched to iloperidone, PANSS-T was analyzed at the end of the study (day 203) as improvement from the baseline of the extension phase Results: A statistical significant association was observed between iloperidone efficacy and SNP rs4528226 genotypes for patients who switched from ziprasidone or placebo to iloperidone. Despite a relative small number of patients available, SNPs rs11851892, rs9643483, rs875326, and rs7837682 showed a similar trend without, however, reaching statistical significance. These results are consistent with the genotype effects observed for iloperidone-treated patients in the short-term phase of the clinical trial. Conclusions: This study is a first step in validating the 6 iloperidone efficacy markers in an independent population. The findings reported here support the application of pharmacogenomics to differentiate medication options and improve individualized treatments for schizophrenia. Vanda Pharmaceuticals sponsored this study.

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» NR1-096

ACTIGRAPHICALLY ASSESSED ACTIVITY AND REST IN SCHIZOPHRENIC PATIENTS TREATED WITH OLANZAPINE

Adam Wichniak M.D., Aleksandra Wierzbicka, M.D., Elzbieta Waliniowska, M.S., Iwona Musinska, M.S., Krystyna Czasak, Eugenia Szatkowska, Wojciech Jernajczyk, M.D.,Ph.D, Marek Jarema M.D.,Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize that patients with schizophrenia treated with olanzapine have decreased activity during the daytime and increased time spent in bed during the night. Promoting activity in those patients is crucial to counteract metabolic disturbances that may be related to treatment with olanzapine.

SUMMARY:

Objective: Weight gain and metabolic disturbances became an issue during olanzapine treatment. As decreased activity and increased rest times are important risk factors for metabolic disturbances and are preventable we investigated the activity pattern in schizophrenic patients treated with olanzapine.
Method: 54 patients treated with olanzapine (OLA) (32 M, 22 F, mean age: 30.2 ? 11.0, mean dose 15.6 ? 6.2 mg) were examined. The patients performed a vigilance task (Mackworth clock test) and filled out sleep diaries, Athens Insomnia Scale, Epworth sleepiness scale to assess their sleep and daytime somnolence. Drug side effects were scored with UKU scale. Mental status was evaluated with the use of the PANSS and CDSS scales. Actigraphic recordings (Actiwatch AW4) were performed for seven days: five days in the open psychiatric ward and two days at home. The patients were compared with age and sex-matched 36 healthy controls (HC) (21 M, 15 F, mean age 30.2 ?10.4) and 19 schizophrenic patients treated with risperidone (RIS) (19 M, 5, F, mean age 26.4 ? 6.7, mean dose 4.3 ? 1,6 mg).
Results: The patients had lower mean 24-h activity than HC (OLA: 89.0 ? 29.5, RIS: 84.4 ? 27.5, HC 131.9 ? 48.6 units; p<0.001) and total activity during the 10-h long period with highest activity during the daytime (OLA: 18393.7 ? 6072.4, RIS: 17684.8 ? 5443.8, HC 24498.1 ? 9149.1 units; p<0.001). During the night the patients had increased time in bed (OLA: 595.4 ? 70.5, RIS: 585.2 ? 62.1, HC 454.4 ? 48.2 min.; p<0.001) but comparable sleep efficiency as HC (OLA: 83.8 ? 6.1, RIS: 86.6 ? 4.5, HC 84.1 ? 6.1 %; ns). The reported differences in activity and rest times were more pronounced in patients treated with high (>15 mg) olanzapine dose. Conclusions: Patients with schizophrenia show significantly reduced activity. Promoting an active lifestyle should be considered as important primary prevention to reduce an increased metabolic disease risk in those patients.

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» NR1-097 - WITHDRAWN

» NR1-098

RELATIONSHIP OF CHANGE IN WHOLE-BODY ADIPOSITY TO PSYCHIATRIC SYMPTOM CHANGE DURING RANDOMIZED ANTIPSYCHOTIC

Michael D. Yingling, BS; Peter A. Fahnestock, MD; Dan W. Haupt, MD; Ginger E. Nicol, MD; Karen S. Flavin, RN, CCRC; Julia A. Schweiger, CCRC; Elizabeth T. Westerhaus, MA; Angela M. Stevens, BS; John W. Newcomer, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant will understand the relationship between fat gain and symptom response in patients taking antipsychotic medications.

SUMMARY:

Background: Antipsychotic treatment can increase adiposity, leading to associated changes in insulin sensitivity and lipid metabolism. Interestingly, some recent reports have suggested a positive predictive relationship between weight gain and efficacy during antipsychotic treatment (REF 1), despite well-known adverse health effects associated with weight gain. However, prior studies have used samples where, due to underlying study designs, most patients are gaining weight. In addition, changes in adiposity (rather than lean mass) underlie antipsychotic treatment-induced weight gain, so this hypothesis might best be tested in a sample where patients are both gaining and losing adiposity during treatment.
Methods: The hypothesis that therapeutic response to antipsychotic treatment is predicted by treatment-induced changes in adiposity was tested in a post hoc analysis of pooled data from two well-controlled, randomized studies of the metabolic effects of antipsychotic agents. In this sample, schizophrenia patients are randomized to 12 weeks of treatment with olanzapine, quetiapine, risperidone, ziprasidone, or aripiprazole, with no other medication changes allowed. Changes in adiposity were calculated using baseline and at endpoint values measured using whole body Dual Energy X-Ray Absorptiometry (DEXA), and changes in psychiatric symptoms are measured using the Brief Psychiatric Rating Scale (BPRS).
Results: No significant predictive relationship was detected between changes in adiposity (measured by change in DEXA total fat from baseline to endpoint) and change in psychiatric symptoms as measured by change in total BPRS score ($F[1,83]=1.69$, $p=0.20$), change in BPRS positive symptoms score ($F[1,83]=1.14$, $p=0.29$), and change in BPRS negative symptoms score ($F[1,83]=1.01$, $p=0.32$) .
Discussion: These results are relevant to the evaluation of risks and benefits during treatment with antipsychotic medications. In the absence of substantial benefits, increased cardiometabolic risk

should be the primary focus of clinical interest when treatment-induced increases in adiposity are observed.

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» NR1-099

ACUTE EFFICACY OF OLANZAPINE LONG-ACTING INJECTION, ORAL OLANZAPINE, AND HALOPERIDOL IN PATIENTS WITH SCHIZOPHRENIA: A CROSS-STUDY COMPARISON

Fangyi Zhao Ph.D., Holland C. Detke, Ph.D., Janice Carlson, Ph.D., David McDonnell, M.D., M.R.C.Psych.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the comparable efficacy of olanzapine long-acting injectable and oral olanzapine.

SUMMARY:

Educational objective: At the conclusion of this presentation, the participant should be able to understand the comparable efficacy of olanzapine long-acting injectable to that of oral olanzapine and oral haloperidol.
Objective: To compare the acute efficacy of olanzapine long-acting injection (OLZ LAI) with that of oral olanzapine (OLZ) and oral haloperidol (HAL) in acutely ill patients with schizophrenia.
Methods: Six-week results from an acute, fixed-dose, randomized, placebo-controlled OLZ LAI study (N=404) were compared with those of 3 fixed-dose oral olanzapine studies (Oral Study 1: OLZ vs HAL vs placebo [N=335]; Oral Study 2: OLZ vs HAL vs low-dose OLZ [N=431]; Oral Study 3: OLZ vs placebo vs low-dose OLZ [N=152]). All patients had to have a Brief Psychiatric Rating Scale (BPRS) score □24 (0–6 scale) at study entry. Efficacy endpoints were compared and effect sizes were calculated for BPRS and/or Positive and Negative Syndrome Scale (PANSS) Total score.
Results: PANSS Total score decreased by 22.5–24.8 points for OLZ LAI, by 12.3–26.7 for oral OLZ, and by 20.0 for HAL. BPRS scores decreased by 14.2–15.4 for OLZ LAI, by 6.7–16.4 for oral OLZ, and by 12.4–12.9 for HAL. Effect sizes vs placebo for the PANSS Total score were 0.7–0.9 for OLZ LAI, 0.3–0.7 for oral OLZ, and 0.2 for HAL.
Effect sizes vs placebo for the BPRS were 0.4–0.5 for OLZ LAI, 0.2–0.7 for oral OLZ, and 0.1–0.6 for HAL. At study endpoint, weight increased by 2.8–3.9 kg for OLZ LAI, 1.7-3.6 kg for oral OLZ, and -0.4–0.9 for HAL. Weight gain of □7% at anytime ranged from 19.1–35.3% for oral OLZ, and 23.6–35.4% for OLZ LAI. The incidence of Parkinsonianism was 2.3–6.2% for OLZ LAI, 7.0–18.5% for oral OLZ, and 41.8–52.5% for HAL. The incidence of akathisia was 1.1–5.7% for OLZ LAI, 8.6–26.8% for oral OLZ, and 34.3–45.9% for HAL.
Conclusion: This cross-study analysis indicates that patients treated with OLZ LAI dosages of 210 mg/2 weeks, 405 mg/4 weeks, and 300 mg/2 weeks had a similar magnitude of symptom reduction as patients treated with 5□2.5, 10□2.5 mg/day and 15□2.5 mg/day oral OLZ and 15□5 mg/day oral HAL during 6 weeks of acute treatment. Sponsored by Eli Lilly and Company.

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Monday, May 18, 2009

12:30 p.m. - 2:00 p.m.
Hall D, Exhibit Level,
Moscone Convention Center

NEW RESEARCH POSTER SESSION 2: PATIENT POPULATIONS & NONPSYCHOTIC DISODERS

» NR2-001

RELATIONSHIPS OF BODY COMPOSITION DATA TO CONCURRENT DRUG ABUSE IN A METHADONE CLINIC

Zack Cernovsky Ph.D., Gamal E. Sadek, M.D., Simon Chiu, M.D., Ph.D., Heba Youssef, M.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to anticipate the possible absence of relationship of body composition data to concurrent substance abuse in methadone maintenance patients and also a lack of relationship of BMI to concurrent substance abuse.

SUMMARY:

Introduction: The relationships between body composition data and the frequency of concurrent drug abuse in methadone maintenance patients have not been sufficiently investigated.
Objective: to examine whether body composition variables (body mass, percent of fat, of water, of bone mass, and of muscle mass, basic metabolic rate, and metabolic age) are differentially correlated with concurrent substance abuse.
Method: Forty-seven patients (25 men, 22 women, mean age 31.0, SD=8.2) of an urban methadone maintenance clinic were recruited to obtain body composition data as measured via bio-electrical impedance by means of Tanita Inner Scan Monitor. Their routine urine tests for concurrent abuse of benzodiazepines, cocaine, oxycodone and other opiates were recorded for 2 or more weeks: the N of tests ranged from 3 to 23 (mean = 10.8, SD=5.3).
Results: The body mass index (BMI) of our patients ranged from 17.5 to 39.3 (mean = 25.2, SD=4.9). No significant Pearson correlations (at $p<.05$, 2-tailed) were found between the body composition variables and concurrent substance abuse (N of positive tests divided by the total N of tests), neither when each drug (e.g., cocaine) was considered individually nor when the frequencies of positive tests for all drugs were added. Similarly, no significant correlations were noted of BMI to concurrent substance abuse.
Conclusion: Our findings imply that concurrent substance abuse is not associated with any particular parameters of body composition among methadone maintenance patients.

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2) Moksnes K, Borchgrevink PC, Kaasa S, Dale O. Clinical pharmacology of methadone for pain. Acta Anaesthesiologica Scandinavica 2008; 52:879-89.

» NR2-002

CONCURRENT DRUG ABUSE IN A METHADONE CLINIC: ITS RELATIONSHIP TO PAST CRIMINAL HISTORY

Zack Cernovsky Ph.D., Heba Youssef, M.D., Gamal E. Sadek, M.D., Simon Chiu, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should learn that, in methadone treatment settings, patients' reports of past criminal activity may be uncorrelated with positive urine screening tests for concurrent substance abuse, except with tests for cocaine abuse which may be more frequently positive among those who report charges of impaired driving

SUMMARY:
Introduction: Concurrent drug abuse by patients in methadone maintenance treatment may be more frequent among those with criminal history.
Objective: to examine whether criminal history of methadone maintenance patients is correlated with concurrent substance abuse.
Method: Forty-seven patients (25 men, 22 women, mean age 31.0, SD=8.2) of an urban methadone maintenance clinic were interviewed about their criminal activity with respect to previous convictions, incarcerations, and with respect to being currently on probation, and asked if their treatment was a condition of probation, if a court date was pending, if there were charges of impaired driving, or charges associated with violence or weapons. The total number of days spent in jails was also recorded. Results of their urine tests for concurrent abuse of benzodiazepines, cocaine, oxycodone, and other opiates were collected for 2 or more weeks: the number of tests per patient ranged from 3 to 23 (mean = 10.8, SD=5.3).
Results: No significant Pearson correlations (at $p<.05$, 1-tailed) were found between reports of criminal activity and concurrent substance abuse (N of positive tests divided by the total N of tests), neither when each drug (e.g., cocaine) was considered individually nor when the frequencies of positive tests for all drugs were added. The only exception was a relationship of urine tests for cocaine to charges of driving while under influence of alcohol ($r=.26$, $p=.041$): those who more frequently tested positive for cocaine had more often charges of impaired driving. Conclusion: Reports of past criminal activity were not associated with an increased frequency of concurrent substance abuse among methadone maintenance patients, with the only exception of more frequent charges of driving while intoxicated in patients who abuse cocaine.

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» NR2-003

ADDICTION TREATMENT OUTCOMES FOR A COHORT OF AFRICAN-AMERICAN PHARMACISTS WITH DIAGNOSES OF SUBSTANCE ABUSE OR DEPENDENCE: IS THERE AN INEQUALITY?

Christopher Hammond B.A., Noni A Graham, M.P.H., R Pomm, M.D., Mark S Gold, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able: 1.To recognize inequalities in healthcare. 2.To understand the pattern of substance abuse and dependence in pharmacists. 3.To identify if there are inequalities with regard to treatment received and health outcomes in African American pharmacists when compared to their peers.

SUMMARY:
In the medical literature there is evidence of inequalities in healthcare for African-Americans leading to poorer health outcomes, even when controlling for socioeconomic status. Pharmacists represent a special case with respect to impaired professionals due to their access to narcotics, but multiple studies have demonstrated similar rates of addiction and post-treatment abstinence (85% completion of monitoring programs). To date there have been no studies investigating the treatments offered to and health outcomes of African-American pharmacists with diagnoses of substance abuse or dependence. We querried the Professionals Resource Network, Inc.(PRN) computer database from 1990-2008 and found 18 African-American pharmacists who were currently or had in the past been monitored for substance abuse or dependence. The cohort consisted of 10 males and 8 females, ages 36-58. While ten (56%) of the pharmacists had diagnoses of polysubstance dependence or abuse, a significant number (ten, 56%) had diagnoses of opioid dependence or abuse and had diverted prescription opiates from their workplace. Five (28%) had a clear history of arrest for diversion of opiates from their medical records. In this population, illicit drug abuse in the absence of prescription drug abuse was uncommon. Fifteen (83%) of the African-American pharmacists were offered residential treatment or intensive outpatient programs and seventeen (94%) were offered 12 step programs. All pharmacists received PRN monitoring consisting of weekly meetings and random urinalysis. With respect to outcome data: twelve (67%) were abstinent and had completed or were still under contract with the PRN. Only ten (56%) had returned to the practice of pharmacy at the time of data collection. Interestingly, nine (50 %) had at least one relapse since their initial diagnosis of substance abuse or dependence.

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1) Gadson SL. Health Equality: the New Civil Rights Frontier. J Natl Med Assoc. 2006; 98(3):324-329.

2) Dabney DA. Onset of Illegal Use of Mind-altering or potentially addictive prescription drugs among pharmacist. J Am Pharm Assoc. 2001; 41(3):392-400.

» NR2-004

HOSTILITY AND IMPULSIVITY OF NICOTINE DEPENDENCE

Jaerin Hwang, Sungho Min, M.D.

EDUCATIONAL OBJECTIVES:
Because epidemiological and psychological characteristics of nicotine dependence are different from those of smoking, the difference between the two should be explored in diverse aspects. And new approaches must be developed to evaluate biological and physiological effects of nicotine.

SUMMARY:
Method: Data were obtained from aged 21.0±1.1 years 550 men who were serving in the Air Force and promoted to an airman 1st class. Information on smoking habits, nicotine dependence status (Fagerstrom Test for Nicotine Dependence, Korean Nicotine Dependence Syndrome Scale), sociodemographic factors and psychological factors (Buss & Durkee Hostility Inventory, Dysfunctional Impulsivity Scale, etc.) were collected through self administered questionnaires.
Results: The smoking rates were 30.1%. Alcohol use and psychological factors including depression, hopelessness, anxiety, hostility and impulsivity were found to be related to smoking status in target population. About one third (11.6%) smokers were moderate to severe nicotine dependence (FTND>3). Especially, the level of hostility and impulsivity were significantly associated with severity of the nicotine dependence in smokers.
Conclusions: This study reports prevalence estimates of nicotine dependence, as distinct from smoking. The results of this study suggest that there is unknown connection between two psychological factors and nicotine dependence (1, 2).

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» NR2-005

DRINKING PATTERNS, TEMPERAMENT AND CHARACTER OF FEMALE INPATIENTS WITH ALCOHOL DEPENDENCE

Jung Sik Lee M.D., Soon Woo Chang, M.D., Sang Baek Lee, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize personality trait and drinking patterns of female alcoholics.

SUMMARY:

Objectives : This study was designed to examine the temperament and character inventory (TCI) scores with demographic and clinical findings of female alcoholic patients, and to find ways helpful in further treatment intervention.
Methods : 43 female alcohol dependent patients and 32 female social drinkers were included in this study. Female patients were divided into positive family loading and negative family loading subgroups. Another differentiation was done according to the presence of spouse alcohol drinking problems. Demographic data, TCI scores of two comparing groups were studied, and clinical characteristics of each group were examined by obtaining the informations about drinking habits and childhood victimization histories, and measuring Beck Depression Inventory Korean version(K-BDI), State-trait Anxiety Inventory(STAI-X2), Buss-Durkee Hostility Inventory (BDHI), Acute Physiological and Psychological Response after Drinking, and Michigan Alcohol Screening Test Korean version(MAST-K).
Results : Higher scores of Harm Avoidance (HA) and Self-Transcendence (ST), lower scores of Reward Dependence (RD), Self-Directedness (SD), and Cooperation (CO) were shown in female patients than the scores of normal control. Female alcoholics scored more highly on BDI and STAI, and were also associated with more suicidal thoughts and attempts. They also showed higher rates of childhood victimization experience like physical abuse.
Conclusion : Study results suggest that the TCI profiles of the female alcoholic patients in comparison with normal control subjects may reflects common comorbid psychiatric conditions like depression, anxiety disorder, and personality disorder. The evaluation of childhood traumatic experience and suicidal risk might be also needed in the treatment process of female alcoholics.

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2) Bergvall AH, Nilsson T, Hansen S: Exploring the link between character, personality disorder, and neuropsychological function. Eur Psychiatry. 2003;18(7):334-344.

» NR2-006

COUNSELOR CHARACTERISTICS PREDICT SUBSTANCE ABUSE TREATMENT RECOMMENDATIONS

Colleen Lewy Ph.D., Holly E. Fussell, Ph.D., Celina Oliver, M.S., Bentson McFarland, M.D., Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the role of clinician characteristics on substance abuse treatment recommendations.

SUMMARY:

The American Society of Addiction Medicine Patient Placement Criteria (ASAM PCC-2R) is considered the gold standard for the development of treatment recommendations for persons with substance use disorders. Using six dimensions, clinicians follow a fixed algorithm to create a treatment plan. Research in primary care has shown that physician gender and age can influence recommendations for treatment of depression. If, similar to findings with physicians, substance abuse counselor characteristics account for discrepancies in patient placement, implications for addictions treatment abound. Since counselor characteristics vary widely, this may help explain why the reliability and validity of the ASAM PCC-2R have produced mixed results.
Thirteen drug and alcohol clinicians (persons self-identified as substance abuse counselors or those in training) conducted an assessment interview with a standardized patient (SP) who was portraying a heroin addicted male. SPs are paid professionals specially trained to portray the persona of a patient role and consistently present the same symptoms to multiple clinicians. For this study, clinicians were asked to place the SP on each of the six ASAM PPC-2R dimensions or areas of assessment and then recommend an overall level of treatment.
Regression analyses showed that counselors "not in recovery" (N= 9) or counselors in training (N = 5) recommended significantly higher overall levels of treatment (more intensive) than counselors "in recovery" (N = 4) or counselors who had completed training (N = 8). Thus, certain types of counselor "experience" are associated with less intensive treatment recommendations.
This pilot study suggests that counselor characteristics may influence ASAM patient placement recommendations. Further research with a larger sample is needed to understand what other factors are important for patient placement in substance abuse treatment.

REFERENCES:

1) Baker, S.L., & Gastfriend, D.R. (2003). Reliability of multidimensional substance abuse treatment matching: Implementing the ASAM patient placement criteria. Journal of Addictive Diseases: 22(Sup. 1), 45-60.

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» NR2-007

CANNABIS USE FOLLOWING LOW DOSE NALTREXONE ADDITION IN OPIOID DETOXIFICATION

Paolo Mannelli,Kathi Peindl PhD, Li-Tzy Wu Sc.D., Ashwin A Patkar, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the utility of specific methods of opiate antagonist administration to treat cannabis abuse and dependence.

SUMMARY:

Introduction. Opioid detoxification outcomes include the ability of patients to maintain abstinence and enter aftercare following treatment completion.
Cannabis shares common mechanisms with opioids and cannabis abuse is associated with relapse risk in opioid dependent patients.
Objective. The addition of very low-dose naltrexone (VLNTX) to methadone taper is associated with reduced withdrawal intensity and increased early abstinence rates. We analyzed the characteristics of cannabis use among opioid dependent patients who completed detoxification.
Methods. 120 opioid addicts completed inpatient detoxification, receiving naltrexone 0.125/0.250 mg per day or placebo, together with methadone in a double blind, randomized, two-site study. They were evaluated 1 and 7 days following treatment completion.
Results. Significantly less patients who received VLNTX used cannabis (Day 1: chi square 38.2(2), p=0.000; Day 7: chi square 7.9(2), p=0.02) as confirmed by self-reports and drug screens.

Cross-sectional analysis shows no differences in demographics, drug use severity or discontinuation rate among individuals who differed for cannabis use. A test for equality of means demonstrates that no cannabis use was associated with lower withdrawal intensity at discharge. In a logistic regression analysis, individuals receiving VLNTX were 8 times less likely to have positive urine screens for cannabis the week after discharge, compared to the placebo group (95% CI=14.3-47.6 for both groups; Wald=5.546; p=0.019), controlling for cannabis use before detoxification. There was no association between opioid and cannabis in patients who did not receive VLNTX.
Conclusions. VLNTX use during opiod detoxification is associated with reduced rate of cannabis use, early after completion. Low dose naltrexone should be tested to explore the relationship between effects of cannabis and opioid substances and to treat cannabis dependence in patients without co-morbid substance abuse.

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» NR2-008

POKER AND PSYCHOSTIMULANTS: A CASE STUDY

Troy Pulas M.D., Dwight Zach Smith, M.D., John Renner, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to decribe the differences between dependence, abuse, misuse, and controlled use of substances and medications. The participant should further be able to discuss the ethics of psychostimulant use in poker and other settings for cognitive enhancement.

SUMMARY:

Poker has become one of the most popular gambling games with over 50 million players worldwide. Many professional poker players earn their livelihood through poker. Because prolonged attention, focus, and low anxiety are desirable attributes, poker players use various substances to alter cognition. These agents include nicotine, caffeine, alcohol, and, more recently, psychostimulants. Many papers have reported on use and neuroethics of psychostimulants but a pubmed literature search revealed no case reports or studies of poker or gambling with the concomitant use of psychostimulants. This report discusses the use of lisdexamfetamine in a 30 year old Asian male with no previous psychiatric history who has been a regular poker player for the past 7 years. This subject routinely spends 30-40 hours playing poker each week. Although he considers poker a hobby, he earns enough money for it to be his primary profession. It is not clear if he qualifies for diagnostic criteria for attention deficit hyperactivity disorder or compulsive gambling disorder. Nevertheless, he is prescribed lisdexamfetamine 50mg daily by a psychiatrist. In the past year the subject experimented with other medications including methylphenidate and modafinil before settling on lisdexamfetamine due to better tolerability of side effects. He reports a dramatic improvement in poker playing and profitability, as well as an increase in attention, concentration, and focus. Without lisdexamfetamine he is limited to 8 hour sessions but while using lisdexamfetamine he routinely maintains a high level of play for 16 hours and even up to 36 hour shifts. This subject also occasionally uses lisdexamfetamine when not gambling but he does not appear to abuse the medication at other times. This case presents a description of a new pattern of medication use behavior that raises several important questions in the areas of addiction psychiatry, neuroethics, and cognitive enhancement.

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2) Lanni C, Lenzken SC, Pascale A, Del Vecchio I, Racchi M, Pistoia F, Govoni S (2008). Cognition enhancers between treating and doping the mind. Pharmacological Research 57(3):196-213.

» NR2-009

THE MEDICATION USE FOR NICOTINE DEPENDENCE AT A PUBLIC TREATMENT PROGRAM IN RIO DE JANEIRO, BRAZIL

Ana Saad M.D., Jorge Antonio Jaber Filho, MD, MBA; Eduardo Hoffmann, Psy. D; Angela Hoffmann, Psy. D; Antonio Tomé, therapist.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the benefits or not of using the medication varenicline for quit smoking at a public program in Rio de Janeiro, Brazil.

SUMMARY:

Objective: Nicotine dependence is a world health problem. The objective of this paper is to present the implementation of a public facility for the treatment of nicotine dependence at Câmara Comunitária da Barra da Tijuca in Rio de Janeiro, Brazil, and the use of varenicline as a specific medication.
Methods: The program includes 12 sessions once a week to reach nicotine abstinence. The first evaluation is done by a psychiatrist. The eligibility for varenicline use includes more than one failure of abstinence as well as the use of other medications without success. The initial dose is 0,5 mg on the first 3 days raising to 0,5 mg twice a day from day 4 to day 7; after that it is increased to 1mg twice a day until12 weeks are completed. It is strongly suggested that the patient picks up a day to quit smoking, between the first and second week of varenicline use. Besides medication, it was also given behavioral and focal group therapy.
Results: There were 132 patients attending the program from July 2007 to November of 2008; 63 (47,7%) reached abstinence being 24 male and 39 female. From the abstinent 32 (50,7%) used varenicline 8 male and 24 female. Nausea was the side effect most reported and a reason for discontinuing the use of varenicline.
Conclusion: We intend to improve the number of patients and the methods for a broader study. Meanwhile, as a new medication in Brazil, it was important to understand the acceptation among patients; the high cost is surely an impediment for wide use.

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» NR2-010

RELATIONSHIPS BETWEEN USE OF ANTIPSYCHOTICS AND CHANGES IN PHYSICAL GROWTH IN CHILDREN AND ADOLESCENTS WITH HIV

Suad Kapetanovic M.D., Lisa Aaron, B.S.,Patricia A. Sirois, Ph.D.,Grace Montepiedra, Ph.D.,Paige L. Williams, Ph.D., Deborah A. Pearson, Ph.D., Kathleen Malee, Ph.D., Patricia A. Garvie, Ph.D., Betsy L. Kammerer, Ph.D., Sharon L. Nichols, Ph.D., Molly L. Nozyce, Ph.D., Mark Mintz, M.D., James M. Oleske, M.D., and the IMPAACT/PACTG 219C Team

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:
1. identify risks and benefits of using antipsychotics in HIV-infected youth with psychiatric disorders.
2. recognize the evolution of the HIV infection into a chronic condition and new resulting psychiatric and behavioral risks.

3. identify areas of need for future research.

SUMMARY:

Background and Significance: HIV-infected (HIV+) youth are at risk for mental illness. Antipsychotics are increasingly prescribed to mentally ill youth. There is evidence that some antipsychotics are associated with excessive weight gain. Objective: Examine relationships between prescribed antipsychotics and changes in physical growth in a cohort of perinatally HIV+ youth. Methods: Analysis of data from Pediatric AIDS Clinical Trials Group Protocol 219C, a longitudinal observational study of HIV+ youth. Inclusion criteria: perinatally HIV+; 3-24 years old; used first antipsychotic for = 1 month; available baseline visit prior to starting the first antipsychotic. Each participant with a prescription for an antipsychotic was matched (sex, age, Tanner stage and baseline BMI z-score) with 1-3 perinatally HIV+ controls without prescriptions for antipsychotics. Outcomes: short- and long-term changes in BMI z-score from baseline to 2-year follow-up. Results: The total sample size including controls was 248 for the short-term analysis, and 206 for the long-term analysis. Youth who were taking antipsychotic medication were found to have increased BMI z-scores, relative to youth who were not taking antipsychotic medications (short-term: slope=0.180, p=0.0064; long-term: 0.323, 0.0013); this finding was associated with atypical antipsychotics as a group (0.187, 0.0064; 0.351, 0.0013), as well as risperidone alone (0.242; 0.0032; 0.374, 0.0011). Conclusion: (Atypical) antipsychotics as a group, as well as risperidone alone, were independently associated with increased BMI z-scores in perinatally HIV+ youth. The direction of the association (risperidone > any atypical > any antipsychotic) suggests that some antipsychotics may be weight-neutral in this population. Clinicians prescribing antipsychotics to HIV+ youth should carefully monitor the growth parameters. Future research should evaluate differential growth outcomes of individual antipsychotics in HIV+ youth.

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» NR2-011

AMPHETAMINE RELATED SYMPTOMS: DESCRIPTIVE ANALYSIS AND REASONING

Ghada Abdel Razek M.D., Y. Abdel Razek,M.D. Mahmoud Rashad,PhD., Mohamed Al-Zahrany ,PhD., Abdalla Al-Johi, PhD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to 1- Recognize the the importance of clinical observation to monitor changes in the presentation of amphetamine dependent patients. 2- Know the different psychotic symptoms associated with amphetamine induced psychosis 3-identify the importance of integrating clinical observation with chemical assessment of the available illicit drugs

SUMMARY:

At the last few years a lot of data in the gulf region reported that amphetamine psychosis became more common and more prolonged. Aim of the work: This study was done to: 1) assess clinical features related to amphetamine withdrawal, 2) assess if there are changes in these features in comparison to other previous studies or not, 3) study the relation between amphetamine and chronicity of psychotic symptoms, 4) Find a reason for such suspected changes if present. Methods: A total of 150 male amphetamine dependent inpatient were selected according to ICD-10 research diagnostic criteria. Patients were subjected to the following procedures: 1) Oral informed consent. 2) Full psychiatric interview. 3) Urine test for common addictive substances on admission 4) Symptoms checklist which have been designed by the authors to assess Clinical features associated with amphetamine 5) Symptom Checklist–90—Revised (Derogates 1994) . Results: Generally the present study shows that the psychotic symptoms were very common with Amphetamine dependent patients and the severity of all symptoms decreased significantly during the different phases of treatment. Delusions and hallucinations were very common during 2nd week (54% and 51% respectively) and persisted for more than 8 weeks in 24% and 10% of patients respectively. Discussion: Some of the results are similar to previous studies as Dalmau et al 1999 and Koyama et al 1991 but still the duration of psychosis is much longer. Conclusion: there is increased risk of psychosis with use of amphetamine and a lot of reasons may play role as starting abuse at early age , sensitization process that may lead to chronic psychosis , and adulterating substances like ephedrine that may be dangerous and can lead to permanent damage of brain serotonin nerve endings.

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» NR2-012

THE IMPACTS OF SUBSTANCE ABUSE AND DEPENDENCE ON NEUROPSYCHOLOGICAL FUNCTIONS IN A SAMPLE OF PATIENTS FROM SAUDI ARABIA

Mohamed Alzahrani Ph.D., Yasser A. Elsayed

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the impacts of substance abuse and dependence on neuropsychologial functions and the factors affecting these impacts.

SUMMARY:

BACKGROUND: A lot of studies were directed to explore the relation between drug abuse and Neuropsychological functions. The interest in studying this relationship is the result of the scientific achievements in the field of neuropsychology. Some studies reported that even after a long duration of disappearance of withdrawal or intoxication symptoms, many patients have obvious deterioration of cognitive functions. AIM OF THE STUDY: The aim of this study was to explore the relationship between the substance use disorders and the executive functions. METHODS: Two groups were selected for this study. An experimental group consisted of 154 patients and further subdivided according to the substance used into three different subgroups: opioid, Amphetamine and Alcohol group which included 49, 56 and 49 patients respectively. The control group was selected matching the experimental group in the demographic characteristics and included 100 persons. Tools used were: Benton Visual Retention Tests, Coloring Making Tests, Stroop Colors-word Test, Symbol Digit Modalities Test, the Five Dots Cognitive flexibility test, Verbal flexibility test. All previous tools were standardized by the researchers prior to application. STATISTICAL ANALYSIS: all the data were subjected to statistical analysis which included the Mean & Standard Deviation, Factor Analysis, Correlations, MANCOVA, and Multivariate Analysis of Co- Variance. RESULTS: There were significant differences between experimental and control groups in the performance of neuropsychological tasks as the experimental group was much worse. Also, there were significant differences among the subgroups of the experimental group as the alcoholic group was much worse on several tests especially tests related to cognitive flexibility, attention and reaction time followed the opioids then the amphetamine group. Patients with longer duration of dependence and multiple hospital readmissions were much worse in comparison to

patients with smaller duration of dependence and less readmission.
DISCUSSION AND CONCLUSION: Drug dependence impacts the neuropsychological functions negatively and the findings were more with alcohol followed by opioids and amphetamine. The more the duration of dependence and the number of relapses the more the negative impacts.

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» NR2-013

ALCOHOL PROBLEM USE IN MALE POPULATION IN COLOMBIA: ASSOCIATION WITH CIGARETTE SMOKING

Jaider Barros-Bermudez M.D., German E. Rueda-Jaimes, MD, Luis A. Diaz-Martinez, MD, MSC, Edwin Herazo, MD, MSc, Adalberto Campo-Arias, MD

EDUCATIONAL OBJECTIVES:

At the end of this poster presentation, the attendees will know the prevalence of alcohol problem use and its correlates in Colombian men

SUMMARY:

Background: Alcohol is the substance most used in men from the Colombian general population. Alcohol intake is related to high number of death due violence and car accidents. These are main cause of death in young and middle age Colombian men. Although, the frequency and correlates of alcohol problems use in men have not been accurately reported.
Objective: To estimate the prevalence and explore some correlates of alcohol problem use in a sample of men from the general population of Bucaramanga, Colombia.
Method: A cross-sectional study was designed. Demographic variables, daily cigarette smoking, daily coffee drink, common mental disorders and alcohol problem use were investigated. Alcohol problem use was measured with the CAGE questionnaire (two or more affirmative answers). Logistic regression model was calculated to adjust associations.
Results: A total of 756 men participated in this research. The mean age was 37.3 years (SD=14.4) and mean years of education 9.9 years (SD=4.2), 54.6% were married, 76.8% were employed, 18.6% reported daily cigarette smoking, 45.9% daily coffee intake, 9.5% common mental disorders, and 10.0% (95%CI 7.9-12.1) scored for alcohol problem use. Daily cigarette smoking (OR=2.1, 95%CI 1.3-3.6) was associated with alcohol problem use, adjusted for common mental disorders (Hosmer-Lemeshow goodness-of-fit, X2=0.33, df=4, p=0.846).
Conclusions: One each ten men in Colombia report alcohol problem use. Only daily cigarette smoking is related to alcohol problem use. More studies are needed.

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» NR2-014

DUAL DIAGNOSIS IN PSYCHIATRIC IN PATIENTS

Jose Gines, David Corcoles M. D., Jose M Arcega M. D., Angeles Malagon M.D., Carles Garcia-Ribera M. D., Anna Merino M. D., Antoni Bulbena Ph.D. M. D.

EDUCATIONAL OBJECTIVES:

Dual diagnosis (substance use disorders and any other pathology in axis I or axis II) is very frequent actually in psychiatric emergency rooms and in psychiatric in-patients.
These pathology means a different use of health care resources and different treatment. Usually this patients have more non psychiatric disorders like HIV, and other infections. We want to determinate in a psychiatric unit the differences between patients with dual diagnosis and others without substance use disorders.

SUMMARY:

We have the results for 161 patients who stayed in a psychiatric unit during 1 year. Thirty-seven of this patients (23%) have a dual diagnosis. We have compared socio-demographic and clinical variables between patients with or without dual diagnosis. We did the analyze using the SPSS 16.0 sotfware package.
We have found significatives differences in syndromic diagnosis (excluding substance use disorder) (p=0.003 chi square); social problems 48.6% in dual diagnosis vs 17.7% (p=0.000 Chi square); HIV 35.1% vs 3.2% (p=0.000), hepatitis C 43.2% vs 2.4% (p=0.000) and in mean age 49.58+17.15 in dual diagnosis vs 40.22+11.13 (p=0.002 Anova).
We didn't found differences in other variables such as gender, immigrants patients, days like in-patients, derivation after discharge or psychiatric backgrounds.
We found that patients with dual diagnosis need more health care and more resources.

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» NR2-015

STUDY OF FACTORS THAT INFLUENCE DRINKING BEHAVIOR AMONG KOREAN PREGNANT WOMEN

Sung-Gon Kim M.D., Ji-Hoon Kim, M.D., Sang-Shin Lee, M.D., Soo-Mi Shin, M.D., Byung-Dae Lee, M.D., Woo-Young Jung, M.D., Ji-Hye Park, M.D.

EDUCATIONAL OBJECTIVES:

This study shows that a quarter of pregnant women aware of their status consume alcohol, which strongly suggests that an anti-drinking educational strategy should be devised to target women of childbearing potential, particular, those at high risk.

Summary:

Objective: Drinking alcohol during pregnancy can result in malformation of the fetus and diverse behavioral problems in newborns. Nevertheless, few studies have been conducted in Korea to determine levels of alcohol consumption during pregnancy and the factors that influence drinking behavior among Korean pregnant women.
Accordingly, a survey was conducted on pregnant women to determine whether they drank alcohol and to identify the result factors involved.
Method: Pregnant women at less than 30 days before expected delivery who visited 3 obstetric and gynecology hospitals (a university hospital, a specialized hospital, and a clinic) were asked to complete a self-report questionnaire. Demographic and obstetric characteristics were investigated, as were consumption of alcohol before and after the realization of pregnancy, frequency of drinking, and average amount consumed.
Result: 1) Six hundred and ninety five subjects of average age 30.8±3.8 years were enrolled. Of these, 25.7% had completed high school education and 37.6% had a career. 67.9% were nulliparous, and 99.4% were aware that consuming alcohol during pregnancy

is harmful. 2) 578 (83.2%) and 173 subjects (24.9%), respectively, consumed alcohol before becoming pregnant and after they were aware of being pregnant. 3) Those that had consumed alcohol before becoming pregnant (X2=48.614, p<0.001) and those with a family history of alcoholism (X2=12.316, p<0.001) were found to be more likely to drink alcohol when pregnant. In addition, those with a lower educational background (X2=8.938, p=0.030), and those with an unintended pregnancy (X2=4.684, p=0.030) were found to be more likely to drink alcohol when pregnant.
Conclusion: This study shows that a quarter of pregnant women aware of their status consume alcohol, which strongly suggests that an anti-drinking educational strategy should be devised to target women of childbearing potential, particular, those at high risk.

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» NR2-016

TRACTOGRAPGY BASED SEGMENTATION OF THE CORPUS CALLOSUM IN ALCOHOL DEPENDENCE

I-Chao Liu M.D.,Chen-huan Chiu, M.D.,Ph.D.,Issac Wy Tseng, M.D., PhD

SUMMARY:
Background: Neuroimaging studies have demonstrated structural and functional damage to certain brain regions in alcohol dependents. Brain white matter is especially vulnerable to chronic alcohol consumption. The aim of this present study was to use an advanced technique, Diffusion Spectrum Imaging (DSI), to investigate the microstructural integrity of corpus callosum (CC) white matter in alcoholism. We subdivide CC using a tractography-based method and the associations between neurobehavioral characteristics and region-specific nerve tracts of CC among alcoholics were also evaluated.
Methods: Twenty-five cases meeting DSM-IV diagnostic criteria of alcohol dependence were recruited from an in-patient setting. In addition to fill out the Barratt Impulsivity Scale (BIS), subjects were assessed using the following tests: Wechsler Adult Intelligence Scale-Third Edition, Wechsler Memory Scale-Third Edition, and Color Trails Tests. All alcohol-dependents and fifteen healthy subjects were imaged in a 3.0-Tesla scanner and Fractional Anisotropy (FA) was used as the index of the integrity of white matter to be compared in this study.
Results: Years of alcohol regular use is found to be negatively associated with FA on all regions of CC connecting primary sensory, temporal, and parietal cortex. The BIS score has an inverse relationship with FA on the prefrontal region of CC. The disruption of nerve connectivity with a low FA was found to be significant in patients with alcohol dependence, comparing with the comparison group.
Conclusions: Our findings support the injury of CC, measured by low FA, in patients with alcohol dependence. The possible explanations on white matter damage have been proposed. The impulsivity level is correlated with nerve disruption of the prefrontal region on CC. Further imaging studies for alcohol dependence ought to explore the associations between nerve connectivity and disease course, disease severity, and deficits on neuropsychological performance.

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» NR2-017

DOES ANY METHOD OF DEFINING FAMILIAL ALCOHOLISM PREDICT REMISSION FROM AN AUD FORTY YEARS LATER?

Shubha Raja M.D., Elizabeth C. Penick, Ph.D., Bjorn Ebdrup, M.D., Joachim Knop, M.D., Elizabeth J. Nickel, M.A., Per Jensen, M.D., William F. Gabrielli, M.D., Ph.D. Ann M. Manzardo, Ph.D., Sreelatha S. Spieker, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be familiar with nine different methods of defining familial alcoholism and their effect on the development and remission from an Alcohol Use Disorder at age forty.

SUMMARY:
Objective: Our previous work showed that a history of alcoholism in the biological father predicted the development of an Alcohol Use Disorder (AUD) in their sons but did not predict its remission. This study asks whether any of nine different methods of defining familial alcoholism predicted remission from Alcohol Abuse/Alcohol Dependence.
Method: The 202 men who completed the 40-year examination were drawn from a cohort of 9,182 births that was extensively studied perinatally and one year later. In their late teens, a sample of high-risk sons of treated alcoholic fathers and low-risk sons of fathers never treated for alcoholism was created from data located in the national Central Psychiatric Register of Denmark and local alcoholism clinics in Copenhagen. This sample was studied at age 20, then at age 30, and at age 40, with a broad array of procedures. These methods included a series of structured interviews, psychometric tests and an examination by a senior psychiatrist. Nine methods of defining familial alcoholism were extracted from the data. Six were based upon the family history method (son's report at age 40), two were based upon archival information, and one was based upon a combination of archival and family history methods. The diagnosis of an AUD and the qualifier "in full remission" was made by the examining psychiatrist according to DSM-III-R criteria.
Results: All nine methods of familial alcoholism were significantly correlated with each other and predicted three major drinking outcome measures. None of the nine methods of defining a family history of alcoholism predicted remission from Alcohol Abuse or Alcohol Dependence.
Conclusion: An unexpected disconnect was found between the effect of a positive family history of alcoholism on the course of alcoholic drinking. Familial alcoholism strongly predicted who would become alcoholic but did not predict who would recover.

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» NR2-018

DISRUPTING RECONSOLIDATION OF ALCOHOL-RELATED MEMORIES REDUCES CUE-INDUCED ALCOHOL-SEEKING BEHAVIOR IN RATS

Christoph von der Goltz M.D., Valentina Vengeliene, Ph.D., Falk Kiefer, M.D., Rainer Spanagel, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize mechanisms and potential therapeutical impact of disrupting reconsolidation of alcohol-related memories.

SUMMARY:
In humans alcohol-seeking behavior is frequently evoked by the retrieval of memories associated with an alcohol experience and it is reasonable to hypothesize that disrupting alcohol-related memories might help to prevent relapses. The reconsolidation hypothesis states that a consolidated memory could again become labile and susceptible to pharmacological disruption after memory retrieval (Nader et al., 2000). While the majority of research on memory reconsolidation has used conditioned aversion paradigms, more recent studies demonstrated that retrieved appetitive drug-related memories also undergo reconsolidation (Lee et al., 2005). Although it has been shown that the reconsolidation of cocaine and morphine-related memories can be disrupted, it remains to be done for alcohol-associated memories. The aim of our study was to investigate whether the behavioral impact of previously conditioned alcohol-related cues is significantly reduced by blocking the reconsolidation of the previously learned alcohol associations that are retrieved by reexposition. For this purpose we applied an animal model for cue-induced relapse to alcohol-seeking behavior. We show that post-retrieval systemic administration of 0.1 mg/kg of the NMDA antagonist MK-801 significantly reduced alcohol-seeking behavior during the following test day as compared to vehicle treated rats. Similarly, memory reconsolidation was disrupted by intracerebroventricular administration of 400 µg of the protein synthesis inhibitor anisomycin. Pharmacological disruption of reconsolidation of alcohol-associated memories may thus provide a potential therapeutic strategy for the prevention of relapse in alcohol addiction.

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» NR2-019

IMPROVEMENT IN EMOTIONAL EXPRESSION IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER TREATED WITH 20 TO 70 MG/DAY LISDEXAMFETAMINE DIMESYLATE

Katic Alain M.D., Lawrence D. Ginsberg, M.D., Rakesh Jain, M.D., Cynthia Richards, M.D., Ben Adeyi, M.S., Tom Babcock, D.O., Bryan Dirks, M.D., Brian Scheckner, Pharm.D., Robert L. Findling, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to evaluate lisdexamfetamine dimesylate effects in children with attention-deficit/hyperactivity disorder on emotional expression, as assessed by the Expression and Emotion Scale for Children. Participants will also be able to evaluate whether sex, history of other psychiatric conditions, common adverse events, or early discontinuation altered LDX effect on emotional expression at endpoint.

Summary:
Objective: To assess the effects of lisdexamfetamine dimesylate (LDX) on emotional expression in children with attention-deficit/ hyperactivity disorder (ADHD).
Methods: Children aged 6 to 12 years with ADHD participated in an open-label, 7-week, dose-optimization study of 20-70 mg/d LDX. The ADHD Rating Scale IV (ADHD-RS-IV) was the primary efficacy measure. The 29-item Expression and Emotion Scale for Children (EESC) was used to assess the effect of LDX on emotional expression, including blunting of affect, emotional lability, and positive expression. These items are rated on a 5-point scale from 1 (not true at all) to 5 (very much true).
Results: Percent (SD) improvement in ADHD-RS-IV total score (N=316) from baseline to endpoint was 69.3% (23.3) (P<.0001). Mean change from baseline EESC total score was -7.4 (18.3) (N=304), indicating improvement (P<=.0001). Changes (SD) from baseline were -2.1 (9.6) for positive emotions (P=.0002), -2.5 (7.7) for emotional flatness (P<.0001), and -2.8 (5.2) for emotional lability (P<.0001). Similar mean changes in emotional expression with treatment were observed in males and females, subjects with or without a history of other psychiatric disorders, and subjects who did or did not report a common (reported by >=5% of subjects) treatment-emergent AE (TEAE). Participants who discontinued before study end (n=28) did not show mean improvement in emotional expression. Common TEAEs (>=5%) included decreased appetite, decreased weight, irritability, insomnia, headache, upper abdominal pain, affect lability, nausea, and vomiting.
Conclusions: There were significant improvements in ADHD-RS-IV with LDX at endpoint. TEAEs were consistent with those seen with long-acting stimulants. Subjects of both sexes, or with or without history of comorbid psychiatric conditions, or commonly observed AEs generally had no mean worsening of emotional expression with LDX treatment.
Supported by funding from Shire Development Inc.

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» NR2-020

PATIENT EXPERIENCE AND SATISFACTION WITH LISDEXAMFETAMINE DIMESYLATE IN ADULTS WITH ADHD

Donna Antonucci M.D., Donna Kerney, Ph.D., Frank A. Lopez, M.D., Michael Manos, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to describe adult patient reported effects of lisdexamfetamine dimesylate after 6 weeks of treatment for ADHD. Effects include reduction in ADHD symptoms and decrease in ADHD symptom interference with school, work, leisure, and personal relationships. Participants will also be able to describe the patients' reports of medication tolerability and their satisfaction with medication.

SUMMARY:
Objective: Lisdexamfetamine dimesylate (LDX) is the first long-acting prodrug stimulant indicated for attention-deficit/hyperactivity disorder (ADHD) in children and in adults. This study assessed patients' perception of ADHD symptom control and their satisfaction with LDX.
Methods: Adult patients with ADHD and initiating LDX treatment responded to phone surveys at baseline, 3, and 6 weeks. Reports of patient responses were shared with patients and their physicians. Patients received a coupon for $25 off a prescription of LDX when they completed the survey.
Results: Patients completed baseline and 6-week surveys (n=1092, mean time 51 days) rating symptoms (1=not at all; 9=very much affected) before and during LDX treatment. Patients reported improvement in symptom ratings (mean baseline vs 6 weeks) for: not able to focus (6.6 vs 4.2); difficulty organizing tasks (6.7 vs 4.1); avoiding or delaying starting tasks (6.9 vs 4.0); restlessness (5.7 vs 3.9); and making decisions impulsively (5.9 vs 3.5) (all P<.01). Patients reported that ADHD symptoms interfered less with their school or work tasks, 6.8 vs 3.5 (1=did not interfere; 9=completely interfered); with their social and leisure activities, 6.1 vs 3.3; and with personal relationships, 6.3 vs 3.4 (all P<.01). LDX tolerability and convenience were rated on average 7.2 and 7.8, respectively (1=not at all; 9=very tolerable/convenient). Patients who took

another medication prior to LDX (n=546) reported greater satisfaction with LDX, 6.8 vs 5.1, (1=not at all, 9=very satisfied, P<.01) and longer duration of symptom control (61% longer, 25% the same, 14% earlier). At least 82% of patients intended to continue using LDX.
Conclusions: Patients who completed a 6-week survey after LDX treatment reported reduction in ADHD symptoms, less symptom interference with school, work, leisure activity, relationships, good tolerability, convenience, and high satisfaction with LDX.
Supported by funding from Shire Development Inc.

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» NR2-021

LONG-TERM EFFICACY AND SAFETY OF OROS® MPH IN AFRICAN AMERICAN ADULTS WITH ADHD

Robert Armstrong M.D., H. Lynn Starr, M.D., C.V. Damaraju, Ph.D., Diane M. Hasner

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be able to understand that osmotic controlled-release methylphenidate (OROS® MPH) appeared to be efficacious and well tolerated by African American adults during treatment for attention-deficit/hyperactivity disorder (ADHD).

SUMMARY:
Introduction: Few studies have evaluated the effects of stimulant treatment for ADHD in African Americans with the disorder. This subanalysis evaluated the safety and efficacy of OROS MPH in a sample of African American adults with ADHD who were enrolled in a long-term, open-label trial (ID CR011557).
Methods: Adults (18–65 years of age, inclusive) with ADHD were enrolled in an open-label study of OROS MPH for either 6 or 12 months. Starting dose of OROS MPH was 36 mg/d; doses were titrated weekly in 18 mg/d increments until minimum clinical response criteria were met or the subject reached the maximum dose (108 mg/d). Safety and efficacy evaluations were performed throughout the treatment period.
Results: Of the 550 patients who received at least 1 dose of study medication, 6.4% (n=35, 10 men and 25 women) were African American. Of these patients, 57.1% (n=20) had not been previously diagnosed with ADHD, and 65.7% (n=23) had not received previous ADHD treatment. The 6- or 12-month study was completed by 42.9% (n=15) of patients; 14.3% (n=5) withdrew due to an adverse event (AE) and the remaining 15 patients withdrew for other reasons. Final mean (SD) OROS MPH dosage was 63.8 mg/d (23.24). Mean (SD) improvement in Adult ADHD Investigator Symptom Rating Scale total score was –17.4 (11.9) from baseline to endpoint. AEs reported by =20% of patients were decreased appetite, headache, nausea, and decreased weight. Small changes in mean (SD) systolic blood pressure (+2.0 mmHg [6.55]), diastolic blood pressure (+0.7 mmHg [5.20]), and pulse (+5.6 bpm [12.78]) occurred. No clinically relevant changes occurred in ECGs.
Conclusions: In this open-label, long-term study, African American adults demonstrated improvement in ADHD symptoms with OROS MPH treatment. OROS MPH appeared to be safe and well tolerated in this small sample of African American adults with ADHD. Supported by Ortho-McNeil Janssen Scientific Affairs, LLC, Titusville, NJ.

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» NR2-022

VIDEO GAMES: A NOVEL METHOD TO IMPROVE ATTENTION IN CHILDREN WITH ADHD

Gupta Bhupendra M.D., Jay Flynn, B.S.; Akash Gupta

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand the implications of video games in helping with ADHD as well as non-traditional treatments.

SUMMARY:
Attention Deficit Hyperactivity Disorder (ADHD) is the most commonly diagnosed behavioral and learning disorder. Children with ADHD are unable to self regulate and are dependent on external stimulation to direct attention. The present studies were conducted to investigate if video gaming can provide a stimulus in improving the attention in children with ADHD. Researchers have shown increased “slow brain waves” or theta waves (tuned out waves) and decreased “fast brain waves” or beta waves (thinker waves) in children with ADHD. EEG neurofeedback was used to focus on decreasing slow brain wave activity and increasing beta/theta ratio. The procedure consisted of using Playstation 2 and video game Gran Turismo. A virtual helmet was placed around the head circumference to hold the sensors. Three sensors were placed beneath the helmet on the head using CZ as an active site, a reference ear site, and one ground/neutral ear site. A wireless receiver was used for programming and communication of the signal processing from the video game hand-held device which transmitted real time EEG signals to the computer while playing the video game. As the subject was playing video game, signals were sent, and a line graph appeared. Data was plotted and quantified for 15 minutes per session and analyzed statistically. Results show that under controlled conditions, video games can significantly improve attention in children with ADHD as determined by the rating scale. It also leads to an improvement in physiological activity in the brain as evident by increased beta wave activity and decreased theta waves. These studies suggest that video games can have implications in improving in children and adults. Video games can be an effective method for behavior modification in children with ADHD. This method can provide a non-invasive method of improving concentration in workplace including pilots, troops, and other places of work.

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» NR2-023

METHYLPHENIDATE TRANSDERMAL SYSTEM USE AND QUALITY OF LIFE IN ADOLESCENTS WITH ADHD

Amann Birgit M.D., Robert Findling, M.D., Richard Civil, M.D., Manisha Madhoo, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be

able to discuss data described in this study pertaining to the effects of MTS on quality of life in adolescents with ADHD.

SUMMARY:
Introduction: This was a randomized, double-blind, multicenter, parallel-group, placebo-controlled, dose optimization study designed to evaluate the safety and efficacy, as well as quality of life (QoL) impact, of methylphenidate transdermal system (MTS) (10–30 mg/9 hour doses) compared with placebo transdermal system (PTS) in adolescent subjects (aged 13 17 years) diagnosed with ADHD.
Methods: At baseline, subjects were randomized in a 2:1 ratio to MTS or PTS, titrated over 5 weeks to an optimal dose of MTS, and maintained on their optimal dose through a 2-week maintenance period. The youth quality of life instrument-research version (Y-QoL), a 56 item, generic, validated instrument, was used to assess QoL at baseline and at week 7.
Results: A total of 217 subjects were enrolled, and the Y-QoL intent-to-treat population was based on a total of 129 subjects. At week 7, between group comparisons of the Y-QoL total perceptual score (LS-mean difference MTS vs PTS) did not show a statistically significant difference; however, a within group comparison (week 7 vs baseline) showed a statistically significant difference for MTS (change of 3.2) but not for PTS (change of 1.5). Both MTS and PTS groups had improved directional changes at Week 7 compared to baseline, though the effect magnitude in the MTS group was more than 2 times that seen in the PTS group. Further examinations of Y-QoL perceptual domains for the MTS treatment group showed a statistically significant improvement from baseline in the "self" (P<.05) and "relationship" (P <.05) domains, though no statistically significant improvements from baseline were noted in the "environment" and "general QoL" domains. Between group comparisons (LS-mean difference MTS vs PTS) were not significant for any Y QoL perceptual domains.
Conclusions: Within the MTS treatment group, some improvements in adolescent quality of life were noted at week 7 when compared with baseline. Supported by funding from Shire Development Inc.

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» NR2-024

SOCIOLINGUISTIC ANALYSIS OF DIALOGUE BETWEEN PSYCHIATRISTS AND ADULTS WITH DEPRESSION AND POSSIBLE COMORBID ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

William Dodson M.D., Robert L. Findling, MD; Corey Eagan; Meaghan Onofrey, MS

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be able to 1) understand the tone, content, and structure of in-office discussions between psychiatrists and adult patients with depression and possible comorbid ADHD and 2) understand the importance of effective interactions between psychiatrists and their patients with depression in regard to recognizing patient cues that may suggest ADHD comorbid with depression.

SUMMARY:
Introduction/Hypothesis: Assessment of attention-deficit/hyperactivity disorder (ADHD) symptoms in adults can be complicated by their nonspecific nature. Furthermore, many ADHD symptoms are present in other psychiatric conditions. Among adults with major depressive disorder (MDD) in the National Comorbidity Survey Replication, the prevalence of ADHD was 9.4%, and among respondents with ADHD the prevalence of MDD was 18.6% (1). Although ADHD is frequently comorbid with depression in adults, ADHD is less often diagnosed (2), and therefore many adults with ADHD are not treated for the disorder. This study reports on the tone, content, and structure of in-office discussions between psychiatrists and adult patients with depression and possible comorbid ADHD.
Methods: In-office visits between 15 psychiatrists and 52 adult patients diagnosed with depression were video and audio taped. Individual patient and psychiatrist interviews were recorded, demographic questionnaires were completed, and Part A of the Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist was administered. Only the transcripts from the 14 visits including patients with a positive screen for possible ADHD on the ASRS were analyzed linguistically.
Results: Visits lasted an average of 15 minutes and were characterized by complex, emotionally charged discussions of continued depressive symptomatology and comorbidities. None of the visits contained discussions of ADHD, although 36% of the visits contained either psychiatrist- or patient-driven language suggesting possible ADHD symptoms. Ninety-two percent of psychiatrists did not suspect ADHD when asked about individual patients post-visit. Conversely, 69% of patients believed that it was possible or probable that they had ADHD.
Conclusions/Discussion: This analysis of psychiatrist-patient interactions suggests that opportunities exist to help psychiatrists recognize patient cues that may suggest possible comorbid ADHD symptoms.Supported by Shire US Inc.

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» NR2-025

BASELINE CHARACTERISTICS AND ATOMOXETINE TREATMENT EFFICACY IN ADULTS WITH ADHD AND ADULTS WITH ADHD AND COMORBID SOCIAL ANXIETY DISORDER

Todd Durell M.D., Lenard Adler, M.D., Richard Rubin, M.D., Meihua Qiao, Ph.D., Bethany Boardman, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to identify baseline disease characteristics that differentiate patients with ADHD from patients with ADHD and comorbid Social Anxiety Disorder and understand the efficacy of atomoxetine treatment in the two patient populations.

SUMMARY:
Introduction: Attention-deficit/hyperactivity disorder (ADHD) in adults is frequently associated with comorbid anxiety disorders (1). The comorbid occurrence of ADHD and anxiety disorders may produce greater impairments or unique treatment challenges. To establish the baseline characteristics of these two patient populations and assess response rates to atomoxetine treatment, post-hoc analyses of data from two clinical trials were conducted.
Methods: Data from 501 adult patients with ADHD (study 1) and 405 with ADHD and Social Anxiety Disorder (SAD; study 2) participating in 2 randomized, double-blind, placebo-controlled studies examining the efficacy and safety of atomoxetine treatment were analyzed (2,3). Statistical tests used were Fisher's exact and analysis of variance.
Results: At baseline, patients with ADHD only had higher Conners' Adult ADHD Rating Scale-Investigator Rated: Screening Version (CAARS) Total and inattention subscale scores.

Patients with ADHD and comorbid SAD had greater symptoms as measured by the Montgomery-Asberg Depression Rating Scale, the Pittsburgh Sleep Quality Index, and the State-Trait Anxiety Inventory. Response rates and mean changes from baseline to endpoint of CAARS Total score and subscores were statistically higher for atomoxetine treatment compared to placebo in both patient groups. Despite receiving a significantly lower daily atomoxetine dose, more patients with ADHD alone responded (=30% reduction of CAARS Total score) to atomoxetine treatment and had greater mean changes from baseline to endpoint in CAARS Total score and subscores compared to patients with ADHD and comorbid SAD. Reports of treatment-emergent adverse events were similar between ADHD patients and patients with ADHD and comorbid SAD.
Conclusion: Significant differences in both baseline characteristics and response to atomoxetine treatment exist between patients with ADHD only and patients with ADHD and comorbid SAD.

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2) Adler L, Spencer T, Brown TE, Holdnack J, Keith Saylor K, Schuh K, Trzepacz PT, Williams DW, Douglas Kelsey D: Once-daily atomoxetine for adult ADHD: A six-month, double-blind trial. J Clin Psychopharmacol 2008; In press

» NR2-026

SELF-REPORTED COMORBID PSYCHIATRIC CONDITIONS AMONG ADULTS AT RISK FOR ADHD

Michael Durkin M.S.C., Robert Armstrong, M.D., Lynn Starr, M.D., Michael L. Reed, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to better understand the prevalence of comorbid health problems with symptoms that overlap with those of ADHD in an adult population at risk for the disorder as indicated by the Adult ADHD Self-Report Scale symptom checklist (ADHD Screener).

SUMMARY:

Introduction: ADHD symptoms are not clearly distinct from other psychiatric conditions, complicating diagnosis. The objective of this survey was to assess, in adults at risk of ADHD, the prevalence of self-reported diagnosed psychiatric conditions and rates of prescription treatment for those conditions.
Methods: Surveys were mailed to a representative sample of 200,000 individuals from a TNS household panel. Variable outgo sampling was used to balance the returned sample to US Census. The survey included a subset of 6 validated screening items from the Adult ADHD Self-Report Scale symptom checklist (ASRS Screener), containing DSM-IV ADHD symptoms for the past 6 months rated on a 5-point scale. Questions were also included about previous diagnoses and prescription treatment for anxiety disorder; bipolar disorder or mania; depression; drug/alcohol addiction; and sleep disorders. Prevalence rates for comorbidities were determined and demographically adjusted prevalence ratios (PR) were calculated using gender, age, income, race, household size, population density, and geographic region as covariates in a generalized linear model.
Results: Surveys were obtained from 105,187 individuals (52.6% return rate), with complete ASRS data obtained from 102,960. A total of 13,421 (13%) were at or above symptom threshold (ASRS+) and considered at risk for ADHD. ASRS+ cases were more likely to report a prior diagnosis of anxiety disorder (PR 1.82), bipolar disorder (PR 2.04), depression (PR 2.27), drug/alcohol addiction (PR 1.77), and sleep disorder (PR 1.69), relative to respondents not symptomatic for ADHD. All PRs were significant at $P<0.0001$. Similar results were seen for rates of prescription treatment.
Conclusions: Psychiatric comorbidities are common in adults at risk for ADHD. To improve management in adults, more research is needed into the relationship between ADHD and comorbidities. Supported by Ortho-McNeil Janssen Scientific Affairs, LLC, Titusville, NJ.

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» NR2-027

PHARMACOKINETICS OF INTRANASAL VERSUS ORAL ADMINISTRATION OF LISDEXAMFETAMINE DIMESYLATE IN HEALTHY ADULTS

James Ermer, Kerry Dennis, B.Sc; Mary Haffey, R.Ph; Walter J. Doll, Ph.D.; Erik P. Sandefer, Ph.D; Mary Buckwalter, M.S.; Richard C. Page, Ph.D.; Brian Diehl, B.S.; Patrick Martin, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to summarize the rate and extent of absorption and conversion to d-amphetamine of lisdexamfetamine dimesylate (LDX) when administered intranasally and describe the pharmacokinetic differences/similarities of intranasal administration compared with oral administration. Altered rate and extent of absorption with different routes of administration may play a role in determining abuse potential of stimulant agents.

SUMMARY:

Objective: To compare the pharmacokinetics of d-amphetamine derived from the prodrug stimulant lisdexamfetamine dimesylate (LDX) after single intranasal (IN) vs oral (PO) administration of LDX. Methods: In this randomized, 2-period, crossover study, healthy adult males without a history of substance abuse (18 to 65 years) were administered single IN (radiolabeled with up to 100 µCi 99mTc-DTPA) and PO doses of LDX 50 mg at least 7 days apart. IN administration was confirmed by scintigraphy. Serial blood samples were drawn (up to 72 hours postdose) to measure d-amphetamine and intact LDX levels. Treatment-emergent adverse events (TEAEs) were assessed.
Results: Eighteen subjects were enrolled and completed the study. The mean (SD) Cmax, AUClast, and AUCinf of d-amphetamine following IN LDX were 35.9 (6.49) ng/mL, 690.5 (157.05) ng•h/mL, and 746.2 (171.58) ng•h/mL, respectively. After PO LDX, the mean (SD) Cmax, AUClast, and AUCinf of d-amphetamine were 37.6 (4.54) ng/mL, 719.1 (157.05) ng•h/mL, and 776.9 (167.69) ng•h/mL, respectively. The 2 routes of administration demonstrated similar median Tmax (4 [IN] vs 5 [PO] hours) and mean (SD) $t_{½}$ (11.3 [1.8] [IN] vs 11.6 [2.8] [PO] hours). TEAEs were more frequent after IN administration, reported by 38.9% of subjects (7/18), compared with 27.8% of subjects (5/18) after PO administration; all AEs were mild or moderate in severity and were consistent with known effects of amphetamine.
Conclusions: The rate and extent of d-amphetamine exposure were similar for both IN and PO administration of LDX. Thus, there is no pharmacokinetic advantage with IN administration should this route be abused. Safety profiles after PO and IN LDX were similar. Supported by funding from Shire Development Inc.

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2) Jasinski DR, Krishnan S: Human pharmacology of intravenous lisdexamfetamine dimesylate: abuse liability in adult stimulant abusers.

[published online ahead of print, July 17, 2008]. J Psychopharmacol

» NR2-028

EFFICACY AND SAFETY OF THE METHYLPHENIDATE TRANSDERMAL SYSTEM IN ADOLESCENTS WITH ADHD

Robert Findling M.D., Richard Civil M.D., Manisha Madhoo M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to describe the effects of MTS on ADHD symptoms in adolescents with ADHD compared with PTS, and they should be able to discuss data pertaining to the safety of MTS in adolescents with ADHD as described in this study.

SUMMARY:

Introduction: This study evaluated the efficacy and safety of the methylphenidate transdermal system (MTS) compared with a placebo transdermal system (PTS) in adolescents with ADHD.
Methods: This was a randomized, double-blind, multicenter, parallel-group, placebo-controlled, dose optimization study designed to evaluate the safety and efficacy of MTS (10–30 mg/9 hour doses) compared with PTS in adolescent subjects (aged 13–17 years) diagnosed with ADHD. At baseline, subjects were randomized in a 2:1 ratio to MTS or PTS, titrated over 5 weeks to an optimal dose of MTS, and then maintained on their optimal dose through a 2-week maintenance period. All efficacy measures were assessed using intent-to treat (ITT) analysis, and the primary efficacy measure, the ADHD-RS-IV, was administered at all study visits. Adverse events were assessed throughout the study.
Results: A total of 217 subjects were enrolled and randomized to double-blind treatment (safety population), 215 subjects were included in the ITT population, and 124 subjects completed the study. The MTS-treatment group demonstrated significantly greater mean reductions from baseline in ADHD-RS-IV total scores as well as ADHD RS-IV hyperactivity/impulsivity and inattentiveness subscale scores compared with the PTS group (P < .0001) across all study visits and at study endpoint. Overall, 386 treatment-emergent adverse events (TEAEs) were reported. Of these, 202 events were considered treatment related, and the majority (98.5%) were of mild or moderate intensity. The most common TEAEs were decreased appetite (25.5% [MTS] vs 1.4% [PTS]), headache (12.4% [MTS] vs 12.5% [PTS]), irritability (11.0%[MTS] vs 6.9% [PTS]), and upper respiratory infection (10.3% [MTS] vs 9.7% [PTS]).
Conclusions: MTS treatment resulted in significantly improved ADHD behavioral symptoms compared with PTS, and most adverse events observed with MTS treatment were mild to moderate in intensity. Supported by funding from Shire Development Inc.

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1) Plizka S. AACAP Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry. 2007;46:894-921.

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» NR2-029

DURATION OF EFFECTS OF LISDEXAMFETAMINE DIMESYLATE ON BEHAVIOR OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN NATURALISTIC SETTINGS

Thomas Frazier, Donald A. Caserta, M.A., M.S.S.A., L.I.S.W., Michael J. Manos, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the comparative effects of medication (lisdexamfetamine dimesylate), behavioral, or combined treatment on general and specific targeted behaviors including following instructions, ability to calm self, and frustration tolerance across the day from 0.5 hours (h) postdose to 12.5 h postdose in children with attention-deficit/hyperactivity disorder during a summer treatment program.

SUMMARY:

Objective: To compare duration of effects of lisdexamfetamine dimesylate (LDX), behavioral (BEH), and combined (COM) interventions on behavior ratings in children with attention-deficit/hyperactivity disorder in a summer treatment program (STP).
Methods: After open-label dose optimization and participation in the first 3 weeks of the 7-week STP, children (20 males, 5 females; aged 6-12 years) received LDX or placebo in double-blind, randomized order. During weeks 4-6, they were exposed to LDX, BEH, or COM, counterbalanced across weeks. Counselors used the Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) Rating Scale at 0.5, 1, 3, 5, 7, and 9 h on days 1-4 and 10.5 and 12.5 h postdose on day 3 each week. Parents rated specific behaviors at 10.5 and 12.5 h postdose on days 1, 2, and 4 each week with the Clinical Global Impressions-Severity (CGI-S) scale. Treatment effects were assessed with repeated-measure ANOVA.
Results: Mean SKAMP (SD) ratings (n=25) to 9 h postdose were worse in the BEH (0.66 [0.39]) condition vs COM (0.36 [0.29]) condition and LDX (0.39 [0.26]) condition; the effect size difference between LDX and BEH was 0.81. The BEH group showed deterioration by 3 h, and LDX and COM were superior to BEH (P<.001) using SKAMP ratings (n=17) to 12.5 h postdose. Parent CGI-S ratings indicated no significant effects on frustration tolerance and ability to calm self, but a significantly better ability to follow instructions in LDX and COM vs BEH at 10.5 h postdose (P=.03). By 12.5 h postdose, CGI-S ratings in all groups were comparable.
Conclusion: LDX and COM demonstrated sustained benefit across the day to 12.5 h postdose, unlike BEH alone where early deterioration of behavior occurred. LDX outperformed BEH by almost a full standard deviation, with a large effect size difference. Parents reported that children were significantly more able to follow instructions through 10.5 h postdose in LDX and COM vs BEH alone.Supported by funding from Shire Development Inc.

REFERENCES:

1) Biederman J, Boellner SW, Childress A, Lopez FA, Krishnan S, Zhang Y: Lisdexamfetamine dimesylate and mixed amphetamine salts extended-release in children with ADHD: a double-blind, placebo-controlled, crossover analog classroom study. Biol Psychiatry 2007; 62:970-976

2) Biederman J, Krishnan S, Zhang Y, McGough JJ, Findling RL: Efficacy and tolerability of lisdexamfetamine dimesylate (NRP-104) in children with attention-deficit/hyperactivity disorder: a phase III, multicenter, randomized, double-blind, forced-dose, parallel-group study. Clin Ther 2007; 29:450-463

» NR2-030

EFFICACY OF ONCE-DAILY ATOMOXETINE ON NON-VERBAL EXECUTIVE FUNCTION IN TAIWANESE CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER

Susan Shur-Fen Gau M.D., Chi-Yung Shang, MD Department of Psychiatry, College of Medicine, National Taiwan University, Taipei, Taiwan; Department of Psychiatry, National Taiwan University Hospital, Taipei, Taiwan

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know that atomoxetine is effective not only in the reductions of ADHD-related symptoms but also in improvement of non-verbal executive function in children with ADHD in ethnic Chinese population.

SUMMARY:

Objective: to assess the efficacy of atomoxetine on non-verbal

executive function in children and adolescents with ADHD.
Methods: Participants included 31 patients with DSM-IV ADHD, aged 8 to 15 years, who were recruited to an open-label 12-week atomoxetine treatment study, and 31 age-, sex-, FSIQ- and parental education-matched school controls. All the subjects were assessed by using the Chinese Kiddie-Schedule for Affective Disorders and Schizophrenia-Epidemiology version, the CPT, the WISC-III and subtests involving executive functions included the Rapid Visual Information Processing (RVIP), Spatial Span (SSP), Spatial Working Memory (SWM), Intra-dimensional/Extra-dimensional Shifts (IED), and Stocking of Cambridge (SOC) of the Cambridge Neuropsychological Test Automated Battery. The primary and secondary efficacy measures were executive functions, and parent reports on the Chinese CPRS-R:S and SNAP-IV scales, respectively. Patients with ADHD were assessed at baseline, 4 weeks, and 12 weeks. Multi-level models were used for data analysis.
Results: Patients with ADHD performed worse in the CPT, IED and RVIP than the controls. Significant improvement in executive function after treatment with atomoxetine for 4 weeks included fewer omission and commission errors, fewer hit reaction time standard errors, and less variability in the CPT; fewer total errors and trials in the IED; higher probability of hits, total correction rejection, and total hits, fewer total misses, and shorter latency in the RVIP; longer span length and fewer total usage errors in the SSP; fewer errors and strategy utilization in the SWM; and more problems solved, fewer mean moves, and shorter subsequent thinking time in the SOC. Atomoxetine significantly reduced ADHD-related symptoms over time.
Conclusions: In addition to efficacy in reducing ADHD core symptoms, our results support that atomoxetine is effective in improving the executive function in patients with ADHD in Taiwan.

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1) Gau SS, Huang YS, Soong WT, Chou MC, Chou WJ, Shang CY, Tseng WL, Allen AJ, Lee P: A randomized, double-blind, placebo-controlled clinical trial on once-daily atomoxetine in taiwanese children and adolescents with attention-deficit/hyperactivity disorder. J Child Adolesc Psychopharmacol 2007; 17:447-60

2) Faraone SV, Biederman J, Spencer T, Michelson D, Adler L, Reimherr F, Seidman L: Atomoxetine and stroop task performance in adult attention-deficit/hyperactivity disorder. Journal of Child & Adolescent Psychopharmacology 2005; 15:664-70

» NR2-031

PREDICTION OF INATTENTION SYMPTOMS ON VERBAL AND SPATIAL WORKING MEMORY AT CHILDHOOD AND ADOLESCENCE

Susan Shur-Fen Gau M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to know that among the three core symptoms of ADHD, inattention predicts decreased verbal and spatial working memory at later age, and therefore, early identification and treatment of inattention is needed.

SUMMARY:

Objective: to investigate the prediction of inattention at early childhood to verbal and spatial working memory at childhood and adolescence
Methods: The sample included 401 probands (male, 85%) with DSM-IV attention-deficit/hyperactivity disorder (ADHD), 213 siblings (male, 42%), and 175 unaffected controls (male, 73%), aged 9 to 17 years (mean age 12.02±2.24). All the subjects were assessed by using the Chinese Kiddie-Schedule for Affective Disorders and Schizophrenia-Epidemiology version for the ADHD symptoms and diagnosis and other psychiatric disorders at childhood and when they were assessed with the WISC-III including digit spans and the Spatial Working Memory (SWM) of the Cambridge Neuropsychological Test Automated Battery. Multi-level models were used for data analysis.
Results: Univariate analyses revealed inattention, hyperactivity, and impulsivity symptoms at childhood significantly predicted decreased digits recalled in the backward digit span task; and increased total errors (4-box, 6-box, and 8-box problems) and strategies utilized in searching the box with blue token in the SWM. If the three ADHD core symptoms were included in the model, only inattention maintained the significant prediction (all p values < 0.001). After further controlling for comorbidity, age of assessment, treatment with methylphenidate, and Full-scale IQ, increased childhood inattention symptoms still significantly predicted worse verbal (p = 0.008) and spatial (p ranging from 0.017 to 0.002) working memory at follow-up.
Conclusions: our findings suggest that childhood inattention symptoms predict verbal and spatial working memory at later developmental stage after taking other ADHD symptoms, demographics, medication, and intelligence into account. Early identification and treatment for inattention is needed to offset impaired working memory at later childhood and adolescence.
Supported by a travel grant from the National Science Council, Taiwan

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1) Martinussen R, Tannock R, Martinussen R, Tannock R. Working memory impairments in children with attention-deficit hyperactivity disorder with and without comorbid language learning disorders. Journal of Clinical & Experimental Neuropsychology: Official Journal of the International Neuropsychological Society 2006; 28:1073-94

2) Klingberg T, Fernell E, Olesen PJ, Johnson M, Gustafsson P, Dahlstrom K, Gillberg CG, Forssberg H, Westerberg H. Computerized training of working memory in children with ADHD--a randomized, controlled trial. Journal of the American Academy of Child & Adolescent Psychiatry 2005; 44:177-86

» NR2-032

EFFECT OF LISDEXAMFETAMINE DIMESYLATE ON SLEEP IN CHILDREN AGED 6-12 YEARS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

John Giblin, M.D., Allison Hudson, Aaron Strobel, Jesse Byrd

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the effect of short-term treatment with lisdexamfetamine dimesylate on both objective (polysomnograph and actigraph data) and subjective (sleep questionnaire) measures of sleep in children with attention-deficit/hyperactivity disorder.

SUMMARY:

Introduction: Treatment with psychostimulants has been associated with sleep disturbances, including both sleep onset and maintenance problems, in children with ADHD. This analysis evaluated the effect of lisdexamfetamine dimesylate (LDX) on sleep in children with ADHD.
Methods: This single center, double-blind, placebo-controlled, parallel-group trial enrolled children aged 6-12 years with a DSM-IV-TR? diagnosis of ADHD. The study included a screening period, 1-week washout, 3-week open-label LDX dose optimization phase, and a 4-week double-blind treatment phase in which subjects were randomized to placebo, 30, 50, or 70 mg/d LDX. Polysomnography and actigraph measures as well as assessments of subjective sleep parameters were performed in all subjects prior to treatment and reassessed after treatment with either LDX or placebo.
Results: A total of 24 subjects were randomized (8 placebo, 3 LDX 30 mg/d, 11 LDX 50 mg/d, 2 LDX 70 mg/d). The mean baseline for latency to persistent sleep (LPS) was 28.79 for LDX and 19.00 for placebo (P= 0.27). At endpoint, mean change from baseline LPS was not significantly different between LDX and placebo (LDX 12.21 vs. placebo -0.29, P=0.80). Secondary PSG/actigraph results generally supported primary endpoint results, although sleep efficiency and NAASO suggested the possibility of improved

sleep quality. Subjective sleep measure results indicate the possibility that responses are influenced by sleep hygiene counseling before and throughout the study.
Conclusions: LDX effects on sleep parameters in children with ADHD support the conclusion that LDX does not contribute to sleep disturbance in this population. Effects on LPS were not significant. NAASO and sleep efficiency data suggest the possibility that LDX may actually enhance quality of sleep. Further study with LDX focusing on sleep quality (e.g., efficiency) rather than sleep onset delays are recommended in children with ADHD.
Supported by funding from Shire Development Inc

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» NR2-033

PARENTAL EVALUATION OF LISDEXAMFETAMINE DIMESYLATE IN THE TREATMENT OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

Lawrence Ginsberg M.D., Valerie Arnold, M.D., Joe Gao, Ph.D., Cynthia Richards, M.D., Robert Findling, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to explain parental attitudes toward lisdexamfetamine dimesylate in the treatment of their children with attention-deficit/hyperactivity disorder.

SUMMARY:

Background: Lisdexamfetamine dimesylate (LDX) is a prodrug stimulant indicated for children and adults with attention-deficit/hyperactivity disorder (ADHD).
Objective: To determine parental assessment of their child's global ADHD status and their satisfaction with LDX treatment.
Methods: A 7-week, open-label, dose-optimization trial evaluated the efficacy of 20, 30, 40, 50, 60, and 70 mg/d LDX in 316 children aged 6 to 12 years with ADHD as determined by the ADHD Rating Scale IV (ADHD-RS-IV) total score. Global improvement was rated with the 7-point Parent Global Assessment (PGA) scale (scored from 1=very much improved to 7=very much worse, compared with the child's behavior at baseline/washout). At study end, parents also completed the Medication Satisfaction Questionnaire, a rating scale that measures satisfaction with the medication, how it compares with their child's previous medication, and whether they would continue using it.
Results: At endpoint, the mean (SD) percent improvement from baseline in ADHD-RS-IV total score was 69.3% (23.3) (P<.0001). Also, 40.8% of parents rated their child as very much improved (score of 1) and 44.3% as much improved (score of 2) on the PGA scale. Parent satisfaction scores showed they were very satisfied (76.0%), moderately satisfied (21.1%), not satisfied (2.3%), and unsure (0.6%) with LDX treatment. Parents rated LDX much better (38.3%), better (19.5%), the same (6.5%), or worse (2.3%) than their child's previous treatment (33.5% indicated they didn't know or there was no prior treatment). Most parents (87.3%) reported that they would "absolutely" or "probably" continue to use LDX. Common adverse events included decreased appetite, decreased weight, insomnia, irritability, headache, and upper abdominal pain.
Conclusion: Most parents reported that their child improved after receiving LDX, and most indicated satisfaction with the medication and would choose to continue LDX treatment.
Supported by funding from Shire Development Inc

REFERENCES:

1) Biederman J, Krishnan S, Zhang Y, McGough JJ, Findling RL: Efficacy and tolerability of lisdexamfetamine dimesylate (NRP-104) in children with attention-deficit/hyperactivity disorder: a phase III, multicenter, randomized, double-blind, forced-dose, parallel-group study. Clin Ther 2007; 29: 450-463

2) Biederman J, Boellner SW, Childress A, Lopez FA, Krishnan S, Zhang Y: Lisdexamfetamine dimesylate and mixed amphetamine salts extended-release in children with ADHD: a double-blind, placebo-controlled, crossover analog classroom study. Biol Psychiatry 2007; 62: 970-976

» NR2-034

COMPARING THE EFFICACY OF MEDICATIONS FOR ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER USING META-ANALYSIS OF EFFECT SIZES

Stephen Glatt Ph.D., Stephen V. Faraone, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe effect size comparisons between stimulant and nonstimulant medications in adults; to assess the difficulty of interpreting differential medication efficacy when a direct comparative trial is not available; and to describe methodologic features of the studies that were associated with the magnitude of their effect sizes.

SUMMARY:

Objectives: To estimate effect sizes; to quantify differences in effect sizes among different drugs used in adult ADHD; and to determine if differences in study design features influence comparison estimates of drug efficacy.
Methods: From multiple databases, we identified double-blind, placebo-controlled studies (after 1979) in adults that defined ADHD using diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition or Fourth Edition, followed >=20 subjects for >=2 weeks, and presented the means (SD) of either change or endpoint scores. Effect sizes, as standardized mean differences, for ADHD outcome scales as total and subscale scores (hyperactive and inattentive) were assessed. A random effects model was used; regression analysis adjusted for study design and Egger's method assessed publication bias. All dependent outcome measures were separate data points in the analysis with variance estimates adjusted by Huber's formula.
Results: We included 19 studies of 13 different drugs. The mean effect size was 0.73 for long-acting stimulants, 0.96 for short-acting stimulants, and 0.39 for nonstimulants (P<.001 vs placebo for all). Effect sizes for nonstimulants were smaller than those for short-acting stimulants (P=.006) and long-acting stimulants (P<.0001); the stimulant classes did not differ significantly from one another. There was significant heterogeneity among short-acting stimulants (P<.001) but not long-acting stimulants and nonstimulants. There was evidence of publication bias for short-acting stimulants (P<.001) but not long-acting stimulants or nonstimulants.
Conclusions: Both long- and short-acting stimulants had a larger effect size than nonstimulants in studies of adults with ADHD, even after correcting for potential confounding effects of differing study designs. Findings were similar to those previously reported for studies of children with ADHD.
Supported by funding from Shire Development Inc.

REFERENCES:

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2) Faraone SV, Biederman J, Spencer TJ, Aleardi M: Comparing the efficacy of medications for ADHD using meta-analysis. MedGenMed 2006; 8:4

» NR2-035

LINKING ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER RATINGS AND CLINICAL GLOBAL IMPRESSIONS SCORES IN STUDIES OF LISDEXAMFETAMINE DIMESYLATE IN ADHD

David Goodman M.D., Richard Weisler, M.D., Lenard A. Adler, M.D., Stephen V. Faraone, Ph.D., Bryan Dirks, M.D., Mohamed Hamdani, M.S.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to discuss the clinical meaning of total and change scores on the Attention-Deficit/Hyperactivity Disorder Rating Scale Version IV (ADHD-RS-IV) in relation to severity and improvement on the Clinical Global Impressions (CGI) scales from 2 similarly designed studies of lisdexamfetamine dimesylate (LDX) in adults and children with ADHD.

SUMMARY:

Objective: To provide additional understanding of the clinical significance of Attention Deficit/Hyperactivity Disorder Rating Scale IV (ADHD-RS) total and change scores in relation to Clinical Global Impressions-Severity or Improvement (CGI-S/I) categories.
Methods: Equipercentile linking technique identified scores on the ADHD-RS and CGI, that have the same percentile rank, in 2 similarly designed, randomized, double-blind, placebo-controlled trials of lisdexamfetamine dimesylate (LDX) in children and adults with ADHD. The methodology can link or equate treatment effects in one scale to effects in another scale that is easier to interpret clinically. A potential limitation to interpreting the link analysis was the use of the same rater for both the ADHD-RS and CGI.
Results: 405 adults and 270 children were included in this analysis. LS mean ADHD-RS change scores ranged from -8.2 to -18.6 for adults and -6.2 to -26.7 for children. Moderately, markedly, severely, and extremely ill adults had mean (SD) baseline ADHD-RS-IV scores of 36.2 (4.86), 42.2 (6.15), 45.4 (5.09), and 53.0, respectively. In children, those moderately, markedly, severely, and extremely ill had scores of 38.8 (6.20), 45.5 (5.87), 48.2 (4.05) and 50.5 (4.04), respectively. At endpoint, 309 of 405 adults and 206 of 270 children were very much, much, or minimally improved. Very much, much, and minimally improved adults had mean (SD) change from baseline ADHD-RS-IV scores of -30.4 (7.82), -20.5 (7.27), and -11.3 (5.95), respectively. Children who were very much, much, and minimally improved had mean (SD) change scores of -33.2 (9.42), -25.7 (7.27), and -9.8 (6.56), respectively.
Conclusions: These results facilitate clinical interpretation of the positive changes on the ADHD-RS scale in 2 clinical trials of LDX. In addition, severity of illness can be established with total ADHD-RS score. The findings were consistent between the 2 populations. Supported by funding from Shire Development Inc

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1) Adler LA, Goodman DW, Kollins SH, et al. Double-blind, placebo-controlled study of the efficacy and safety of lisdexamfetamine dimesylate in adults with attention-deficit/hyperactivity disorder. J Clin Psychiatr 2008; 69: In press

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» NR2-036

ASSESSMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) DOCUMENTATION FROM CANDIDATES REQUESTING AMERICANS WITH DISABILITIES ACT (ADA) ACCOMMODA

Javed Joy M.D., Rose J. Julius DO MPH,Rashida Akter MD, David A. Baron, DO

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the importance of accurate and comprehensive documentation, identify the common pitfalls made, discuss the supporting role of psychometric testing, and describe the common co-morbidities among the candidates applying for ADA accommodation, on the basis of ADHD for high stakes medical examination

SUMMARY:

Purpose: Every year increasing numbers of candidates request special accommodations for high stakes medical licensing examinations, due to Attention Deficit Hyperactivity Disorder (ADHD), on the basis of the Americans with Disabilities Act (ADA). This poses significant challenges for both the applicant and the medical boards, and has significant financial, legal and ethical implications. The purpose of this survey was to review all applications requesting ADA accommodations on the basis of ADHD for the National Board of Osteopathic Medical Examiners (NBOME) COMLEX exam. The primary outcome measurement was whether the documentation provided by the applicants met the DSM-IV-TR criteria for ADHD.
Methods: The authors reviewed all requests for special accommodations on the basis of ADHD submitted to the National Board of Osteopathic Medical Examiners (NBOME) from 2005-2007. There were 50 requests in total submitted. All were reviewed by the investigators independently, then cross checked to determine inter-rater reliability. Prior to review, the files were sanitized by the NBOME staff, removing all personal identifiers in order to protect the candidates' confidentiality.
Results: Of all applicants, only 14% (7/50) provided sufficient documentation to support a diagnosis of ADHD. Inter-rater reliability for this study demonstrated consistently high agreement among the raters.
Conclusions: The majority of applicants who request special testing accommodations on the basis of ADHD do not provide adequate documentation to the medical boards to support the diagnosis. To our knowledge, this is the first paper of its kind investigating the documentation provided for ADA accommodations for ADHD on any high stakes medical examination.

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» NR2-037

EFFECTS OF EXTENDED RELEASE METHYLPHENIDATE ON THE FREQUENCY OF CYTOGENETIC ABNORMALITIES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY

Vinod Kumar M.D., James D. Tucker, Ph.D., Yinong Zhou, M.D., Rafael Muniz, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize that extended-release methylphenidate (MPH-ER) treatment is not associated with genotoxicity in pediatric patients with attention-deficit hyperactivity disorder (ADHD) and is safe and well tolerated.

SUMMARY:

Background: Chromosomal aberrations (CAs), micronuclei (MN), and sister chromatid exchanges (SCEs) in MPH-treated pediatric ADHD patients have been previously reported. This study replicated this work in a larger population.
Methods: A randomized, 3-month, open-label study evaluated potential genotoxic effects of MPH-ER treatment (10-60 mg/d)

plus behavioral therapy (BT) versus BT alone in treatment-naïve (no psychostimulant medications) children 6-12 yr with ADHD. BT consisted of a multimodal approach (non-compliance, impulse behavior, organizational skills). Change from baseline for primary endpoints of frequency of CAs/100 cells, excluding gaps and MN/1000 binucleated cells, and for the secondary endpoint SCEs at 3 mo (84 d) were evaluated by blinded investigators using a Poisson model comparing rate ratios between baseline and endpoint. Efficacy was measured by change from baseline on the Conners ADHD/DSM-IV Scales for Parents (CADS-P) and severity and global improvement ratings of Clinical Global Impression (CGI-S and CGI-I).
Results: 109 children (mean 8.4 yr; 66 males) were randomized to MPH-ER plus BT (n=53) or BT (n=56). In the MPH-ER plus BT and BT groups, CAs decreased by 40% and 56% (treatment ratio [TR]=1.34; P=0.53), MN by 37% and 26% (TR=0.85; P=0.28), and SCEs by 6% and 5%, respectively (TR=0.99; P=0.81). MPH-ER plus BT and BT resulted in mean changes in CADS-P total score, CGI-S, and CGI-I of -17.0 vs -7.0, -1.9 vs -0.6, and 1.9 vs 3.0, respectively. The most frequently occurring adverse events (>10% of patients) in the MPH-ER plus BT versus BT groups were decreased appetite (19.2% vs 0), headache (13.5% vs 1.9%), and upper respiratory tract infections (11.5% vs 9.6%).
Conclusion: Chromosomal aberrations, micronuclei, and SCEs decreased with MPH-ER exposure similarly to BT. MPH-ER treatment was not genotoxic in treatment-naive ADHD pediatric patients, was efficacious, and was generally well tolerated.
The study was funded by Novartis Pharma AG.

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1) El-Zein RA, Abdel-Rahman SZ, et al. Cytogenetic effects in children treated with methylphenidate. Cancer Lett. 2005;230:284-291.

2) Stopper H, Walitza S, Warnke A, et al. Brief review of available evidence concerning the potential induction of genomic damage by methylphenidate. J Neural Transm. 2008;115:331-334.

» NR2-038

CHANGES IN EMOTIONAL EXPRESSION RELATED TO MEDICATION USED TO TREAT ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER

Michael Manos Ph.D., Matthew Brams, M.D., Ann Childress, M.D., Robert L. Findling, M.D., Frank A. López, M.D., Peter S. Jensen, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to define changes in emotional expression in patients with ADHD, describe the paucity in the reporting of this phenomenon in the literature, and understand the need for improved, systematic, and validated reporting of emotional changes in children treated for ADHD.

SUMMARY:

Introduction: Changes in emotional expression (CEE) in patients receiving medications for the treatment of attention-deficit/hyperactivity disorder (ADHD) has yet to be fully characterized. Given the paucity of clinical trials that have systematically investigated CEE as a function of the medical treatment of ADHD, and to differentiate to what extent such effects occur as a function of the disorder, we conducted a comprehensive literature search to analyze CEE in children with ADHD.
Methods: Articles published from January 1, 1988 through August 31, 2008 were identified through a PubMed search. Randomized placebo controlled trials (n = 20 or more subjects) that investigated monotherapy with amphetamine, methylphenidate, guanfacine, atomoxetine, clonidine, or lisdexamfetamine for ADHD in children (0-18 years of age) with no prespecified comorbidities were selected.
Results: Of 148 articles that met all selection criteria, 48 reported a CEE of some type; 8 studies included 2 active investigational treatment arms, which resulted in 56 total reports of CEE associated with medication for the treatment of ADHD. Inconsistency was evident in: a) descriptors attached to CEE; b) informants reporting on the presence of CEE; c) time of day a CEE was observed; d) whether emotional side effects attenuated over time; e) whether base rates were reported; f) whether CEE or other specific side effects were measured; or g) when measured, whether CEE were probed via rating scales or spontaneously reported. Few studies (11%) reported base rates and, if included, they were reported as a mean raw score of a rating scale. Six studies reported a base rate, placebo rate, and drug rate of CEE. Positive CEE were generally not reported.
Conclusions: To fully delineate CEE as an effect of treatment versus an effect of the disorder, implementation of a validated scale to probe for CEE in controlled clinical trials is needed. Supported by funding from Shire Development Inc.

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2) Carson GA, Kelly KL. Stimulant rebound: how common is it and what does it mean? J Child Adolesc Psychopharmacol. 2003;13:137-142.

» NR2-039

METHYLPHENIDATE TRANSDERMAL SYSTEM IN THE TREATMENT OF ADULTS WITH ADHD: A PRELIMINARY REPORT

Barrie Marchant M.S., Frederick W. Reimherr M.D., Corinne Halls M.S., Erika D. Williams, M.S.W., Robert E. Strong D.O., Doug C. Christopherson B.S., Reid Robison M.D., John L. Olsen M.D.

EDUCATIONAL OBJECTIVES:

After reading this poster the reader will be able to describe the outcome of a clinical trial of Methylphenidate Transdermal System (MTS) in an adult sample.

SUMMARY:

Introduction: ADHD affects 3 to 5% of children and persists into adulthood in approximately 65% of affected subjects (1). Methylphenidate Transdermal System (MTS) provides gradually increasing plasma levels of methylphenidate and the unique benefits of reduced blood level variability, and the ability to control duration of daily medication exposure by removal of the patch (2).
Methods: This placebo controlled double-blind randomized trial enrolled males and females 18-65 who met the Utah and/or DSM-IV-TR criteria for ADHD. The crossover phase involved two 4-week treatment arms. Dosing was flexible based on treatment response and tolerance. Outcome was measured by the Wender-Reimherr Adult Attention Deficit Disorder Scale (WRAADDS), Connors' Adult ADHD Rating Scale (CAARS) and Clinical Global Impression – Severity scale (CGI-S). An ANOVA design assessed treatment effects on WRAADDS and CAARS scores. The McNemar's test assessed categorical response defined as CGI-S =3. Cohen's d calculated effect sizes.
Results: 80 subjects were enrolled, 59 furnished double-blind data and 45 completed the trial. MTS proved superior to PBO: Total CAARS (MTS=29.1±17.6; PBO=50.2±18.4, p<.001); Total WRAADDS (MTS=10.7±6.9; PBO=18.2±6.4, p<.001). Effect sizes were large: CAARS (d=.9), WRAADDS (d=.9). Sub-scales of the WRAADDS had similar treatment effects. Using CGI-S criteria, 66% of subjects improved on MTS versus 20% on PBO (p<.001). PBO subjects averaged 27.6±5.1 mg. ATX subjects averaged 23.5±6.7 mg. Numerous MTS subjects experienced erythema with 5 reporting moderate discomfort. Changes in EKG, pulse and BP measures were not significant.
Discussion: Treatment with MTS was associated with lower ADHD symptoms compared to PBO. All ADHD symptoms (Attention+Disorganization, Hyperactivity+Impulsivity, Emotional

Dysregulation and ODD) responded to treatment at significant levels. While most side effects were similar to oral forms of methylphenidate, subjects also experienced erythema.

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1) Faraone SV, Biederman J, Mick E: The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. Psychol Med. 2006; 36(2):159-65

2) Pelham WE Jr, Manos MJ, Ezzell CE, Tresco KE, Gnagy EM, Hoffman MT, Onyango AN, Fabiano GA, Lopez-Williams A, Wymbs BT, Caserta D, Chronis AM, Burrows-Maclean L, Morse G: A dose-ranging study of a methylphenidate transdermal system in children with ADHD. J Am Acad Child Adolesc Psychiatry 2005; 44:522-9

» NR2-040

EVALUATION OF THE QUALITY OF LIFE IN ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER TREATED WITH OROS METHYLPHENIDATE – THE CONQOL STUDY

Paulo Mattos M.D., Daniel Segenreich, M.D., Gabriela Macedo Dias, M.D., Bruno Nazar, M.D., Eloisa Saboya, Psy.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to consider questions related to quality of life in adults with attention deficit hyperactivity disorder.

SUMMARY:

Background: Attention Deficit Hyperactivity Disorder (ADHD) persists into adulthood and is associated with lower quality of life (QoL) indexes. Methylphenidate (MPH) is a commonly prescribed medication for this condition. Although there is plenty of data concerning its safety and efficacy, there are few studies on measures of QoL. Objective: to assess the effectiveness of osmotic, controlled release, once-a-day MPH (OROS MPH) through the impact on QoL in adults with ADHD. Methods: Analysis of a 12-week multicenter open trial involving 60 patients. Subjects started on 18mg and titreated up weekly in 18 mg/day of OROS MPH increments to optimal response judged by investigator. The functional measures were Adult ADHD Quality of Life Scale (AAQoL), State and Trait Anxiety Inventory (STAI) scores, Hamilton Depression Rating Scale (HAM-D) scores, Clinical Global Impression (CGI), and safety evaluations. A mixed analysis of fixed effects model was used to evaluate the treatment response. Results: Overall 83.3% of subjects completed the study, and the average dose of OROS MPH was 56.1 ± 13.3/mg at week 12. The Total AAQoL score showed an improvement of 21.9 ± 2.3 (SE) points ($P < 0.0001$). All AAQoL subscales reflected significant improvement (Productivity= 19.0 ± 3.2 SE; Psychological health= 14.7 ± 2.4 SE; Life perspectives= 15.6 ± 2.4; Relationships= 20.6 ± 2.7; $P < 0.0001$). A statistically significant reduction on CGI-I (-1.7 ± 0.1), HAM-D (-3.3 ± 0.6), STAI (state anxiety= -9.4 ± 1.3; trait anxiety= -10.7 ± 1.3), and ASRS (Attention Deficit= -11.3 ± 1.0; Hyperactivity= -9.2 ± 0.9) scores was observed ($P < 0.0001$). Three subjects discontinue the study due to adverse events. No serious adverse events were reported. Side effects observed were similar to other OROS MPH studies. Conclusion: This study has shown that treatment of adult ADHD with OROS MPH is associated with an improvement in measures of QoL and ADHD. This study was supported by Janssen-Cilag Brazil.

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» NR2-041

INTERNAL CONSISTENCY AND VALIDITY OF THE ADHD RATING SCALE IV FOR ADULTS

Keith McBurnett Ph.D., Stephen V. Faraone, Ph.D., Lenard A. Adler, M.D., Thomas J. Spencer, M.D., Scott Kollins, Ph.D., Richard Weisler, M.D., David Goodman, M.D., Stephen Glatt, Ph.D., Joseph Biederman, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to assess the internal consistency of the Attention-Deficit/Hyperactivity Rating Scale, Investigator Administered and Scored Version IV (ADHD-RS-IV-Inv) and to evaluate the reliability and validity of this measure used in clinical trials of ADHD medications. Participants will be able to evaluate the process of refining diagnostic criteria for adult ADHD and better understand which symptoms are most responsive to treatment.

SUMMARY:

Objective: To assess internal consistency and validity of the Attention-Deficit/Hyperactivity Rating Scale, Investigator Administered and Scored Version VI (ADHD-RS-IV-Inv) with NYU/MGH adult ADHD prompts in adults with ADHD for determining clinical change in a study of lisdexamfetamine dimesylate (LDX). LDX is the first prodrug stimulant used to treat ADHD.
Methods: This was a 4-week, randomized, double-blind, placebo-controlled, forced-titration (30 to 70 mg/d) study of LDX in adults with ADHD. Ordinal logistic regression evaluated relationships between demographics and baseline scores on ADHD-RS-IV-Inv items, inattentive and hyperactive/impulsive subscales, with dose as independent and item score as dependent variables. Internal consistency was assessed by Cronbach's a(alpha) and item-rest correlations of each item with the other items. Correlations between the ADHD-RS-IV-Inv and Clinical Global Impressions-Severity (CGI-S) and -Improvement (CGI-I) scales were assessed by Spearman's rank correlations.
Results: A total of 420 subjects contributed data to the analyses. Internal consistency of the ADHD-RS-IV-Inv scale was relatively high at all visits (Cronbach's a from 0.770 at visit 2 to 0.945 at visit 6). Cronbach's a increased between visits 2 (0.770) and 3 (0.912), with smaller increases at later visits. CGI-S scores were correlated with the ADHD-RS-IV-Inv (Spearman's $p=0.518$, $P<.0001$) at baseline. CGI-I ratings were correlated with ADHD-RS-IV-Inv ratings at visits 3 to 6 ($P<.0001$) and with change in ADHD-RS-IV at study end ($P<.0001$).
Conclusions: Reliability of the ADHD-RS-IV-Inv scale increased during the trial and was substantial at endpoint, possibly reflecting improved skills of administrators over time at delivering or scoring the scale. Correlation with CGI-I also provided evidence of convergent validity. This suggests that ADHD-RS-IV-Inv with adult prompts is reliable and valid for assessment of ADHD in adults.
Supported by funding from Shire Development Inc.

REFERENCES:

1) Adler LA, Spencer TJ, Milton DR, Moore RJ, Michelson D: Long-term, open-label study of the safety and efficacy of atomoxetine in adults with attention-deficit/hyperactivity disorder: an interim analysis. J Clin Psychiatry 2005; 66:294-299

2) Adler LA, Spencer TJ, Williams DW, Moore RJ, Michelson D: Long-term, open-label safety and efficacy of atomoxetine in adults with ADHD: final report of a 4-year study [Epub ahead of print]. J Atten Disord 2008

» NR2-042

INCIDENCE OF VEHICULAR COLLISIONS AND CITATIONS AMONG DRIVERS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD): A GROWING PROBLEM

Richard Merkel M.D., Margaret T. Davis, B.A., Brian S. Cox, B.S., Melissa Moore, M.D., Roger C. Burket, M.D., Daniel J. Cox, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to: 1) recognize that driving safety for individuals with ADHD is a significant public health concern; 2) appreciate the severity of this problem given males with ADHD have higher collision rates not only in adolescence as is the trend in the general population, but as adults; 3)Take this information into account when weighing treatment options for this high risk group (consider treatments shown to mitigate risk).

SUMMARY:
The core symptoms of ADHD: inattention, impulsivity and hyperactivity could interfere with safe operations of a motor vehicle. In fact, adolescents with ADHD have 4 X more at-fault collisions, receive 3 X more citations and are 8 X more likely to have their license suspended. The purpose of this study was to investigate the effects of sex and age on the frequency of self-reported vehicular collisions and citations among drivers with ADHD.
Using a cross-sectional, internet-based survey of drivers with ADHD, our survey was posted on five internet websites (e.g. CHADD) for six months. Of all qualifying surveys, 156 were from male and 283 were from female drivers diagnosed with ADHD. Overall, the sample included 142 adolescents (16-18 years), 161 young adults (19-25 years), and 136 middle-aged adults (ages 26-62 years).
In the previous 12 months, 28% reported receiving a citation, 34% reported being involved in a collision and 44% reported either a collision or a citation. Adolescents and females reported significantly fewer citations (p =.05 and .03 respectively). While occurrence of collisions steadily increased with age for males (p=.008), collisions declined among middle-aged female ADHD drivers as in the general population (Figure 1).
While it has been reported that adolescent ADHD drivers have more collisions than their peers, this may actually increase with age. Middle-aged adult ADHD male drivers reported 1.1 collisions in the past 12 months, while a similar national survey of the general population reported only 0.06 collisions in the past 24 months. To the extent that long acting stimulant medications improve driving of those with ADHD, it may be prudent to consider use of medications with all ages of ADHD drivers.

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1) Barkley RA, Cox D: A review of driving performance and adverse outcomes in adolescents and adults with attention deficit/ hyperactivity disorder. J Safety Res 2007;38:113-128.

2) Fischer M, Barkley RA, Smallish L, Fletcher K: Hyperactive children as young adults: driving abilities, safe driving behavior, and adverse driving outcomes. Accid Anal Prev 2007;39:94-105.

» NR2-043

METHYLPHENIDATE TRANSDERMAL SYSTEM USE AND SLEEP QUALITY IN ADOLESCENTS WITH ADHD

Judith Owens M.D., Robert Findling, M.D., Richard Civil, M.D., Manisha Madhoo, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be able to demonstrate an understanding of the effects of MTS compared with PTS on sleep quality in adolescents with ADHD and discuss data pertaining to the safety of MTS in adolescents with ADHD as described in this study.

SUMMARY:
Introduction: This was a randomized, double-blind, multicenter, parallel-group, placebo-controlled, dose optimization study designed to evaluate the safety and efficacy, as well as the impact on sleep quality, of methylphenidate transdermal system (MTS; 10–30 mg/9 hour doses) compared with placebo transdermal system (PTS) in adolescent subjects (aged 13–17 years) diagnosed with ADHD.
Methods: Study subjects were screened for 2 weeks prior to a washout period of up to 30 days, depending on the subject's previous medication treatment. At baseline, subjects were randomized in a 2:1 ratio to MTS or PTS, titrated over 5 weeks to an optimal dose, and maintained on their optimal dose through a 2-week maintenance period. A 5-item, post-sleep questionnaire (PSQ) assessed sleep quality at baseline and end of study. Adverse events were assessed at all study visits.
Results: A total of 217 subjects, with a mean (SD) age of 14.6 (1.3) years, were enrolled and randomized to double-blind treatment (safety population), 215 subjects were included in the intent-to-treat population, and 124 subjects completed the study. There were no significant differences between treatment groups at study endpoint in the percent of subjects rating overall sleep quality as either "Good" or "Very good" (62.0% [PTS] vs 64.4% [MTS]) or in the mean (SD) hours of sleep the previous night (8.7 [1.9] vs 8.7 [2.6]). Furthermore, all insomnia-treatment emergent AEs reported, regardless of treatment group, were of mild to moderate intensity and the majority (80.0%) resolved with continued treatment.
Conclusions: MTS treatment resulted in no significant differences in overall sleep quality compared with PTS, and in subjects treated with MTS, little change from baseline in sleep quality was noted. These results suggest MTS, worn for 9 hours, generally has limited effect on and does not diminish overall sleep quality in adolescents with ADHD.Supported by funding from Shire Development Inc.

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1) Sung V, Hiscock H, Sciberras E, Efron D. Sleep problems in children with attention-deficit/hyperactivity disorder: prevalence and the effect on the child and family. Arch Pediatr Adolesc Med. 2008;162:336-342.

2) Owens J. The ADHD and sleep conundrum: a review. J Dev Behav Pediatr. 2005;26:312-322.

» NR2-044

EFFICACY AND SAFETY OF THE METHYLPHENIDATE TRANSDERMAL SYSTEM IN ADOLESCENTS WITH ADHD AS EVALUATED BY CLINICIANS AND PARENTS/ LEGAL GUARDIANS

Melmed Raun M.D., Robert Findling, M.D., Richard Civil, M.D., Manisha Madhoo, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be able to demonstrate an understanding of the efficacy and safety of MTS in adolescents with ADHD compared with PTS and discuss MTS efficacy measures in adolescents with ADHD, as evaluated by either clinicians or parents/legal guardians, described in this study.

SUMMARY:
Introduction: This was a randomized, double-blind, multicenter, parallel-group, placebo-controlled, dose optimization study designed to evaluate the safety and efficacy of methylphenidate transdermal system (MTS) (10-30 mg/9 hour doses) compared with placebo transdermal system (PTS) in adolescent subjects (aged 13-17 years) diagnosed with ADHD as rated by clinicians and parents/legal guardians.
Methods: At baseline, subjects were randomized in a 2:1 ratio to MTS or PTS, titrated over 5 weeks to an optimal dose, and maintained on their optimal dose through a 2-week maintenance period. All efficacy measures were assessed using intent-to- treat (ITT) analysis. The clinician-completed ADHD-RS-IV and the parent/ legal guardian-completed Conners' Parent Rating Scales-Revised Short Form (CPRS-R) were administered at all study visits. The Clinical Global Impressions and the Parent Global Assessment scales were used to assess ADHD severity at baseline and symptom improvement at each subsequent visit. Adverse events (AEs) were assessed throughout the study.

Results: A total of 215 subjects were included in the ITT population. The MTS-treatment group demonstrated a significantly greater mean decrease from baseline on both ADHD-RS-IV and CPRS-R total scores when compared with the PTS group (P<.0001) at study endpoint. Furthermore, the majority of clinicians (81.7%) and parents (74.1%) rated ADHD symptoms as improved at endpoint compared with baseline for subjects receiving MTS. The majority (98.5%) of AEs were of mild or moderate intensity, and the most commonly reported MTS treatment-emergent AEs included decreased appetite (25.5%), headache (12.4%), irritability (11.0%), and upper respiratory infection (10.3%).
Conclusions: MTS treatment resulted in significantly improved ADHD behavioral symptoms compared with PTS as rated by both clinicians and parents/legal guardians, and most adverse events were mild to moderate in intensity. Supported by funding from Shire Development Inc.

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» NR2-045

SELF-REPORTED SYMPTOM-BASED PREVALENCE OF ADHD IN THE US COMPARED WITH RATES OF PREVIOUS DIAGNOSIS

Michael Reed Ph.D., Mike Durkin, Ph.D., Robert Armstrong, M.D., Lynn Starr, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should recognize that the rate of adults having symptoms indicating ADHD risk as specified by the Adult ADHD Self-Report Scale symptom checklist (ASRS Screener) compared with rates of actual diagnosis and treatment suggest that ADHD is currently underdiagnosed and undertreated in adults.

SUMMARY:

Introduction: ADHD symptoms are often subtle in adults and may be shared with other disorders, making diagnosis difficult. The objective of this survey was to assess self-reported symptom-based prevalence of ADHD risk in the US compared with rates of previous diagnosis and treatment.
Methods: Surveys were mailed to a representative sample of 200,000 individuals from a TNS household panel. Variable outgo sampling was used to balance the returned sample to US Census. The survey included a subset of 6 validated screening items from the Adult ADHD Self-Report Scale symptom checklist (ASRS Screener), containing DSM-IV ADHD symptoms rated on a 5-point scale for the past 6 months. Questions about previous ADHD diagnosis and treatment were also included. Prevalence rates were determined and adjusted prevalence ratios (adjusting for demographics) were calculated for gender, age, income, race, household size, population density, and geographic region using generalized linear modeling. Chi-square tests were used to test main effects among demographics.
Results: Surveys were obtained from 105,187 individuals (52.6% return rate). Of all, 55,029 men and 47,831 women had complete ASRS data. 7379 men (13.4%) and 6042 women (12.6%) were at or above symptom threshold (ASRS+) and considered at risk for ADHD. Prior diagnosis of ADHD in the total sample was reported in 4.8% of men and 3.2% of women. Among ASRS+ cases only, 15.7% of men and 9.7% of women reported a prior ADHD diagnosis. Only 4.3% of ASRS+ men and 3.3% of ASRS+ women reported current treatment for ADHD. Main effects for ADHD risk were found (P<0.001) for age, gender, income, race, population density, and geographic region.
Conclusions: Rates of ADHD risk compared to current rates of diagnosis and treatment suggest that many adults with ADHD symptoms have not been diagnosed and are not receiving treatment. Supported by a grant from Ortho-McNeil Janssen Scientific Affairs, LLC, Titusville, NJ.

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2) Kessler RC, Adler L, Ames M, Demler O, Faraone S, et al: The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. Psychol Med 2005; 35(2): 245–256

» NR2-046

METHYLPHENIDATE TRANSDERMAL SYSTEM IN THE TREATMENT OF ADULTS WITH ADHD: A PRELIMINARY REPORT

Frederick Reimherr M.D., Barrie K. Marchant M.S., Corinne Halls M.S., Erika D. Williams, M.S.W., Robert E. Strong D.O., Doug C. Christopherson B.S., Reid Robison M.D., John L. Olsen M.D.

EDUCATIONAL OBJECTIVES:

After reading this poster the reader will be able to describe the outcome of a clinical trial of Methylphenidate Transdermal System (MTS) in an adult sample.

SUMMARY:

Introduction: ADHD affects 3 to 5% of children and persists into adulthood in approximately 65% of affected subjects (1). Methylphenidate Transdermal System (MTS) provides gradually increasing plasma levels of methylphenidate and the unique benefits of reduced blood level variability, and the ability to control duration of daily medication exposure by removal of the patch (2).
Methods: This placebo controlled double-blind randomized trial enrolled males and females 18-65 who met the Utah and/or DSM-IV-TR criteria for ADHD. The crossover phase involved two 4-week treatment arms. Dosing was flexible based on treatment response and tolerance. Outcome was measured by the Wender-Reimherr Adult Attention Deficit Disorder Scale (WRAADDS), Connors' Adult ADHD Rating Scale (CAARS) and Clinical Global Impression – Severity scale (CGI-S). An ANOVA design assessed treatment effects on WRAADDS and CAARS scores. The McNemar's test assessed categorical response defined as CGI-S =3. Cohen's d calculated effect sizes.
Results: 80 subjects were enrolled, 59 furnished double-blind data and 45 completed the trial. MTS proved superior to PBO: Total CAARS (MTS=29.1±17.6; PBO=50.2±18.4, p<.001); Total WRAADDS (MTS=10.7±6.9; PBO=18.2±6.4, p<.001). Effect sizes were large: CAARS (d=.9), WRAADDS (d=.9). Sub-scales of the WRAADDS had similar treatment effects. Using CGI-S criteria, 66% of subjects improved on MTS versus 20% on PBO (p<.001). PBO subjects averaged 27.6±5.1 mg. MTS subjects averaged 23.5±6.7 mg. Numerous MTS subjects experienced erythema with 5 reporting moderate discomfort. Changes in EKG, pulse and BP measures were not significant.
Discussion: Treatment with MTS was associated with lower ADHD symptoms compared to PBO. All ADHD symptoms (Attention+Disorganization, Hyperactivity+Impulsivity, Emotional Dysregulation and ODD) responded to treatment at significant levels. While most side effects were similar to oral forms of methylphenidate, subjects also experienced erythema.

REFERENCES:

1) Faraone SV, Biederman J, Mick E: The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. Psychol Med. 2006; 36(2):159-65

2) Pelham WE Jr, Manos MJ, Ezzell CE, Tresco KE, Gnagy EM, Hoffman

MT, Onyango AN, Fabiano GA, Lopez-Williams A, Wymbs BT, Caserta D, Chronis AM, Burrows-Maclean L, Morse G: A dose-ranging study of a methylphenidate transdermal system in children with ADHD. J Am Acad Child Adolesc Psychiatry 2005; 44:522-9

» NR2-047

ADHD TREATMENT RESPONSE MEASUREMENT WITH THE ADULT SELF REPORT SCALE

Richard Rubin M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand application of the ADHD Adult Self Report Scale to practice and have reference measurement scores.

SUMMARY:

OBJECTIVE: While DSM criteria guide description of a patient's ADHD core symptoms, managing treatment requires their quantitative measure. The Adult Self Report Scale (ASRS), developed under World Health Organization auspices, assesses the ADHD core symptoms on a frequency basis and provides validated clinical severity thresholds for each symptom. APA 2008 NR6-030 presented the first case series applying the pilot ASRS to office clinical practice. This 2009 poster adds to that data, employing the validated ASRS V.1.1. METHOD: This series consists of adults diagnosed as ADHD without significant comorbidities who pursued an initial treatment course with approved medicines in the author's practice. The 37 participants completed the V.1.1 ASRS at initial evaluation, and then again when response from the first medicine of choice was expected, a minimum of 4 weeks for long acting stimulants and 6 weeks for atomoxetine. The CGI-Severity scale was used to judge satisfactory remission to a score of 1 (normal) or 2 (borderline). Quantitative ASRS calculations include: 1) the total symptom scores at baseline; 2) the number of significant symptoms at baseline; 3) the outcome total symptom scores; and 4) the outcome number of significant symptoms. RESULTS: With a possible range of 18 to 72, the total group baseline ASRS mean was 49.9 in a range of 33 to 69. The lowest possible ASRS score consistent with DSM ADHD criteria is 26. The mean number of significant symptoms at baseline was 13.2 out of 18 maximum, in a range of 7 to 18. At outcome measurement, total group symptom load mean was 27.3, with a range of 8 to 49. The mean of remitters was 18.5 and non-remitters 37.6. The outcome number of significant symptoms was 4.9 for the entire group, 1.2 for remitters, and 9.2 for non-remitters.
CONCLUSION: This case series of ADHD treatment outcomes supports the clinical utility of the Adult Symptom Rating Scale for assessing treatment response.

REFERENCES:

1) Kessler R, Adler L, Ames M et al: The World Health Organization Adult ADHD Self-Report Scale. Psychol. Med. 2005;35:245-256

2) http://www.med.nyu.edu/psych/assets/adhdscreen18.pdf.

» NR2-048

EFFICACY AND SAFETY OF OROS® MPH IN ADULTS WITH PREVIOUSLY UNDIAGNOSED ADHD

H. Lynn Starr M.D., C.V. Damaraju, Ph.D., Diane M. Hasner, Robert B. Armstrong, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize that attention-deficit/hyperactivity disorder (ADHD) appears to be an under-recognized condition in adults and be aware that osmotic controlled-release methylphenidate (OROS® MPH) appears to be effective and well tolerated in adults with previously undiagnosed ADHD.

SUMMARY:

Introduction: Although there is increasing awareness of ADHD in adults, it is often under-recognized. Data from a study of OROS MPH in adults with ADHD were used to examine patients with and without a prior diagnosis of ADHD.
Methods: This was a post-hoc analysis of a double-blind, dose-escalation study of OROS MPH in adults with ADHD (ID CR011560). Patients 18–65 years of age (inclusive) were randomized to placebo or OROS MPH for 7 weeks of treatment. Doses were initiated at 36 mg/d and titrated over 5 weeks until minimum protocol-defined improvement in symptoms was demonstrated or until maximum dose was reached (108 mg/d).
Results: Of the 226 adults in the ITT analysis set, 53% (n=119) reported no prior formal diagnosis of ADHD. Women were less likely to have been previously diagnosed than men (38% vs 54%). ADHD symptoms and other characteristics at baseline were similar in patients with and without a prior diagnosis. For patients with no prior diagnosis, the OROS MPH group had significantly greater improvement than the placebo group at endpoint on the AISRS total score (LS mean improvement 12.0 vs 6.2, P=0.0094 from ANCOVA), and numerically greater improvement on the Conners' Adult ADHD Rating Scale–Self Report: Short Version total score (LS mean improvement 13.4 vs 8.3, P=0.0692). The OROS MPH group had significantly better scores than the placebo group on the CGI-I at endpoint (LS means 2.87 vs 3.46, P=0.0042). OROS MPH appeared to be well tolerated. There were no serious treatment-emergent AEs or deaths. Headache, decreased appetite, and dry mouth were the most commonly reported AEs (>20% of the OROS MPH group).
Conclusions: Approximately half of the adults with ADHD in this study were not previously diagnosed; aside from gender, baseline characteristics did not distinguish these patients. OROS MPH treatment improved symptoms of ADHD in these patients and was well tolerated. Supported by Ortho-McNeil Janssen Scientific Affairs, LLC, Titusville, NJ.

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2) Adler LA, Biederman J, Zimmerman B, et al: Efficacy and safety of OROS methylphenidate (Concerta) in adults with attention-deficit/hyperactivity disorder: a randomized, placebo-controlled, double-blind, parallel group, dose-escalation study. J Clin Psychopharmacol.

» NR2-049

HOW REPRESENTATIVE ARE PARTICIPANTS IN A CLINICAL TRIAL FOR ADHD? COMPARISON WITH ADULTS FROM A LARGE OBSERVATIONAL STUDY

Craig Surman M.D., Michael C. Monuteaux, Sc.D., Carter R. Petty, M.S. Stephen V. Faraone, Ph.D., Thomas J. Spencer, M.D., Nicole F. Chu, B.A., Joseph Biederman, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:
Recognize the high rate of comorbidity in adults with ADHD.
Recognize that clinical trials for ADHD treatments often exclude subjects with such comorbidity.
Be aware that there are significant mental health and functional differences between subjects with ADHD who do and do not meet entry criteria for clinical trials. Appreciate that broader eligibility criteria may increase the external validity of such trials.

SUMMARY:

OBJECTIVE: Clinical trials have demonstrated that pharmacotherapies can safely treat ADHD in adulthood. Eligibility criteria in these trials may significantly limit their external validity by excluding a significant portion of adults with ADHD in the general population. In particular, exclusion criteria may frequently exclude individuals with comorbid mental health conditions, which are common in the adult ADHD population.
METHOD: The authors addressed the representativeness of clinical trials by comparing 146 adult Clinical Trial participants

with DSM-IV ADHD, and a Community Sample comprised of 127 adults with DSM-IV ADHD and 123 non-ADHD controls. Subjects were compared on socioeconomic status, Hollingshead Occupational code, cognitive measures, lifetime psychopathology and global assessment of function (GAF) ratings.
RESULTS: Adults with ADHD in the Community Sample had higher rates of lifetime psychiatric comorbidity, lower GAF, and lower occupational codes than those in the Clinical Trial. The excluded portion of the Community sample had higher rates of lifetime psychiatric comorbidity and lower GAF than clinical trial participants.
CONCLUSIONS: Adults with ADHD participating in the Clinical Trial had less evidence of functional impairment and endorsed less psychiatric comorbidity than the majority of Community Sample subjects with ADHD. This suggests that findings from clinical trials may have limited external validity for adults with ADHD in the general population, particularly for those adults with ADHD with the greatest burden of comorbid psychopathology. Data analyzed in this work comes from studies supported by grants from the National Institute of Health to Stephen Faraone (R01MH57934) and to Thomas Spencer (R29MH57511). Novartis Pharmaceuticals Corporation supported a portion of the cost of active medication in the latter study.

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2) Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am J Psychiatry. 2006;163:716-723.

» NR2-050

INFERIOR FRONTAL CORTEX (IFC) DYSFUNCTION DURING AN INHIBITION TASK IN ADULT ADHD COMPARED WITH CONTROL SUBJECTS USING FMRI

Jennifer Townsend B.A., Lara Foland-Ross, B.A., James McGough, M.D., Jeff Fischer, B.A., Susan Y. Bookheimer, Ph.D., Lori L. Altshuler, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the basic inhibition functional network in control subjects and identify the regions of dysfunction in adult subjects with ADHD.

SUMMARY:

Objective: To investigate the neural biological underpinning of inhibition, specifically in the inferior frontal cortex (IFC), in adult Attention-Deficit/Hyperactivity Disorder (ADHD) and control subjects using fMRI.
Methods: Sixteen adult ADHD subjects (6F/10M; age=35.4 yrs. ±11.6 yrs.) and 16 matched control subjects (6F/10M; age=35.9 yrs. ± 11.1 yrs.) underwent fMRI scanning while performing an inhibition task known to activate the IFC. Behavioral data, including response time and accuracy, were simultaneously recorded. FSL was used to analyze whole-brain activation patterns when subjects performed the Go-NoGo task, requiring subjects to inhibit motor response to letter stimuli. Contrasts were made for each subject comparing the NoGo vs. Go conditions, and these contrasts were entered into a between-group random effects analysis.
Results: Behavioral results showed no differences between the two groups in either response time (p=.35) or accuracy (p=.92). Within-group results showed activation of inferior frontal lobe regions in controls subjects and subjects with ADHD. Random effects between-group analyses revealed significantly greater activation in control compared with ADHD subjects in bilateral cingulate, right IFC (BA44) and middle frontal gyrus (BA10), regions normally activated in this task. Additionally, other significant differences were found in the left middle frontal gyrus (BA 46/9), bilateral superior frontal gyrus (BA6/9), bilateral precentral gyrus (BA6), bilateral inferior parietal lobule (BA40), left insula and bilateral superior temporal gyrus (BA22) (See Figure 1). The reverse comparison showed no areas of significantly greater activation in ADHD compared with controls subjects.
Conclusion: Main features of ADHD include not only difficulties with attention, but difficulties in inhibition as well. This study provides evidence of dysfunction in the neural network responsible for inhibition, including IFC and cingulate, in adult ADHD.

REFERENCES:

1) Aron AR (2007) The Neural Basis of Inhibition in Cognitive Control. The Neuroscientist, 13, 214-228.

2) Suskauer SJ, Simmonds DJ, Fotedar S, Blankner JG, Pekar JJ, Denckla MB, Mostofsky SH. (2008). Functional magnetic resonance imaging evidence for abnormalities in response selection in attention deficit hyperactivity disorder: differences in activation associated with response inhibition but not habitual motor response. J Cogn Neurosci. Mar;20(3):478-93.

» NR2-051

IMPROVEMENT IN EXECUTIVE FUNCTION IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER TREATED WITH 20 TO 70 MG/DAY LISDEXAMFETAMINE DIMESYLATE

Atilla Turgay M.D., Lawrence Ginsberg, M.D., Rakesh Jain, M.D., Joseph Gao, Ph.D., Cynthia Richards, M.D., Robert L. Findling, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to evaluate and discuss the effect of treatment with 20 to 70 mg/day of lisdexamfetamine dimesylate (LDX) in children diagnosed with attention-deficit/hyperactivity disorder (ADHD) on executive function as assessed by the Behavior Rating Inventory of Executive Function. Deficits in executive function are thought to play a central role in the impairments associated with ADHD.

SUMMARY:

Objective: To assess the effects of lisdexamfetamine dimesylate (LDX) on executive function in children with attention-deficit/hyperactivity disorder (ADHD).
Methods: This open-label, 7-week, dose-optimization study of 20 to 70 mg/d LDX evaluated children aged 6 to 12 years with ADHD. The ADHD Rating Scale IV (ADHD-RS) was the primary efficacy assessment; safety measures included physical examinations, adverse events, and vital signs. Secondary assessments included Behavior Rating Inventory of Executive Function (BRIEF) and Expression and Emotion Scale for Children (EESC). Percent change from baseline for ADHD-RS was analyzed by 1-sample t-test and change from baseline for BRIEF, EESC, by similar analyses, post hoc.
Results: Overall percent (SD) improvement in ADHD-RS total score from baseline to endpoint was 69.3% (23.3) (P<.0001). Mean change scores from baseline (SD) were available for BRIEF in 308 and for EESC in 304 of 316 subjects. Mean change scores for BRIEF of -17.9 (12.5) for global executive composite (GEC), -15.4 (12.6) for behavioral regulation index (BRI), and -17.6 (12.3) for metacognition index (MCI) all demonstrated significant improvement with LDX (pooled doses) compared to baseline (P<.0001). Mean (SD) baseline and endpoint BRIEF GEC, BRI, and MCI scores were similar at all dose levels. Mean change scores for EESC of -7.4 (18.3) for total, -2.1 (9.6) for positive emotions, -2.5 (7.7) for emotional flatness, and -2.8 (5.2) for emotional lability all showed significant improvement with LDX (pooled doses) compared to baseline (P<.001). Treatment-emergent AEs in >=10% of subjects were decreased appetite, decreased weight, irritability, insomnia, headache, upper abdominal pain, and initial insomnia.
Conclusions: There were significant improvements in ADHD-RS scores, executive function, and emotional expression scores with LDX at endpoint. TEAEs were consistent with those seen with

long-acting stimulants.
Supported by funding from Shire Development Inc.

REFERENCES:

1) Biederman J, Krishnan S, Zhang Y, McGough JJ, Findling RL. Efficacy and tolerability of lisdexamfetamine dimesylate (NRP-104) in children with attention-deficit/hyperactivity disorder: a phase III, multicenter, randomized, double-blind, forced-dose, parallel-group study. Clin Ther 2007; 9:450-463

2) McCandless S, O' Laughlin L. The Clinical Utility of the Behavior Rating Inventory of Executive Function (BRIEF) in the diagnosis of ADHD. J Atten Disord 2007;10:381-389.

» NR2-052

SUSTAINED EFFICACY OF LISDEXAMFETAMINE DIMESYLATE OVER 13 HOURS AS ASSESSED BY EFFECT SIZE IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

Sharon Wigal Ph.D., Scott Kollins, Ph.D., Ann Childress, M.D., Ben Adeyi, M.S., Liza Squires, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to evaluate and discuss the efficacy of lisdexamfetamine dimesylate (LDX) in relation to magnitude of effect size of LDX as assessed by repeated assessments of deportment, attention, and academic productivity compared with placebo over 13 hours postdose in children aged 6 to 12 years with attention-deficit/hyperactivity disorder.

SUMMARY:

Objective: To examine maintenance of efficacy of lisdexamfetamine dimesylate (LDX) in children with attention-deficit/hyperactivity disorder (ADHD) by magnitude of effect size at all time points over 13 hours (h) postdose.
Methods: Children (aged 6 to 12 years) with ADHD were enrolled in a laboratory school study of LDX including open-label, dose-optimization (4 weeks) and randomized, placebo-controlled, 2-way crossover (1 week each) phases. The Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP Deportment [-D] and Attention [-A]) and Permanent Product Measure of Performance (PERMP Attempted [-A]/Correct [-C]) scales were measured predose and 1.5 to 13 h postdose. Safety measures included treatment-emergent adverse events (TEAEs). Current analyses examined least squares (LS) mean effect size for maintenance of effect throughout the 13 h of the study.
Results: 111 of 129 enrolled subjects completed the study. Overall LS (SE) effect size (LDX vs placebo) for SKAMP-D was -1.7 (0.18) and at the time points 1.5, 5, and 13 h postdose was -0.7 (0.14), -1.4 (0.16), and -0.4 (0.14), respectively. At 1.5, 5, and 13 h postdose, SKAMP-A LS (SE) effect size was -0.6 (0.14), -1.2 (0.15), and -0.8 (0.14), respectively. At 1.5, 5, and 13 h postdose, PERMP-A LS (SE) effect size was 0.6 (0.14), 1.4 (0.16), and 1.1 (0.15) while PERMP-C LS (SE) effect size at 1.5, 5, and 13 h postdose, was 0.7 (0.14), 1.4 (0.16), and 1.1 (0.15), respectively. TEAEs during dose optimization included decreased appetite (47%), insomnia (27%), and headache (17%), which decreased in the crossover phase (6%, 4%, and 5%, respectively).
Conclusions: Postdose effect sizes demonstrated LDX efficacy with maintenance of effect on deportment, attention, or academic productivity scores over 13 h. Overall effect sizes were robust, with the largest effect sizes being reported during the middle of the classroom day. Supported by funding from Shire Development Inc.

REFERENCES:

1) Biederman J, Boellner SW, Childress A, Lopez FA, Krishnan S, Zhang Y. Lisdexamfetamine dimesylate and mixed amphetamine salts extended-release in children with ADHD: a double-blind, placebo-controlled, crossover analog classroom study. Biol Psychiatry 2007; 62:970-976

2) Biederman J, Findling RL, Krishnan S, McGough JJ, Zhang Y. Efficacy and tolerability of lisdexamfetamine dimesylate (NRP-104) in children with attention-deficit/hyperactivity disorder: a phase III, multicenter, randomized, double-blind, forced-dose, parallel-group study. Clin Ther 2007; 29:450-463

» NR2-053

BEFORE SCHOOL ADHD SYMPTOMS AND FUNCTIONING IN YOUTH TREATED WITH THE METHYLPHENIDATE TRANSDERMAL PATCH (MTS)

Timothy Wilens M.D., Paul Hammerness, M.D., Linsey Utzinger, B.A., Anne Georgiopoulos, M.D., Robert Doyle, M.D., Kerry Brodziak, B.A., MaryKate Martelon, M.P.H., Joseph Biederman, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to 1) Examine the use of methylphenidate treatment of ADHD in the morning. 2) Learn potential effects of ADHD treatment on functioning in the morning. 3) Examine the potential usefulness of a functional scale of before school activities in school aged youth

SUMMARY:

Objective. To examine the effects of the MTS on before school ADHD symptoms and functioning in children with ADHD. Methods. This was a randomized cross-over study in which subjects were treated weekly with 10 mg and 20 mg MTS or placebo patch for a total of 4 weeks applied in the early morning. Primary efficacy measures included the ADHD Rating Scale (RS) and a newly developed multi-item scale capturing before-school functioning (Wil-Hammer). Results. We ascertained the predetermined sample of 25 subjects completing the study. The sample was primarily male and between the ages of six and twelve years (mean of 9 years). There were highly significant reductions in the ADHD RS and Wil-Hammer total scores between active drug and placebo treatment at endpoint. There were no serious adverse effects and the medication was relatively well tolerated in this brief cross-over study. Conclusions. These data show that MTS is effective not only for morning ADHD symptoms, but also in improving associated activities and functioning that occur before-school in ADHD children. This study also signals the potential utility of a new instrument to examine before school functioning in ADHD youth. Support for the study, medication/placebo, and presentation was from Shire Pharmaceuticals, Inc.

REFERENCES:

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2) Wilens TE, Spencer TJ: The stimulants revisited, in Child and Adolescent Psychiatric Clinics of North America. Edited by Stubbe D. Philadelphia, Saunders Press, 2000, pp 573-604

» NR2-054

RESPONSE AND SYMPTOMATIC REMISSION IN A LONG-TERM TRIAL OF LISDEXAMFETAMINE DIMESYLATE IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

Joel Young M.D., Greg Mattingly, M.D., Richard Weisler, M.D., Liza Squires, M.D., Ben Adeyi, M.S., Bryan Dirks, M.D., Thomas Babcock, D.O., Brian Scheckner, Pharm.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to explain the outcome of long-term treatment of adults with ADHD using optimized doses of LDX in terms of response and symptomatic remission. These parameters may provide greater clinical relevance compared with changes in rating scale scores.

SUMMARY:
Objective: To evaluate response and symptomatic remission in adults with attention-deficit/hyperactivity disorder (ADHD) in a long-term trial of lisdexamfetamine dimesylate (LDX) treatment.
Methods: This open-label, single-arm study enrolled adults (18 to 55 years) diagnosed with ADHD. Treatment began at 30 mg/d LDX. At weekly visits 2 through 5 (weeks 1-4), the dose was increased or decreased in 20-mg increments until an optimal dose between 30 and 70 mg/d was attained. The maintenance phase continued for an additional 11 months. Primary and secondary efficacy measures were the ADHD Rating Scale Version IV (ADHD-RS-IV) with adult ADHD prompts and the Clinical Global Impressions-Improvement (CGI-I) scale, respectively. Response was defined as a reduction in ADHD-RS-IV score of >=30% and a CGI-I score of <=2 relative to the baseline score of the preceding double-blind study. Symptomatic remission was defined as an ADHD-RS-IV total score of <=18.
Results: The study enrolled 349 subjects; 191 completed. The mean (SD) ADHD-RS-IV change from baseline score in the intent-to-treat population (n=345) was -24.8 (11.7), P<.0001 at endpoint. Of subjects who entered the maintenance phase (n=327), criteria for response were met by 95.7% and symptomatic remission by 85.0% at any point in the study. Of those who had response at visit 5, 75.2% maintained their response through the maintenance phase. Of those in remission at visit 5, 65.7% remained in remission through maintenance. Median time to first remission was 22 days. Common adverse events included upper respiratory tract infection, insomnia, headache, dry mouth, and decreased appetite.
Conclusions: Long-term treatment with LDX resulted in significant improvement in ADHD symptoms in adults, with a majority achieving sustained response and symptomatic remission over 11 months of follow-up. Symptomatic remission provides clinicians with an additional measure of response to treatment.
Supported by funding from Shire Development Inc

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1) Biederman J, Mick E, Faraone SV: Age-dependent decline of symptoms of attention deficit hyperactivity disorder: impact of remission definition and symptom type. Am J Psychiatry 2000; 157:816-818

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» NR2-055

SELF IMAGE PERCEPTION OF 171 CHILDREN AND ADOLESCENTS WITH CLEFT LIP AND PALATE FROM 23 DIFFERENT COUNTRIES

Alaa Abd-Elsayed, Morgan Livingstone CCLS

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should start thinking of the reason of this phenomenon

SUMMARY:

Self image perception of 171 children and adolescents with cleft lip and palate from 23 different countries Alaa A Abd-Elsayed1 MD, MSc and Morgan Livingstone 2 CCLS
1 Outcomes Research Department, Cleveland Clinic, Cleveland, Ohio, USA.2 CCLS, Toronto, Canda
Introduction: Children's drawings have been studied as indicators of self image, cognitive ability and interpersonal relationships. Art therapy is an amazing tool that helps connect children with their feelings in a non threatening way and to also gain insight into the concerns and inner life of patients. Art therapy has been used with a variety of pediatric medical populations, including cancer, kidney disease, juvenile rheumatoid arthritis, chronic pain, and severe burns (Malchiodi, 1999). Understood as a way of discovering strengths, art therapy can be a bridge from the sad and lonely places of illness to the joy of human connection and understanding (Ulman & Levy, 1975). In our study it was used to initiate interactions with children prior to cleft lip and or palate surgery, a population that is thought to have considerable problems with self-confidence and self-perception.
Methods: As part of a private practice and during missions to multiple countries, 171 children from 23 countries including Australia, Botswana, Botswana, Canada, Ecuador, Egypt, England, Ethiopia, France, Ghana, India, Iran, Ireland, Israel, Jamaica, Jordan, Kenya, Mexico, Morocco, Spain, Syria, U.A.E and USA were asked to participate in an art therapy session with a child life specialist prior to reparative cleft lip surgery. Each child was asked to lie down upon a large piece of paper to have his or her outline traced. Then the child was asked to draw himself as he sees himself or herself now within the outline, including his face. Pictures were taken of the drawings. The pictures were later reviewed to examine how the children depicted their mouths.
Results: 171 children, 120 males and 50 females, ranging from 5 to 17 years old were asked to participate in this activity. This study was carried out in 23 countries, over a period of 7 years from 2000 to 2007. When examining the faces drawn by the children, all drew their mouths as normal, without any depiction of a cleft lip.
Conclusions: Children with cleft palate and cleft lip, independent of the age, sex, culture, had a normal representation of their self image.

REFERENCES:

1) Malchiodi, C. A. (Ed.). (1999). Medical art therapy with children. London: Jessica Kingsley.

2) Ulman, E., & Levy, B. (1975). An experimental approach to the judgment of psychopathology from paintings. In E. Ulman & P. Dachinger (Eds.), Art therapy in theory and practice (pp. 393– 402). New York: Schocken.

» NR2-056

ASSOCIATION OF PANDAS(PEDIATRIC AUTOIMMUNE NEURODEVELOPMENTAL DISORDER ASSOCIATED WITH STREPTOCOCCAL INFECTION) WITH PERVASIVE DEVELOPMENTAL DISORDER

Asad Amir M.D., Imran Anjum MD, Valerie D'Aurora BS, Bliss Chalemian MD, Javed Iqbal MD

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand the association of PANDAS(Pediatric Autoimmune Neurodevelopmental disorder associated with Streptococcal Infection)with Pervasive Developmental Disorder.

Summary: The Pediatric Autoimmune Neuropsychiatric Disorder Associated with Group A Streptococcal Infection (PANDAS) has been described by the National Institute of Mental Health as the abrupt pediatric onset or exacerbation of Tic disorder and/or Obsessive Compulsive Disorder temporally related to Group A Streptococcal Infection. Since clinical studies identify a post infectious autoimmune-mediated etiology, the use of Penicillin during the acute phase and for prophylaxis, tonsillectomy, immunomodulatory therapies such as plasma exchange and intravenous immunoglobulin may be indicated and have been reported to alleviate the symptoms of PANDAS. Since pediatricians frequently follow their patients longitudinally, they play a primary role in the detection of acute behavioral changes, and are instrumental in first considering a diagnosis of a possible PANDAS infection. There is considerable research associating PANDAS with the symptoms of childhood-onset obsessive compulsive disorder, Tic Disorder and ADHD. However, there are limited studies showing an association between the symptoms of pervasive developmental disorder and PANDAS. In this report, we present a 7 year old Caucasian male with a past psychiatric history of ADHD and learning disabilities (reading and comprehension) who presented with an abrupt onset of agitated, self injurious and extremely assaultive behavior commencing 3-4 weeks after an episode of scarlet fever. Clinical features also

included emotional lability, irritability, poor concentration, regressive behavior, impulsivity, hyperactivity, poor scholastic performance, secondary nocturnal enuresis, circumscribed, stereotyped patterns of behavior, and vocal tics. There was a dramatic exacerbation of these symptoms, leading to an aggressive unprovoked physical attack on his younger brother. We review the temporal correlation between high titers of ASO antibodies and disruptive behavioral and social changes in this patient, as well as clearly demonstrate the successful treatment and spontaneous remission in conjunction with decreasing ASO titers following antibiotic treatment. Moreover, we emphasize the need for frequent screening and prompt psychiatric consultation for patients presenting to their pediatricians or primary care physicians, with a considered diagnosis of PANDAS.

REFERENCES:

1) Mabrouk, AA, Eapen V. Challenges in the Identification and Treatment of PANDAS: A Case Series. Journal of Tropical Pediatrics 2008;1-3.

2) Besiroglu, L, Agargun MY, Ozbebit O, et al. Therapeutic Response to Plasmapharesis in Four Cases with Obsessive-Compulsive Disorder and Tic Disorder Triggered by Streptococcal Infections. Turkish Journal of Psychiatry 2007;18(3):270-276.

» NR2-057

ATOMOXETINE FOR HYPERACTIVITY IN CHILDREN WITH SEVERE AUTISTIC DISORDERS: AN OPEN-LABEL STUDY

Chawanun Charnsil M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to consider benefit and risk of atomoxetine in treating hyperactivity symptoms in severe autistic disorders.

SUMMARY:

OBJECTIVE: This study aimed to examine the effects of atomoxetine on attention deficit and hyperactivity symptoms (ADHSs) found in children with severe autistic disorders.
METHOD: Severe autistic children (Childhood Autistic Rating Scale of 37 or more) with ADHSs were given atomoxetine for 10 weeks. The Aberrant Behavior Checklist, Hyperactivity subscale (ABC-H subscale) and the Clinical Global Impression – Improvement scale (CGI-I scale) were used for the assessment of ADHSs at baseline, week 6, and week 10.
RESULTS: 8 boys and 4 girls with a mean (SD) age of 10.6±2.9 years participated in this study. Due to gastrointestinal symptoms, an irritable mood, and sleep problems, three patients discontinued atomoxetine before week 6 assessment. The data of these patients, therefore, were excluded from the analysis. Although CGI-I score at week 10 were rate as improvement(5 subjected was rated as much improved,3 as minimally improved,there was no significant decrease of ABC-H subscale score (33.89 ± 7.18 at baseline to 31.78 ± 7.61 at week 10, p=0.62) . In addition, no significant benefit was found on other ABC subscales.
Conclusions: The benefit of atomoxetine on ADHSs found in a previous study carried out in mild autistic children was not found in our severe autistic children

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» NR2-058

OPTIMAL RESPONSE TO OROS MPH AMONG CHILDREN AND ADOLESCENTS WITH ADHD: THE ANALYSIS OF DEMOGRAPHIC & CLINICAL CHARACTERISTICS

Ying-Sheue Chen M.D., Chou Wen-Jin, M.D., Chen Shin-Jaw, M.D., Chang Hsueh-Lin, M.D., Lin Chih-Chien, M.D., Yeh Chin-Bin, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to learn the operational definition of optimal response in the treatment of ADHD. Severe pretreatment ADHD symptoms, and positive family history of ADHD will reduce the optimal response to OROS-MPH. The interaction of body weight and dosage of OROS-MPH was needed to be considered in increasing OROS-MPH dosage forcefully in order to achieve the remission status. The subjects with heavier body weight need higher dosage.

SUMMARY:

Background: The optimal-response (OR) means achieving a remission status during treatment of ADHD which is defined as a score of "0 or 1" on each of the first 18 items in ADHD SNAP-IV scale. Recently, we found 66% of patients received OROS-MPH reaching OR. The report explored the role of demographic and clinical factors in achieving OR.
Method: A prospective study consisted 6-week titration and 4-week maintenance phase was conducted. Subjects, aged 6-18, with DSM-IV ADHD diagnosis who were taking IR-MPH for at least 1 month were recruited. They were shifted to OROS-MPH. During the 6-week titration phase, subjects who did not achieve "OR", their OROS-MPH dosage were increased forcefully to higher dose level (18mg, 36 mg, and 54 mg daily). At the end of titration phase, the final titration dose was maintained for another 4 weeks. The differences in the rate of OR were analyzed by their demographic and clinical factors.
Results: 521subjects were recruited at 6 medical centers in Taiwan and 290 subjects achieved OR. Total score of baseline SNAP-IV, family history of ADHD, dosage and body weight (BW), were found significantly affected the OR to OROS MPH. 68% of subjects with baseline SNAP-IV scores less than 40 comparing to 49% of patients with SNAP–IV scores above 40 achieved OR (odds ratio:2.17, p<0.0001). 61.45% of 279 patients without family ADHD history achieved OR while 43.4% of 53 patients with family ADHD history remitted (odds ratio: 2.00, p=0.022). The OR is found related to their OROS-MPH dosage and body weight (odds ratio, 2.18-1.58, p=0.004-0.05). Gender, age, type of ADHD, pre-shift Ritalin dosage, and comorbidities had no effect on their OR to OROS MPH.
Conclusions: Patients with more severe ADHD symptoms and positive family history of ADHD had lower OR to OROS MPH. The interaction of body weight and daily dosage of OROS-MPH also played significant roles in reaching OR.

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» NR2-059

DIFFUSION TENSOR IMAGING ABNORMALITIES IN KOREAN ATTENTION DEFICIT/HYPERACTIVITY DISORDER BOYS

Jeewook Choi M.D., Bumseok Jeong, M.D., Ph.D., Seyeon Lee, M.D.,Jiyoung Ahn,M.D.,Ph.D., Younghee Seo, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize neural substrates of ADHD, especially in terms of white matter tract networking, using Diffusion Tensor Imaging which is one of the cutting edge neuroimaging tools.

SUMMARY:
Objective: Attention-deficit/hyperactivity disorder (ADHD) is hypothesized to result from abnormalities in neuronal circuits involving prefrontal cortex, striatum, and cerebellum. Diffuse tensor imaging (DTI) was applied to explore the abnormalities of white matter (WM) tracts in Korean boys with ADHD. Methods: Subjects with ADHD were recruited by advertisements targeted towards boys who visit at child and adolescent clinics on the St. Mary's hospital. Healthy control subjects were also recruited by advertisement targeted towards boys who are elementary school-aged and have no history of Axis I (DSM-VI) psychopathology. The St. Mary's Hospital IRB approved all procedures. DSM-IV criteria on structured diagnostic interview (K-SADS-PL-K: Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version-Korean version) were used for diagnosis. Fifteen boys with ADHD (mean age 9.3±1.8), and 9 age-, gender-matched controls (mean age 9.2±1.8) received DTI assessments, twelve directional diffusion tensor images acquired with a 1.5T Siemens MRI. Fractional Anisotropy (FA) maps of WM were compared between groups with a voxel-wise analysis after intersubject registration to MNI space (at least 10 consecutive voxels and p<.005). Results: There is no difference between groups in demographic variables except IQ, which is higher in healthy control group (F=5.77, p=.006). ADHD group showed decreased FA than healthy control group in left cerebellar middle peduncle, right supplement motor area, left precentral region, and right external capsule. ADHD group also showed increased FA in right middle occipital WM. Conclusion: The findings in ADHD group support previous ADHD hypothesis of the functional abnormalities in corticocerebellar circuit, and suggest that ADHD might have more complicated pathology of neuronal circuit including occipital visual system.

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2) Pavuluri MN, Yang S, Kamineni K, Passarotti AM, Srinivasan G, Harral EM, Sweeney JA, Zhou XJ: Diffusion Tensor Imaging Study of White Matter Fiber Tracts in Pediatric Bipolar Disorder and Attention-Deficit/Hyperactivity Disorder.Biol Psychiatry. 2008 Nov 20. Epub ahead of print

» NR2-060

EFFECTS OF GUANFACINE EXTENDED RELEASE ON SECONDARY MEASURES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND OPPOSITIONAL SYMPTOMS

Daniel Connor M.D., Thomas Spencer, M.D., Christopher Kratochvil, M.D., Frank A. López, M.D., Andrew Lyne, M.Sc., C.Stat., Gerald Tremblay, M.D., J.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participants should be able to describe the efficacy of the extended-release formulation of the nonstimulant selective a2A-adrenoceptor agonist guanfacine (guanfacine extended release [GXR]) in the treatment of both oppositional and core ADHD symptoms in children with ADHD, as well as the impact of GXR treatment on self-reported parent stress and symptoms of disruptive behavioral disorders.

SUMMARY:
Introduction: Guanfacine extended release (GXR) has demonstrated efficacy for the treatment of attention-deficit/hyperactivity disorder (ADHD). The primary objective of this randomized, placebo-controlled, flexible-dose study was to evaluate the effects of GXR on oppositional symptoms in children aged 6 to 12 years with a diagnosis of ADHD and oppositional symptoms. Primary results are reported in a separate abstract. Secondary efficacy measures included the 40-item Conduct Problem Subscale (CPS) of the New York Parent Rating Scale–School-Aged (NYPRS-S), the Parent Stress Index–Short Form (PSI/SF) questionnaire, and the Clinical Global Impressions–Improvement (CGI-I) scale that measured changes in both ADHD and oppositional symptoms.
Methods: Subjects (N=217) were randomized 2:1 to receive GXR or placebo. All subjects randomized to GXR started on a dose of 1 mg/d, which could be titrated by 1 mg each week during the 5-week, dose-optimization period to a maximum of 4 mg/d, then maintained at their optimal dose for 3 additional weeks.
Results: Significantly greater symptom reductions from baseline were seen on the CPS of the NYPRS-S in the GXR group relative to placebo beginning 3 weeks into the dose-optimization phase of the study and continuing through the dose-maintenance period (-16.0 vs -9.6 at endpoint, P<0.001). Least squares mean improvement on the PSI/SF at endpoint was 17.0 for the GXR group compared with 7.7 for placebo (P=0.002). Investigators rated a significantly greater percentage of GXR-treated subjects as "very much improved" or "much improved" on the CGI-I compared with placebo beginning 3 weeks into the dose-optimization period (71.5% vs 32.0%, P<0.001 at endpoint). Most TEAEs (eg, somnolence, sedation, fatigue) were mild or moderate. There were no serious TEAEs.
Conclusion: This analysis further supports the clinical efficacy of GXR for treating oppositional symptoms in children with ADHD.

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» NR2-061

EFFECT OF ARIPIPRAZOLE ON QUALITY OF LIFE AND CAREGIVER STRAIN IN THE TREATMENT OF IRRITABILITY ASSOCIATED WITH AUTISTIC DISORDER

Patricia Corey-Lisle Ph.D., George Manos, Ph.D., William H Carson, M.D., Robert D McQuade, Ph.D., Andrei Pikalov, M.D., Ph.D., Suja Mathew, B.S., Diane K Ammerman, Pharm.D., Michael Nashat, Pharm.D., Ben Handen, Ph.D., Ronald N Marcus, M.D., Randall Owen, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be able to define the constructs of health-related quality of life and caregiver burden, understand the benefit of including perspectives from both the patient and caregiver in evaluations of new therapies and understand the short-term effects of aripiprazole on these measures in the treatment of irritability associated with autistic disorder in children and adolescents.

SUMMARY:
Evaluate the impact of aripiprazole (ARI) on quality of life and caregiver burden in the treatment of irritability in children and adolescents (aged 6-17 years) with autistic disorder.
Methods: Two 8-week, double-blind, randomized, placebo-controlled studies comparing the efficacy of aripiprazole (Study 1: flexibly dosed 2-15 mg/day; Study 2: fixed-dose 5, 10, 15 mg/day) with placebo in the treatment of irritability associated with autistic disorder using the Pediatric Quality of Life (PedsQL) (1) and Caregiver Strain Questionnaire (CGSQ) (2).
Results: In Study 1, 51 subjects were randomized to placebo and 47 to ARI. In Study 2, 52 subjects were randomized to placebo and 53 to 5 mg/day, 59 to 10 mg/day and 54 to 15 mg/day of ARI. Both trials demonstrated efficacy at endpoint on the primary outcome measure, the Aber-

rant Behavior Checklist Irritability Subscale ($p<0.05$). In Study 1, ARI demonstrated improvement vs. placebo on the PedsQL Combined Scales Total score (least-squares mean treatment difference [TD] [95% CI] = 11.4 [6.1, 16.8]), and the Emotional, Social and Cognitive Functioning Subscales. ARI also demonstrated improvement vs. placebo on the CGSQ Global Score (TD = -1.9 [-2.7, -1.2]), and the Objective, Subjective Externalized and Subjective Internalized Strain Subscales. In Study 2, ARI (15 mg/day only) demonstrated improvement vs. placebo on the PedsQL Combined Scales Total score (TD = 8.2 [1.2, 15.2]), the Emotional and Cognitive Functioning Subscales, and on the CGSQ Global Score (TD = -1.1 [-1.9, -0.3]) and Objective, Subjective Externalized and Subjective Internalized Strain Subscales. Conclusion: Aripiprazole, particularly when flexibly dosed, improved health-related quality of life, and reduced caregiver burden, in treatment of children and adolescents (6-17 years) with irritability associated with autistic disorder.

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2) Brannan AM, Heflinger CA, Bickman L. The Caregiver Strain Questionnaire: Measuring the impact on the family of living with a child with serious emotional disturbance. J Emotional and Behavioral Disorders 1997; 5:212-222

» NR2-062

TEMPORAL RELATIONSHIP BETWEEN CANNABIS USE AND DEPRESSION AMONG ADOLESCENTS IN THE UNITED STATES

Hon Ho, M.D., M.P.H., Christian Hopfer, M.D., John K. Hewitt, Ph.D., Brett C. Haberstick, Ph.D., Jeffrey Lessem, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the temporal relationship between cannabis use and depression among adolescents in the United States, and the dose effect of cannabis use in such relationship.

SUMMARY:

OBJECTIVE: To evaluate the temporal relationship between cannabis use and depression (1).
METHOD: Data from the National Longitudinal Study of Adolescent Health, a national probability sample of United States adolescents followed into young adulthood, were used.
Characteristics: 10,778 female and 10,519 male participants, age between 11 and 21, were interviewed at three waves; 52% were Caucasian, 23% African American, 13% Hispanic, 8% Native American, and 2% Asian. The mean age (and standard deviation [SD]) at Wave 1 was 16.2 (SD=1.7) and at Wave 3 was 22.5 (SD=1.8).
Analytic Strategy: To evaluate the temporal relationship between prior cannabis use and later depression based on CES-D scores (2), adolescents who had depression at Wave 1 or Wave 2 (Waves 1 and 2 were one year apart) were excluded (n=9,803 after exclusion). Logistic regression was used to evaluate the association between cannabis use during Wave 1 or Wave 2 and depression during Wave 3 (Waves 2 and 3 were five years apart). To evaluate the temporal relationship between prior depression and later cannabis use, adolescents who used marijuana at Wave 1 or Wave 2 were excluded (n=7,521 after exclusion). Logistic regression was use to evaluate the association between depression during Wave 1 or Wave 2 and cannabis use during Wave 3.
RESULTS: Prior cannabis use was a statistically significant predictor of later depression, even after adjusted for socioeconomic status, drug and alcohol use, age, gender, and race (odds ratio [OR]: 1.27; 95% confidence interval [CI]: 1.07, 1.49). Prior cannabis use of more than ten times was a stronger predictor of later depression (adjusted OR: 1.33; CI: 1.07, 1.64). However, prior depression was not a statistically significant predictor of later cannabis use (adjusted OR: 1.06; CI: 0.90, 1.26).
CONCLUSIONS: Cannabis use increases the risk of depression, but not vice versa, and the risk seems to be dose-dependent. Study supported by 5P01HD031921, 1R01DA021913.

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2) Goodman E, Capitman J: Depressive symptoms and cigarette smoking among teens. Pediatrics 2000; 106:748-755

» NR2-063

SAFETY AND TOLERABILITY OF ARIPIPRAZOLE IN THE TREATMENT OF IRRITABILITY ASSOCIATED WITH AUTISTIC DISORDER (CN138-178 / CN138-179)

Lisa Kamen M.H.A., Randell Owen,M.D., Jully Kim, Pharm.D., George Manos, Ph.D., William H Carson, M.D., Robert D McQuade, Ph.D., Taro Iwamoto, Ph.D., Raymond Mankoski, M.D., Ph.D., Ronald N Marcus, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to understand the short-term safety and tolerability of aripiprazole in the treatment of irritability in children and adolescents (aged 6-17 years) with autistic disorder.

SUMMARY:

Objective: Evaluate the safety and tolerability of aripiprazole in the treatment of irritability in children and adolescents (aged 6-17 years) with autistic disorder.
Methods: Data derived from two 8-week, double-blind, randomized, placebo-controlled studies comparing the efficacy of aripiprazole (flexibly dosed 2-15 mg/day and fixed dose 5, 10, 15 mg/day) with placebo in the treatment of irritability associated with autistic disorder (1).
Results: 313 subjects comprised the safety sample (aripiprazole 212, placebo 101). Both trials demonstrated efficacy at endpoint on the primary outcome measure, the Aberrant Behavior Checklist Irritability Subscale ($p<0.05$) (2). Discontinuation rates due to adverse events (AE) were 10.4% for aripiprazole and 6.9% for placebo. The most common AEs (>1%) leading to discontinuation in the aripiprazole group were (vs. placebo): sedation (3.3% vs. 0%), drooling (1.9% vs. 0%), tremor (1.9% vs. 0%), extrapyramidal disorder (1.4% vs. 0%) and vomiting (1.4% vs. 0%). There were two serious AEs in the aripiprazole group: presyncope and aggression. AEs were mostly mild-to-moderate in severity, and, except for fatigue, there were no apparent dose-related relationships. The incidence of non-akathisia EPS-related AEs was 17.9% (vs. 2.0% for placebo) and the incidence of akathisia events was 3.3% (vs. 8.9% for placebo). The adjusted mean change in body weight and median BMI at endpoint was higher in the aripiprazole group than the placebo group (LOCF: 1.6 kg vs. 0.4 kg and 0.7 kg/m2 vs. 0.2 kg/m2 respectively, p=0.001 for both). There were no meaningful differences between aripiprazole and placebo in the median percent changes from baseline to endpoint in metabolic and glucose laboratory measurements.
Conclusions: Aripiprazole was generally safe and well-tolerated in this population. Long-term safety and tolerability studies may be warranted.

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1) Lecavalier L: Behavioral and emotional problems in young people with pervasive developmental disorders: prevalence, effects of subject characteristics, and empirical classification. J Autism Dev Disord. 2006; 36:1101-1114

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» NR2-064

EXPOSE TO CHRONIC AIRCRAFT NOISE AND EMOTION, BEHAVIOR CHARACTERISTICS IN KOREAN CHILDREN

Myung Ho Lim M.D., Ki Chung Paik, M.D., Young June Jeon, M.D., Won Seok Lim, M.D., Kyung Kyu Lee, M.D., Seok Bum Lee, M.D., Hyun Woo Kim, M.D., Myung Ho Lim, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to study the influence of chronic aircraft noise exposure on children's emotional and behavioral characteristics in Korean children.

SUMMARY:

Objective : It has been known that chronic noise exposure causes various influences on early childhood development, education, school performance and health. This study was focused on the influence of chronic aircraft noise exposure on children's emotional and behavioral characteristics in Korean children.
Methods : We enrolled 586 4th~6th grade children of seven primary schools near airbases in Korea. The Korean version of Child Behavior Checklist, Korean Personality Inventory for Children, Kovac's Children's Depression Inventory, and Spielberger State-Trait Anxiety Inventory involving 2 schools in a helicopter noise-impacted urban area and 3 schools in a fighter plane noise-impacted urban area were compared with those of children from 2 matched control schools in low-aircraft noise-impacted urban areas in Korea.
Results : Family discomfort(P=0.001) and autistic symptoms(P=0.046) of Korean personality inventory for children were significantly higher among children in schools in a helicopter and a fighter plane noise environment compared to the low noised schools. Also, Spielberger State Anxiety Inventory was significantly higher among children in schools in a helicopter and a fighter plane noise environment compared to the low noise schools(P=0.020). Child Behavior Checklist, Kovac's Children's Depression Inventory, Spielberger Trait Anxiety Inventory were not associated with a aircraft noise among children in schools compared to the low noised schools.
Conclusion : Children in a chronic aircraft noise environment schools was shown to be associated with a higher rate of autistic behavior and family discomfort. Also there was a possibility for chronic aircraft noise exposure to be associated with family environment function other than depression and anxiety.

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» NR2-065

PREDICTORS OF IMPROVEMENT IN FUNCTIONAL DISABILITY FROM ADMISSION TO 120 DAYS POST DISCHARGE IN ADOLESCENT PSYCHIATRIC INPATIENTS

Liza A. Maldari Ph.D., David L. Pogge, Philip D. Harvey

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to : understand the predictors of improvement in functional disability associated with inpatient treatment in adolescents; understand the relative importance of clinical as compared to cognitive improvements associated with antipsychotic treatment

SUMMARY:

Background. Functional disability in psychotic disorders is correlated with cognitive impairments and treatment of cognitive impairments have been hypothesized to potentially improve functional outcomes. These relationships hold up in both adults and adolescent populations. Much less is known about these relationships in nonpsychotic conditions and there is essentially no information about the relative importance of treatment of cognitive impairments, relative to symptomatic changes, for improving functional outcomes. Methods. Hospitalized adolescent inpatients (n=106) who received their first treatment with antipsychotic medications were examined with clinical (depression, psychosis, mania, and disruptive behaviors), cognitive, and intellectual assessments, and ratings on a scale of functional disability (The HONOSCA) at the time of admission and 120 days after discharge. Results. Statistically significant (p<.05) improvements were found for clinical symptoms, functional disability, and cognitive performance from baseline to endpoint. Regression analyses, controlling for IQ scores, found that a composite measure of clinical change accounted for 37% of the variance in functional improvements from admission to 120 day follow-up (p<.001), while cognitive changes accounted for 1% of the variance in those change scores. Adjusting scores for medication adherence and subjective satisfaction with treatment did not influence these results. Conclusions. In nonpsychotic adolescent patients with low levels of cognitive impairments at baseline, improvements in cognitive functioning were much less important than clinical changes for improving functional disability.

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» NR2-066

COMPARATIVE SEVERITY & OUTCOME OF ADHD IN A PSYCHIATRIC PRIVATE PRACTICE: HIGH-RISK/ LOW-INCOME VS MIDDLE-CLASS YOUTH

Godehard Oepen M.D., Joseph Llinas, M.D., Edward J. Federman, Ph.D., Richard N. Akins, M.D., M.B.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to desribe the challenge of comparative severity & outcome of ADHD in high-risk/low-income vs middle-class youth, able to identify demographic and environmental factors that increase risk for psychiatric disorders in youth, and describe an integrated treatment model that meets the challenge.

SUMMARY:

Youth from families with limited resources and from marginalized communities are at higher risk for psychiatric and behavioral disorders than their more affluent peers. Despite controversy about whether universal preventive measures or selected interventions offer the best approach to this problem1, there is limited data about the comparative severity and outcome of psychiatric conditions in high- vs. average-risk youth in everyday practice settings. At Alabama Psychiatric Services, an integrated psychiatric private practice with more than one million covered lives, we compared the prevalence, severity and naturalistic outcome of high-risk youth and middle-class controls with ADHD, a major factor in emotional disorders, violence and risk taking behaviors. High-risk youth were more than twice as likely to be diagnosed with ADHD as controls (p<.0001) and trended toward having more severe ADHD (p<.08) and comorbid (i.e., oppositional defiant disorder, p<.10) conditions. Outcome analysis showed no differences in clinically significant improvement2 or remission between high-risk youth

and controls. The discussion shows how the described integrated model of care can be adopted in other settings to meet the needs of high-risk youth, without first settling the long-term public health controversy encircling this issue.

REFERENCES:

1) Frankford, Evelyn R Changing Service Systems for High Risk Youth through State level Strategies" Am J Public Health 2007, vol.97/#4, pp.31-38

2) Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J Consult Clin Psychol. Feb 1991;59(1):12-19.

» NR2-067

SUICIDALITY AND DELIBERATE SELF-HARM IN ADOLESCENT BORDERLINE PERSONALITY DISORDER

Uday Patil M.A., Marianne Goodman, M.D., Joseph Triebwasser, M.D., Elizabeth Diamond, M.A., Larry Siever, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant will be able to identify the symptom dimensions of Borderline personality disorder (BPD) that predict an onset of suicidality and deliberate self-harm in BPD adolescents. Participants will be able to recognize that the prodromal features of adolescent suicidality and deliberate self-harm germinate with unusual sensitivity and moodiness in young children, and culminate in marked impulsivity and aggression in pre-teens.

SUMMARY:

BACKGROUND: Suicide is the third leading cause of death in teenage Americans. Each year, one in five engage in suicidal ideation, and four percent engage in non-lethal deliberate self-harm (DSH). The risk of suicide increases 50-100 times after an incident of DSH. Borderline personality disorder (BPD) is an important risk factor for suicidality and DSH in adulthood, but limited data exist on which symptom dimensions of BPD are associated with suicidality and DSH.
METHODS: We collected data on suicidality and DSH by surveying parents of offspring with BPD. A 200-item questionnaire covered clinical variables from infancy through adulthood, particularly in the domains of self-injury, impulsive behavior and emotional dysregulation. Responses on BPD offspring (identified as such with embedded diagnostic criteria and a professional diagnosis of BPD) were compared to those on non-BPD siblings. Clinical variables in earlier epochs were used to predict adolescent suicidality and DSH.
RESULTS: Parents responded on 184 children diagnosed with BPD during adolescence (13 to 19) and their non-BPD siblings. Suicidal behavior and DSH co-occurred in more than half of the BPD offspring, and this co-occurrence was predicted by disrupted peer relations and victimization before adolescence. DSH was present in 87% of the probands, and was predicted uniquely by impulsivity. Suicidality was frequently endorsed, including suicidal thoughts (74%), suicidal threats (60%), and suicide attempts (44%). Attempts were uniquely associated with outwardly directed aggressive acts in adolescence. These rates of suicidality and DSH were significantly higher than in the non-BPD siblings.
CONCLUSIONS: Probands have markedly high rates of suicidality and DSH. These symptoms may be among the most telling correlates of a diagnosis of BPD, even more so than emotional dysregulation, impulsive behavior, affective sensitivity, or temperamental disturbances.

REFERENCES:

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» NR2-068

SCREENING AND BRIEF INTERVENTION FOR UNDERAGE DRINKING IN UNDERSERVED POPULATIONS

Ashwin A. Patkar, M.D., Alex Kemper, M.D., Rowena Dolor, M.D., John Anderson, M.D., Jayaselvi Thanaseelan, M.D., Lillian Robinson, Ph.D., Robert Hubbard, Ph.D.,Kathleen S.Peindl,Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, participants should be able to recognize the importance of screening for alcohol use among adolescents and the clinical utility of Brief Interventions to address underage alcohol use.

SUMMARY:

Objectives: About 1/3rd of 18-20 year old young adults drink heavily in the past month. Adolescence is the ideal time to intervene with individuals involved in alcohol use because successful interventions during this period can have long-term benefits. As a part of a NIAAA initiative to address rural underage drinking, the PARTNER (Prevention Approaches To UNdERage Alcohol Use) project examined the feasibility of a Screening, Brief Intervention and Referral to Treatment (SBIRT) approach for adolescent alcohol use in a primary care setting in an open-label, prospective design. Methods: The SBIRT model developed for adult alcohol users was modified for use in the adolescent population and implemented at 4 primary care practices in North Carolina. An integrated treatment model that involved co-location of the behavioral therapist at the primary care practice was developed. The CRAFFT questionnaire was used as a screening tool. Outcome measures included proportion of adolescents who volunteered for screening and those with positive screen who agreed for brief intervention. Results: A total of 153 adolescents were consented and screened. 3 (1.96%) refused to participate after consenting. Out of the 150 participants (59.3% women, 56.7% African-American, 10% Latino), 24 (6.24%) screened positive. There was a trend for more girls (75%) than boys (25%) to report positive screens on CRAFFT (p=.067). There was a significant main effect of age on positive screens for alcohol (F=25.6, p<.001) with positive screen reported more by older adolescents (mean age=18.6) compared to negative screens (mean age=16.5). 20 (82.5%) of adolescents who screened positive participated in the brief intervention.
Conclusion: The SBIRT Model for underage drinking appears to be feasible in a primary care setting. The high acceptance rate for a Brief intervention suggests that adolescents are willing to participate in brief behavioral strategies to address underage drinking. Further research is required to examine the effectiveness of brief intervention in this population.

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» NR2-069

EFFECTS OF ARIPIPRAZOLE ON METABOLIC MEASURES IN PEDIATRIC AND ADOLESCENT PATIENTS: A POOLED ANALYSIS OF PLACEBO-CONTROLLED TRIALS

Andrei Pikalov M.D., John W Newcomer, M.D; Ross A Baker, Ph.D., M.B.A.; Stephen Kaplita, M.S.; Jian Han, Ph.D.; Suja Mathew, B.S.; Raymond Mankoski, M.D., Ph.D.; William H Carson, M.D.; R Andrew Forbes, Ph.D; Margaretta Nyilas, M.D.; Taro Iwamoto, Ph.D.; Randall Owen, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the audience will be able to describe the metabolic effects of aripiprazole in pediatric and adolescent patients in the worldwide clinical development program.

SUMMARY:
Objective: Metabolic side-effects that can occur during antipsychotic treatment in children and adolescents are recognized as a concern by clinicians, patients and caregivers, offsetting potential benefits (1, 2). In the present analysis the metabolic effects of aripiprazole in pediatric and adolescent patients from the aripiprazole worldwide development program were evaluated.
Methods: Metabolic measures in the aripiprazole- and placebo-exposed patients were compared with analysis of covariance (ANCOVA) using last observation carried forward (LOCF).
Results: Aripiprazole produced limited mean changes (mg/dL) versus placebo in fasting plasma glucose (aripiprazole +0.3, placebo -1.2; p=0.38), total cholesterol (aripiprazole -5.8, placebo -8.5; p=0.22) and fasting triglycerides (aripiprazole -2.5, placebo -0.9, p=0.79). Statistically significant changes in body weight were observed (aripiprazole +1.6 kg, n=381, placebo: +0.3 kg, n=187, p<0.001).
Conclusions: The results inform evidence-based clinician decisions and reinforce the need for realistic management of weight gain and metabolic monitoring in all children/adolescents being treated with antipsychotic medications.

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» NR2-070

A CASE-CONTROL ASSOCIATION STUDY OF 5-HYDROXYTRYPTAMINE 1A RECEPTOR GENE IN ATTENTION DEFICIT HYPERACTIVITY DISORDER IN A KOREAN SAMPLE

Se-Hoon Shim, M.D, Ph.D., Hyun-Woong Ahn, M.D, Young Hwangbo, M.D, Ph.D., Young -Joon Kwon, M.D, Ph.D., Hee-Yeon Jeong, M.D, Ph.D., Bun-Hee Lee, M.D, Ph.D., Yong-Ku Kim, M.D, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able : 1)To recognize that the 5-HT1A gene may be a risk factor in the development of ADHD; 2)To think that serotonin's regulatory control over dopaminergic neurotransmission is an important fact contributing to the hypothesis that serotonin may be responsible to some degree in mediating ADHD behaviour particularly the hyperactive and impulsive components of the disorder.

SUMMARY:
Purpose: The majority of research into the neurobiology of ADHD has targeted the dopaminergic system. It is well accepted that dopamine(DA) and 5-HT do not operate in the brain on a mutually exclusive basis but rather are closely interconnected and exert regulatory control over each other. 5-HT exerts an influence over DA-mediated behaviors, which may be directly relevant to the serotonergic hypothesis of ADHD. While the 5-HT system may be involved in motor activity, less is known about which receptors are responsible for the various mechanisms of motor control. Different 5-HT receptor subtypes have been shown to mediate the regulation of 5-HT over DA neurotransmission including the 5-HT1A receptor. We hypothesized that the 5-HT1A receptor gene may be a good candidate for genetic studies of ADHD. Accordingly, we investigated the association of 5-HT1A receptor gene with ADHD.
Methods: 78 ADHD subjects and 107 controls were enrolled in this study. All of the ADHD subjects completed a comprehensive and standardized diagnostic and psychological evaluation battery. The genotype and allele frequencies of patients and controls were analyzed.
Results: There was a significant difference in the genotype frequencies of SNP rs6295 (-1019 C/G) between the ADHD and control group (?2=6.23, p=0.044). The ADHD group had a higher GG genotype percentage than the controls. There were more robust findings in the allele frequencies of SNP -1019C/G between the ADHD and control group (?2=5.71, p=0.017). In the ADHD group, the -1019 G allele was found with a higher frequency (76.9%) than the -1019 C allele (23.1%). The GG genotype group had a higher score in the all subscale and total score than CG and CC genotype group in the parents version of Korean version of the ADHD Rating Scale and ADHD diagnostic system, although these differences were not significant. C allele carriers had an odds ratio of 0.47. C-allele carriers were associated with lower risk of ADHD.
Conclusions: There was a significant association between the SNP -1019C/G and ADHD in Korean children. Our results suggest that SNP -1019C/G might play a significant role in the pathogenesis of ADHD. Especially, C allele might have protective effects against ADHD. More studies are needed to confirm these findings.

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» NR2-071

CO-EXPOSURE TO ENVIRONMENTAL LEAD AND MANGANESE AFFECTS THE INTELLIGENCE OF SCHOOL-AGED CHILDREN

Cho Soo-Churl M.D., Yeni Kim, M.D., Ph.D., Boong-Nyun Kim, M.D., Ph.D., Yun-Chul Hong, M.D., Ph.D., Min-Sup Shin, Ph.D., Hee-Jeong Yoo, M.D., Ph.D., Jae-Won Kim, M.D., Ph.D., Soo-Young Bhang, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize that neurodevelopment of children might be adversely affected by exposure to lead (Pb) and Manganese (Mn). In particular, the participant may be able to identify the joint effects and interactions of these heavy metals on the intelligence of children.

SUMMARY:
Objective: The aims of this study were to investigate the association of a community's level of Pb and Mn on the intellectual function of its school-aged children and to explore the effects of joint exposure of these two heavy metals.
Method: The study participants were recruited from four cities of South Korea. From each city, we chose one school that was located at the center of the city. After being given a detailed explanation, 287 children and their parents gave consent to participate in the study. Of the 287 children, 279 children completed both the blood Pb and Mn samplings and the IQ measurements. Of these patients, 18 children were excluded from the analyses because of low birth weight (<2.5 kg, N = 17) or seizure disorder (N = 1), resulting in 261 students being included in the final analysis.
Results: The mean blood concentrations of Pb were 1.73 μg/dL (SD 0.8, median = 1.55, range 0.42-4.91) and of Mn were 14.3 μg/L (SD 3.8, median = 14.0, range 5.30-29.02). After adjustment for covariates, we found a significant relationship between the blood concentration of both heavy metals and the full-scale IQ. To analyze the interaction between blood Pb and Mn concentrations, children were divided into 2X2 groups of Pb and Mn blood concentrations. The 'high level group' was defined as having a higher

blood level of the respective heavy metal than the median level of the study population, and the 'low level group' was defined as having a lower blood level than the median level of the study population. Analysis for the interactive effect of Pb and Mn on intelligence showed that children with both high blood concentrations of both Pb and Mn had the lowest IQ. Regression analyses indicated the additive effect of Pb and Mn on the full-scale and verbal IQ of the children.
Conclusions: The present study shows that there may be an additive interactive effect of Pb and Mn on the intelligence of school-aged children.

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» NR2-072

PREDICTORS OF RESPONSE AND REMISSION IN PEDIATRIC PATIENTS WITH BIPOLAR DISORDER TREATED WITH ZIPRASIDONE

Michelle Stewart Ph.D., Christoph U. Correll, M.D., Elizabeth Pappadopulos, Ph.D., Francine Mandel, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify individual predictors of antipsychotic response.

SUMMARY:

Objective: To determine predictors of response and remission in children and adolescents with bipolar mania.
Methods: Children and adolescents aged 10–17 years (N=218) with bipolar I disorder (Young Mania Rating Scale [YMRS] score = 17, symptomatic for = 7 days) were given ziprasidone (ZIP: 80–160 mg/d) or placebo (PBO) for 4 weeks. Predictors of response (= 50% decrease in YMRS) and remission (YMRS = 12) were assessed at weeks 1–4 and last observation carried forward end point (LOCF). Groups were first compared using Cochran-Mantel-Haenszel (CMH) tests. Forced entry (FEM) and stepwise selection (SSM) models determined individual predictors of response and remission in the ZIP-treated cohort only (n=149).
Results: There were more responders in the ZIP group (CMH: ZIP vs PBO: week 3, 53% vs 29% [p=0.002]; week 4, 62% vs 35% [p=0.003]; LOCF, 53% vs 22% [p<0.0001]). However, logistic regression at week 4 or LOCF found no clear predictors of response. This was supported by FEM and SSM analyses at weeks 1–4 and LOCF (R2: 0.01–0.07, not significant). More patients on ZIP were in remission at week 3 (CMH: ZIP vs PBO, 51% vs 34% [p=0.028]) and LOCF (49% vs 27% [p=0.0002]). Logistic regression at week 4 or LOCF found standard titration speed (p=0.03, week 4) and low baseline YMRS score (p=0.007: week 4; p=0.01: LOCF) predicted remission. FEM found low baseline YMRS to be a significant predictor of remission at weeks 1–4 and LOCF. SSM confirmed low baseline YMRS and identified standard titration speed (week 4: odds ratio [OR] 2.53, [p=0.004]) and lack of comorbid attention deficit hyperactivity disorder (ADHD) (LOCF: OR, 2.06 [p=0.05]) as additional predictors.
Conclusions: In ZIP-treated patients, low baseline YMRS predicted remission most consistently. Further studies are required to confirm whether standard titration speed and a lack of comorbid ADHD are additional predictors of remission. Supported by Pfizer.

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» NR2-073

CDRS-R SUBSCALE ANALYSIS IN A RANDOMIZED PLACEBO-CONTROLLED TRIAL OF ESCITALOPRAM IN DEPRESSED ADOLESCENTS

Daniel Ventura Ph.D., Adelaide Robb, M.D., Anjana Bose, Ph.D., Andrew Korotzer, Ph.D., Stavros Tourkodimitris, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the four subscales that comprise the CDRS-R and understand the effects of treatment on these symptom domains in depressed adolescent patients.

SUMMARY:

Introduction: Adolescent depression is a serious disorder that affects up to 8.3% of adolescents. Understanding symptom domains that respond to treatment may be helpful for clinicians in tracking patient response over time. A post-hoc analysis of CDRS-R subscale scores from a placebo-controlled adolescent depression trial explored the effects of escitalopram on four symptom domains.
Methods: Male and female adolescents (12-17 years) with DSM-IV defined major depressive disorder were randomly assigned to 8 weeks of double-blind treatment with escitalopram 10-20mg/day (N=155) or placebo (N=157). The prospectively-defined primary efficacy parameter was change from baseline to Week 8 in Children's Depression Rating Scale-Revised (CDRS-R) total score. In a post hoc analysis, treatment effects on CDRS-R subscale scores (Mood, Behavior, Subjective, and Somatic subscales) were explored with an ANCOVA model, using the last observation carried forward (LOCF) approach.
Results: Mean baseline CDRS-R total score at baseline was 57.6 for escitalopram and 56.0 for placebo. Significant improvement was seen in the escitalopram group relative to placebo at endpoint in CDRS-R total score (-22.1 vs. -18.8; P=0.022; LOCF). Relative to placebo, escitalopram significantly improved the CDRS-R Mood Subscale scores (-6.4 vs. -5.0; P<0.01) and Behavior Subscale scores (-5.7 vs. -4.8; P<0.05), but not CDRS-R Subjective Subscale or Somatic Subscale scores.
Conclusion: This post-hoc analysis of the adolescent depression trial showed that, in this trial, the subscales measuring core depressive symptoms were most sensitive to treatment effects. Supported by funding from Forest Laboratories, Inc.

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» NR2-074

PATIENT ASSESSED QUALITY OF LIFE VS. CLINICIAN ASSESSMENT IN A TRIAL OF ARIPIPRAZOLE IN PEDIATRIC PATIENTS WITH BIPOLAR DISORDER

Richard Whitehead B.S., Chien-Feng Chen, Ph.D.; Edward Kim, M.D., M.B.A.; William H. Carson, M.D.; Taro Iwamoto, Ph.D.; Suja Mathew, B.S.; Andrei Pikalov, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize an association between patient based subjective measures as assessed by the pediatric version of the Quality of Life

Enjoyment and Satisfaction Questionnaire (PQ-LES-Q) and clinician assessed objective measures (YMRS Total Score and CGI-BP Overall) during acute and long-term treatment of pediatric patients with Bipolar Disorder.

SUMMARY:
Introduction: The pediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q) is made up of 14 items that assess quality of life (QoL) with total score and one item overall assessment. QoL measures yield information independent of symptom measures. This post-hoc analysis investigated correlation between patient's assessment in QoL and objective clinical assessment (YMRS, CGI-BP).
Methods: 296 children (age 10-17) with BP participated in a 4-wk double-blind trial of aripiprazole (10 or 30 mg/day, fixed doses) vs. placebo (PBO). Completers entered 26 wk extension. Primary outcome was mean change from baseline on YMRS Total Score. Secondary measures included mean changes on CGI-BP Overall, PQ-LES-Q Total (T) and the Overall item (O).
Results: YMRS Total Score and CGI-BP Overall improved vs. PLB with both doses of aripiprazole at wk 4 and wk 30; $p<.05$ and $p<.01$ respectively, LOCF). Both aripiprazole arms showed improvement on PQ-LES-Q(T) and (O); however they did not reach statistical significance. Observed Cases analysis (OC) demonstrated a correlation at wk 4 and wk 30 between % change in PQ-LES-Q(T) and % change in YMRS ($r = -.18$ & $-.29$, respectively; $p<.03$). When 4 wk YMRS Total improvement was put into categories (<20%; 20-30%; 30-50%; >50% reduction), % change in mean PQ-LES-Q(T) was 1.7, 2.3, 12.5, & 10.4 per category (trend analysis p= .007; regression = p=.01; OC). At 30 wks % change in mean PQ-LES-Q(T) was 3.3, NA, -2.6, 16.6 (p=.02; Linear regression = p=.02; OC). When CGI-BP Overall was put into 4 categories (=0; -1; -2; =-3 point change) at 4 wks, % change in mean PQ-LES-Q(O) was .02, .15, .27, .43 per category (trend analysis $p<0.05$; OC) and at 30 wks, % change in mean PQ-LES-Q(O) was -1, 0, .63, 64 (p=.02; OC).
Conclusion: In this trial of pediatric patients with BP there was positive correlation between patient-assessed QoL measures and clinician-based assessment. Supported by funding from Otsuka Pharmaceutical Co., Ltd.

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» NR2-075

THE PRO-INFLAMMATORY CYTOKINE INTERLEUKIN-18 AND ITS RELATED MOLECULES ARE IMPLICATED IN COGNITIVE DECLINE OF ALZHEIMER'S DISEASE PATIENTS

Paola Bossu Ph.D., Antonio Ciaramella, Ph.D., Diego Vanni, M.S., Francesca Salani, M.S., Carlo Caltagirone, M.D., Gianfranco Spalletta M.D., Ph.D. and Giuseppe Scapigliati Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize the link between inflammation and Alzheimer's Disease, and identify the cytokine IL-18 and its whole system as new possible mediators of AD-related cognitive impairment.

SUMMARY:
Introduction: Inflammatory processes are implied in the pathogenesis of Alzheimer's Disease (AD) and pro-inflammatory cytokines contribute to synaptic dysfunction and loss, neuronal death and cognitive impairment. Interleukin (IL)-18, in particular, is a pleiotropic pro-inflammatory cytokine, likely involved in neuroinflammation and neurodegeneration. We recently found in AD patients an association between two functional IL-18 gene polymorphisms and both disease susceptibility and outcome. Then, we reported that AD-derived PBMC released higher amounts of IL-18, as compared to cells of control subjects, and the levels of IL-18 were significantly related to cognitive function in AD patients. Objective and method: To better define the involvement of IL-18 in AD, in this study we used a PCR array to evaluate the expression of a panel of 24 genes related to IL-18 in unstimulated and LPS-treated PBMC obtained from 10 AD patients and healthy controls (HC). Results: AD patients had a lower basal expression of IL-1F7 than HC. Interestingly, LPS stimulation was able to induce in AD, as compared to HC, an higher gene expression increment of IL-4, IL-12, and notably, of IL-18, IL-18Rß and IL-1F7. This last molecule inhibits the IL-18 activity by binding the IL-18BP and forming a complex with IL-18Rß. Since in previous studies we did not find any significant alteration of IL-18BP protein expression in AD patients, we next evaluated the specific protein expression of IL-18 receptors in AD blood cells. The IL-18 receptor a and ß chains were examined by flow cytometry analysis on lymphocytes and monocytes obtained from both AD and HC subjects. The expression of IL-18Rß on lymphocytes was significantly higher in AD patients, with respect to HC, confirming the PCR array results. Conclusions: On the basis of such results, the whole IL-18 system seems to be specifically altered in AD patients, supporting the view that IL-18 is involved in the pathophysiology of AD cognitive decline.

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» NR2-076

PLANNING IN DEPRESSION AND ANXIETY: THE IMPORTANCE OF USING DIFFERENT INDICATORS FOR FEATURING ITS IMPAIRMENT

Silvia Fernandez Biesa M.D., Antonieta Nieto, Ph.D., Jose Barroso, Ph.D., Ivan Galtier, Ph.D., Belen Curbelo, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to: Get to know, in patients suffering from depression and anxiety, the frequency of mistakes in their ability to plan. Get to know, in patients suffering from depression and anxiety, those parameters that can be used in cognitive assessment as indicators of planning impairment.

SUMMARY:
Background: Executive functions impairment has been reported in depression and anxiety. Planning is one relevant component of executive functions. Processing speed can affect planning ability. The aim of this study is to analyze naïve anxiodepressive patients performance through a planning and a processing speed task. Also, we study the relationship between performance and anxiodepressive symptomatology and patients' cognitive complaints. Method: 20 naïve patients who meet DSM-IV-R criteria for adaptative disorder, MDD, PD or GAD are studied. MADRS and HARS are used to assess depressive and anxious symptomatology. SOC, a computerized version of the "Tower of London", and Matching to sample (MTS), both from CANTAB, are used to assess planning and processing speed respectively. A selection of items from the DEX-BADS is used to measure the subjective assessment of cognitive impairment.
Results: 45% of the patients presents impairment on SOC Perfect

Solutions (trials completed in minimum moves). However, Time of Planning is only increased in 5% on more complex trials. 25% present impairment on MTS latency on the more demanding trials (MTS 2-8). 57% of the patients reports having noticed cognitive changes which correlates with MTS mean latency (MTS 8: r=0.509; p<0.05; MTS 2-8 (r=0.494; p<0.05)) but doesn't correlate with SOC measures. No correlation is found between scores on MADRS, HARS or number of previous episodes and performance. Conclusions: In general, the amount of time spent in planning prior to act isn't increased but almost 50% of patients do not solve the planning task in the minimum number of moves. Given the slowness shown on MTS, a more structured task, these results suggest that patients have difficulties in self-regulation on non-structured tasks and do not spend enough time in organizing and planning their execution. These difficulties could have important repercussions in real life situations. Supported by funding from Almirall and Eli Lilly.

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» NR2-077

DELIRIUM AND PSYCHO-ACTIVE MEDICATIONS IN TERMINAL CANCER

Pierre Gagnon, MD, Pierre Allard, MD, PhD, Bruno Gagnon, MD, PhD, Chantale Mérette, PhD, François Tardif, MSc, Claudia Émond, MSc, Valérie Jomphe, MSc.

EDUCATIONAL OBJECTIVES:

Objective 1: Identify the psycho-active medications prescribed in terminal cancer which will influence the occurrence of delirium
Objective 2: Analyze the profile of prescription of psycho-active medications before and after a delirium in terminal cancer
Objective 3: Criticize current pharmacological strategies of delirium treatment in terminal cancer

SUMMARY:

Background: Antipsychotics, benzodiazepines and corticosteroids are often prescribed in terminal cancer but no accurate and extensive analysis of these drugs taken prior and after a delirium episode has been published.
Objective: To describe the use of antipsychotics, benzodiazepines, and corticosteroids before and after the occurrence of an episode of delirium in terminal cancer patients.
Methods: 1516 patients admitted in 7 palliative care units in Canada were followed prospectively from admission until death during a 3 year period (average survival: 21 days; average age: 68.4 years). Data on medication were collected daily. Benzodiazepines, corticosteroids, and antipsychotics doses were converted in equivalent units (mg. of lorazepam, dexamethasone, and haloperidol). Delirium symptoms, as rated with the Confusion Rating Scale (CRS), were correlated with doses of medications. The fifth day preceding, the day of, and the fifth day after delirium detection were identified as t-5, t0 and t+5 respectively.
Results: The prevalence of significant delirium symptoms on admission (as defined by a CRS =2) was 20% (n = 507) and the incidence during stay was 46% (n = 701). An increase in antipsychotics of 45% between t-5 and t0 (mean daily doses of 1.61mg and 2.34mg, respectively) was observed and doses kept increasing until day t+5 (2.82mg). Benzodiazepines increased by 108% between t-5 and t+5 (mean daily doses of 2.17mg and 5.55mg, respectively) (All between p<0.03 and p<0.001).
Conclusions: In a large cohort of terminal cancer patients, an increase in antipsychotics and benzodiazepines as well a decrease in corticosteroids doses were observed between the fifth day prior and the fifth day after the formal detection of a delirium episode. The observed increase in benzodiazepines remains a controversial practice in delirium management, contrary to the observed increase in antipsychotics and decrease in corticosteroids which reflect current recommendations.

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» NR2-078

EXTENDED-RELEASE MEMANTINE (28 MG, ONCE DAILY) IMPROVES ATTENTION AND VERBAL FLUENCY IN PATIENTS WITH MODERATE TO SEVERE ALZHEIMER'S DISEASE

Stephen Graham Ph.D., George T. Grossberg, M.D., Facundo Manes, M.D., Ricardo Allegri, M.D., Ph.D., Luis Miguel Gutierrez Robledo, M.D., Ph.D., Sergio Gloger, M.D., Lei Xie, Ph.D., Xinwei Daniel Jia, Ph.D., Michael Tocco, Ph.D., James L. Perhach, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the potential benefits of extended-release memantine treatment on frontal lobe functions (eg, attention and verbal fluency) in patients with moderate to severe Alzheimer's disease.

SUMMARY:

Objectives: Memantine is approved for the treatment of moderate to severe Alzheimer's disease (AD). In the US, it is currently administered orally in two daily 10-mg doses (20 mg/day) as an immediate-release tablet or solution. We recently evaluated the safety, tolerability, and efficacy of an oral, once-daily, extended-release memantine formulation (28 mg, memantine ER) in outpatients with moderate to severe AD on stable cholinesterase inhibitor (ChEI) treatment. Top-line results were reported previously; this analysis examined patients' performance on frontally mediated tasks of attention and verbal fluency.
Methods: A 2-week, single-blind, placebo-only period was followed by a 24-week, double-blind period of treatment with memantine ER or placebo. Attention was assessed post hoc, using the Severe Impairment Battery (SIB) attention domain, consisting of digit, visual, and auditory spans, and presented as a change from Baseline to Week 24 (LOCF, OC). The pre-specified measure of verbal fluency was the change in the number of animals the patient could name in one minute. The data were analyzed using ANCOVA. (Sponsored by Forest Laboratories, Inc.)
Results: A total of 677 patients [MMSE: mean (SD) 10.8 (2.9); range 3-17] were randomized to receive memantine ER (n=342) or placebo (n=335). Compared to the placebo/ChEI group, the memantine ER/ChEI group at Week 24 performed significantly better on both the attention subscore (LOCF: LS mean difference (LSMD)=0.3; P=0.004) and on verbal fluency (LOCF: LSMD=0.5; P=0.004). OC analyses yielded similar results. Furthermore, at Week 24, only the memantine ER/ChEI group showed a statistically significant improvement over baseline (paired t-test) on both measures (attention: LOCF and OC; verbal fluency: OC only).
Conclusion: Treatment of patients with moderate to severe AD with once-daily, extended-release memantine (28 mg) is associated with significant improvements in frontal lobe functions, such as attention and verbal fluency.

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NR2-079

EXTENDED-RELEASE MEMANTINE (28 MG, ONCE DAILY) IMPROVES BEHAVIOR IN PATIENTS WITH MODERATE TO SEVERE ALZHEIMER'S DISEASE

George Grossberg M.D., Facundo Manes, M.D., Ricardo Allegri, M.D., Ph.D., Luis Miguel Gutierrez Robledo, M.D., Ph.D., Sergio Gloger, M.D., Lei Xie, Ph.D., Xinwei Daniel Jia, Ph.D., James L. Perhach, Ph.D., and Stephen M. Graham, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the potential benefits of memantine treatment on behavioral symptoms in patients with moderate to severe Alzheimer's disease.

SUMMARY:

Objectives: Memantine is approved for the treatment of moderate to severe Alzheimer's disease (AD). In the US, it is currently administered orally in two daily 10-mg doses (20 mg/day) as an immediate-release formulation (tablet or solution). We recently evaluated the safety, tolerability, and efficacy of an oral, once-daily, extended-release memantine formulation (28 mg, memantine ER) in outpatients with moderate to severe AD on stable cholinesterase inhibitor (ChEI) treatment. Top-line results were reported previously; this report is a detailed post-hoc analysis of behavior, assessed by the Neuropsychiatric Inventory (NPI).

Methods: A 2-week, single-blind, placebo-only period was followed by a 24-week, double-blind period of treatment with memantine ER or placebo. Behavioral efficacy parameters were the changes from Baseline to Week 24 (LOCF, OC) for the total and individual NPI item scores, analyzed using ANCOVA. (Sponsored by Forest Laboratories, Inc.)

Results: A total of 677 patients [MMSE: mean (SD) 10.8 (2.9); range 3-17] were randomized to receive memantine ER (n=342) or placebo (n=335). Compared to the placebo/ChEI group, the memantine ER/ChEI group performed significantly better on the total NPI score at Week 24 (LS Mean Difference -2.7: P=0.005; LOCF), and also at Weeks 12 and 18. The memantine ER/ChEI group also performed significantly better on the NPI items of delusions, agitation/aggression and irritability/lability (Weeks 8, 12, and 24), and nighttime behavior (Week 24). The OC analyses yielded similar results. Furthermore, at Week 24, the memantine ER/ChEI group showed a statistically significant improvement over baseline (LOCF, OC; paired t-test) on the NPI total score and the scores of these four items.

Conclusion: Treatment of patients with moderate to severe AD with once-daily, extended-release memantine (28 mg) is associated with significant behavioral improvements. The benefits on particular NPI symptoms support prior clinical experience.

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NR2-080

MEMANTINE TREATMENT IN PATIENTS WITH ALZHEIMER'S DISEASE: BRAIN IMAGING AND NEUROPSYCHOLOGICAL RESULTS OF AN OPEN-LABEL, MULTI-CENTER TRIAL

Robert Hofbauer Ph.D., Mike Weiner,M.D. Carl Sadowsky,M.D. Judith Saxton,Ph.D. Robert K. Hofbauer,Ph.D. Stephen M. Graham,Ph.D. Sung Yun Yu,Ph.D. Hai-An Hsu,Ph.D. James L. Perhach, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the potential benefits of memantine treatment on hippocampal atrophy and on cognitive abilities in patients with Alzheimer's disease.

SUMMARY:

Objectives: To assess changes in brain volume and cognitive abilities in patients with Alzheimer's disease (AD) during periods of treatment with and without memantine.

Methods: Forty-seven patients with AD (MMSE 15-23) were maintained on ChEI treatment during a 24-week, observational lead-in period (Weeks 1-24), followed by 24 weeks of open-label memantine-ChEI treatment (Weeks 25-48). The patients underwent MRI at Weeks 1, 24 (Baseline), and 48 (Endpoint), and a battery of cognitive evaluations at Weeks 1, 24, 28, 36, and 48. The primary outcome measure was the annualized rate of change (%) in total brain volume (TBV) during Weeks 25-48, compared with the rate during Weeks 1-24. Other a priori measures included differences in the annualized rate of change in Right and Left Hippocampal Volume (RHV, LHV) and Brain Ventricular Volume (VV), as well as changes in performance on a battery of cognitive tests. Changes between the two periods were also analyzed post hoc, using Markov chain models. All comparisons were performed using paired t-tests; OC results are presented. (Sponsored by Forest Laboratories, Inc.)

Results: The change in RHV during Weeks 25-48 was the only MRI measure that was significantly different from the changes observed during Weeks 1-24 (-5.5 ± 12.0% vs -10.8 ± 7.2%; P=0.04), and it was also significantly smaller than the value that would be expected from the changes observed in the lead-in period (Markov chain analysis; P<0.001). Also, mean improvements on confrontation naming ability (Boston Naming Test) and executive function (Trail Making Test-B) during Weeks 25-48 were significantly different from the mean declines observed for Weeks 1-24 (P=0.034 and P=0.001, respectively).

Conclusions: In some patients with AD, memantine-ChEI treatment may slow the atrophy of the right hippocampus, suggesting a possible effect on disease progression, while providing a clinically meaningful slowing of decline in language abilities and executive function.

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NR2-081

POST-STROKE DEMENTIA: COGNITIVE FUNCTION EVALUATION WITHIN THE FIRST SIX MONTHS AFTER A STROKE

Angela Iragorri M.D., Olga L. Pedraza M.D, Msc, Pablo Reyes, Sandra Plata, Laura Castiblanco M.D, Fabián Gil, Diana Torres M.D, Erick Sánchez M.D, Luis Morillo M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the importance of screening for dementia in patients suffering stroke

SUMMARY:

Objective: Numerous studies have indicated the prevalence of post-stroke (within one year) dementia varies from 9% to 30% in developed countries. Unfortunately, the prevalence of post-stroke dementia in Latin American countries is unknown. The purpose of this study was to determine the number of patients who develop dementia during the first 6 months after a stroke.

Methods: Subjects (n=217) were patients admitted to San Ignacio University Hospital with the diagnosis of ischemic stroke between February of 2004 and February of 2005. Each subject and its family were interviewed and the IQCODE was applied. Patients with

the diagnosis of dementia before admission were excluded from the study. Patients without dementia at admission were evaluated using a standardized battery of evaluations which included: functionality tests (Barthel and Lawton), a depression test (Yesavage), a behavioral test (Kertesz), Hachinski Score and neuropsycological tests (MMSE, semantic and phonologic fluency, naming, Grober and Buschke, Rey figure, remote and recent memory, block design cubes, visual fluency, metaphors and similarities). For this group evaluation was repeated 6 months after stroke. Patients with severe global aphasia were excluded from analyses.
Results: 35 patients with dementia before admission and 7 patients with severe global aphasia were excluded from the study. Twenty-four patients died during the following-up phase of the study, 35 patients were lost during follow-up and 30 patients denied participation in the study. Eighty six patients were included in the study and evaluated six months after stroke; dementia was diagnosed during follow-up in 38 of them (44.1%).
Conclusion: The prevalence of poststroke dementia was 44.1% within the first six months among patients attending a University Hospital in Bogota , Colombia. Supported by Pontificia Universidad Javeriana Research funds

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2) Haring H. Cognitive impairment after stroke. Current Opinion in Neurology 2002; 15: 79-84

» NR2-082

MEMORY DYSFUNCTIONS OF THE MILD AND MODERATE TBI WITH FRONTAL LOBE INJURY

Jin-Sung Kim M.D., Bon-Hoon Koo, MD., Min-Ji Kim. MD., Kwang-Hun Lee, MD., Young-Hoon Han MD., Hye-Jeong Hong, MA.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand that TBI patients with frontal lobe injury have different memory abilities by severities of TBI.

SUMMARY:

The purpose of this study was to assess memory dysfunctions of the mild and moderate TBI patients with frontal lobe injury. The 110 patients were selected from both hospitalized and outpatient referrals. Among these patients, 20 patients(18.2%) are mild TBI with frontal lobe injury(FLI), 16 patietns(14.5%) are midl TBI without FLI, 51 patients(46.4%) are morderate TBI with FLI and 23 patients(20.9%) are moderate TBI without FLI. All of patients was administrated memory test using Korean version of Memory Assessment Scale(K-MAS). As results, summary scale scores including Immediate, Verbal, Visual and Global memory abilities did not showed any difference between TBI patients with and without frontal lobe injury, but showed different results by types at severities. TBI patient with frontal lobe injury showed higher Global memory ability than TBI patients without frontal lobe injury patients at mild traumatic brain injury state, but moderate TBI patients showed lower Verbal and Global memory abilities than TBI patients without frontal lobe injury at moderate traumatic brain injury state. Some subscale scores and Cued recall: list recall score showed same results as above. It suggested that assessment tool or paradigm(clinical vs. experimental, theoretical) of memory abilities in TBI patients with frontal lobe injury was selectively applied considering TBI severities.

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1) Vakil, E. (2005). The effect of moderate to severe traumatic brain injury (TBI) on different aspects of memory: A selective review. Journal of Clinical and Experimental Neuropsychology 27: 977-1021.

2) McDonald, B. C., & Flashman, L.A., & Saykin, A.J. (2002). Executive function following traumatic brain injuy: Neural substrates and treatment strategies. NeuroRehabilitaition 17: 333-344.

» NR2-083

SKIN TOLERABILITY OF RIVASTIGMINE TRANSDERMAL PATCH: LARGE PLACEBO-CONTROLLED MULTICENTER TRIAL IN MILD TO MODERATE ALZHEIMER'S DISEASE

Martin Farlow, Jeffrey Cummings, Jason Olin

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to review the skin-tolerability profile of the rivastigmine transdermal patch and understand how these results compare with data obtained with older patches that use 'reservoir' technology.

SUMMARY:

Purpose: Patches offer non-invasive smooth and continuous drug delivery, and are associated with potentially enhanced efficacy and improved systemic tolerability. On the other hand, patches have the potential to cause skin irritation. Modern 'matrix patches' are designed to minimize skin irritation. Rivastigmine has been available as a matrix patch for >1 year in the USA. The purpose of this analysis was to describe the skin tolerability profile of a modern 'matrix' patch.
Methods: The development program for rivastigmine patch included a 24-week double-blind randomized clinical trial (RCT) in 1,195 patients with mild to moderate Alzheimer's disease. Long-term (52 weeks) safety and tolerability were assessed in an open-label extension of this RCT. A targeted scale was used to collect skin irritation data (rather than relying on spontaneous adverse event reports), and was expected to provide a conservative estimate of skin tolerability.
Results: During the RCT, 98.2% of patients using the 4.6 mg/24 h rivastigmine patch reported 'no, slight or mild' irritation as their most severe application-site reaction. 89.6% of patients using the 9.5 mg/24 h rivastigmine patch reported 'no, slight or mild' irritation as their most severe reaction. Irritation seldom led to discontinuation (e.g., 2.4% in the 9.5 mg/24 h patch group). During the open-label extension >90% of all patients experienced 'no, slight or mild' irritation as their most severe reaction, comparable to results from the double-blind RCT. There was no trend towards an increase in the severity of adverse skin reactions over time. Symptoms most commonly reported with rivastigmine patch were erythema and pruritus.
Conclusion: Overall, rivastigmine patch was well tolerated. Of patients who experienced skin irritation, most reported slight or mild skin erythema that was not severe enough to lead to discontinuation. Irritation rates compare favorably over older patches using 'reservoir' technology, and appear to represent an advance in drug delivery design.

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» NR2-084

A 24-WEEK PLACEBO-CONTROLLED TRIAL OF RIVASTIGMINE CAPSULE IN PATIENTS WITH PARKINSON'S DISEASE DEMENTIA: ANALYSES OF NEUROPSYCHIATRIC INVENTORY ITEMS

James E. Galvin, James B. Leverenz, Daniel Weintraub, Jason Olin

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to review the data on the effect of rivastigmine treatment on neuropsychiatric symptoms in patients with Parkinson's disease

dementia.

SUMMARY:

Purpose: In a previously published randomized, double-blind, 24-week trial in PDD, rivastigmine capsules demonstrated statistically significant improvements versus placebo on both primary (cognitive and global) and secondary outcomes, including the total 10-item Neuropsychiatric Inventory (NPI-10) score. The purpose of these secondary analyses was to examine treatment effects on the 12-item NPI (NPI-12), including the 12 individual NPI items.
Methods: The current analysis investigated rivastigmine–placebo differences on NPI-12 individual item scores, using the observed case (OC) approach with patients who were experiencing symptoms at baseline (i.e. patients reporting a score of > 0 on any individual item). Treatment differences at 24 weeks were assessed using the van Elteren test blocking for country.
Results: In total, 541 patients participated in the study (mean age 72.7 years, 35% women, baseline MMSE 19.3). 449 patients (290 rivastigmine, 159 placebo) provided data for this analysis. In patients experiencing respective symptoms at baseline, rivastigmine was significantly superior to placebo in improving euphoria/elation ($p = 0.04$) and irritability/lability ($p = 0.03$). In addition, numerical improvements that did not reach statistical significance were seen for delusions, hallucinations, agitation/aggression, anxiety, apathy/indifference, disinhibition, aberrant motor behavior, and appetite/eating change. Rivastigmine was associated with non-significant worsening on depression/dysphoria and sleep/night-time behavior.
Conclusion: Rivastigmine led to numerical improvements compared with placebo on most NPI items. PDD patients suffering from these symptoms may find relief with rivastigmine in terms of symptom resolution or reduction, in addition to the benefits previously described regarding the cognitive and functional effects of cholinesterase inhibitor treatment.

This study was supported by Novartis Pharma AG.

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2) Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J: The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. Neurology 1994;44:2308–2314

» NR2-085

UNDERREPRESENTATION OF ELDERLY MINORITY IN ANTIDEPRESSANT TRIALS

Geena Athappilly M.D., Maria German,M.D., Moises Martinez,M.D, Shunda McGahee, M.D., Maria Llorente,M.D.

EDUCATIONAL OBJECTIVES:

Studies have suggested that elderly minority are underrepresented in clinical trials. The implications of this exclusion are multi-fold. Different polymorphisms of CYP450 exist and vary by race. This study aims to examine and demonstrate the level of representation of elderly minority in clinical trials involving antidepressants for the treatment of depression and thereby, questions the generalizability of clinical trials.

SUMMARY:

Methods: A Pub Med Search was conducted using the key words "antidepressant clinical trials" and search criteria: English, human, randomized, controlled trials, and 1990-present. Among these trials, only studies that reported depression as the outcome measure were included. Variables compared were age, gender, race, ethnicity, setting, funding source, study N and duration. In order to asses the representation of elderly minority, the studies were divided into two groups by age. Results: 115 studies met the inclusion criteria. 70.4% were in the younger group, and 63.2% were female. In the older group, 64.1% of the study population was female. 56.5% of the studies did not report race. Of the remaining 43.5% which did, Caucasians ranged from 64.9-99.6%. In the older group, Caucasians ranged from 65-99.6%. 72.2% of the 115 trials did not comment on ethnicity, and in the older group, the breakdown was as follows: 67.6%-African Americans, 79.4%-Hispanics, 76.5%-Asians, and 67.6%-other. The funding sources for the older group were: 26.5% Federal, 50% Pharma, 2.9% Other, 11.8% Both.
Conclusions: The results of this literature review suggest that minorities are underrepresented in antidepressant clinical trials in adult populations. It was surprising that even more recently published studies failed to adequately describe the race and/or ethnicity of the study population. It was also surprising that Federally-funded projects seemed to be no more representative of diversity, than Pharma studies. Clinical differences between the elderly minority and the majority population represented in most antidepressant clinical trials call into question the generalizability of results of these studies to guide diagnosis, management, and treatment of a diverse group of elderly.

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» NR2-086

EFFECT OF ETHNICITY ON PSYCHIATRIC DIAGNOSIS IN A GROUP OF FOREIGNERS PRESENTED TO MENTAL HEALTH SERVICES IN SAUDI ARABIA

Ghada Taha, Farouk Lotaief, M.D., Ghada Abdel Razek, M.D., Yasser Abdel Razek M.D., Khaled Abdel Azim, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to Identify the impacts of ethnic and cultural background on clinical presentation and variation in psychiatric diagnoses

SUMMARY:

Background: Previous studies reported that ethnic differences exist in patterns of psychiatric diagnosis and management, increasing the overloads on and demands from psychiatric services. Aim: To study the demographic and clinical characteristics of a group of foreigners utilizing psychiatric emergency room service in a large governmental Saudi hospital for mental health and to study the influence of ethnic/cultural background on clinical presentation and variation in psychiatric diagnosis. Methods: All foreign patients presented to the psychiatric emergency room over 1 year duration were involved. Demographic and clinical data were obtained cross-sectional. All patients were assessed twice; first in ER and second time either in psychiatric ward after admission or in the outpatient clinic if not admitted.. Results: A total of 112 foreign patients were included. Help seeking behavior was significantly different between groups. Admission rates were high especially among South East Asians. Psychotic and stress related disorders were more likely diagnosed in South East Asians and Asians while Mediterranean and African patients were more likely diagnosed with affective disorders. Although there was significant diagnostic difference between ER and final diagnosis, however, it was more related to the nature of presenting symptoms and symptoms after observation rather than to the effect of ethnicity. Discussion: This preliminary study shows that the ethnic background of foreign population may possibly influence psychiatric diagnosis and disposition from psychiatric emergency room. South East Asians are more likely to be hospitalized and labeled with psychotic and neurotic disorders than other ethnicities. However, there is still probability of diagnostic bias because of cultural gap between clinicians and foreign patients.

REFERENCES:

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2) Primm AB: Understanding the significance of race in the psychiatric clinical setting. Focus, 2006, 1, 6-8

» NR2-087

THE EFFECT OF TYPE-D PERSONALITY AND A PARTNER ON EMOTIONAL DISTRESS

Ko Young-Hoon M.D., Moon-Soo Lee, M.D., Ph.D., Hong Euy Lim, M.D., Ph.D., Young-Min Park, M.D., Ph.D., Sook-Haeng Joe, M.D., Ph.D., Chang-Su Han, M.D., Ph.D., Rhee-Hun Kang, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the effect of Type D personality and the existence of a partner on depression.

SUMMARY:

Objective: Type D personality is known to be a risk factor for the negative outcomes of cardiovascular disorder. The cultural difference of the combined effect of type D personality and other mediating factors in Asian population has not been reported. We tried to find out the influence of type-D personality in relation with the various measures on symptoms of anxiety and depression. Methods: Normal controls (N = 953), patients with hypertension (N = 175), and with coronary heart disease (N = 111) were recruited. All the participants completed self-report measures on type-D personality, screening instruments including a questionnaire upon socio-demographic aspects (sex, age, education level, poorly perceived health and history of psychiatric treatments), state subscale of Spielberger State and Trait Anxiety Inventory, and Center for Epidemiologic Studies Short Depression Scale. Results: In multivariable logistic regression analysis, type-D with a partner (OR = 5.62; 95% CI = 3.84 – 8.24), and type-D with no partner (OR = 7.01; 95% CI=4.24 – 11.61) were significant predictors of anxiety, adjusting for all other variables. In addition, type-D with a partner (OR = 9.28; 95% CI = 5.87 – 14.67), and type-D with no partner (OR = 19.01; 95% CI = 10.81 – 33.45) were significant predictors of depression, adjusting for all other variables. Poorly perceived health status was also a significant predictor of both anxiety and depression. In multivariable analysis to identify the difference within type-D personality in relation to the presence of a partner, type-D with no partner group (OR: 1.81; 95% CI=1.13-2.90) remained a significant predictor of depression, but did not a predictor of anxiety, adjusting for all other variables. Conclusion: Type-D patients without a partner were related with increased risk of symptoms of depression. Clinicians need to identify type-D patients, as they tend to show more clinically significant depression and anxiety as psychiatric problems.

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» NR2-088

CULTURAL IDENTITY, QUALITY OF LIFE, AND MENTAL HEALTH IN FIRST-GENERATION IMMIGRANTS

Maria Zapata-Vega M.D., Maria A. Ruiperez, Ph.D., Juan E. Mezzich, M.D.,Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the impact of cultural identification in the quality of life and the mental health of first-generation immigrants.

SUMMARY:

Objectives: The aim of this study is to assess the relationship between cultural identity and measurements of quality of life (QOL) and mental health (MH).

Methods: A sample (N=236) of first-generation Latino, Korean and Chinese psychiatric patients in New York completed a set of 3 scales: the Modified Cortes, Rogler, and Malgady's bicultural scale (M-CRM-BS), the Multicultural Quality of Life Index, and the Personal Health Scale (PHS) which is a 10-item MH screening composed of three subscales assessing psychiatric symptoms, functioning, and one's insight into the need for professional help. Using the M-CRM-BS, subjects were classified into groups based on their identification with their culture of origin only ("traditional", n=95), the mainstream-US culture only (n=18), both ("bicultural", n=102), or none (n=21).

Results: A statistical significant difference was found among the four groups of cultural identification on QOL mean scores ($F=5.65$, $p=0.001$), PHS mean total scores ($F=7.34$, $p<0.001$) and its symptoms ($F=3.25$, $p=0.023$) and functioning ($F=3.68$, $p=0.013$) subscales. Games-Howell post-hoc test showed that the "bicultural" group had significantly higher mean QOL scores than the "traditional" group (5.78, SD=2.02 vs. 4.69, SD=1.74, $p=0.001$). Bonferroni post-hoc test showed that the "bicultural" group had significantly lower MH screening mean scores than the "traditional" group, including the PHS total scores (8.46, SD=4.9 vs. 11.63, SD=4.94, $p<0.001$), symptoms (2.04, SD=1.2 vs.2.56, SD=1.17, $p=0.023$) and functioning (1.98, SD=1.74 vs. 2.78, SD=1.7, $p=0.013$) subscales.

Conclusions: Bicultural identification (as opposed to identifying solely with the culture of origin) in first-generation mentally ill immigrants is associated with both better quality of life and better mental health measurements. These findings challenge the conventional unidirectional model of assimilation and encourage biculturalism as a potential asset to enhance the wellbeing of immigrants.

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» NR2-089

BODY APPEARANCE, WEIGHT PRECOCCUPATIONS, AND EATING HABITS-GENDER DIFFERENCES IN MEDICAL STUDENTS- A STUDY IN MUMBAI, INDIA

Tushita Mayanil M.D., Neena Sawant, M.D., Shubhangi Parkar, M.D., Ph.d.,Biswarup Ghosh, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand gender differences in Indian medical students regarding perceptions of appearance beliefs, satisfaction with body areas,weight preoccupation, eating behaviors and its correlation with appearance beliefs and weight preoccupation.

SUMMARY:

Body image being the underlying theme in eating disorders has been a subject of extensive research and is conceived as one's attitudinal disposition towards physical self and includes cognitive and behavioral components. Though medical school curriculum exposes the medical students to scientific knowledge of the human body, they are not immune to the influence of the media. Obsession with "ideal" body image is no longer a female preoccupation only. Our study has been done in Mumbai,India where eating disorders- traditionally a Western diagnosis have only rarely been found. Methods- After a valid consent,280 second & third year medical students filled out proformas designed to study their

knowledge of body image, MBSRQ(Multidimensional Body Self Relations Questionarre)-69 item self report inventory for body image constructs and EAT(Eating Attitudes Test). 204 completed proformas were analysed for gender differences using chi square, unpaired t test and Pearson's coefficient where applicable.
Results & Discussion-Mean age for males was 21.26 years and females was 21 years. 83% felt media/TV was the main source of information about body image and eating practices. Female medical students had significantly higher overweight preoccupation whereas males scored significantly more in fitness orientation and health evaluation. 52% of males perceived their weight as normal compared to only 36% of the females. 7-10% of medical students had incorrect eating practices like starvation and skipping meals though majority ate a well balanced meal inspite of an academically demanding schedule.Both genders had a significant negative correlation of eating behaviours with appearance evaluation and body areas satisfaction and positive correlation with overweight preoccupation. Implications-Though tradionally a "Western" disorder, weight and body image preoccupation and incorrect eating behaviors needs to explored in medical students especially females in developing countries.

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» NR2-090

DROP-OUT FROM IN-PATIENT TREATMENT FOR EATING DISORDER : THE ROLE OF PERSONALITY FACTORS

Alexandra Pham-Scottez M.D., Ludovic Gicquel, MD., Roland Dardennes, PhD., Frederic Rouillon, PhD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to better understand the role of personality and Personality Disorders in the eating disordered patient's decision of premature termination of hospitalization.

SUMMARY:

Objective : Eating Disorders are associated with a chronic and long-term course, and drop-out from treatment is a serious problem which remains poorly understood. The purpose of this study was to identify personality factors associated with drop-out from adult in-patient treatment for Eating Disorders.
Method : 100 consecutive patients hospitalised in an Eating Disorder Unit were included. All patients were assessed for demographic variables, clinical features and DSM-IV Personality Disorders (SIDP-IV) and personality factors (NEO-PI-R, TCI).
Results : Data indicated that only comorbidity with a DSM-IV personality Disorder and a low Self-Directedness TCI score were statistically predictive of premature discharge. No other personality factor, demographic or clinical feature was associated with drop-out.
Conclusion : Personality Disorders are important clinical predictors of premature discharge from hospitalisation for the treatment of Eating Disorders. The implications for clinical practice, in order to diminish the rate of drop-out, and for future research in this area will be discussed.

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» NR2-091

DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF QUETIAPINE FOR ANOREXIA NERVOSA: PRELIMINARY REPORT

Pauline Powers M.D., Megan Klabunde, M.A., Mary Ellen Trunko, M.D., Patti Lowery, Vikas Duvvuri, M.D., Ph.D., Walter Kaye, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of presentation the participant will:
(1) understand the complications in recruiting anorexia nervosa patients for clinical drug trials
(2) be able to describe key symptoms of anorexia nervosa and common co-morbid disorders that should be assessed in the evaluation of possible effective pharmaceutical agents
(3) be able to describe the possible benefits and risks of atypical antipsychotics in the management of anorexia nervosa

SUMMARY:

Introduction: The treatment of anorexia nervosa (AN) is complex. The atypical antipsychotics may be helpful. An open study with quetiapine was associated with improvements in depression, anxiety, and obsessive compulsive symptoms. Methods: Adult patients were recruited who met DSM-IV-TR criteria for AN and were at least 15% below ideal body weight. After psychiatric evaluation, laboratory testing, and physical assessment, a test battery was completed and patients were randomized to placebo or quetiapine. Dose ranged from 100-400 mg. Periodic assessments were performed during the 8 week study. Results: During the last two years 207 patients have been screened, 24 enrolled, and 17 have been randomized to study drug. All 17 were seen at least once after randomization. Nine patients have completed the study. Mean age of the patients was 33 years (range 18-61), all but one were female, and mean body mass index at baseline was 15.9. For the total group there was modest weight gain of slightly less than 2 lbs. in 8 weeks, a mean improvement in the Hamilton Depression Index score (p=.0031), and an improvement in the mean Trait score of the State Trait Anxiety Inventory (p=.0120). Among subjects who received placebo, rather than quetiapine, there was an improvement in the Drive for Thinness scale of the Eating Disorder Inventory-2 (p=.0454) and a trend for an improvement in the Body Dissatisfaction scale (p= .0661). There were three serious adverse events requiring hospitalization; two patients were on placebo and one was on quetiapine. None of these events were thought due to the study drug. Conclusions: There were improvements in measures of anxiety and depression in the entire group. It remains to be seen if there are differences between the two subgroups. As noted by other authors, enrolling AN patients in drug trials is difficult. This study was supported by a grant from AstraZeneca Pharmaceuticals.

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» NR2-092

IMPULSIVITY, BUT NOT SENSATION-SEEKING, AS A CHARACTERISTIC TRAIT IN BULIMIC SPANISH WOMEN

María Tajes-Alonso, María J. Gastañaduy-Tilve, M.D., Ramón Ramos-Ríos, M.D., Pablo Martínez-Gómez, M.D., Isabel González-Lado, M.D., Silvia Martínez-Formoso, M.D., Manuel Arrojo-Romero, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participants should be able to recognize some of the characteristic traits of women with bulimia nervosa that could be important for the management of the

disorder and of its most frequent comorbidities.

SUMMARY:

Objectives: Impulse control disorders (ICD) have been frequently reported in patients with bulimia nervosa (BN) and the personality traits of impulsivity and sensation-seeking are considered two of the most important predictors of the occurrence of ICD. The aim of this study is to measure impulsivity and sensation-seeking traits in a clinical sample of patients with BN.
Methods: Impulsivity, sensation-seeking and novelty seeking were assessed in 32 bulimic patients from the Eating Disorders Unit of Santiago de Compostela (Spain) and 38 healthy controls using the Barrat Impulsivity Scale (BIS-11), the Sensation-Seeking Scale-Form V (SSS) and the revised version of the Temperament and Character Inventory (TCI). Both groups were matched by age and educational background.
Results: Compared to healthy controls, bulimic patients show higher mean scores in global (53.84 vs. 39.39, p< 0.01), cognitive (17.13 vs. 12.13, p < 0.01) and motor impulsivity (19.28 vs. 11.32, p < 0.01) measured by the BIS-11. There were no significant differences in global scores of the SSS and novelty seeking dimension of the TCI. Similarly, no significant differences were noted in the subscales scores. Only a statistical trend toward higher "boredom susceptibility" mean score in the group of patients (3.59 vs. 2.84, p = 0.09) was found, that can be justified by the significant correlations of this trait with cognitive (r =0.353, p< 0.01) and motor impulsivity (r = 0.342, p< 0.01).
Conclusions: Bulimic patients were more impulsive in cognitive and motor areas than healthy controls. In contrast with previous reports, our results do not confirm the link between high sensation-seeking and bulimia nervosa. These results may be corroborated by further studies including larger sample sizes and patients with comorbid ICD.

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» NR2-093

THE EFFECT OF MEMANTINE ON SERUM TOTAL ANTIOXIDANT CAPACITY IN ALZHEIMER'S DEMENTIA

Jin Sook Cheon M.D., Byoung Hoon Oh, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand a mechanism of treatment effect of memantine on Alzheimer's dementia.

SUMMARY:

Objectives: To evaluate whether memantine causes change in a peripheral blood marker of oxidative stress, to identify influencing factors, and to suggest its usefulness to measure the effect of memantine in clinical practice. Methods: The subjects were consisted with 66 patietns with Alzheimer's dementia and 60 healthy aged controls. The demographic data were obtained by the structured interviews. The cognitive disorder was assessed by the MMSE, severity of dementia by the CDR and the GDS, and function by the ADL. The serum total antioxidant capacity (TAC) was measured by chemiluminescence method, once in the control group and three times (before memantine administration, 1 month after memantine administration and 2 months after memantine administration) in the patient group. Results: 1) As compared with TAC before memantine administration (mean 1.762, SD 0.133 mmol/L), TAC (mean 2.096, SD 0.172 mmol/L) increased at 2 months after, higher than TAC at 1 month after (mean 1.865, SD 0.283 mmol/L) and TAC of controls (mean 1.935, SD 0.194 mmol/L) (p<0.001, respectively). 2) TAC of patient group was different according to MMSE, CDR, GDS and ADL before, according to sex and age at 1 month after, and according to ADL at 2 months after memantine admnistration (p<0.005, respectively). 3) Effect of memantine on TAC correlated with sex, age and duration of dementia at 1 month after memantine administration, so did with severity of dementia (p<0.05, respectively). Conclusion: To evaluate effect of memantine treatment on moderate to severe Alzhimer's dementia, a peripheral blood marker of oxidative stress seemed to be preferable to clinical scales.

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» NR2-094

OVEREXPRESSION OF CELL CYCLE PROTEINS OF PERIPHERAL LYMPHOCYTES IN PATIENTS WITH ALZHEIMER'S DISEASE

Jaewon Chung M.D., Hyeran Kim, M.D., Ph.D.,Young-Ah Kwon, M.S., Inn Sook Ahn, M.A., Seonwoo Kim, Ph.D., Sangmee Ahn Jo, Ph.D., Doh Kwan Kim, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the association between cell cycle dysregulation and Alzheimer's disease.

SUMMARY:

Objective: Early recognition of Alzheimer's disease (AD) is important to facilitate early treatment. Biological markers for AD will help clinicians make objective diagnoses early during the course of dementia. A failure of regulation of the cell cycle has been proposed as a mechanism of neuronal apoptosis in AD. Moreover, previous studies have suggested that cell cycle dysregulation begins earlier than the onset of clinical manifestations in AD. The authors have previously demonstrated that the lymphocytes of AD patients, like neurons, are more vulnerable to cell death than those of control subjects. In the present study, the authors examined the lymphocyte expression of cell cycle proteins in AD, dementia controls (DC), and normal controls (NC). Method: One-hundred eleven subjects (31 AD, 31 DC, and 50 NC) were recruited. Dementia patients underwent neuropsychological evaluation. Peripheral venous blood was obtained from all study subjects. Cell cycle proteins CDK2, CDK4, CDK6, cyclin B, and cyclin D were measured in peripheral lymphocytes. Cell cycle protein expression in the three groups was compared after adjusting for age and sex. Results: Cell cycle proteins CDK2, CDK4, CDK6, cyclin B, and cyclin D were significantly higher in AD patients than in normal controls. The DC group manifested intermediate levels of cell cycle proteins compared to AD patients and NC subjects. Conclusions: The present study indicates that cell cycle proteins are upregulated in peripheral lymphocytes of AD patients. Cell cycle dysregulation in peripheral lymphocytes may present a promising starting point for the identification of peripheral biomarkers of AD.

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» NR2-095

FAMILY CAREGIVERS OF HOSPITALIZED PATIENTS WITH DEMENTIA REPORT GREATER DEPRESSIVE SYMPTOMS THAN CAREGIVERS OF OUTPATIENTS WITH DEMENTIA

Gary Epstein-Lubow M.D., Mathew Hinckley, B.A., Ellen Darling, B.A., Ivan W. Miller, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to list several factors that may contribute to increased depressive symptoms in family caregivers of patients with dementia.

SUMMARY:

Setting: Brown University; Butler Hospital Hypothesis: We hypothesized that caregivers of hospitalized patients with dementia would report greater depression compared with caregivers of outpatients with dementia.
Methods: Caregivers of individuals with dementia were recruited during the process of care-recipient treatment in either an outpatient clinic for memory disorders or an inpatient geriatric psychiatry service. Demographic information was collected along with self-adminstered measures of depression [The Center for Epidemiological Studies – Depression Scale, 10-item version (CES-D)], stress, burden and grief. Statistical analyses were conducted to determine group differences and predictors of depression severity.
Results: Forty-one inpatient and 44 outpatient caregivers (total N = 85) were recruited. The two groups did not differ except caregivers of inpatients were significantly younger and less likely to reside with the care recipient. Regarding depression, 63.4% of caregivers of inpatients and 43.2% of caregivers of outpatients scored within the clinical depressive symptoms range on the CES-D. Independent sample T-tests showed that caregivers of inpatients had greater severity of depression, burden, and grief. In linear regression models, when controlling for age and co-residence status, caregiving for inpatients remained a significant predictor of greater depression (Total R2 = .099; p = .046), but inpatient caregiving did not predict burden or grief.
Discussion/Significance: Some demographic differences do distinguish caregivers of inpatients and outpatients with dementia; however, caregiving for a hospitalized patient with dementia appears to be an additional independent risk factor for depression severity.

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» NR2-096

AGE-RELATED CHANGES IN THE VISUAL PROCESSING OF FACES: POTENTIAL SUPPORTIVE INTERVENTIONS FOR PERSONS WITH DEMENTIA

Jason Greenhagen B.S., Ann D. Gathers, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to 1) demonstrate an understanding of facial processing strategies; 2) understand the progression of normal face processing in aging; and 3) consider alternative compensatory strategies for better facial recognition in social settings.

SUMMARY:

Previous data support changes in face processing and recognition in the typical aging and dementia populations. The basic cognitive mechanism for these changes is still unknown. The current pilot study investigated the effects of aging on two types of face processing: featural, identification by individual face features such as the eyes or nose; and configural, identification by spacing between features. Based on existing developmental and aging literature, this study posed that older adults rely on configural processing less than young adults. To address this hypothesis, 13 young adults (18-35 years) and 13 older adults (60 years and greater) participated in a behavioral same/different face-matching task in which featural or configural manipulations occurred in different face pairs. Overall, reaction and accuracy rates indicated increased difficulty in face processing with age. Older adults were slower and less accurate than younger adults. Contrary to the hypothesis, older and younger adults were equally proficient at configural processing tasks, but younger adults performed significantly better on featural processing tasks than older adults. Face processing findings in aging may provide insight into compensatory strategies to benefit the social and personal lives of older adults and their families.

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» NR2-097

SUCCESSFUL AGING IN OLDER ADULTS WITH SCHIZOPHRENIA: PREVALENCE AND ASSOCIATED FACTORS

Fayaz Ibrahim M.D., Carl I. Cohen, M.D., Paul M. Ramirez, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognise the variables associated with successful aging and will be able to identify better targets for intervention among persons with schizophrenia.

SUMMARY:

Objective: Little is known about the prospects for successful aging among persons with schizophrenia.This study contrasts the prevalence of successful aging in older adults with schizophrenia with their age peers in the general community, and also examines variables associated with successful aging in the older population with schizophrenia.
Methods: The schizophrenia group consisted of 198 community-dwelling persons aged 55 years and older who developed schizophrenia before age 45 years. A community comparison group (N = 113) was recruited using randomly selected block-groups. The three objective criteria proposed by Rowe and Kahn were operationalized using a 6-item summed score. Moos' Ecosystem Model was used to examine the association of 16 predictor variables with the Successful Aging Score in the schizophrenia group.
Results:The community group had significantly higher Successful Aging Scores than the schizophrenia group (4.3 vs. 3.0; t=8.36, df=309, p<.001). Nineteen percent of the community group met all six criteria on the Successful Aging Score versus 2% of the schizophrenia group, and there were significant group differences in the distribution of the scores. In regression analysis, only 2 variables –fewer negative symptoms and a higher Quality of Life Index—were associated with the Successful Aging Score within the schizophrenia group.
Conclusion: Older adults with schizophrenia rarely achieve successful aging and it occurs much less commonly than among their age peers. Only two significant variables were associated with successful aging, neither of which are easily remediable. The elements that comprise the components of successful aging such as health, adaptive functioning, and social engagement may be better targets for intervention.

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» NR2-098

OVERGENERALITY OF AUTOBIOGRAPHICAL MEMORY IN PATIENTS WITH EARLY ALZHEIMER'S DISEASE

Luisa Jurjanz, Markus Donix, M.D., Christina Brons, M.D., Katrin Poettrich,Ph.D., Peter Winiecki, Ph.D., Vjera A. Holthoff, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand that in very early AD patients autobiographical memory reveals an excess of overgenerality of categoric memories and the implications for daily functioning such as social problem solving.

SUMMARY:

Objectives: This study was aimed at identifying whether patients suffering very early Alzheimer's disease (AD) reveal an excess of categoric memories during autobiographical memory (ABM) retrieval by administering an ABM specificity measure. Specificity of autobiographical memories has implications for every day social problem-solving performance and is therefore an important clinical feature.
Method: Sixteen very early AD patients (aged 63.1 years ± 5.78; MMST 27.6 ± 0.81) and 16 healthy controls (HC; aged 62.9 ± 5.73), matched for gender and educational level underwent a cued-recall task. Participants were presented cue words (positive/negative) and were required to produce a specific autobiographical memory within 60 seconds. Responses were rated as categoric, extended or specific. A battery of neuropsychological tests provided an independent estimate of cognitive deficit severity in several cognitive domains.
Results: Compared to HC, AD participants produced significantly higher numbers of categoric and extended memories and significantly fewer specific memories. No difference was revealed between both groups related to the valence of the cue words.
Conclusion: In early AD autobiographical memory retrieval revealed an excess of overgenerality of memories. The data suggest a stop at the categoric description stage and a lack of cognitive resources to conduct a directed search for a specific memory.

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» NR2-099

EFFECTS OF APOLIPOPROTEIN E GENOTYPE ON MORTALITY IN PATIENTS WITH ALZHEIMER'S DISEASE

Shin Gyeom Kim M.D., Han Yong Jung, MD, PhD1, So Young Lee, MD, PhD1, Eun Young Shin, MD1, Yu Jin Lee, MD1, Joon Ho Park, PhD1, Yeon Jung Lee2, MD,Sung Il Woo, MD, PhD2

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that the e4 allele of apolipoprotein has associated with an increased risk and earlier onset of Alzheimer's disease, but whether it affects mortality in patients with the disease is not consistently confirmed. This study is the first report about the effect of the e4 allele on mortality in oriental ederly with AD and provides an ethnic information about variation in association between AD and apolipoprotein.

SUMMARY:

Background/Objectives: The e4 allele of apolipoprotein(APOE) has associated with an increased risk and earlier onset of Alzheimer's disease(AD), but whether it affects mortality in patients with the disease is not consistently confirmed. This study aimed to assess the effect of APOE e4 allele on mortality in patients with AD.
Methods: APOE genotyping had been performed on 200 patients recruited from patients with probable AD registered in the Dementia and Age-associated Cognitive Decline Clinic of an university hospital and in a service program for the early detection and management of dementia in the community between 1996 and 2006. All the subjects had been examined according to the protocol of the Korean Version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet (CERAD-K) at baseline. Subjects were dichotomized into 88 patients with and 112 patients without at least one e4 allele. Cox's proportional hazards regression models were used to identify the effect of the selected variables including the e4 allele on mortality.
Results: Forty patients with and 49 patients without the e4 allele were had died by December 2006. Median survival from onset of AD did not differ by the e4 allele carrier status(10.2 years in the e4-positive group, 9.1 years in the e4-negative group). There were no differences between e4-positive and e4-negative group in age at baseline, sex, education, age at onset, duration of AD, severity of dementia. Significant factors that affects mortality during the follow-up included age at baseline and age at onset. Adjusting for age at baseline and age at onset, the presence of an e4 allele did not show increased risk of mortality (RR = 0.98, 95% CI = 0.64-1.49) and the risk of effect of the e4 allele not vary by age, sex, education in this sample.
Conclusions: This study provide the first information about the effect of the e4 allele on mortality in oriental ederly with AD. The APOE e4 allele was not associated with mortality in patients with AD.

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» NR2-100

THE RIVASTIGMINE TRANSDERMAL PATCH COMPARED WITH THE RIVASTIGMINE CAPSULE IN PATIENTS SWITCHED FROM DONEPEZIL: SAFETY DATA FROM THREE CLINICAL TRIALS

Jason Olin Ph.D., Carl H. Sadowsky, M.D., Xiangyi Meng, Ph.D.

EDUCATIONAL OBJECTIVES:

Treatment of Alzheimer's disease (AD) with cholinesterase inhibitors is often associated with gastrointestinal (GI) adverse events (AEs). At the conclusion of this presentation, the reader will have ascertained that the rivastigmine transdermal patch is associated with a favorable tolerability profile, with fewer GI AEs and discontinuations due to AEs than the rivastigmine capsule, in patients (pts) with moderate AD who have switched from donepezil.

SUMMARY:

Objective: To analyze data from three open-label trials to compare the safety and tolerability of switching to rivastigmine capsule or transdermal patch from donepezil in pts with moderate AD.
Method: Study US38 was a 25-week, randomized, parallel-group study investigating the switch (immediate or after 7 days' withdrawal) from donepezil to rivastigmine transdermal patch (4.6 mg/24 hr). Two studies investigated the switch from donepezil to rivastigmine capsules (3–12 mg/day). Study US13 was a 26-week, single-arm, immediate-switch study. Study US18 was a 26-week,

sequential cohort study. Pts switched immediately or after 7 days' withdrawal. Safety outcomes included adverse events (AEs), discontinuations due to AEs and serious AEs (SAEs).
Results: At baseline, pts receiving the rivastigmine patch (n=261) had a mean (SD) age of 77.3 (8.0) years, dementia duration of 3.9 (2.6) years and MMSE score of 18.3 (3.99). Pts receiving rivastigmine capsules (n=331) had a mean (SD) age of 78.1 (7.8) years, dementia duration of 3.6 (2.2) years and MMSE score of 17.9 (4.4). One hundred and eighty four (70.5%) pts receiving the patch experienced at least one AE, and 23 (8.8%) experienced an SAE, compared with 276 (83.4%) and 55 (16.6%) pts, respectively, who received capsules. Of the pts who experienced an AE, 10 (3.8%) and 109 (32.9%) experienced nausea, and 11 (4.2%) and 80 (24.1%) experienced vomiting with the patch and the capsule, respectively. Discontinuations due to AEs occurred in 38 (14.6%) pts who received the patch, the most common reasons being application site reaction and disease progression. Discontinuations due to AEs occurred in 64 (19.3%) pts who received the capsule, most commonly owing to nausea and vomiting.
Conclusions: The rivastigmine transdermal patch appears to provide a better tolerability profile than rivastigmine capsules, particularly in terms of GI AEs and discontinuations due to these AEs.
This study was funded by Novartis Pharmaceuticals Corp.

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» NR2-101

A CROSS-SECTIONAL COMPARISON OF THE CLINICAL FEATURES OF ADULT VERSUS GERIATRIC BIPOLAR PATIENTS IN AN URBAN OUTPATIENT SETTING

Ilyse Rosenberg D.O., James Prosser, M.D., Khayti Shah, M.D., Igor Galynker, M.D., Melinda Lantz, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to compare and contrast bipolar disorder among geriatric patients compared to younger patients. In particular comparing psychiatric com-morbidities, history of suicide, history of violence, and past non-psychiatric hospitalizations.

SUMMARY:

Introduction: Geriatric bipolar disorder is a chronic and debilitating disease associated with increased morbidity and mortality. There is little published data on its prevalence, epidemiology or clinical features. Methods: We reviewed 133 patient charts with the diagnosis of bipolar disorder in an urban outpatient clinic setting from June 2006 to September 2007: 67 patients 55 and older, and 66 patients younger than 55. The average age of the Age > 55 group was 62.6 years. The average age of the Age < 55 group was 41.0 years. We compared the groups based on age, frequency of comorbid axis one diagnosis, comorbid axis two diagnosis, psychopharmacology management, co-morbid medical diagnosis, history of violence, history of suicide, past hospitalizations, and psychiatric symptoms Results: The prevalence of geriatric bipolar patients was 4.3% compared to 9.1% for the younger subset. Statistical significance was noted between the age groups for the frequency of two or more co-morbid axis one disorders (5.9% geriatric vs. 25.5% for younger patients); frequency of co-morbid borderline personality disorder (4.5% for geriatric patients vs. 24.6% for younger patients), history of suicide attempts (14.9% for geriatric patients vs. 43.9% for younger patients); history of violence (1.5% for geriatric patients vs. 15.1% for younger patients), and number of non-psychiatric hospitalizations (1.39 for geriatric patients vs. 0.12 for younger patients). Conclusion: Geriatric bipolar patients have more co-morbid axis one diagnosis, lower rates of suicide, lower rates of past violence, and more non-psychiatric admissions compared to younger adults. The management of bipolar disorder is complex and reflects the multiple co-morbid conditions associated with an aging population.

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» NR2-102

SWITCHING FROM DONEPEZIL TO RIVASTIGMINE TRANSDERMAL PATCH: CLINICAL OUTCOMES AND PREFERENCE OVER 25 WEEKS IN PATIENTS WITH ALZHEIMER'S DISEASE

Carl Sadowsky M.D., Alan Dengiz, M.D., Xiangyi Meng, Ph.D., Jason T. Olin, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the reader will understand that switching to the rivastigmine transdermal patch from donepezil in patients (pts) with mild-to-moderate Alzheimer's disease (AD) is associated with maintenance of cognition, behavior and global functioning during long-term treatment.

SUMMARY:

Objective: Clinical benefits of rivastigmine are well established in pts with AD. Previous studies have shown the benefit of switching from donepezil to rivastigmine capsules. This analysis evaluates the long-term efficacy associated with switching from donepezil to the rivastigmine transdermal patch in pts with mild-to-moderate AD.
Method: In this randomized, prospective, open-label, parallel-group study, pts (aged >=50 years; Mini-Mental State Examination [MMSE] score 10–24) were switched immediately or after 7 days' withdrawal from 5–10 mg/day donepezil to rivastigmine transdermal patch (4.6 mg/24 hr). A 5-week phase was followed by a 20-week, open-label extension. Efficacy outcomes included cognition (MMSE), behavior (neuropsychiatric inventory [NPI]), global functioning (Clinical Global Impression of Change [CGIC]) and pt preference. Activities of daily living (ADLs) were also assessed. 95% confidence intervals (CIs) for the mean change from baseline were reported.
Results: A total of 261 pts (mean age 77.3 ± 8.04 years; 58% female; mean dementia duration 3.9 ± 2.61 years) received rivastigmine. The Week 5 mean CGIC scores suggested no worsening in either group (3.9 immediate vs 4.0 delayed switch). The percentage of pts with no decline (CGIC rating <=4) was 82.5 and 75.2%, respectively. At Week 25, there was no significant deterioration from baseline in cognitive function. The combined mean change from baseline in NPI score was 0.2 (95% CI [–1.4, 1.8]). The mean change from baseline in ADCS-ADL score was –4.1 (95% CI [–5.4, –2.8]). More pts (55%) preferred rivastigmine transdermal patches to a tablet.
Conclusions: In the absence of a placebo control, the results of this study suggest that most pts with mild-to-moderate AD may be switched from donepezil to the rivastigmine transdermal patch with no significant deterioration in cognition, behavior and global functioning. This study was funded by Novartis Pharmaceuticals Corp.

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» NR2-103

INTERACTIVE WEB-BASED NETWORKING TOOL FOR LINKING SERVICES AND INTERVENTIONS RESEARCH TRAINING AND EDUCATION PROGRAMS

Brian Shanahan, Stephen J. Bartels, M.D., M.S.., Martha L. Bruce, M.D., M.P.H., Jürgen Unützer, M.D., M.P.H., Yvette Sheline, M.D, Jo Anne Sirey, Ph.D, Gwenn Smith, Ph.D., Jeffrey Lyness, M.D., Patricia Arean, Ph.D., Yeates Conwell, M.D., Benjamin Druss, M.D., M.P.H., Paul Duberstein, Ph.D., Joseph Gallo, M.D., M.P.H., Anand Kumar, M.D., Benoit Mulsant, M.D., Bruce Pollock, M.D., Ph.D., David Steffens, M.D., M.H.S.

EDUCATIONAL OBJECTIVES:

Identify how geriatric mental health researchers will benefit from increased interaction with mentors and colleagues. Recognize the importance of having a pool of researchers dedicated to finding novel interventions and services in geriatric mental health. Discuss how interactive Web-based tools can be used to assist in mentoring and career advancement of geriatric mental health researchers.

SUMMARY:

Objective: By 2011, the youngest members of the 78-million baby boomer generation will turn 65, and, by 2030, around one-fifth of the US population will be over 65.1 The 2003 Report of the Subcommittee on Older Adults for the President's New Freedom Commission on Mental Health recognized the dearth of clinicians and researchers and identified support for mental health and aging research as a major priority.2 The mounting public health burden of mental illness in this population requires an increase in specialized investigators that can research geriatric mental health disorders and introduce interventions to treat them

Methods: MedEdSeminar is a Web-based collaboration system that supports distance mentoring and career advancement for junior investigators who are preparing to submit applications for independent research funding for geriatric mental health research. The site provides an environment in which to share resources (ie, articles, event announcements) and a Live Meeting tool to facilitate live mentoring between geographically dispersed mentors and scholars.

Results: The Web site is currently utilized by members of two workgroups comprising junior investigators and mentors who are participants in geriatric psychiatry research training programs funded by the NIMH. Since 2004, MedEdSeminar has hosted over 50 live seminars for workgroup members.

Conclusion: The MedEdSeminar hub links senior investigators (mentors) and their trainees (scholars) through live interactive meetings, thereby enabling the development and dissemination of geriatric mental health ideas and findings. This online community of researchers benefit from sharing current information about research and interventions in the field and gaining feedback from mentors about proposed research projects in order to better their chances of obtaining independent research funding that will support the field of geriatric mental health research.

Funding acknowledgement: This project has been funded with federal funds from the National Institutes of Health, Department of Health and Human Services, under Contract No. HHSN271200664098C.

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» NR2-104

PERSONALITY DISORDERS AND GENDER IDENTITY: TRANSSEXUALS VS. HETEROSEXUALS

Dragana Duisin M.D., Gordana Nikolic-Balkoski,MD,Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to:
[no data]

SUMMARY:

INTRODUCTION: Contemporary research approaches in the field of gender identity and gender identity disorders (GID) have mainly been restricted with two variables: gender and sex orientation while correlation between personality and personality psychopathology and GID is very much neglected.

Objectives: Basically this paper deals with the relationship of personality disorders (PD?s) and gender identity among persons with transsexual and heterosexual identity. Research subject refers on PD's in correlation with sex and gender differentiation in order to establish the validity of our main hypothesis that there is a relation between PD's and gender identity. Furthermore we've searched for correlation between PD's, sex and gender assuming that PD's strongly associate with gender identity, but not with sex identity.

Methods: Research was carried out in two year period. Chosen sample consisted of 60 adult persons: target group comprising of 30 healthy individuals with transsexual identity (9 female and 21 male) and control group of 30 healthy individuals with heterosexual identity (15 female and 15 male). Groups did not differ significantly in age. Patients within target group were diagnosed according to DSM-IV criteria for homosexual transsexualism. We have used psychiatric examination, psychological evaluation and SCID-II screen (First M.B. et al., 1997) - comparative version for ICD-10 and DSM-IV (only PD's joint for both classification systems).

For statistic analysis we have used: c2 test, Value Spearman's correlation test and discriminant analisys.

Results: All examined PD's were significantly correlated with type of gender identity while none of them with sex. Significant difference between harmonized gender identity subjects and subjects with GID (both sexes) was the type of PD.

Substantial difference in type of PD was also found by comparison of both sexes GID individuals to heterosexual individuals. Transsexuals of both sexes had notable presence of Avoidant, Paranoid and Emotionally unstable PD. Avoidant and Paranoid PD's represent the most significant difference between gender disharmonized subjects (transsexuals) and gender harmonized subjects (heterosexuals) and they were substantially more frequent among males than females.

Conclusions: The results indicate significant personality psychopathological aspects in a substantial proportion of subjects with gender identity disorder (namely transsexuals) and notable correlation of verified

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» NR2-105

MARITAL AND SEXUAL SATISFACTION AMONG PARTNERS OF MEN WITH AND WITHOUT SEXUAL DYSFUNCTION

Ajit Avasthi M.D., Rajinder Kaur,M.A.; Sandeep Grover, M.D.; Om Prakash,M.D.; Parmanand Kulhara, M.D., FRCPsych.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the importance of evaluation of partners of men presenting with sexual dysfunction for overall better outcome of sexual dysfunction.

SUMMARY:
Introduction: In the treatment of couples where the male partner has sexual dysfunction, it often becomes apparent that female partners also undergo lot of distress and the relationship between the couple is also affected. However, this has received little research attention. Methodology: We evaluated the female partners of men with and without sexual dysfunction (n = 50 in each group) and compared their psychological functioning, sexual and marital functioning, quality of life, and dyadic adjustment. Results: There was no difference in sociodemographic profile of participants across the 2 groups. As expected, significantly more number of spouses of men with sexual dysfunction reported sexual dissatisfaction. Spouses of men with psychosexual dysfunction reported significantly poor quality of life, significantly more relationship problems and significantly more psychological problems (Anxiety, depression, somatic symptoms and anger/hostility). Conclusion: For better outcome of psychosexual dysfunction, their partners should also be evaluated for psychological distress and marital satisfaction.

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» NR2-106

HOW DO PEDOPHILES COMPARE WITH OPIATE ADDICTS AND HEALTHY CONTROLS ON MEASURES OF NEUROCOGNITIVE FUNCTIONING?

Cristina Nesci B.A., Curren Katz, MA, Matthew Steinfeld, MA, Igor I. Galynker, MD, Lisa J. Cohen, PhD

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be able to appreciate differences between the neuropsychological underpinnings of pedophiles, opiate addicts and healthy controls.

SUMMARY:
Objective: To compare pedophiles to opiate addicts and healthy controls on measures of neurocognitive functioning associated with the frontal lobe. Introduction: Pedophilia has been hypothesized to be an addictive disorder. As with substance abuse disorders, it is characterized by failure to inhibit destructive, reward-driven behavior. This study explored whether pedophiles and/or opiate addicts have deficits in frontal lobe-related executive functions, which are typically associated with impairments in behavioral inhibition. Given the profound social cost of these disorders, elucidation of any neurocognitive substrates which may either link them or distinguish them is important. Methods: 51 male pedophiles recruited from an outpatient facility, 53 opiate addicts in sustained remission recruited from a residential treatment program, and 84 healthy controls recruited from media advertisements were tested on a battery of neuropsychological tests. Included were Controlled Oral Word Association, Stroop Color-Word Test, Matching Familiar Figures Test (MFFT), Porteus Mazes, Trailmaking Test, and Wisconsin Card Sorting Test (WCST). MANOVA's with follow-up univariate F tests and paired comparisons were used to compare test scores across groups. Results: On omnibus tests, groups differed significantly on MFFT, Stroop, and WCST. On MFFT, opiate addicts and controls differed significantly on one subtest and pedophiles and opiate addicts differed marginally on two subtests. On Stroop, opiate addicts and controls differed significantly on three subtests. On WCST, both pedophiles and opiate addicts significantly differed from controls on one subtest. Conclusion: Both patient groups appear to have some executive deficits relative to controls. Opiate addicts may show increased cognitive impulsivity relative to pedophiles. Such findings may contribute to the development of maximally effective psychopharmacological and psychotherapeutic interventions for these patient groups.

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» NR2-107

SUICIDAL RISK IN MOOD DISORDERS: RELATIONSHIP WITH CLONINGER'S TEMPERAMENT AND CHARACTER

Marwa Abdel Meguid M.D., Moustafa Kamel, M.D., Abdel Naser Omar,M.D., Yasser Abdel Razek, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to know the importance of assessment of suicidal risk in patients with mood disorders through its correlation to the personality profile.

SUMMARY:
Background: Suicide, the most serious complication in patients with mood disorders, is the cause of death in 15 to 25% of untreated patients with mood disorders. Aim Of the study: To assess suicidal risk in patients with mood disorders through its correlation to the personality profile of those patients. Subjects & Methods: The cases were selected from inpatients admitted in the Institute of Psychiatry. The sample is a selective one including the first 50 patients admitted at the institute and fulfilling the criteria of bipolar or unipolar mood disorders according to DSM-IV. Patients were diagnosed by SCID-I, personality was assessed TCI-R, Suicidal ideation was assessed using Beck scale for suicide ideation. Results: 64% of patients did not have a previous history of suicide, 22% were classified as ideators and14% with previous suicidal attempts. Correlation of Cloninger temperament and character to Scores of patients in Beck Scale for suicide ideation revealed Direct relationship with total scales of personality dimension reaching point of statistical significance with Harm Avoidance (HAt) ($p=0.017$) and Correlation held with history of suicidality revealed a higher mean scores of HA1 (Anticipatory worry and pessimism vs. uninhibited optimism) among patients with previous suicide attempts with significant statistical difference. Also higher mean scores of RD2 (Openness to warm communication vs. aloofness) among patients with previous suicide attempts with significant statistical difference. Conclusion: Suicidal risk in patients with mood disorders is correlated to their personality profiles. Personality assessment in patients with mood disorders is essential to predict risk of suicide in those patients.

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» NR2-108

DIFFERENCES IN SUICIDAL INTENTION, DEPRESSION, AND DISSOCIATION AMONG SELF-POISONING PATIENTS WITH MOOD DISORDER AND THOSE WITH PERSONALITY DISORDER

Shuntaro Ando M.D., Toshihiko M, M.D., Ph.D., Rie O, M.D., Aya H, M.D., Daisuke, Y, M.D., Hotsumi K, M.D., Takao N, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able

to recognize that personality disorder patients may commit self-poisoning with nearly the same level of suicidal intention and the same level of depressive and dissociative psychopathology exhibited by self-poisoning mood disorder patients.

SUMMARY:
Objective: To clarify the psychopathological differences between self-poisoning patients with mood disorder and those with personality disorder.
Methods: Of the 73 patients who were admitted to an emergency unit due to self-poisoning between March and July 2008, we selected 32 inpatients (25 women, 7 men; average age 31.2 ± 8.9 years) who met the ICD-10 criteria for either mood disorders (F3: mood disorder group) or disorders of adult personality and behavior (F6: personality disorder group). The shortened version of Beck's Suicide Intent Scale (SIS), the K10 Anxiety and Depression Test, and the Adolescent Dissociative Experience Scale (ADES) were all administered along with the clinical interview.
Results: Among the items on the SIS, only one revealed a significant difference between the two groups: the patient's "reaction to the act". Specifically, patients in the mood disorder group were more likely to feel disappointed about having recovered from a comatose state than patients in the personality disorder group. No significant difference was found between the groups' results on either the K10 test or the ADES; both groups received high total scores on both tests (K10: mood disorder group, 33.1 ± 9.5; personality disorder group, 33.4 ± 9.4. ADES: mood disorder group, 3.6 ± 2.3; personality disorder group, 4.1 ± 2.0). These findings indicate that there is no significant difference between the two groups in terms of intensity of suicidal intention or severity of depression and/or dissociation.
Conclusion: Our results suggest that personality disorder patients may commit self-poisoning with nearly the same level of suicidal intention and the same level of depressive and dissociative psychopathology exhibited by self-poisoning mood disorder patients.

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» NR2-109

THE DEVELOPMENT OF A STRUCTURED INTERVIEW USING THE SUICIDE RISK ASSESSMENT AND MANAGEMENT MANUAL (S-RAMM) AND AN ASSESSMENT OF INTERRATER RELIABILITY

Elizabeth Cummings, M.D., Emma Unoh M.D., Ijaz Atif M.D., Alexia Papaconstantinou M.D., Harry Kennedy M.D., Helen O'Neill M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand the evidence supporting the use of the Suicide Risk Assessment and Management Manual (S-RAMM), structured professional judgment tool and have an awareness of how a structured interview may facilitate its use in a wider setting. Finally, it is anticipated that, because of its simplicity and ease of use, a participant would be able to use this structured interview to assess and manage suicide risk.

SUMMARY:
Introduction: We undertook to develop a structured interview based on the Suicide Risk Assessment and Management Manual (S-RAMM) and thereafter to assess interrater reliability. The S-RAMM is the first validated structured professional judgment tool for suicide risk assessment. It is analogous to the HCR-20.
Methods: 4 investigators assessed 15 patients in the Central Mental Hospital, a forensic hospital, in Ireland using a structured interview developed by the first two authors. Generalised Kappa was calculated using Excel. Interviews took approximately 15 minutes.
Results: N=15, male= 100%. Mean Age 49 years (standard deviation 12.6 years). Generalised Kappa Values: B1 History of Deliberate Self Harm 0.838, B2 Seriousness of previous Suicidality 0.715, B3 Previous Hospitalisation 0.938, B4 Mental Disorder 0.782, B5 Substance Abuse Disorder 0.763, B6 Personality 0.636, B7 Childhood Adversity 0.690, B8 Suicide in the Family 0.931, B9 Age, Gender and marital status 0.731, C1 Suicidal ideation , communication and intent 0.99, C2 Hopelessness 0.704, C3 Psychological Symptoms 0.617, C4 Treatment Adherence 0.015, C5 Substance Use 0.99, C6 Psychiatric Admission and Discharge 0.99, C7 Psychosocial Stress 0.794, C8 Problem Solving Deficits 0.725, C9 Age, Gender and marital status 0.731, F1 Access to preferred method of suicide 0.574, F2 Future Service Contact 0.643, F3 Future Response to drug treatment 0.418, F4 Future response to Psychosocial Intervention 0.409, F5 Future Stress 0.303. P values were typically of the order of 0.0001.
Conclusion: Our study showed substantial agreement between raters on most factors and almost perfect agreement on some. This provides support for this structured interview as a time-efficient and pragmatic suicide risk assessment and management tool.

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» NR2-110

RELIGIOUS AFFILIATION AND SUICIDAL BEHAVIOR IN PATIENTS WITH BIPOLAR DISORDER

Kanita Dervic M.D., Juan J. Carballo, M.D., Enrique Baca-Garcia, M.D., Hanga Galfalvy, Ph.D., Ossama T. Osman, M.D., Maria A. Oquendo, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to :1-Recognize the correlation between suicidal behavior and several socio-demographic factors, clinical features and co-morbid conditions in patients with bipolar disorder; 2-Identify possible protective role for religious affiliation as a resource that correlates with lower risk for suicide

SUMMARY:
Objectives: Patients with bipolar disorder (BD) are prone to suicidal behavior, yet possible protective mechanisms are rarely studied. This study investigated a possible protective role for moral objections to suicide (MOS)/religious beliefs against suicidal behavior in patients with BD, who were in a depressed phase.
Methods: We compared 149 patients with BD who reported religious affiliation (BD-RA) and 51 BD patients without religious affiliation (BD-WRA) in terms of socio-demographics, clinical characteristics and history of suicide attempts.
Results: With regard to sociodemographics, the BD-RA patients were more likely to have children (41.8% vs. 15.7%, P=.001), and had more family oriented social networks (66.1% vs. 24.4%, P<.001). In terms of clinical history; BD-RA group had fewer past suicide attempts (63.1% vs. 80.4%, P=.023), less suicides in first degree relatives (2.8% vs. 14%, P=.003) and were older at the time of first suicide attempt (24.5±11.6 vs. 20.4±9.6, P=.047). As for co-morbid conditions, BD-RA group had less co-morbid alcohol and substance abuse (49.7% vs. 74.5%, P=.002); less childhood abuse experience (44.1% vs. 63.3%, P=.022); lower lifetime aggression (20.1±6.2 vs. 22.1±6.0, P=.049) and greater MOS (11.2±6.7 vs. 6.4±3.7, P<.001). After controlling for confounders, higher aggression level (P=.001) and lower MOS/religious beliefs (P<.001) were found to have significant association with past suicide acts in BD. Both groups did not differ with regards to the level of suicide ideation, depression, hopelessness, impulsiv-

ity, severity of manic symptoms, adverse life events nor perceived total reasons for living.
Conclusions: This study suggests that higher moral objections to suicide/religious beliefs are associated with less suicidal acts and may have protective effect against suicide in depressed bipolar patients. It is important to consider these factors during the diagnostic assessment and with therapeutic intervention in this population.

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» NR2-111

RISK FACTORS FOR LOW PLAN/IMPULSIVE SUICIDE ATTEMPTS (LPI-SA)

Serena Fox M.D., Anita Jothy, MD, Mudassar Tariq, MD, Muhammad Majeed, MD, Igor Galynker, MD, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to delineate clinical risk factors for low plan/impulsive suicide attempt (LPISA) and anticipate the need for tailored treatment plans for individuals who present with suicidal ideation without a plan (low plan) in the presence of high risk clinical features.

SUMMARY:

Objective: This review investigates clinical characteristics of low plan/impulsive suicide attempts (LPI-SA). It will alert clinicians to patients who present with suicidal ideation without a plan, but more at risk for impulsive suicide attempts than previously thought. Behavioral factors, age and gender, substance use, and neurobiological findings will be discussed.
Context: Forty-three% of acute suicide attempts (SA) have been described as unplanned. Currently, clinicians rank patients with suicidal ideation (SI) without a plan at lesser risk for future SA than those with one. This designation may overlook a subgroup of individuals with low plan SI at risk for acute, impulsive SA (conceived hours or minutes before implementation), and thereby affect treatment.
Method: PubMed, Medline, and PsycINFO were searched for English-language articles that evaluate 'low plan', 'unplanned', or 'impulsive' suicide attempts by adults and adolescents. Additional keywords were combined: behavior, age, gender, alcohol dependence, neurobiological, genetic.
Results: LPI-SA is associated with individuals who are younger or adolescent, female, less depressed (or depressed and alcoholic) and prone to alcohol-related aggression or externalizing behaviors. Most impulsive attempters experience SI prior to an attempt but are less likely to believe their attempt will cause death. Differences in mean scores on trait impulsivity between impulsive and non-impulsive attempters were not significant. LPI-SA strongly predicts relapse and time to relapse in treated alcohol dependent patients. Emerging neurobiological evidence links LPI-SA to serotonergic but not estrogenic genetic markers.
Conclusion: Younger, more aggressive, alcohol dependent patients may be at higher risk for LPI-SA than previously recognized. Women and adolescents with co-occurring alcohol abuse may be particularly vulnerable. Treatments need to address acute SA risk, alcohol disorders and relapse prevention.

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» NR2-112

CORRELATION BETWEEN GROSS DOMESTIC PRODUCT AND SUICIDE RATES IN COLOMBIA

Edwin Herazo M.D., Andrea Carolina Acevedo, Econ, Adalberto Campo-Arias, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the correlation between Gross Domestic Product (GDP) and suicide rates in Colombia since 1995 to 2007.

SUMMARY:

Introduction: Suicide is a result of a complex interaction of individual, social and economical factors. Some investigations suggest an association between GDP and suicide rates. However, this correlation needs to be explored in Colombian population.
Objective: To estimate the correlation between GDP and suicide rates in Colombia since 1995 to 2007.
Method: An ecological study was designed. Official information about GDP and suicide rates of the last thirteen years was collected. Correlation between these variables was calculated using Pearson's product moment correlation (rho). It was accepted as a significant correlation a coefficient higher than (+/-) 0.30 and p value less than 0.05.
Results: The Colombian GDP varied from USD$ 2,101.78 to USD$ 2,565.69, expressed in US Dollars of 1994; and suicide rates, from 4.03 per 100,000 inhabitants to 5.26 per 100,000 inhabitants. The correlation between these indicators was negative (Pearson´s rho= -0.80; p=0.001).
Conclusions: There is a negative correlation between GDP and suicide rate in Colombian population. Improving economic indexes would reduce psychological burden that increase suicide rates. More researches are necessary.

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» NR2-113

CASE-CONTROL STUDY OF THE RELATIONSHIP OF DEPRESSIVE SYMPTOMS TO SUICIDE IN A COMMUNITY-BASED SAMPLE OF INDIVIDUALS WITH SCHIZOPHRENIA IN CHINA

John Kasckow, MD, PhD, Nancy Liu M.S., Gretchen L. Haas, PhD, Michael R Phillips, MD, MPH

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to better understand risk factors for completed suicides in patients with schizophrenia especially with regards to depressive symptoms and depression-associated factors.

SUMMARY:

BACKGOUND: Suicide is the leading cause of premature death among people with schizophrenia. Most studies on completed suicide among persons with schizophrenia suggest that suicide is associated with a history of depression, symptoms of agitation, worthlessness and hopelessness.
METHODS: To test the relationship between depressive symptoms in schizophrenia and suicide, we conducted a secondary analysis from a large psychological autopsy study in mainland China that used a version of the structured clinical interview for DSM-IV (SCID) adapted for interviewing Chinese. The original dataset included 519 suicides and 536 unintentional injury decedents. From this, we identified a community-based sample of 74 suicides (cases) and 25 accidental deaths (controls) among persons with schizophrenia. Our hypothesis stated subjects dying from suicide would have more depressive symptoms and depression-associated

problems. A 'depression symptom severity score' based on the number, severity, and persistence of depressive symptoms 2 weeks before death was derived from the structured psychiatric examination; a 'dysfunction due to depressive symptoms score' was assessed, based on informants' reports about the effect of depressive symptoms on decedents' functioning in the month before death; and a 'chronic stress score' was assessed based on duration and severity of the psychological effect of negative life events over the prior year.
RESULTS: Subjects who died by suicide had a mean age of 44 (SD = +/- 15) years; 70% were female and 68% lived in rural settings. Control subjects had a mean age of 46 (SD = +/- 17) years; 63% were female and 71% were from rural settings. Those who died by suicide had a significantly higher prevalence of most of the 9 symptoms of a DSM IV Major Depressive Syndrome, a higher overall depression severity score, greater dysfunction due to depressive symptoms, and higher levels of chronic stress (all effects significant at $p < 0.05$).
DISCUSSION: This study of a community-based sample of individuals with DSM-IV schizophrenia who died by suicide in a non-western culture extends findings from Western culture studies that point to depressive symptoms as a risk factor for suicide in schizophrenia. Findings underline the importance of routine screening for depressive symptoms among patients with schizophrenia.

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» NR2-114

HOW PEOPLE COPE BY ATTEMPTING SUICIDE

Yvette Kaunismaki M.D., Marta Elliott, PhD, Barbara Kohlenberg, PhD, Morgan Green, MA, Barbara Larsen, MA

EDUCATIONAL OBJECTIVES:

At the conclusion of the presentation, the participant should be able to describe ways in which attempted suicide is used to cope with seemingly hopeless situations, and how survivors of suicide attempts transform their experience into short- and long-term plans to address their problems with less self-destructive methods. In addition, participants should be able to describe the typical psychosocial circumstances in which attempted suicide takes place.

SUMMARY:

The purpose of this study is to analyze how individuals use attempted suicide as a coping mechanism. This study is important because there is a need to systematically explain the subjective outlook that results in attempted suicide so as to learn how to meet the needs of suicidal individuals before they make an attempt on their lives. Thirty-five individuals in hospital subsequent to a suicide attempt were interviewed in depth to gather narrative accounts of the circumstances preceding their suicidal behavior. Special attention was paid to the social context in which the attempt occurred, the immediate triggers of the attempt, individuals' description of their motivation for attempting suicide, and how they felt just before and after their attempt. The interview transcripts were analyzed using grounded theory-based qualitative methodology. The results indicate that many suicide attempts occur in the context of grave financial strain, and are triggered by interpersonal conflict, particularly with one's intimate partner. Suicide survivors frequently describe unbearable pain, hopelessness, and a feeling of injustice with no way out. Taking action against themselves is typically described as an effort to end the pain, rather than to end their lives. Suicide attempts offer a method of coping that gets across the severity of their emotional pain to others and elicits treatment in the form of 72-hour confinement to hospital. While in-patient treatment is described as far less than optimal, suicide survivors often find meaning and hope in the aftermath of their behavior, and use their period of hospitalization to develop problem-based solutions to the circumstances leading up to their attempt.

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» NR2-115

PREDICTIVE VALIDITY OF THE SUICIDE BEHAVIOR QUESTIONNAIRE-REVISED IN COLOMBIAN PSYCHIATRY PATIENTS WITH SUICIDE RISK

Andres Rangel-Martinez-Villalba M.D., German Eduardo Rueda-Jaimes,M.D., Paul Anthony Camacho Lopez, M.D., M.Sc.

EDUCATIONAL OBJECTIVES:

At the end of this poster presentation, the attendees will know the psychometric properties of the Suicide Behavior Questionnaire-Revised and its predictive validity for suicide attempt and suicide in psychiatry patients.

SUMMARY:

Background: The usefulness in clinical practice of self-report questionnaires is questionable.
Objective: The aim is to establish the psychometric properties of the Suicide Behavior Questionnaire-Revised in psychiatry patients with suicide risk and its predictability for suicide or suicide attempt.
Methods: This was a validation study. Patients who assisted to psychiatry consult and their attending psychiatry found them to have suicide risk were assessed with the Suicide Behavior Questionnaire-Revised scale, a four item version; reasons for living scale; and a semi-structured interview for suicide risk. A 30 days follow up were completed to all patients to establish the predictive validity with suicide attempt or suicide.
Results: 211 patients were surveyed. The mean age was 31.5 years old (SD=14.48). 37.44% of the sample were male. The Cronbach's alpha was 0.664. The Suicide Behavior Questionnaire-Revised showed a correlation of -0.546 with the Reasons for Living ($p<0.001$) and 0.380 with the semi-structured interview for suicide risk ($p<0.001$). With a cutpoint equal or higher than thirteen the scale showed a positive predictive value of 10.17% and a negative predictive value of 98.25%.
Conclusion: The Suicide Behavior Questionnaire-Revised was useful for the assessment of psychiatry patients with suicide risk. This scale could be applied as a screening instrument in psychiatry patients with suicide risk to predict suicide attempt in the first month of treatment because of its excellent negative predictive value. Otherwise, those patients who have a score higher than thirteen should be assess and follow by a specialized team in suicide.

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1) Osman A, Bagge CL, Gutierrez PM, Konick LC, Kopper BA, Barrios FX.The Suicidal Behaviors Questionnaire-Revised (SBQ-R):Validation with Clinical and Nonclinical Sample, Assessment. 2001; 8; 443

2) Cotton CR, Peters DK, Range LM. Psychometric properties of the Suicidal Behaviors Questionnaire. Death Stud. 1995; 19:391-97

» NR2-116

LIFETIME HISTORY OF SUICIDE ATTEMPTS IS ASSOCIATED WITH POORER SOCIAL SKILLS IN PATIENTS WITH BIPOLAR PATIENTS TYPE I

Cristiana Castanho de Almeida Rocca, Lena Nabuco de Abreu, Luciana Gerchmann, Beny Lafer

EDUCATIONAL OBJECTIVES:

[no data]

SUMMARY:
Background: Lifetime history of suicide attempts is frequently associated with bipolar disorder (BD) and can be associated with some risk factors, such as severity of depressive symptoms, impulsivity, hopelessness and familial conflicts. Even during remission, patients with bipolar disorder can present social skills deficits. However, no study has been conducted in order to evaluate social skills in bipolar patients with a past history of suicide attempts.
Method: We studied a group of 28 euthymic patients with bipolar disorder: 12 BPI outpatients with a history of suicide attempt and 16 BPI outpatients non-attempters. The groups of patients were compared with 31 healthy controls in a social skills measure. All participants were assessed using a self-report questionnaire, the Brazilian Social Skills Inventory (IHS – Del Prette).
Results: Patients with a history of suicide attempts presented lower IHS scores for the domains that assessed conversational skills and social self-confidence ($p<0.001$), social openness to new people and situations ($p= 0.001$) and self-control of aggressiveness and individual reactions to aversive stimuli that require the management of anger and aggressiveness ($p= 0.041$) when compared with healthy controls and bipolar patients without previous suicide attempts.
Conclusion: Our results suggest that BPI outpatients with a history of suicide attempts present inhibited behaviour in relation to other people and their environment. They have difficulties to face situations that involve interacting with new people and they have to make efforts to control the aggressiveness. Further research may verify if these social skills deficits are associated with other risk factor that may lead to higher suicidality in Bipolar Patients.

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1) Rocca CCA, Macedo-Soares MB, Gorenstein C, Tamada RS, Issler CK, Dias RS, Schwartzmann AM, Lafer B. Social dysfunction in bipolar disorder: pilot study. Australian and New Zealand Journal of Psychiatry 2008; 42:686!692

2) Carballo JJ, Harkavy-Friedman J, Burke AK, Sher L, Baca-Garcia E, Sullivan GM, Grunebaum MF, Parsey RV, Mann JJ, Oquendo MA.Family history of suicidal behavior and early traumatic experiences: additive effect on suicidality and course of bipolar illness? J Affect Disord. 2008 Jul;109(1-2):57-63.

» NR2-117

EFFECTIVENESS OF A PRACTICE GUIDELINE FOR AMBULATORY TREATMENT OF COLOMBIAN PATIENTS WITH SUICIDE RISK

German Rueda-Jaimes M.D., Andres Mauricio Rangel-Martinez-Villalba, MD., Paul Anthony Camacho, MSc, MD., Maria Teresa Lopez-Camargo, MD.

EDUCATIONAL OBJECTIVES:
At the end of this poster presentation, the attendees will know the use and the effectiveness of a practice guideline for the ambulatory treatment of patients with suicide risk

SUMMARY:
Background: There are some guidelines for the treatment of patients with suicide risk, although, their effectiveness have been rarely evaluated.
Objective: The aim was to study the effectiveness of a practice guideline for the ambulatory treatment of Colombian patients with suicide risk.
Methods: This study used a quasi-experimental design. The practice guideline for the ambulatory treatment of patients with suicide risk has been developed by a private mental health institute in Colombia. The patients were classified in four different suicide risk levels, low, middle, high and high immediate. The guideline established that patients with suicide risk lower than high immediate could be treated in home with medical care. The control group was established with those patients who their insurance service did not allow the application of the guideline; therefore, usual care was offer to them. The outcome was measured by suicide attempts or suicide within the first 30 days of the treatment.
Results: 103 patients were included in the intervention group and 73 in the control group. The patients in the intervention group had a mean age of 31.3 years (SD = 13.5) and 32.0% were male; the patients in the control group had a mean age of 31.5 years (SD = 15.6) and 46.6% were male. The relative risk for suicide attempt within the first month was 0.19 (CI95%; 0.04-0.96). None patient died by suicide. Formal survival analyses revealed a significantly lower suicide rate in the intervention group for the first 30 days ($p=0.027$). The median for hospitalization days was 2 in the intervention group and 7 in the control group ($p<0.001$).
Conclusion: The use of the practice guideline was protector for suicide attempt and also diminished the hospitalization days compared with the usual care. Randomized clinical trials should be conducted to confirm these results.

REFERENCES:

1) Jacobs DG, Baldessarini RJ, Conwell Y, Fawcett JA, Horton L, et al. Practice Guideline for the Assessment and Treatment of Patients with Suicidal Behaviors. APA Guidelines. 2003.

2) Hvid M, Wang AG. Preventing repetition of attempted suicide-I. Feasibility (acceptability, adherence, and effectiveness) of a Baerum-model like aftercare. Nord J Psychiatry. 2008; 17:1-6.

» NR2-118

EXTENDED RELEASE QUETIAPINE FUMARATE (QUETIAPINE XR) IN MAJOR DEPRESSIVE DISORDER (MDD): SUICIDALITY DATA FROM ACUTE AND MAINTENANCE STUDIES

Richard Weisler M.D., Hans Eriksson, M.D., Ph.D., M.B.A., Willie Earley, M.D., Johan Szamosi, M.Sc

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should have knowledge of the prevalence of suicide in patients with major depressive disorder, and understand the results of this analysis evaluating the risk for suicidal ideation/behavior with quetiapine XR.

SUMMARY:
Objectives: Suicidal behavior and ideation are significant complications in MDD (1,2). This analysis evaluated incidence of suicidal ideation/behavior with extended release quetiapine fumarate (QTP XR) in MDD.
Methods: Data from prospectively planned pooled analysis of six previously reported randomized, placebo (PBO)-controlled, 6 to 10-week studies (4 monotherapy; 2 adjunct therapy). Patients (pts) (18-65 years; DSM-IV diagnosis of MDD) received QTP XR 50 (n=181), 150 (n=910), 300mg/day (n=685) or PBO (n=957). Data from a maintenance study (12-18-week open-label, stabilization phase, up to 52-week randomization phase) in pts randomized to QTP XR (50-300mg/day; n=391) or PBO (n=385) were also evaluated. Incidence and relative risks (RR; adjusted for study by Mantel-Haenzel stratification) for suicidal ideation/behavior in randomized safety populations were assessed by Columbia-type review and classification. Suicidal ideation/behavior was defined by Columbia classification codes of 1, 2, 3, or 4 (complete suicide, suicide attempt, preparatory acts towards imminent suicidal behavior, and suicidal ideation, respectively).
Results: During acute randomized treatment, incidence of suicidal ideation/behavior following Columbia analysis was 1.1% (n=2), 0.7% (n=6), 0.7% (n=5) for QTP XR 50, 150, and 300mg/day, respectively vs 0.7% (n=7) PBO. Adjusted RR (95% CI) for suicidal ideation/behavior vs PBO were 0.40 (0.08, 2.04), 0.88 (0.30, 2.58) and 0.72 (0.23, 2.26), respectively.In the maintenance study (randomization phase), incidence of suicidal ideation/behavior was 0.3% (n=1), QTP XR vs 0.5% (n=2), PBO; adjusted RR (95% CI) was 0.66 (0.11, 3.91) with QTP XR. No completed suicides were recorded in any studies during

randomized treatment.
Conclusions: These data show no evidence of increased risk of suicidal ideation/behavior with QTP XR monotherapy or adjunct therapy in pts with MDD not considered to be of high suicide risk at baseline. Funded by AstraZeneca

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2) Oquendo MA, Galfalvy H, Russo S, Ellis SP, Grunebaum MF, Burke A, Mann JJ: Prospective study of clinical predictors of suicidal acts after a major depressive episode in patients with major depressive disorder or bipolar disorder. Am J Psychiatry 2004; 161(8):1433-1441

» NR2-119

CONSTRUCT VALIDITY OF A SUICIDE TRIGGER STATE

Zimri Yaseen, MD, Matthew Johnson, PhD, Igor I. Galynker, MD, PhD

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, participants should be able to identify how suicidal behavior may be associated with a distinct near-psychotic panic state, as measured by the STS-2 scale.

SUMMARY:
Aims: Factors that trigger a person with suicidal ideation to actually attempt suicide are not known. This study aims to assess the validity of a novel psychopathological construct – a 'suicide trigger state' as measured by the Suicide Trigger Scale 2 (STS-2) specially developed for this purpose.
Methods: A 39 item 3 response category scale, the STS-2, and an established scale of general psychopathology, the SCL-90-R, were administered to 141 adult psychiatric inpatients admitted to the hospital with a chief complaint of suicidal ideation. Item response theory analysis, principal component analysis with Promax and Varimax rotation, and receiver operator curve analysis of the components were applied the STS-2 responses. In addition, components were correlated with the SCL-90-R.
Results: IRT analysis demonstrated a statistically significant association between the STS-2 score and a past history of suicide attempt with a p-value of 0.03. PCA analysis yielded a two-component solution accounting for 43% percent of the variance. There was good agreement between Varimax and Promax rotated solutions. The first component was loaded most heavily by items testing near-psychotic somatization, while the second component was loaded most heavily by items indicating loss of control and a sense of doom and entrapment. Under ROC analysis both subscales generated by the Varimax rotation were good predictors of a history of suicidal attempt in the study subjects (AUC 0.735, 0.844, respectively). The STS-2 and its subscales did not correlate significantly with Axis I diagnosis or other demographic variables of the study subjects.
Conclusion: The STS-2 is significantly associated with history of suicide and is independent of demographic and established Axis I diagnostic factors indicating wide applicability. This suggests that the STS is indeed measuring a suicide associated trigger state with properties of near-psychotic somatization, loss of control, and a sense of entrapment and doom.

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2) Galynker, I.,Ieronimo C., Perez-Aquino A., Lee Y. and Winston, A. (1996). Panic attacks with psychotic features. Journal of Clinical Psychiatry 57, 402-406.

» NR2-120

LEAVING LAS VEGAS: HOMICIDE ON TELEVISION VS. UNITED STATES HOMICIDE DATA

Christopher Janish B.A., Melanie Buskirk, B.S., Timothy Lineberry, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to discuss the association between alcohol and homicide in the U.S. and define the differences between popularly portrayed homicides on television. The participant will be able to identify potential public health implications secondary to this difference.

SUMMARY:
Introduction: "Police procedurals", dramatic television series portraying police criminal investigations, are extremely popular and reach > 43 million viewers annually. Previous research demonstrates television can impact individual health behaviors and public health perceptions. Homicide, a complex social and public health problem, resulted in the loss of over sixteen-thousand lives in the US in 2005. The majority of perpetrators use alcohol prior to their crime. We sought to define how representative homicides in "police procedurals" were versus previous epidemiologic data and data from the Centers for Disease Control (CDC) National Violent Death Reporting System (NVDRS).
Methods: The two most popular police procedurals, CSI and CSI: Miami were defined as comparators based on their relative heterogeneity of portrayed homicides, and DVD availability. The seasons of 2003, 2004, and 2005 were chosen to correspond temporally with 2005 CDC NVDRS data. Each episode was analyzed for victim and offender sex, age, race, method, relationship to victim, and associated alcohol/drug consumption.
Results: 11 of 301 (<4%--chi-squared $p<0.0001$) television perpetrators used alcohol. Victims were significantly less likely ($p<0.0001$) to be under alcohol's influence compared to 2005 NVDRS data. Offenders were much more likely ($p<0.0001$) to be strangers than to have a relationship with the victim.
Discussion: Results from the two highly rated series we analyzed, CSI and CSI: Miami, clearly reflect differences between murders depicted in the media versus U.S. data. This potentially biases public perception of both the role of alcohol and drug use in homicide and who commits and is at risk for homicide. Correspondingly, this lack of understanding by the public of the true prevalence of substance use in murders may be a factor in support, or lack thereof, for public policy decisions related to substance use and treatment.

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1) Malmquist CP. Homicide : a psychiatric perspective. 2nd ed. Washington, DC: American Psychiatric Pub.; 2006.

2) Karch DL, Lubell KM, Friday J, Patel N, Williams DD. Surveillance for Violent Deaths -- National Violent Death Reporting Systems, 16 States 2005. In: Department of Violence Prevention. Atlanta, GA: Center for Disease Control and Prevention; 2005. p. 1-43, 5.

» NR2-121

THE ART OF PSYCHO-TRAUMATOLOGY (INTRODUCING THE HEALING ENVIRONMENT)

Omar Mohamed M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to get familiar with the role of psychiatry in disaster response, and also be introduced to the idea of the healing environment as an essential element in the recovery process.

SUMMARY:
This poster is intended to introduce the topic of the healing environment as an essential part of coping with mental health effects of trauma and disasters. The poster first divides disasters into natural and man-made, and then discusses the effects of disasters on individuals and societies. The mental health consequences of disasters, the role of psychiatry before, during and after disasters, and the importance of psychological first aid are also briefly included. Finally the art of psycho-traumatology, namely the idea of the

healing environment (turning a disaster zone into a healing space) and the four elements of the healing environment are introduced in detail towards the end of this poster.

REFERENCES:

1) Harvard Program in Refugee Trauma

2) National Center for PTSD

» NR2-122

LITERATURE REVIEW OF CARVING AS DOMESTIC VIOLENCE: CASE REPORT OF SPOUSE CARVING

Lissette Rodriguez M.D., Indhira Almonte, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify, diagnose and treat cases of domestic abuse with flesh carving.

SUMMARY:

After an extensive literature search of domestic violence cases with carving, we found that no case have been reported. We will present the first case reported of carving on spouse. We will include multiple pictures of name and last name of the abuser carved in the patient different parts of her body including both breast,leg, abdomen and back. The carvings were between 6 to 12 inches.

REFERENCES:

1) Kimuna, Sitawa R, Djamba, Yanyi K. Gender based violence: Correlates of physical and sexual wife abuse in Kenya. Journal of Family Violence. Vol 23(5)July 2008, 333-342.

2) Waters, Dana P;Westermeyer, Jerry F; Gralewski, Carolyn; Schneider, Mary F;Warkentin, Monica. Lifestyle among abuse-reporting outpatients. Journal of Individual Psychology. Vol 64(1)Spr 2008, 55-66.

» NR2-123

POSTTRAUMATIC EMBITTERMENT DISORDER: SERBIAN WAR VETERANS' EXPERIENCE

Radomir Samardzic M.D., Zeljko Spiric, M.D., Ph.D., G. Mandic-Gajic, M.D., Ph.D., Natasa Milosevic, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to [no data]

SUMMARY:

Objective: Epidemiological studies have shown that higher rate of posttraumatic mental disorders are associated with reduced psychosocial support. This study focuses on the postwar adjustment of war veterans in the wars in former Yugoslavia since 1991. Method: The data about psychosocial adaptation in 220 Serbian war veterans (mean age = 44.70, SD = 10.10) were analyzed in the retrospective case-control study conducted in the period Jun-December 2005. The self-report on postwar social support was assessed by the Questionnaire designed for that occasion, posttraumatic stress disorder (PTSD) by the Impact of Event Scale (IES cut-off score = 2.0), and comorbid psychopathology with the Symptom Check List-Revised (SCL-90-R). Self report measures of various forms of psychosocial support were assessed on the 5-point scale (1=very negative, 5=very positive). Statistical analysis was performed using descriptive and analytical non-parametric methods. Results: PTSD veterans (n=91) have assessed state institutions help about housing problem with 1.69 (SD=0.93) and non-PTSD (n=129) veterans with 1.88 (SD=0.97). Social responses to their war engagement PTSD war veterans have evaluated with 2.25 (SD=0.98) and non-PTSD veterans with 2.63 (SD=0.99). Most veterans from both groups reported feelings of bitterness, resignation, rage, helplessness and a sense of injustice and humiliation towards the society regarding their war engagement. Conclusions: Psychological disturbances in the postwar adaptation of the war veterans in this study are significantly similar to the reactive disorder described in the aftermath of German reunification, which has been called the posttraumatic embitterment disorder. Thus, issues of greater social support and justice are likely to be powerful factors for better postwar psychological adjustment.

REFERENCES:

1) Weiss, D, Marmar C. The Impact of Event Scale-Revised. In: J. Wilson & T. Keane, (Ed.) Assessing psychological trauma and PTSD, New York, Gilford, 1997

2) Linden M, Rotter M, Baumann K, Lieberei B. Posttraumatic embitterment disorder: definition, evidence, diagnosis, treatment. Cambridge: Hogrefe & Huber Publishers. 2007

» NR2-124

GENDER DIFFERENCES IN TORTURE VICTIMS IMPRISONED DURING CIVIL WAR IN EX-YUGOSLAVIA

Zeljko Spiric M.D., Radomir Samardzic, M.D., Ph.D., Goran Knezevic,Ph.D., Vladimir Jovic, M.D., Ph.D., ; Goran Opacic, Ph.D., Ivanka Vidakovic

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize gender differences in victims of torture during civil wars in ex-Yugoslavia, regarding frequency of torture types and indices of consequent general psychopatology.

SUMMARY:

Objective: The aim of this study was to assess gender differences in sample of 486 (aged 14-81 years), clients of Centre for Rehabilitation of Torture Victims, Belgrade, Serbia, who were imprisoned during civil wars in ex –Yugoslavia. Method: The study subjects were 411(84.57%) men, and 75 (15.43%) women. Clients were compared regarding results from a special questionnaire of 81 different forms of psychological, physical and sexual abuse and ill treatment. Symptom Checklist (SCL-90-R) was used for assessing of general psychopathology. Results: Men experienced more different types of torture than women (23.1 to 15.1). Most frequent types of torture were: kicking or beating (86%), for men, and death or mutilation threats directed against close persons (65%) for women. Most prominent gender differences in experienced torture types were: kicking or beating (86% to48%), and forcing to remain in one position (53% to 21%) more frequent in men group, and rape by person of opposite sex (13.3% to 0.2%), and genital infection as consequence of rape (9.3% to 0.5%) more frequent in women group. Significant differences were in almost all types of sexual abuse which were more frequent in women group: verbal sexual humiliation or threats (32% to 17.3%), touching of genitals (20% to 15.1%), forcing to sexual action except actual rape (14.7% to 3.4%), use of animals or objects for sexual purposes (6.7% to 0.7%). Somatization, depression, anxiety, interpersonal sensitivity, and fobic anxiety were significantly higher in women compared to men group measued by SCL-90-R. Conclusion: Significant gender differences were found in victims of torture imprisoned during civil war in ex-Yugoslavia. Men experienced more various types of torture than women. Experience of sexual abuse types of torture were more frequently present in women. General psychiatric symptoms measured by SCL-90-R were more prominent in women.

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2) Basoglu M, Paker M, Ozmen E, Tasdemir O, Sahin D. Factors related to long-term traumatic stress responses in survivors of torture in Turkey. JAMA 1994; 272: 357-263.

» NR2-125

TRAUMA COPING MECHANISMS AND PSYCHOLOGICAL DISTRESS AMONG SOLDIERS

DEPLOYED IN AFGHANISTAN

Jan Vevera M.D., M Preiss Ph.D., I Provoost Ph.D., Z Bubenik MD, M Psutka MD, M Plodr MD Ph.D., J Bancarel MD, P Bob Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that increasing telephone and email contacts might assist military personnel in dealing with traumatic experiences The majority of military personnel were calm and relaxed during deployment.. Personnel who completed one or more deployments reported less anxiety symptoms and the security situation was less likely to affect their mood in comparison with individuals participating in their first deployment.

SUMMARY:

Background: Research from the US shows that up to 25% of veterans received a mental health diagnosis, mostly posttraumatic stress disorder –PTSD while European studies reported substantially lower numbers – around 3%. Herein we explore the nature of coping mechanisms of military personnel in Kabul who served at a military camp, repeatedly attacked by the insurgents. We expected to find phone and email communication to be the most useful coping mechanism in dealing with stress, furthermore, to find a high prevalence of anxiety symptoms as the study was conducted in an operational theatre

Method: Cross-sectional study using a modified version of the Strous Questionnaire in 385 European soldiers experiencing at least one rocket attack.

Results: In dealing with trauma 60 % of the responders find useful obtaining additional information and 54 % being in touch with friends or relatives. Responders felt during deployment calm (84 %) and relaxed (80 %). Previously deployed soldiers report that the security situation was less likely to affect their mood (p=0.02). The prevalence of Acute Stress Reactions and PTSD were less than 1 %.

Conclusions: Seeking information and being in touch with friends or relatives were identified as most helpful in dealing with trauma. The fact that despite missile attacks, the vast majority of soldiers were calm and relaxed was not consistent with US studies. This might be related to shorter periods of deployment as well as to different protective factors operating. However, emphasis in current diagnostic systems (DSM IV, ICD 10) as well us in research and advocacy groups overstates the contribution of trauma variables to contextual factors such as resilience and age of military personnel and post-deployment stressors such as lack of social support and availability of health care. Ignoring those factors lead as to miss some of rare opportunities for safe and available primary prevention in psychiatry.

REFERENCES:

1) Engelhard IM, van den Hout MA, Weerts J, Arntz A, Hox JJ, McNally RJ: Deployment-related stress and trauma in Dutch soldiers returning from Iraq. Prospective study. Br J Psychiatry 2007; 191:140-5

2) Strous RD, Mishaeli N, Ranen Y, Benatov J, Green D, Zivotofsky AZ: Confronting the bomber: coping at the site of previous terror attacks. J Nerv Ment Dis 2007; 195(3):233-9

» NR2-126

RISK FACTORS IN POSTPARTUM PSYCHIATRIC DISORDERS

Nesrin Karamustafalioglu, Nesrin Tomruk, M.D., Evrim Oztekin, M.D., Ozlem Tanriover, M.D., Rahsan Erim, M.D., Cahide Ucar, M.D., Nihat Alpay, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation the participant should be able to identify the postpartum period as a time of high risk for psychiatric disturbances and to realize marital discordance, lack of social support, financial difficulties and adverse life events as contributing psychosocial factors.

SUMMARY:

Introduction: Postpartum (PP) period is a time of high risk for the occurence of psychiatric disorders. A multifactorial causal model, incorporating biological, psychosocial and developmental variables has been proposed. Among these, psychosocial risk factors have been frequently reported. Identifying these risk factors is essential to develop appropriate intervention strategies. In this study, it was aimed to identify the psychosocial risk factors contributing to the development of PP psychiatric disorders. Method: 39 patients hospitalized with PP psychiatric disorder between March-September 2008 in Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, were included in the study. A matched control group of 61 mothers were recruited from a General Training Hospital's well child unit. PP period was defined as up to 6 months after delivery. A semistructured form evaluating demographic, psychosocial variables and reproductive data was performed. Results: The majority of the patients were bipolar. Four factors emerged as contributing risk factors and all were statistically significant compared to the control group. The majority of the PP patients (85%) reported lack of social support especially for the care of the baby. Two thirds had marital dissatisfaction, while 67% had adverse life events, and 54% had financial difficulties. Conclusion: In this study, the frequently reported psychosocial risk factors have been found to be related to PP disturbances; indicating that women are more prone to developing PP disorders whan certain risk factors are present. Marital relationship, social support, life events and economic status are important in this context. Traditional social supports such as extended family may be weakening with urbanisation in Turkey. These results emphasize the need for identifying the psychosocial risk factors in PP disorders, so that the necessary interventions could be undertaken.

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» NR2-127

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (RTMS) IN PREGNANT WOMEN WITH MAJOR DEPRESSIVE DISORDER

Deborah R. Kim, M.D., Juan M. Gonzalez, M.D., Pilar Cristancho, M.D., Laura Wakil, M.D., Samuel Parry, M.D., Michal A. Elovitz, M.D., Karl Rickels, M.D., Michael E. Thase, M.D., John P. O'Reardon, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the preliminary feasibility, safety and efficacy data for the use of 1 Hz repetitive transcranial magnetic stimulation in pregnant women with major depressive disorder

SUMMARY:

Specific Aim: To evaluate the feasibility and safety of repetitive transcranial magnetic stimulation (rTMS) in pregnant women with major depressive disorder (MDD). Methods: This open-label pilot study examined the feasibility and safety of 1Hz right –sided dorsolateral prefrontal cortex (RDLPFC) rTMS in pregnant women with MDD. Eligible women were 18 - 39 years old, 14 – 34 weeks gestational age (GA), and had a Hamilton Depression Rating Scale (HDRS) = 14. Each subject received 20 sessions of rTMS. Repeated pulses at 1 Hz frequency were delivered in 60 second trains followed by inter-train intervals of 60 seconds (100%MT). The total study dose was 6,000 pulses. Non-stress test fetal cardiotocography (NST), uterine tocometry and fetal growth ultrasounds were performed. Primary outcomes were number of sessions attended and results of NST, tocometry and ultrasounds. Changes in HDRS and clinical global improvement (CGI) scores

from baseline to week 4 were assessed. Subjects were considered responders if HDRS score decreased by = 50. Descriptive statistics are used. Sample Characteristics: 4 women completed treatment. At study entry, the mean age was 29 (SD 8.2) and mean GA was 25 (SD 2.9). At baseline, mean HDRS was 26.8 (SD 4.6) and CGI-severity was 4.8 (SD 0.5). Results: All subjects had 100% session attendance. No abnormalities in fetal heart rate, uterine tocometry or fetal ultrasounds were associated with rTMS. HDRS decreased by 63% to a mean HDRS of 10.2 (SD 6.7).3/4 subjects were responders. Post-treatment CGI-S was 2.8 (SD 0.5). No serious adverse events were seen in the mother or fetus, with transient headache the only adverse event of note. Conclusions: rTMS is feasible, safe and effective in this sample of pregnant women with MDD. Although sample size is small, the novelty of a non-invasive treatment for MDD in pregnancy, along with encouraging preliminary safety and efficacy results, will likely stimulate interest among medical professionals.

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2) Ziad Nahas, Daryl E. Buhning, Monica A. Molloy, John A. Oustz, S. Craig Risch and Mark S. George. Safety and feasibility of repetitive transcranial magnetic stimulation in the treatment of anxious depression in pregnancy: a case report. J Clin Psychiatry 1999 60(1):50-2.

» NR2-128

ABUSE EXPERIENCES BEFORE AND DURING PREGNANCY AND THEIR RELATIONSHIP WITH ANTENATAL DEPRESSION AND EATING DISORDERS

Antoinette M. Lee, Ph.D, Catherine S. K. Tang, Ph.D., C. Y. Chan, BSoc. Sc., Siu-Keung Lam, M.D., Kwok-Yin Leung, M.B.B.S., M.Sc., F.R.C.O.G.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the significance of abuse experiences during pregnancy, and to understand the relationship between different forms of abuse before and during pregnancy and depressive and disordered eating symptoms in the antenatal period.

SUMMARY:

Background and Objectives: Intimate partner abuse affects many women. Past studies showed significant relationship of childhood abuse with depression and eating disorders (1, 2). However, the impact of more proximal abuse experiences on antenatal mental health is much less examined. The aim of the study is to estimate the prevalence of emotional, physical and sexual abuse by partner immediately before and during pregnancy, and to examine if these were associated with increased risks of depression and eating disorders in early pregnancy.

Methods: A cross sectional survey of 504 pregnant women attending two regional hospitals in Hong Kong were assessed with the Abuse Subscale of the WHO Multi-Country Study on Women's Health and Domestic Violence Core Questionnaire (Version 10), Edinburgh Postnatal Depression Scale, and Eating Attitudes Test-26 at first antenatal presentation. Participants were asked to complete the Abuse Subscale with reference to two time points: during the one year before pregnancy (retrospective report) and at present (first trimester).

Results: Participants' mean weeks of gestation was 12.1 (SD = 1.14). Emotional abuse was the most prevalent form of abuse, with prevalence of 10% and 4.8% in the year before and during pregnancy respectively. Rates of physical (before: 2.4 %, during: 0.8 %) and sexual abuse (before: 0.4%, during: 0.2%) were lower but also of concern. Women experiencing emotional abuse before pregnancy (OR 2.41, 95% CI: 1.30-4.48, p<.01) and during pregnancy (OR 4.27, 95% CI: 1.82-10.02, p<.01) had more than 2- and 4-fold increased risk of depression respectively. Neither physical nor sexual abuse was associated with depression. Increased risk of eating disorders was not predicted by any form of abuse.

Conclusion: Emotional abuse is a significant problem with adverse impact on pregnant women's mental health. Identification of and intervention for emotionally abused pregnant women is important in preventing antenatal depression. This study was supported by a grant from the General Research Fund of the Research Grants Council of the HKSAR (Ref: CERG HKU7470/06H)

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» NR2-129

PREDICTORS OF INCIDENCE OF PPD: THE POTENTIAL ROLE OF SEPARATION ANXIETY

Mauro Mauri, MD, Mary Katherine Shear, MD,Susanna Banti, MD, Annalisa Oppo, Psy D., Chiara Borri, MD, Valeia Camilleri, Daniele Ramacciotti, MD, Maria Sole Montagnani, MD, Sonia Cortopassi, MD, Cristina Rambelli, MD

EDUCATIONAL OBJECTIVES:

To identify and assess whether mood or anxiety spectrum phenomena and family history of psychiatric disorders predict cumulative incidence of postpartum depression above and beyond established risk factors

SUMMARY:

Objective: To examine whether mood or anxiety spectrum assessment and family history of psychiatric disorders predicts cumulative incidence (1st- 6th month postpartum) of postpartum depression.

Method 600 women, presenting for ultrasound examination were assessed at baseline and approximately every two months up to 6 months postpartum. During pregnancy, participants completed Postpartum Depression Predictors Inventory-Revised (PDPI-R) (Beck et al., 2002), Family History Screen (FHS) (Weissman et al., 2000), Mood Spectrum (Dell'Osso et al., 2002) and Panic-Agoraphobic Spectrum (Cassano et al., 1999). Each spectrum instrument consists of a group of factors pertaining to component clinical features. Mood spectrum includes 6 depressive factors (Cassano et al., 2008) and 9 manic-hypomanic factors (Cassano et al., 2009), panic agoraphobic spectrum includes ten factors (Rucci et al., 2008). During postpartum, participants completed the Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987), women who exceeded the EPDS cut-off score of 13 were administered the SCID-I to confirm the diagnosis of PPD. A stepwise logistic regression model was performed to identify the role of each specific factor of the Spectra instruments in early predicting the risk for PPD, adjusting for the PDPI-R.

Results: The cumulative incidence of PND was 4.4% (N=25). PDPI-R during pregnancy predicted PND, but mood spectrum did not. Family history of panic disorder (RR=2.1; 95% CI: 1.06-4.4) 'Separation Anxiety' (RR=1.3; 95%CI=1.1-1.5) and 'Loss Sensitivity' (RR=0.5; 95% CI= 0.3-0.98) of the Panic-Agoraphobic Spectrum predicted cumulative incidence of PPD.

Conclusion: Our results suggest that panic-related symptoms, especially separation anxiety, predicts PPD. In addiction to previously identified risk factors, (personal-family history of Depression, lack of social-environmental support, low income, etc.), these panic symptoms should be assessed when managing pregnant and postpartum women.

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2) Beck CT. Revision of the postpartum depression predictors inventory. J Obstet Gynecol Neonatal Nurs 2002;31(4):394–402.

» NR2-130

MOTHER-INFANT ANTIDEPRESSANT LEVELS AND MATERNAL DEPRESSION: IMPACT ON NEONATAL OUTCOMES

Dorothy Sit M.D., Eydie Moses-Kolko, M.D., Diane Hunker, Ph.D., M.B.A., Sonia Jones-Ivy, M.D., Joseph Helsel, B.S., James Perel, Ph.D. and Katherine L. Wisner, M.D., M.S.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize exposures to shorter acting agents, maternal depression, and smoking may contribute to risk for neonatal signs. Effective antidepressant and smoking cessation treatments could improve outcomes of newborns of depressed mothers.

SUMMARY:

Objectives. We explored the relationships between neonatal outcomes and cord and maternal plasma antidepressant levels and maternal major depressive disorder.
Methods. The investigators enrolled 21 mother-infant pairs with antidepressant exposure across pregnancy. Mothers were assessed with the Structured Clinical Interview for DSM-IV to confirm the diagnosis of Major Depressive Disorder. Depression ratings, antidepressant dose and smoking frequency were obtained at 20, 30, 36 weeks gestation and delivery. Cord and maternal blood samples were obtained at delivery. Neonatal outcome was assessed with the Peripartum Events Scale (PES).
Results. One-third (7/21) of infants had neonatal signs defined by a PES score of one or more. Newborns with signs were exposed to shorter acting serotonin reuptake inhibitors only. Of the affected infants, three (43%) had preterm and four (57%) had full-term births. Five newborns with signs (71%) were exposed to higher cord-to-maternal levels ratios (0.56-1.64) of venlafaxine, escitalopram, citalopram and sertraline; two (29%) were exposed to lower cord-to-maternal levels ratios (0.19-0.34) of sertraline. Among the neonates with signs, 5 (71%) had mothers with major depression; in contrast, 6 of 14 healthy infants (43%) had depressed mothers. Three of 7 affected neonates (43%) had exposure to maternal smoking, compared to only 2 of 14 healthy newborns (14%).
Conclusion. These data suggest that exposures to shorter acting agents, maternal depression, and smoking may contribute to risk for neonatal signs. Effective antidepressant and smoking cessation treatments could improve the outcomes of newborns of depressed mothers.

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1) Hendrick V, Stowe ZN, Altshuler LL, Hwany S, Lee E, Haynes D. Placental passage of antidepressant medications. Am J Psychiatry 2003; 160:993-996.

2) Loughhead AM. Stowe ZN, Newport DJ, Ritchie JC, DeVane CL, Owens MJ. Placental passage of tricyclic antidepressants. Biol Psychiatry 2006; 59:287-290.

» NR2-131

THYROID HORMONE LEVELS AND THYROID ANTIBODIES IN POSTPARTUM PSYCHIATRIC INPATIENTS

Nesrin Tomruk M.D., Nesrin Karamustafalioglu, M.D., Ozlem Tanriover, M.D., Rahsan Erim, M.D., Evrim Oztekin, M.D., Gozde Yapici, M.D., Nihat Alpay, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation the participant should be able to recognize the importance of biological factors and to interpret thyroid hormone and antibody levels in postpartum psychiatric disorders.

SUMMARY:

Introduction: Thyroid diseases are the most common endocrine diseases and may cause many psychiatric disorders. Thyroid hormone levels may also be temporarily abnormal in acute hospitalizations, referred to as Euthyroid Sick Syndrome (ESS). It is reported to be 5-30% in acute psychiatric inpatients, the most frequent being high T4 and TSH levels. The vulnerability and risk for mental illness is high in the postpartum (PP) period. Among the biological risk factors, hormonal changes may play an important role. A relationship between thyroid hormone dysfunction and perinatal mood has been postulated. In this study it was aimed to investigate the prevalence of abnormal thyroid tests and thyroid antibody levels in acute PP psychiatric inpatients. Method: Thyroid hormone and thyroid antibody (antimicrosomal, antithyroglobuline) levels were measured in 34 consecutive postpartum (6 months) psychiatric inpatients between March-September 2008. Results: The majority of the patients (59%) were bipolar. Among 34 patients, one had hyperthyroidism and one other case had elevated antimicrosomal antibody level, with decreased TSH, increased T3 and normal T4 levels. There were high T3 in 35%, low T4 in 26%, high TSH in 12%, low TSH in 12%, low T3 in 9% and high T4 in 6% of the patients. Only in 38% of the patients all three hormone levels were in normal range. Conclusion: Although affective illness and female gender are risk factors for thyroid disease and thyroid dysfunction is postulated to be aetiologically related to PP psychiatric disturbances, the prevalence of thyroid disease was not higher than reported both in general population and psychiatric inpatients. However, ESS was considerably high; these nonspecific alterations may also be related to perinatal changes in hypothalamic-pituitary-thyroid axis. The most prevalent abnormalities were high T3 and low T4 levels in our group. Assessment of thyroid function as a contributing factor in PP psychiatric patients is essential.

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2) Harris B. Postpartum depression and thyroid antibody status. Thyroid 1999; 9(7):699-703.

Monday, May 18, 2009

3:00 p.m. - 5:00 p.m.
Hall D, Exhibit Level,
Moscone Convention Center

NEW RESEARCH POSTER SESSION 3: YOUNG INVESTIGATOR POSTERS 1

» NR3-001

PSYCHIATRIC COMORBIDITY IN SOCIAL PHOBIA - RELATIONSHIP WITH DURATION OF UNTREATED PERIOD

Hong-min Choi M.D., Young-Do Kwon, M.D., Se-Won Lim, M.D., Kang-Seob Oh, M.D.,Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize that the longer duration of untreated period with social phobia patients have the more comorbid depressive disorders

SUMMARY:
objective: depressive and other anxiety disorders are commonly found to coexist with social phobia patients. we investigated psychiatric comorbidity, and compared with comorbid depressive disorder group and with comorbid anxiety disorder group in social phobia to document difference in demographic and clinical features. methods: a total of 292 outpatients with social phobia were included in this study. all the patients were evaluated using clinical instruments for the assessment the presence of comorbid other psychiaric disorders and various clinical features; korean version of mini international neuropsychiatric interview plus, self-report questionnaires (beck anxiety inventory, beck depression inventory, anxiety sensitivity index and state-trait anxiety inventory) and clinical rating scales (hamilton anxiety scale, hamilton depression scale and global assessment of functional score). Results: thirty two percent of social phobia patients were found to at least one comorbid psychiatric diagnosis. there were no differences between comorbid depressive disorder group and comorbid anxiety disorder group in demographic characteristics (sex, education, presence of occupation, marital status). In addition, there were no differences in age, onset age of social phobia, total score of beck anxiety inventory, beck depression inventory, anxiety sensitivity index and state-trait anxiety inventory, hamilton anxiety scale, hamilton depression scale and global assessment of functional score between both group. however, cormorbid depressive disorder group have more longer illness duration of social phobia than anxiety disorder comorbidity group. conclusion: the results of this study demonstrate that the longer duration of untreated period with social phobia patients have the more comorbid depressive disorders than comorbid anxiety disorders. these results suggest that early treatment of social phobia may reduce the risk of depressive disorder comorbidity.

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1) Chartier MJ, Walker JR, Stein MB. Considering comorbidity in social phobia. Soc Psychiatry Psychiatr Epidemiol. 2003 Dec;38(12):728-34.

2) Wittchen HU, Fehm L. Epidemiology, patterns of comorbidity, and associated disabilityies of social phobia. Psychiatr Clin North Am. 2001 Dec;24(4):617-41. Review.

» NR3-002

STARTLE REACTIVITY IN SOCIAL ANXIETY DISORDER DURING SPEECH ANTICIPATION IN VIRTUAL REALITY

Randi Heller B.A., Brian R. Cornwell, Ph.D., Arter Biggs, B.A., Daniel S. Pine, M.D., Christian Grillon, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should: 1) understand specific social cues of public speaking that elicit fear and anxiety in individuals with Social Anxiety Disorder (SAD); 2) be aware of the specificity of heightened fear in SAD patients while being the center of attention because it could lead to a more precise focus for treatment; and 3) recognize the startle reflex as a useful and dependable measure of anxiety.

SUMMARY:
A detailed understanding of how individuals diagnosed with Social Anxiety Disorder (SAD) respond physiologically under social-evaluative threat is lacking. We aimed to isolate the specific components of a socially threatening situation that distinguish SAD patients from healthy individuals. Seventeen individuals diagnosed with SAD and seventeen healthy individuals were asked to prepare and deliver a short speech in a virtual reality (VR) environment. The VR environment simulated standing center stage before a live audience and allowed us to gradually introduce social cues during speech anticipation. To measure fear reactivity, startle eye-blink responses were elicited periodically by loud white-noise bursts presented during anticipation, speech delivery, and recovery in the VR environment.
SAD individuals reported greater distress and state anxiety than healthy individuals across the entire VR procedure. Analyses of startle reactivity revealed a robust group difference during speech anticipation in VR, specifically as audience members directed their eye gaze and turned their attention toward the participants. SAD individuals, compared to healthy controls, show greater potentiated startle specifically when they perceived themselves as occupying the focus of others' attention. This response is indicative of a strong phasic fear response. Our results show that potentiation of startle under social-evaluative threat is emerging as a reliable biomarker marker for trait social anxiety. These findings also suggest that our VR environment is sufficiently realistic to provoke fear and anxiety in individuals who are highly vulnerable to socially threatening situations.

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1) Grillon C: Models and Mechanisms of Anxiety: Evidence from Startle Studies. Psychopharmacol 2008 199(3): 421-437

2) Cornwell BR, Johnson L, Berardi L, Grillon C: Anticipation of Public Speaking in Virtual Reality Reveals a Relationship Between Trait Social Anxiety and Startle Reactivity. Biol Psychiatry 2006 59: 664-666

» NR3-003

POSSIBILITY OF QT DISPERSION AS NEUROPHYSIOLOGICAL MARKER IN SOCIAL PHOBIA

Youngdo Kwon M.D., Hong-min choi, M.D.,Se-won Lim,M.D.,Ph.D., Kang-seob Oh, M.D.,Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be able to recognize the relationship between social phobia and QT dispersion

SUMMARY:
Objectives:Social phobia is one of the most common anxiety disorders. It is frequently accompanied with automic nerve system symtoms, which are related to imbalance of the automic nerve system. According to former studies, QT dispersion such as the maximum interlead difference in QT interval is an indicator of the automic nerve system disparity of the heart itself; myocardial infarction etc.The objective of this study is to investigate possibility of QT dispersion as neurophysiological marker by verifying the hypothesis that the QT dispersion of social phobia patient group is higher than the normal control

Methods:This research has targeted 15 physically healthy social phobia outpatients(10 men, 5 women, the average age 26±2.6), the research has the control group of mentally physically healthy 15 people (10 men, 5 women, the average age 26±2.6) and the proportion of males to females is equal. All QT interval measurements were performed manually with an accurate caliber (Digital Vernier Calipers) with an accuracy of 1/100mm by one person. Rate-corrected QT interval(QTc)is measured by using Bazett's formula
Results: QT dispersion(QTd) and rate-corrected QT dispersion(QTcd) are significantly higher in the patient group than in the control group. QTd (55±27 ms vs. 20±7 ms, $P < 0.0001$) QTcd (58±26 ms vs. 21±7 ms, $P< 0.0001$)
This result shows statistically unchanged difference between two groups by analyzing (using ANCOVA) considering ages. RR interval and heart rate are no difference between two group ($P = 0.897$, $P = 0827$)
Conclusion: Our study shows association between social phobia and increase of QT dispersion. Previous studies showed the QT dispersion is associated an increase of sympathetic nerve system and cardiac disease. Therefore, measurements of QT dispersion could be used as supplementary tool for diagnosis of social phobia. The major limitation of this study is the small number of sample size.

REFERENCES:

1) Nahshoni, E., Gur, S., Marom, Z., Levine-Pore, J., Weizman, A., Hermesh,H., QT dispersion in patients with social phobia. J. Affect. Disord 78 (2004) 21–26.

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» NR3-004

AN OPEN STUDY OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION IN TREATMENT OF OBSESSIVE-COMPULSIVE DISORDER

SE JOUNG LEE, Young-Eun Jung, MD, Ho-Jun Seo, MD, Won-Myong Bahk, MD, PhD, Tae-Youn Jun, MD, PhD, Jeong-Ho Chae, MD, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to improve OCD symptoms

SUMMARY:

Objective: There are several evidences that repetitive transcranial magnetic stimulation(rTMS) may be useful for the treatment of obsessive-compulsive disorder(OCD). This study was conducted to investigate the efficacy of rTMS for patients with OCD and the factor associated with clinical response.
Method: Data of 24 patients with OCD treated rTMS(right prefrontal, 1 Hz, 20min, 15 daily session) from January 2003 to July 2008 were collected. Demographic data and clinical data were investigated.
Results: Subjects had an overall significants improvements in the CGI score. Good social and occupational adjustment is a predictor of treatment response.
Conclusion: Low-frequency rTMS of the right prefrontal cortex produced significant improvement of OCD. Further studies are indicated to assess to the efficacy of rTMS in OCD and to clarify the predictive factors that response to rTMS.

REFERENCES:

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2) Chae JH, Nahas Z, Wassermann E, Li X, Sethuraman G, Gilbert D, Sallee FR, George MS: A pilot safety study of repetitive transcranial magnetic stimulation (rTMS) in Tourette's syndrome. Cogn Behav Neurol 2004;17(2):109-117

» NR3-005

PSYCHOLOGICAL TESTS AS PREDICTORS OF FEAR CONDITIONING AND EXTINCTION IN HUMANS

Karen Martinez M.D., Franco JA; Ojeda B; Castro-Couch M; Segura G; Milad MR; Quirk GJ

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the role of fear extinction in the etiology and treatment of anxiety disorders and identify how psychological tests could be used clinically to predict fear extinction responses.

SUMMARY:

There is increasing recognition that people with anxiety disorders show altered fear learning and fear extinction. Thus, it would be useful to be able to predict fear learning and extinction, for diagnosis and treatment purposes. Because it is not practical to carry out psychophysical testing on a large scale, we sought to determine if simple psychological tests could predict fear learning and extinction in normal adults. We used tasks that rely on the same orbitofrontal and cingulate regions implicated in fear expression and extinction, namely Stroop interference tasks and the WCST. Nineteen healthy adults (8 female and 11 male aged 21-39) were administered a series of tests that included the State-Trait Anxiety Inventory, the Multi-Source Interference Task (a counting Stroop task), the Wisconsin Card Sorting Test (WCST) and the Emotional Stroop Task (EST). Subjects were then trained in a well established fear conditioning and extinction paradigm which consists of associating a colored light with an electrical current and then extinguishing this association. Skin conductance responses (SCR) were recorded as a physiological measure of fear. During conditioning, higher SCR measures were associated with longer latency to threat in the EST ($r=0.749$; $p=0.000$) and higher state anxiety inventory scores ($r=0.604$; $p=0.006$). This association with EST was stronger for women ($r=0.810$; $p=0.015$) and only seen for women with the state anxiety inventory($r=0.687$; $p=0.06$). No associations could be seen with conditioning and MSIT or WCST. During recall of fear, less fear during this phase was associated with higher state anxiety inventory scores ($r=-0.847$; $p=0.009$) and more cognitive flexibility in the WCST ($r=-0.783$; $p=0.022$) only in women. Finally, upon evaluation of renewal of fear, subjects with longer latencies to threat words in the EST were associated with less renewal of fear ($r=-0.502$; $p=0.029$) and this association was stronger for women ($r=-0.905$; $p=0.02$). Multiple linear regression models showed that the EST latency and the score on the State Anxiety Inventory could predict the scores on fear conditioning ($R=0.891$; $p=0.019$) and fear renewal ($R=0.895$; $p=0.018$). These results suggest that psychological tests could indeed be used to predict acquisition of fear and contextual renewal of fear, particularly in women.

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» NR3-006

PREGABALIN: BEYOND THE GENERALIZED ANXIETY DISORDER

ALFONSO MOZOS-ANSORENA M.D., Pérez-García M.,M.D., Páramo-Fernández M.,Ph.D.,Núñez-Iglesias J.,M.Ph.D., Brenlla-Gonzalez, J,Ph.D., Portillo-Díez J.; Alonso San-Gregorio J.,M.D., Pérez-Pérez J.,M.D., Tortajada-Bonasselt I.,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize Pregabalin showed to be useful beyond the generalized anxiety disorder:in the somatomorph disorder resistant to the

antidepressant treatment, in serious depression, bipolar disorder, discontinuation of benzodiazepine and in alcoholic detoxification.

SUMMARY:

INTRODUCTION:Pregabalin showed its efficacy in the generalized anxiety disorder.Recent investigations deal with its potential usefulness in the somatomorph disorder resistant to the antidepressant treatment, in serious depression,bipolar disorder, discontinuation of benzodiazepine and in alcoholic detoxification. OBJETIVE:description of sociodemographic and health variables of patients hospitalized in a Psychiatric Hospitalization Unit under treatment with pregabalin since February 2006 to May 2008. MATERIALS AND METHODS:10 women and 8 men(average age = 57.78±15.69 years).Variables are analyzed through a statistic package,using frequency tables and distribution graphics. RESULTS:SOCIODEMOGRAPHIC PROFILE:Married persons (33.3%).Most of them live together with own family(55.6%).A 38.9% have primary education.A 72.2% are pensioners.HEALTH PROFILE:Axis I:The disorders stand out due to the consumption of drugs(33%),the depressive disorders and the somatomorph disorders(both 28%).Axis II: 22% show a personality disorder.The most frequent somatic diagnosis is the osteomuscular pathology(33.3%),and neurological pathology(22.2%).We observe anxious symptomatology at the moment of admission in more than 75% of the patients.The stipulated dose of pregabalin has been varied,ranging between 75 mg/day(33.3%)and 300 mg/day (33.35).An 83% is also administered with an ansiolytic treatment and a 66.7% with antidepressants.CONCLUSIONS:In our sample, the patients treated with pregabalin show the following profile:woman aged 58, married,who lives with own family,she did primary studies and is a pensioner.She shows a disorder due to the consumption of drugs with/without a depressive or somatomorph disorder.She suffers from osteomuscular pains and has an anxiety symptomatology when admitted.She receives a dose of 75 or 300 mg/day of pregabalin,together with an ansiolytic and/or antidepressant.Therefore,the pregabalin showed to be useful beyond the generalized anxiety disorder.

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» NR3-007

ALEXITHYMIA IN OBSESSIVE-COMPULSIVE DISORDER

Daeyoung Roh, Chan-Hyung Kim, M.D., Ph.D., Se-Joo Kim, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize OCD is related to alexithymia ;understand the relationships between alexithymia and obsessive-compulsive symptom dimensions

SUMMARY:

Previous studies have suggested an association between alexithymia and obsessive-compulsive disorder (OCD). The purpose of the current study was to evaluate difference of the alexithymia between obsessive-compulsive patients and normal controls. This study was also designed to elucidate the relationships between alexithymia and obsessive-compulsive symptom dimensions. 45 subjects with OCD and 45 normal controls completed Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), Korean version of 20 item Toronto Alexithymia Scale (TAS-20K), Hamilton Anxiety Scale, and Montgomery-Asberg Depression Rating Scale. OCD was associated with significantly higher scores of alexithymia. The alexithymia of obsessive-compulsive patients was explained by anxiety and age of onset. The YBOCS score and Obsessions score in obsessive compulsive patients were correlated with TAS-20K score. 'Sexual/religious obsessions' dimension out of five symptom dimensions was significantly associated with alexithymia. These findings suggest that early onset groups of OCD may be associated with alexithymia and patients with sexual/religious obsession dimensions may tend to be alexithymic. In the future, prospective studies are needed with large groups of obsessive-compulsive patients concerning about obsessive compulsive symptom dimensions related with alexithymia using factor analysis.

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» NR3-008

SYMPATHETIC NERVOUS FUNCTION AND CATECHOL-O-METHYLTRANSFERASE GENETIC POLYMORPHISM IN PATIENTS WITH PANIC DISORDER

Song Yoon-Jae, Woo-Yong Shin, M.D., Eun-Ho Kang,M.D., Hoondong Choe,M.D, Bum-Hee Yu, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to catechol-o-methyltransferase genetic polomorphism coudl moderate sympathetic function in panic disorder.

SUMMARY:

Background: Abnormalities of the sympathetic nervous function has long been known as one of the possible etiologies of panic disorder. The catechol-O-methyltransferase(COMT) affects sympathetic activities, and the COMT genetic polymorphism has been suggested to be related to panic disorder. The aim of this study was to examine the relationship between the COMT genetic polymorphism and sympathetic nervous function in patients with panic disorder.

Methods: Fifty-eight patients with panic disorder and 58 age-matched normal control subjects were compared in terms of the finger temperature which is known to be a useful marker reflecting sympathetic nervous function. Genotyping for the COMT Val158Met polymorphism was performed using polymerase chain reactions.

Results: There was a significant interaction effect between the COMT genetic polymorphism and diagnosis in terms of finger temperature (F1, 106=5.158, p=0.025), and the post hoc analysis revealed that panic patients with the L allele carriers showed significantly lower finger temperature than those with the H allele carriers (t1, 56 = -2.042, p=0.046).

Conclusions: This study suggests that the COMT L alleles may be related to higher sympathetic nervous function in panic disorder.

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» NR3-009

SUBGENUAL CINGULATE GYRUS DEEP BRAIN STIMULATION FOR REFRACTORY MAJOR DEPRESSIVE DISORDER: A MULTI-CENTRE UPDATE

Peter Giacobbe B.S.C., Sidney H. Kennedy MD FRCPC, Helen S. Mayberg MD, Andres M. Lozano MD PhD FRCSC, Raymond W. Lam MD FRCPC, Guy Debonnel MD FRCPC, Theodore Kolivakis MD FRCPC, Andrew Howard MD FRCPC, Abbas Sadikot MD PhD FRCSC, Christopher Honey MD PhD FRCSC

EDUCATIONAL OBJECTIVES:
The participant should be aware of ongoing developments in the evaluation of Deep Brain Stimulation (DBS) to subgenual cingulate gyrus – Brodmann area 25 (SCg25) for Major Depressive Disorder that is resistant to > 4 treatments.

SUMMARY:
Background: Pilot data support the effectiveness of DBS to SCg25 for MDD with resistance > 4 treatments (Mayberg et al, 2005; Lozano et al, 2008). Replication of methodology and expansion of sample size in sites other than Toronto are important for verifying this hypothesis.
Methods: Three academic centres in Canada (McGill University, University of British Columbia and University of Toronto) recruited 21 patients who met stringent criteria for MDD resistant to 4 or more treatments, comparable to previously published inclusion/ exclusion criteria. Bilateral quadripolar DBS electrodes were implanted in white matter immediately adjacent to SCg25 using MRI-guided stereotactic localization. Surgeries were completed November 1, 2005 to August 31, 2008.
Results: Eighteen patients have completed 6 months of post surgery evaluation and 17 have been evaluated after one year. Improvement in depressive symptomatology was seen in 78% of patients. The mean baseline Hamilton Rating Scale for Depression 17 Item-HRSD-17 was 27.4 and the mean at last follow-up was 16.6 showing a 40% improvement in scores over time. Of patients who were responders or partial responders at months 4-6 compared to baseline, 72% sustained improvement at last follow-up, which was defined as a consistent HRSD-17 score that did not increase more than 20%. In all patients, the greatest improvements at 1 year (HRSD-17) were seen in the depression (mood, work, guilt and retardation) and anxiety (psychic, somatic, hypochondriasis) symptom clusters(46% and 45%, respectively).
Conclusions: The results confirm this study's initial findings at 6 months that DBS to SCg25 is an effective intervention for MDD resistant to > 4 treatments in the majority of eligible patients and suggest that benefits are sustained in approximately three quarters of patients.

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» NR3-010

UNUSUAL PRESENTATION OF HYPOXIC DELIRIUM

Stanislav Grabylnikov M.D., Irmute Usiene M.D.PGY II, Amel Badr M.D., Javed Iqbal M.D., Mohammad Niazi M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to identify and diagnose carbon monoxide –induced delirium, perform differential diagnosis, predict and identify neurological sequelae and create treatment plan.

SUMMARY:
Carbon monoxide intoxication may result in neuropsychiatric abnormalities that can be overlooked or not fully appreciated. Estimates show that 50% of individuals with carbon monoxide poisoning will develop neurologic, neurobehavioral, or cognitive sequelae. CO- related cognitive impairments include impaired memory, attention, executive function, motor, visual spatial, slow mental processing speed ,mood symptoms (depression or mania), delusions, hallucinations.
We present a patient with h/o seizure disorder and no prior psychiatric history. The patient was neurologically stable, free from psychiatric symptoms and lived alone in an apartment where a constant carbon monoxide furnace leak was later discovered. Over the period of six weeks the patient gradually became isolative, had decreased appetite, minimal and irregular food intake, had difficulties maintaining personal hygiene, poor sleep and reported fearful and anxious mood. The patient started to believe that aliens from another planet were invading the Earth and on the day of presentation called his parents and made a statement that he saw aliens on TV and he believed that people in the neighborhood are aliens too. The patient was treated with Risperdal and after a period of five days his condition was much improved. We concluded that the patient had suffered Hypoxic Delirium secondary to carbon monoxide poisoning. He was discharged in stable condition with plan to follow up with a neurologist.

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» NR3-011

CHANGES IN RCBF AFTER LEFT HIGH FREQUENCY AND RIGHT LOW FREQUENCY RTMS ON DLPFC IN REFRACTORY DEPRESSIVE AND ANXIETY DISORDERS

Eun Jin Jahng M.D., Jung-Ah Min, M.D., Hyewon Lee, M.D., Ho-Jun Seo, M.D., Yong-An Chung, M.D., Jeong-Ho Chae, M.D, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize therapeutic effect of left 20Hz and right 1Hz DLPFC rTMS in drug-resistant depression and anxiety disorders.

SUMMARY:
Objective: Recently, studies have reported high frequency rTMS applied to the left dorsolateral prefrontal cortex (DLPFC) improved depressive symptoms and low-frequency rTMS applied to the right DLPFC improved depressive and anxiety symptoms. We examined the changes in regional cerebral blood flow (rCBF) and symptom severity before and after randomly assigned left high frequency and right low frequency DLPFC rTMS in refractory depression and anxiety disorders.
Methods: The clinical symptoms and images of brain perfusion Tc-99m ECD Single Photon Emission Computed Tomography (SPECT) were obtained and reconstructed using statistical parametric mapping (SPM) in 21 patients with drug-resistant depression and anxiety disorders (14 male, 7 female; mean age: 35.4 years), both before and after rTMS . rTMS were randomly assigned to left high frequency (20Hz, 2 seconds on, 28 seconds off, 20 minutes, 15 times) and right low frequency (1Hz, 20 minutes, 15 times) with 100% of motor threshold.
Results: After rTMS, increased rCBF was detected in the left precentral gyrus, postcentral gyrus, parahippocampal gyrus, and culmen. No area with decreased rCBF after rTMS was noted. Improvement in depressive symptoms was found (Clinical Global Impression (CGI);P=0.04, Hamilton Depression Rating Scale (HDRS); P=0.01). Right 1Hz rTMS (N=13) induced increased rCBF in left putamen, globus pallidus, thalamus, culmen, postcentral gyrus, parahippocampal gyrus, hippocampus and clinical improvement in CGI (P=0.02), HDRS (P=0.05). Left 20 Hz rTMS (N=8) induced increased rCBF in left fusiform gyrus, inferior prefrontal cortex, precentral gyrus, and parahippocampal gyrus and improvement in Beck Depression Inventory (P=0.04), HARS (P=0.02).
Conclusions: We found changes in the rCBF and improvements of clinical symptom severities with rTMS in drug-resistant depression and anxiety disorders. Differential effects on rCBF and clinical features by left 20 Hz rTMS and right 1Hz rTMS were noted.

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» NR3-012 - WITHDRAWN

» NR3-013

ASSOCIATION BETWEEN DOPAMINE D2-RECEPTORS IN LIMBIC BRAIN REGIONS AND THE PERSONALITY TRAIT SOCIAL DESIRABILITY: IMPLICATIONS FOR SOCIAL PHOBIA

Simon Cervenka M.D., Christer Halldin, Ph.D., Lars Farde, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand how research on the biological background of personality traits can further our knowledge on the pathophysiology of psychiatric disorders. In particular, the present findings should provide the participants with a theoretical model of how dopaminergic neurotransmission can influence specific symtom dimensions in anxiety disorders such as social phobia, knowledge which may eventually inform treatment decisions.

SUMMARY:

OBJECTIVE: The dopamine system has a role in social behavior and personality, as supported by animal research and studies in human subjects (1). In particular, recent molecular imaging studies have shown a negative correlation between dopamine D2-receptor binding in the striatum and socially desirable responding, which represents a tendency to adjust behavior to gain approval (2). The emotional and cognitive aspects of social behavior suggest involvement of brain regions outside of the striatum, such as limbic structures. The aim of the present study was to explore associations between the personality trait social desirability and dopamine D2-receptor binding in both striatal and extrastriatal brain regions.
METHOD: We examined 16 healthy control subjects with Positron Emission Tomography and the radioligands [11C]raclopride for striatal regions and [11C]FLB 457 for extra-striatal regions. Regional D2-receptor binding potential values were analyzed in relation to scores on the social desirability scale of the inventory Swedish universities Scales of Personality.
RESULTS: D2-receptor binding in the hippocampal-amygdala complex showed statistically significant negative correlations to social desirability (p=0.008), whereas a trend-level correlation in the same direction was found for striatum.
IMPORTANCE: The results add to previous evidence in support of a role for the dopamine system in socially desirable behavior, and extend this research into brain regions of relevance to fear and learning. Patients with social phobia experience fear of negative evaluation, a disposition which could be underlying also the personality trait of social desirability. The present findings of associations between a dopaminergic marker and socially desirable behaviour thus demonstrate how research on the biological underpinnings of personality can provide new leads to the pathophysiology of psychiatric disorders.

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2) Reeves SJ, Mehta MA, Montgomery AJ, Amiras D, Egerton A, Howard RJ, Grasby PM: Striatal dopamine (D2) receptor availability predicts socially desirable responding. Neuroimage 2007; 34(4):1782-9

» NR3-014

AN FMRI STUDY FOR READING THE MIND IN MALE SCHIZOPHRENIC PATIENTS

Inkyung Oh M.D., Jung-Woo Son, M.D., Ph.D., Sang-Ick Lee, M.D., Ph.D., Chul-Jin Shin, M.D., Ph.D., Sie-Kyeong Kim, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that impaired TOM ability is not only explained intelligence and symptom severity, and implies that impaired TOM circuit is trait marker in schizophrenia.

SUMMARY:

Objective : 'Theory of mind (TOM)' refers to the ability to infer one's own and other person's mental states. Several studies have shown that schizophrenic patients had poorer TOM performance relative to controls. The aim of this study was to compare activated brain regions in male schizophrenic patients with normal controls during verbal TOM task using fMRI.
Method : Fourteen male schizophrenic patients and fifteen male normal controls participated in this study. The patient group underwent Positive and Negative Syndrome Scale (PANSS) and Clinical Global Impression-Severity (CGI-S). The subjects were scanned while tasks consist of six blocked design comprising 2 condition that are first order false belief and physical causality. The data were analyzed using SPM2 software (uncorrected p<.01, extent threshold ?=10).
Results : The patient group had average level of intelligence and mild psychotic symptoms. They showed significantly poor performance on first order belief task and less activation of the left medial frontal gyrus and left precuneus during first order false belief task compared with the control group. Especially, the left medial frontal gyrus replicated in other conditions that entered age and IQ as covariates.
Conclusions : We found less activation in medial frontal gyrus in schizophrenia. These results consisted with previous fMRI studies in schizophrenia. This study suggests that schizophrenic patients have impaired TOM processing.

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2) Marjoram D, Tansley H, Miller P, MacIntyre D, Owen DGC, Johnstone EC, Lawrie S: A theory of mind investigation into the appreciation of visual jokes in schizophrenia. BMC Psychiatry 2005; 24:5-12.

» NR3-015

THE RELATIONSHIP BETWEEN SEXUAL RESPONSE-RELATED BRAIN ACTIVITY AND SEXUAL HORMONES IN HEALTHY HETEROSEXUAL MALES: FMRI STUDY

Young Hee Seo, Bumseok Jeong, M.D., Ph.D., Jeewook ChoIi, M.D.,Ph.D., Ji-Woong Kim, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that both normal ranged prolactin may be related with visual, motor, somatosensory and executive system, but not subcortical structure as hypothalamus, and normal ranged baseline testosterone may be related with bilateral cingulate cortex for sexual behavior in healthy heterosexual male. Both prolactin and testosterone might have different role in brain during visual erotic stimulation.

SUMMARY:

Background: Sexual response of human can be affected to various factors including sexual hormones, age, sex, social pressure of gender role and even medication. Little is, however, known about correlations between sexual response-related brain activity and sexual hormones. Thus, the present fMR study was performed to identify the relationship between visual erotic stimuli-induced brain activity and sexual hormones levels measured before visual erotic stimulation.

Methods: Twelve healthy, heterosexual men (30.5±6.6yr) without any mental disorder and sexual dysfunction were recorded the 3T fMRI signals of brain activation elicited by passive viewing erotic (Ero) and emotionally positive (Pos) pictures. Subjects were measured blood testosterone and prolactin concentration just before fMR scanning. Local analysis of mixed effect modeling and estimation for group average were performed to explore the relationship of brain activity with the concentration of sexual hormones before visual erotic stimulation.
Results: The subjects showed several visual erotic stimuli-related brain regions including left hypothalamus, bilateral dorsolateral prefrontal cortices, intraparietal lobules. Prolactin level were positively correlated with most of the activated regions excluding left hypothalamus, while testosterone with both bilateral anterior cingulate cortex and left frontal pole. Neither prolactin nor testosterone showed negative relationship with brain activity.
Conclusion: Our results suggested the normal ranged prolactin level before visual erotic stimulation in healthy men may be positively related with cortical, rather than subcortical, activities during the visual erotic stimulation and testosterone may be related with emotional processing of sexual stimuli. The present findings provide the suggestion about the role of sexual hormones on sexual behavior-related brain activity and the preliminary data to investigate the pathophysiology of sexual dysfunction disorders.

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» NR3-016

CHANGES IN BRAIN GLUCOSE METABOLISM AFTER 12-WEEK TREATMENT WITH ESCITALOPRAM IN PATIENTS WITH PANIC DISORDER: 18FDG-PET STUDY

Woo-Yong Shin M.D., Yoon-Jae Song, M.D.Eun-Ho Kang, M.D., Hoondong Choe, M.D., Bum-Hee Yu, M.D, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the pathophysiology of panic disorder, in terms of neural pathway and some abnormal neural pathways are trait marker for panic disorder.

SUMMARY:

Background: Panic disorder shows abnormalities of some neural pathways in brain, but little is known about the mechanism of pharmacotherapy in terms of changes in the neural pathways. The aim of this study was to examine the changes in brain glucose metabolism using 18FDG-PET after 12-weeks of treatment with escitalopram in panic disorder patients.
Methods: Nineteen patients with panic disorder and 19 age-matched normal control subjects were compared at baseline by the voxel-by-voxel analysis using the statistical parametric mapping(SPM) 2. Automated region-of-interest analysis was performed to examine the changes of brain glucose metabolism in the regions where the brain glucose metabolism was found to be significantly different between panic patients and normal control subjects.
Results: Decreased glucose metabolism was found in right dorsolateral prefrontal cortex (Z=3.62, uncorrected p=0.0001), right cingulate (Z=3.64, uncorrected p=0.0001), and right middle temporal cortex(Z=3.60, uncorrected p=0.0001) in patients with panic disorder. After 12 weeks of pharmacotherapy, panic patients showed no significant changes of glucose metabolism in these regions (all p values>0.1) in spite of marked improvement of panic symptoms.
Conclusion: We suggest that right dorsolateral prefrontal cortex, right cingulate, and right middle temporal cortex should be related to the development of panic disorder. Decreased glucose metabolism in these regions may be a trait marker of panic disorder, and long-term pharmacotherapy may be needed to alter the metabolic abnormalities of panic disorder.

REFERENCES:

1) Gorman JM, Kent JM, Sullivan GM, Coplan JD: Neuroanatomical hypothesis of panic disorder, revised 2000;157;493-505.

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» NR3-017

ADDING CBT TO THE ACUTE IMPATIENT TREATMENT OF UNIPOLAR DEPRESSIVE DISORDERS

Stephan Koehler, Koehler S.,Hoffmann S., Unger T.,Fyrich T.,Mackert A.,Steinacher B.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the meaning of psychotherapy in the treatment of depressive disorders for the outcome treatment. CBT is an evidence-based psychotherapy for the treatment of depressive disorders also in acute management. The study shows that even for the short time of impatient treatment additional effects can be achieved by CBT. Our main goal is to list the reader the importance of combined therapy in depression.

SUMMARY:

The advantage of additional psychotherapy in opposite to single medical treatment of depressive disorders is, still controversial, especially in an acute-impatient setting.
In order of quality assurance and the development of treatment guidelines, we compared the efficacies of the basic psychiatric health care to an additional cognitive behavioural single psychotherapy on impatient treatment of unipolar depressive disorders according to DSM-IV in an incident sample of 224 patients. In addition to a pharmacological treatment, 114 patients had a CBT that dealt with the acute symptoms and was part of the multiple professional treatment. By acquiring the entry and discharge pathology we tried to find differences between both of these treatment strategies.
We used the DSM-IV checklists for diagnosing the disorder. The Hamilton depression score and the Beck depressions inventory were used to asses the severity of depressive symptoms. Plus, we also used the Brief Symptom Inventory to capture the disease burden and the Dysfunctional Attitude Scale (DAS) to evaluate dysfunctional cognitions and their persuasiveness by the CBT. The medical doctors had to fill in the Clinical Global Impressions Score and the Global Assesment of Functioning to evaluate severity of the disease.
All these tests were used in the beginning and in the end of the treatment. Additionally, we used the SKID II to analyse the influence of personality disorders as a determining factor for treatment outcome. Variance analyses showed that the basic psychiatric treatment using both as a single means and in combination with CBT could reduce depressive symptoms significantly. Patients who had CBT showed less severe depressive symptoms and a lower disease burden than patients without psychotherapy. The results of this clinical study give clear support that additional psychotherapy has also a positive effect on the outcome of the acute impatient treatment of depressive disorders.

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2) Paul A. Pirraglia, Allison B. Rosen, Richard C. Hermann, Natalia V. Olchanski, and Peter Neumann Cost-Utility Analysis Studies of Depression Management: A Systematic Review Am J Psychiatry 2004 161: 2155-2162

» NR3-018

QUALITY OF SUICIDE ASSESSMENT IN THE PSYCHIATRIC EMERGENCY SETTING

Christopher Chee B.S., Benjamin K.P. Woo, M.D., Satinder Mahal, B.S., Conrado Sevilla, M.D., and Tai P. Yoo, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the importance of documentation in suicide assessment and be aware of the pitfalls involved in assessing suicidal patients.

SUMMARY:

Introduction: Suicidal ideation and attempts are common reasons for emergency psychiatric evaluation. The APA's published guidelines for assessing and treating suicidal patients emphasize the importance of documentation in the suicide risk assessment. This study aimed to evaluate the quality of suicide assessment in the psychiatric emergency setting by measuring adherence to these guidelines in the form of documented process indicators. Methods: A retrospective chart review was conducted on 145 involuntarily admitted patients deemed a danger to self during June 2006. Each patient's medical record was reviewed against 19 process indicators determined from published literature: suicidal ideation, current suicidal plan, previous attempts, family history of suicidal behaviors, recent substance abuse, command hallucinations to harm self, firearm access, history of abuse, recent stressful life events, hopelessness, self injurious behaviors, impulsivity/aggression, previous psychiatric diagnoses, signs of major depressive episode, new onset of severe medical condition, barriers to suicide and/or reason for living, social support system, contract for safety, and follow-up of removal of medications from patients who attempted overdose. Results: Of the 19 indicators, 3 were documented in about 75% and 9 were documented in 50% to 75% of assessments. None documented all 19 of the indicators. The most commonly documented indicators were access to firearm (75.9%), recent stressful life events (75.2%), and contract for safety (74.5%). Separating patients by admission to the inpatient unit, the admitted group was more likely to have documented command hallucinations (P=.02) and previous psychiatric diagnoses (P=.001). Conclusions: Overall, documentation of process indicators in emergency suicide risk assessments was less than optimal. Potential areas for improvement is early resident training in systemic suicide assessment, posting guidelines, and use of checklists.

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» NR3-019

VALIDITY OF THE GENERAL PRACTITIONER ASSESSMENT OF COGNITION(GPCOG) IN COMMUNITY

Bokyung Sohn M.D., Lee DW.,M.D.,Ph.D.,Choi YM.M.D.Ph.D.,Kim BS.M.D.Ph.D.,Kim MS.,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize and understand the importance of GPCOG as a screening test of dementia.

SUMMARY:

Specific purpose: General practitioner assessment of cognition(GPCOG), developed by Brodaty, is a novel and promising screening test of dementia. We have already proved the validity of Korean version of GPCOG(GPCOG-K) in clinical population in the previous study. In this study, the authors evaluated validity of GPCOG-K in community.
Content: GPCOG has nine cognitive and six informant items. Through nine cognitive items, we can evaluate ability of patient's memory and cognitive function. Six informant items are performed by caregiver of elderly. These items show longitudinal changes of memory, language and instrumental activities of daily living.
Method: Total 92 people aged 65 and older living in community were evaluated from January 1 2008 to November 30 2008. Through history taking, mental status exam, and neuropsychological battery of Consortium to English a Registry of Alzheimer's Disease Korean version(CERAD-K(NP)), they were divided into two groups, i.e., dementia group and normal control group. And then Mini Mental Status Exam and GPCOG-K was performed. Consensus diagnoses of dementia was established according to dementia of the Alzheimer's type of Diagnostic and Statistical manual of Mental disorders 4th edition(DSM-IV) and probable Alzheimer's disease of National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related disorders Association(NINCDS-ADRDA) by psychiatrists. Receiver operator characteristic(ROC) analyses were used to assess the GPCOG-K nine cognitive items, six informant items, total score and MMSE score.
Results: There were 25 people in dementia group and 67 people in normal control group. Mean Age was 79.88 years old in dementia group and 75.46 in normal group. Mean educational level was 2.60 years in dementia group and 5.90 years in normal group. At cut point, sensitivity and specificity of GPCOG-K total score were 0.841 and 0.870 in dementia group. MMSE were 0.873 and 0.696. In Receiver Operating Characteritics(ROC) analysis, Area Under the Curve(AUC) of GPCOG-K was 0.900(95% CI 0.822-0.978) and that of MMSE was 0.820(95%CI 0.703-0.938). AUC of Each nine cognitive and six informant items was also wider than MMSE.
Conclusions: In this study, GPCOG-K was superior to MMSE in detecting dementia. Because dementia shows gradual onset and progression, six informant items of GPCOG-K which evaluate longitudinal changes of patient's cognitive function.

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» NR3-020

SCREENING FOR DISSOCIATIVE DISORDERS AT INTAKE INTERVIEW: EXPERIENCES IN AN OUTPATIENT PSYCHIATRY TRAINING CLINIC

Laura Diamond, M.D, Victoria Balkoski, M.D., Robert Hubbell, Psy.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:
1) Recognize the difficulties in evaluating for rare disorders, especially in a training clinic setting.
2) Appreciate the lack of consistent evaluation and questioning patients about dissociative disorder symptoms.
3) Identify factors, such as patient self-report, that may or may not affect clinical diagnosis.

SUMMARY:

Background. Rates of dissociative disorders (DD) diagnosis across settings has varied significantly, from 4-21%.1,2 Prior studies used screening tests or structured interviews to determine diagnosis. The purpose of this study was to assess if including five questions specific to symptoms of DD during initial intake interview revealed increased diagnosis of DD in the Albany Medical

Center Outpatient Clinic (OPC).
Methods. All PGY-III psychiatry residents rotating at the OPC completed a short questionnaire enquiring about their familiarity of DD. They then underwent a 30 minute training session about how to integrate five questions, developed from the Dissociative Experiences Scale and the Dissociative Disorders Interview Schedule, into the intake interviews. Intakes of all potential patients were conducted by PGY-III residents with direct faculty supervision, per regular procedure. For each intake, the resident documented demographic information and Axis I-V diagnoses. This data was collected and the rate of diagnosis was determined. A chart review was done of existing cases and corresponding information was collected for comparison.
Results. A total of 67 out of 192 intakes completed over an 11 month period at the OPC were documented. One patient was diagnosed with Dissociative Identity Disorder (DID). Of the 279 existing cases, one had Dissociative Disorder NOS ruled out, one had DID diagnosed later, and one with reported "dissociative symptoms" was not diagnosed.
Conclusions. Despite implementing a series of questions designed to elicit symptoms of DD, it did not result in an increase the rate of diagnosis at the OPC. The OPC diagnostic rate of DD was much less than the literature suggests. Reasons included: poor response rate of documentation and unfamiliarity with DD, which are rare. Of note, patients often reported dissociative symptoms before the questions were asked, but were not necessarily diagnosed.

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» NR3-021

COMPARATIVE STUDY IN AN ACUTE PSYCHIATRIC UNIT: DIFFERENCES BETWEEN PERSONALITY DISORDER INPATIENTS AND GENERAL PSYCHIATRIC INPATIENTS

David López Gómez, M.D., Jesús J. Marín Lozano, M.D., Mª Eva Román Mazuecos, M.D., Ainoa Muñoz San José, M.D., Santiago Kassem Vargas, M.D., Mª Fe Bravo Ortiz, M.D. Ph. D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to realize that patients diagnosed of a Personality Disorder have specific characteristics compared to general psychiatric inpatients, both demographic and clinical; therefore, they should be managed accordingly.

SUMMARY:
Objective: The aim of this study is to measure the prevalence of Personality Disorders among inpatients in an Acute Psychiatric Unit and to check if there are any clinical or sociodemographic differences among them and general psychiatric inpatients. Method: A retrospective case-series study has been done with a sample of 1,261 inpatients, all of whom were admitted to an Acute Psychiatric Unit at a General Hospital in Madrid, Spain, from January 2006 until October 2008. The data have been analyzed with SPSS 15.0. The sample was divided into two groups according to the absence (63.8%) or presence (36.2%) of Personality Disorder when discharged from hospital. We have related this depending variable with: gender, length of hospital stay, mean age, nationality, marital status, history of suicide attempts, history of alcohol and/or substances misuse, and history of Eating Disorders. Results: Statistically significant differences ($p<0.05$) were found when comparing all variables studied between both groups. The Personality Disorder group had a higher proportion of women (11.6% more), a shorter length of stay (2 days less), and was younger (4.5 years less) than the other group. Prevalence of Personality Disorder in divorced/separated (40.9%) and single (40%) patients was significantly higher than in married (27.4%) and widowed (22.8%) patients. Concerning their medical history, the Personality Disorder group had higher rates of Suicide Attempts (17% more), Alcohol and/or Substances Misuse (19.5% more), and Eating disorders (13.9% more). Conclusion: From these results, we conclude that inpatients diagnosed of a Personality Disorder are demographically and clinically different from those without it. Discussion: These findings show that this group of patients has its own characteristics and support the idea of creating specific programs and units for Personality Disorder patients.

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» NR3-022

NEUROPYSCHIATRIC OUTCOMES IN PATIENTS RECEIVING CARDIOTHORACIC TRANSPLANTATION AT THE MAYO CLINIC: A SINGLE INSTITUTION, TWENTY-YEAR COHORT

Farrah Mateen M.D., Sheila Jowsey, MD, Diederik van de Beek, MD, PhD, Eelco F.M. Wijdicks, MD, PhD.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize the frequency and impact of psychiatric disease on patients who have underwent heart or lung transplantation.

SUMMARY:
Objective: To determine the frequency and range of psychiatric disorders in a large cohort of patients who have undergone lung or heart transplantation at this institution.
Background: Lung transplantation is an increasingly common therapeutic option for select patients with end-stage respiratory insufficiency. Heart transplantation is performed as a therapeutic option for some patients with end-stage heart disease.
Design/Methods: The clinical, laboratory, and imaging records of all patients in the Mayo Clinic lung and heart transplantation cohorts (1988 - 2008) were retrospectively reviewed for select psychiatric diagnoses following transplantation.
Results: One hundred and twenty lung recipients (50% women; mean age 50 years(range 21-73); 60 living, average survival 3.4 years, average follow up 3.7 years) were identified. Heart transplant patients included 289 adults and 24 children (28% women, median age 52 years, 218 living, average follow up 6.3 years). Psychiatric diagnoses including anxiety and/or depression occurred in 27% of heart transplant recipients. A majority of lung transplant patients (>60%) received a psychiatric diagnosis with major depressive disorder, anxiety, and delirium being the most common.
Conclusions/Relevance: Psychiatric diagnoses are common in post-lung transplant and post-heart transplant patients. Prognostic value of psychiatric illness in the setting of post-transplant survival will be explored.

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» NR3-023

META-ANALYSIS OF PATERNAL AGE AND RISK OF SCHIZOPHRENIA IN THE OFFSPRING

Brian Miller M.D., Erick Messias, MD, PhD, MPH, Jouko Miettunen, PhD, Johanna Löhönen, MSc, Antti Alaräisänen, MD, Marjo-Riita Järvelin, MD, PhD, Hannu Koponen, MD, PhD, Pirkko Räsänen, MD, PhD, Brian Kirkpatrick, MD, MSPH, Matti Isohanni, MD, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to discuss paternal age as a risk factor for schizophrenia in the offspring.

SUMMARY:

Background: Advanced paternal age is a well-replicated and relatively robust risk factor for schizophrenia in the offspring. A recent meta-analysis of paternal age and schizophrenia did not adjust for gender and study design effects, did not use the same age classes across studies, and did not consider all available studies. We estimated the overall effect size and tested for a sexually dimorphic effect of paternal age on risk of schizophrenia. Methods: Studies were identified by searching Pub Med, the reference lists of identified studies, and previously unpublished data from the Northern Finland 1966 Birth Cohort. We attempted to contact authors of all identified studies and requested summary data stratified by gender and uniform five-year paternal age groups. Studies were excluded if greater than 20% of cases had a diagnosis of non-affective psychosis, there was significant overlap in the study population, or if the requested summary data were not available. Results: A total of 8 studies met the inclusion criteria, including 5 cohorts and 3 case-control studies. We found a J-shaped association between paternal age and schizophrenia risk in the offspring (reference paternal age of 25-29). Effect sizes were similar between cohort and case-control studies. There was no evidence of sexual dimorphism for the paternal age effect. Conclusions: Further studies are needed to investigate mechanisms for this association, including the increased risk in offspring of fathers under age 25.

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» NR3-024

INSOMNIA IN THE UNITED STATES: PREVALENCE AND ASSOCIATED FACTORS; RESULTS FROM NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES 2004-2005)

Tuan-Anh Nguyen M.D., Gilbert Ramos, MA, Stephanie Riolo, MD, MPH.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to :
1. Determine the point prevalence of insomnia symptoms and syndrome in the general adult US population.
2. Identify associated factors for insomnia in general adult US population.

SUMMARY:

OBJECTIVES: Estimate prevalence of insomnia in the general adult US population and identify commonly associated factors. METHOD: Data were obtained from the NHANES 2004-2005, a population-based survey that uses probability sampling techniques and weighted analyses to produce national estimates of health information. Participants: 6,127 persons aged 20 to 85 years. RESULTS: Over 15% of respondents met DSM IV criteria for insomnia in the past month. Of these, 16% reported initial insomnia, 20% frequent awakening, 27% feeling unrested in the morning, and 18% excessive daytime sleepiness. In the past month, 8.6% of respondents had taken sleeping pills often. The average time to initiate sleep is 20.7 minutes. Of the total sample, 13% slept < 6 hours sleep per night, 22 % slept 6 hours, 57% slept 7-8 hours, and 8 % slept > 9 hours per night. More than 23% of respondents told their doctor they have trouble sleeping, females more likely than males, 28 % vs. 19%. Only 7% of respondents were diagnosed with a sleep disorder by their doctors (no difference by gender). Rates of insomnia in women were higher than in men, 19% vs.12%. Divorced respondents had higher rates (20%) than those who were married (14%) or single (15%). There were no significant differences in rates of insomnia by race or age. Insomnia is more common in people who are obese (18%), living under poverty level (23%), abusing alcohol (18%), smoking cigarettes (22%), or using illegal drugs (21%). Among respondents who met DSM-IV criteria for MDD, 52% met criteria for insomnia. Among people with insomnia 47% had MDD. CONCLUSIONS: Insomnia is common in general adult population. Women, individuals who are divorced, individuals living in poverty, and obese persons are at increased risk for sleep disturbances. Insomnia is strongly associated with depression and also with alcohol abuse, cigarette smoking, and illegal drug use. The presence of insomnia should alert clinicians to determine an underlying etiology.

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» NR3-025

GLOBAL MENTAL HEALTH: AN UPDATE

Geoffrey Oravec M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the global burden of mental illness in the world today, identify epidemiological differences between mental illness and resources in different geographic regions, and understand the disparity of mental health resources between developing and developed nations.

SUMMARY:

Objective: The purpose of this study was to compile the most recent statistics on international mental health including diseases, expenditures and resources by geographical region and economic status so as to identify ongoing global concerns. Method: The author performed a literature search with keywords including "mental health," "epidemiology," "global," and "statistics;" and subsequently reviewed 18 articles published between 2004 and 2008 and compared these findings with the WHO Mental Health Atlas statistics revised in 2005. Results: The most recent studies on global mental health conducted within the past four years show little progress in reducing the disparity of mental health resources both between WHO ascribed geographical regions and World Bank designated income categories. The total number of disability-adjusted life years (DALYs) due to neuropsychiatric conditions in low and middle-income countries (LAMICs) is more than twice that of high-income countries. Despite this, LAMICs spend significantly less of their GDP on mental health care. As a result, LAMICs have fewer resources to treat a greater burden of mental illness than do high-income countries; with an estimated 76-85% of the population in need of mental health care unable to receive services in LAMICs, compared to 35-50% in high-income countries. Geographically, SE Asia and Africa continue to be problematic with 100% of SE Asia and 90% of Africa reporting less than 1 psychiatrist per 100,000 people; and 50% of SE Asia and 70% of Africa spending less than 1% of the national health budget on mental health. Conclusions: Mental illness remains one of the

leading causes of disability in the world today, yet despite increasing awareness progress has been slow in reducing the disparity in mental health care across economic and geographic divides. The success of future endeavors will rely on encouraging domestic initiative while continuing to provide international support.

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» NR3-026

RISK FACTORS FOR DEPRESSION WITHIN OBESE POPULATIONS: RESULTS FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES 2004-2005)

Stephanie Riolo M.D., Tuan-Anh Nguyen, MD, MPH.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:
1. Demonstrate an understanding of the complexity of the relationship between depression and obesity.
2. Identify potential risk factors for depression in obese persons.

SUMMARY:

Objective: Past studies report mixed results regarding the relationship between obesity and depression. Most recent studies suggest that there may be risk factors for depression within discrete obese populations that account for inconsistent finds. Specifically age, gender, race, and type of obesity (e.g. morbid obesity) may moderate/mediate the relationship between depression and obesity. Data from the NHANES 2004-2005 were used to examine whether gender or degree of obesity influence the relationship between depression and obesity. Methods: Secondary data analysis was performed using cross-sectional data from 4,627 participants aged 20 to 85 years. Weighted analyses were used to produce national estimates. Obesity was defined as body mass index (BMI) of 30-39 and morbid obesity as BMI > 40. Depression was defined using the Diagnostic and Statistical Manual of Mental Disorders, fourth edition. Results: Depression was associated with both morbid obesity (p=0.01) and obesity (p=0.04). These associations remained significant after controlling for gender, race, poverty, education, and marital status (obesity p=0.04, morbid obesity p=0.01). When analyses were stratified by gender, depression was associated with obesity (p=0.05) and morbid obesity (p=0.01) in women; however, there was no significant association between depression and obesity in men, regardless of BMI. Conclusion: Converging evidence suggests that subtypes of obesity may have different relationships with depression. Gender appears to be important in the relationship between depression and obesity; however, further research is needed to explore why (e.g., gender specific stigma regarding obesity).

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» NR3-027

2-YEAR NATURALISTIC DEPRESSIVE SYMPTOM IN CHINESE COLLEGE STUDENTS

Song Yuqing, Yueqin Huang, Ph.D, Dan Liu, Ph.D, Johnny. S.H. Kwan, Fuquan Zhang, MD, Pak C. Sham MBBS, Ph.D, Siu Wa Tang, MD, Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify that half to one year after entering college is ciritical period to evaluate depressive symptoms of the students. Personality and stressful life events predicted depressive symptoms of college students.

SUMMARY:

Background: Depression is becoming one of the major mental health of college student facing1. Identifying the naruralistic course of derepssion and the factors that precipitate depression on campus is an increasingly crucial public health goal.
Objectives: We assessed prospectively the association between measures of personality, parental style, stressful life events, and depressive symptoms in Chinese college students.
Design:A prospective follow-up study, including four repeated assessments.
Setting and subjects: 1038 freshmen in two key universities in Mainland China finished Self-reported questionnaires.
Main outcome measure: Depressive symptoms were repeated measured by CES-D2 every half-year interval up to two years. Personalities were assessed through Eysenck Personality Inventory-Neuroticism, Rosenberg Self-esteem Scale, and Frost Perfectionism Scale. Parental style was assessed by EMBU at baseline. Stressful life events were assessed by Chinese version of adolescents self-rating life events checklist.
Results: Mixed effect model was used to analysis the four waves of CES-D scores of the students. The total scores of CES-D of wave 2 (coef=1.09, 95%CI=0.49-1.70, p<0.001) and wave 3 (coef=1.00, 95%CI=0.41-1.59, p<0.001) were significanlty increased compared with base line scores. Neuroticism (coef=0.76, 95%CI=0.62-1.90, p<0.001), maladaptive perfectionism(coef=0.08, 95%CI=0.04-.012, p<0.001), and average stressful life events (coef=0.20, 95%CI=0.17-0.24, p<0.001) were predicted increasing of CES-D scores. While, self-esteem (coef=-0.35, 95%CI=-0.44 - -0.26, p<0.001) and adaptive perfectionism (coef=-0.07, 95%CI=-0.12- -0.12, p=0.006) predicted drecreasing of CES-D scores. The predict effect of parenting style was not found.
Conclusions: Half to one year after entering college is ciritical period to evaluate depressive symptoms of the students. Personality and stressful life events predicted depressive symptoms of college students.

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» NR3-028

EFFECTS OF PRENATAL EXPOSURE TO MATERNAL MALNUTRITION ON ADULT RISK OF SCHIZOPHRENIA

Ming-Qing Xu Ph.D., Ezra Susser, M.D. DrPH, David St. Clair, M.D. Ph.D., Lin He, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the increased risk for schizophrenia among individuals with prenatal exposure to maternal malnutrition and to discuss risk of prenatal malnutrition.

SUMMARY:

OBJECTIVE: Intrauterine malnutrition may increase risk of schizophrenia. The main evidence comes from 1944-5 Dutch Hunger Winter and 1959-61 Chinese famines. The most exposed cohorts, conceived at the height of the famines, had a two fold increased risk of developing schizophrenia in adult life. In this study, the authors tested the hypothesis in a second Chinese cohort that exposure to famine at conception or during early gestation

increases risk of schizophrenia, and determined whether there was a risk difference between urban and rural areas and between Han Chinese and ethnic minorities.
METHOD: The risk of schizophrenia was examined in Liuzhou area of Guangxi Autonomous region (AR). Rates were compared among those born, before, during and after the famine years in the area as a whole and then looking at urban and rural areas separately. All psychiatric case records for the years 1971 through 2001 were examined. Clinical and sociodemographic data on patients with schizophrenia were extracted by psychiatrists blind to nature of exposure. Data on number of births and deaths in the famine years were also available and cumulative mortality was estimated from later demographic surveys. Evidence of famine was verified, and mortality adjusted relative risks were calculated for the region as a whole and for urban and rural areas separately.
RESULTS: The birth rate dropped by approximately 50% for the region as a whole paralleled by a doubling of overall mortality. Mortality-adjusted relative risk was 1.46 and 2.042 (1960 and 61) for the region as a whole. The effect was restricted to the rural areas with urban area showing no increased risk. Rates were similar in ethnic minorities and Han Chinese.
CONCLUSIONS: These data fully endorse findings from the earlier two famine studies. Prenatal exposure to famine is now one of the most robust and best documented environmental exposures identified to date for increased risk of schizophrenia in human populations.

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» NR3-029

CONVERGENT EVIDENCE SHOWS A POSITIVE ASSOCIATION OF THE INTERLEUKIN-1 GENE COMPLEX LOCUS WITH SUSCEPTIBILITY TO SCHIZOPHRENIA

Ming-Qing Xu Ph.D., David St. Clair, M.D. Ph.D., Lin He, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that the IL1B gene or the Interleukin-1 Gene Complex may play a moderate role in the etiology of schizophrenia in the Caucasian population.

SUMMARY:

OBJECTIVE: Recent genetic studies have revealed that the IL1 gene complex (IL1 alpha, IL1 beta and IL1 receptor antagonist) is associated with schizophrenia, but contradictory findings have also been reported.
METHOD: To assess whether the genetic variants in the IL1 gene complex are implicated in vulnerability to schizophrenia, the authors quantitatively assessed the association of the IL1 gene complex locus and schizophrenia using meta-analytic techniques, selecting 14 studies which included 2145 cases, 3148 controls and 221 parent-offspring trios. Potential sources of heterogeneity between studies were also explored.
RESULTS: In a combined analysis, the summary allele-wise odds ratio for schizophrenia of the rs16944 (IL1B gene; T511C) polymorphism was 0.892 (95% confidence interval: 0.806 to 0.987).When applying stratified analysis to this polymorphism, the summary allele-wise odds ratio was 0.883 (95% confidence interval, 0.795 to 0.975) in 9 population-based case-control studies and 0.850 (95% confidence interval: 0.727 to 0.993) in Caucasian samples. In a stratified analysis of the rs1143634 (IL1B gene; T3953C) polymorphism, the pooled genotype-wise results in a dominant model were also statistically significant both in a population-based study subgroup with summary odds ratio of 0.637 (95% confidence interval: 0.410 to 0.989) and a caucasian-population subgroup with summary odds ratio of 0.624 (95% confidence interval: 0.400 to 0.972). Neither combined nor stratified analyses found any association of the rs1800587 (IL1A gene; T889C) or rs1143634 (IL1B gene; T3953C; TaqI) with schizophrenia susceptibility. No publication bias for the positively associated results was detected.
CONCLUSIONS: The results of the present study suggest that the IL1B gene or the Interleukin-1 Gene Complex may play a moderate role in the etiology of schizophrenia in the Caucasian population.

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» NR3-030

TPH1 IS ASSOCIATED WITH MAJOR DEPRESSIVE DISORDER AND FLUOXETINE TREATMENT RESPONSE IN TAIWANESE PATIENTS

Hui Hua Chang,M.S., Po See Chen, M.D., Ph.D., Po-Wu Gean,Ph.D.

EDUCATIONAL OBJECTIVES:

The study was designed to compare the allele frequencies of TPH1 in major depressive disorder (MDD) patients and healthy controls. At the conclusion of this presentation, the TPH1 218A/C genotype and allele frequencies were different between healthy controls and MDD patients in Taiwan. TPH gene variants are therefore a possible modulator of fluoxetine antidepressant activity.

SUMMARY:

Introduction: The heritability of depression is estimated to 30% to 40%, and the serotonin (5-HT) system has been studied related to the original of depression. Among the system, tryptophan hydroxylase (TPH) is a key rate-limiting enzyme in the biosynthesis of serotonin, which may influence with response to SSRI/SNRI. The current study aimed to compare the allele frequencies of TPH1 in major depressive disorder (MDD) patients and healthy controls. We also investigated the possible association between TPH1 A218C and SSRI/SNRI treatment response in Taiwanese MDD patients.
Materials and methods: 105 healthy controls and 115 outpatients with MDD were recruited from the National Cheng Kung University Hospital. All of them were genotyped for the TPH1 218A/C (rs1800532) polymorphism. Patients were randomized assigned to either fluoxetine or venlafaxine treatment group. The 21-item Hamilton Rating Scale for Depression (HAM-D) was administered to evaluate depressive symptoms at baseline and bi-weekly over 6 weeks of treatment.
Results: The TPH1 218A/C genotype and allele frequencies were significantly different between healthy controls and MDD patients in Taiwan. TPH1 218A/C polymorphism was no associated with short-term antidepressant treatment outcome, after repeated-measures analysis of variance of HAM-D score percentage change over time. However, the genotype distributions of TPH1 218A/C showed significant association with short-term response in subgrouping analysis by medications.
Conclusion: This study indicates that the TPH1 218A/C genotype and allele frequencies were different between healthy controls and MDD patients in Taiwan. TPH gene variants are therefore a possible modulator of fluoxetine antidepressant activity. Further research with large sample sizes is needed to confirm the role of TPH1 218A/C.
Keywords: major depressive disorder, selective serotonin reuptake inhibitors, tryptophan hydroxylase, treatment response, single

nucleotide polymorphisms

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» NR3-031

ETHNIC DIFFERENCES IN THE PERCEPTION OF GENETIC RISK IN A BIPOLAR GENETIC STUDY

Olusola Fagbami M.B.B.S, Evaristus A. Nwulia, M.D., MHS, Maria Hipolito, M.D, Mariano Erpe, MS, William B. Lawson, M.D. Ph.D., NIMH Bipolar Collaborative.

EDUCATIONAL OBJECTIVES:

Upon reading this poster, the participant should identify key differences between African Americans and Caucasians in their interpretation of the causes and best treatment of bipolar disorder. Furthermore, the disparity between Black and White Americans on the level of mistrust of handling of scientific data, as well as its historical origin constitutes the overarching educational objective of this presentation. Finally, we would like the participant to understand the potential role of focused e

SUMMARY:

Objective: African Americans (AA) are consistently underrepresented in genetic studies of affective disorders. The goal of this study is to determine if significant differences exist in the knowledge and perception of genetic risk of bipolar disorder (BD), between AA and Caucasian (CA) participants in a bipolar genetic study.

Method: 1032 participants (17% AA) were administered questionnaires inquiring of their knowledge on the causes and most effective treatment of BD; their attitude towards identification of true bipolar risk gene; and their perception of the safety in handling of genetic research information.

Results: 84.2% of the Caucasians in the study attributed the cause of BD to hereditary factors versus 57.7% of the African Americans (P<0.001). More Caucasians than African Americans (53.4% vs.47.8%) correctly identified the most effective treatment for BD; but the difference was not significant (P<0.07). Though significantly (P < 0.05) more CA than AA identified better understanding of brain function and development of new treatment as benefits of gene identification, AA were more optimistic that genetic studies of BD may lead to identification of a gene therapy. Finally, AA expressed more distrust and wariness concerning handling of genetic information, identifying this as potential tool for discrimination of the mentally ill and for racial discrimination

Conclusion: This study revealed more profound negative attitude towards genetic studies of BD amongst AA participants in this study, but also opens the legitimate question of safe-handling of genetic information. This differential mistrust, as well as the significant gap in information regarding knowledge of the disease perspective of BD may underlie the recurring difficulty in recruitment of AA for genetic studies of mood disorders. There is therefore a huge need for educational efforts targeting AA populations, with the goal of improving ethnic representations in studies of the genetic origins of BD.

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» NR3-032

ASSOCIATION OF THE SEROTONIN TRANSPORTER PROMOTER AND DOPAMINE D4 RECEPTOR GENE POLYMORPHISMS WITH DECISION-MAKING IN HEALTHY VOLUNTEERS

Rayeon Ha, Se Joo Kim, M.D., Ph.D., Jee In Kang, M.D., Kee Namkoong, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to demonstrate that emotional decision-making performance measured by Iowa Gambling Task (IGT) was not affected by any triallelic serotonin transporter promoter (5-HTTLPR) or dopamine D4 receptor (DRD4) gene polymorphisms, but we found the significant interaction effect of these two genes on decision-making.

SUMMARY:

Objectives: The Decision-making means the ability to select the most advantageous response from various possible behavioral choices and the IOWA Gambling Task (IGT) is one of the most frequently used neuropsychological tasks to assess the decision making in ambiguous situations. Previous studies suggested the modulation of decision-making processes by serotonin and dopamine system. We aimed to examine the relationships between triallelic serotonin transporter promoter (5-HTTLPR), dopamine D4 receptor (DRD4) 48 bp VNTR polymorphisms and emotional decision-making performance measured by IGT. And we also investigated the interaction effect of these two genes on IGT. Methods: 159 subjects (82 males, 77 females) were tested with the IGT and the functional polymorphisms of the 5-HTTLPR and the DRD4 48bp VNTR were genotyped for each subject. The mean age of the subjects was 23.0±2.2 and the mean duration of education was 15.4±1.0 years. Two-way multivariate analysis of variance (MANOVA) and a post hoc t-test were conducted to examine the main and interaction effects of 5-HTTLPR and DRD4 genotypes on the total IGT score. Results: We could not find any significant multivariate main effects of 5-HTTLPR (F=0.46, p=0.50) or DRD4 (F=0.25, p=0.62) gene polymorphisms on total IGT score. However, there was a significant effect of the interaction between 5-HTTLPR and DRD4 genes on total IGT score (F=7.00, p=0.009). In the presence of the 5-HTTLPR S'S' genotype, subjects with DRD4 2R- genotype had higher total IGT score compared to subjects with DRD4 2R+ genotype (t=-2.34, p=0.02). Conclusion: The DRD4 genotypes influence on emotional decision-making differently according to the background of 5-HTTLPR genotypes.

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» NR3-033

GENOTYPING IN TDM – AN EQUATION

Astrid Hader, T. Jahner, D. Melchner, J. Kirchheiner, E. Haen

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize, when TDM should be amended with genotyping or not.

SUMMARY:

In our laboratory we routinely use dose-related reference ranges for Therapeutic drug monitoring (TDM) which is used to improve the benefit/risk ratio of drug treatment. Thus we are able to identify individual patients with abnormalities in drug metabolism, such as liver and/or kidney disease, drug-drug-interactions, and gene polymorphism; results are returned to the treating physician

together with a clinical pharmacological comment [1]. To find out whether genotyping or determination of drug concentrations is more reliable in identifying poor and rapid drug metabolizers we used a published PCR method to analyse polymorphisms in the genetic code of the drug metabolizing cytochrome P450-isoenzyme 2C19 (CYP2C19). Serum concentrations of Citalopram or Escitalopram, both substrates of CYP2C19, were determined by high performance liquid chromatography [2]. We then compared the results of the clinical pharmacological estimation of drug concentration with the genotyping results in the same patient.
In 121 samples we found 87 extensive metabolizers (EM), 28 intermediate metabolisers (IM) and 5 poor metabolisers (PM). 20 of the EM (17,4%) showed serum concentrations too high for the prescribed dosage which were not explicable. 9 (32%) of the IM had appropriate serum concentrations, 19 (68%) concentrations too high for the prescribed dosage: 11 of these could be explained by drug-drug-interactions, 8 (28,5%) could not. 4 of the PM had too high concentrations: in 3 cases we were not able to explain this by any another reason, in 1 case we identified a drug-drug-interaction. 1 PM showed an appropriate concentration. The next steps will be similar equations for other CYP450-isoenzymes, e.g. CYP1A2 with clozapine- and olanzapine serum concentrations to confirm our first results. These show that the determination of serum concentrations cannot be replaced by genotyping the patients.

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» NR3-034

GENETIC MARKERS FOR SUICIDE RISK IN SCHIZOPHRENIA

Eric Olsson M.D., Urban Ösby, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

The educational objective of this poster is to highlight the importance of finding new prognostic tools for understanding and evaluating the risk for suicide in schizophrenic patients.

SUMMARY:

Around 10 % of patients with schizophrenia will die from suicide. Suicide is the specific cause of death that leads to the largest number of potential years of life lost. Therefore improved prediction of increased suicide risk is of great importance in order to improve prognosis in schizophrenia.
Molecular genetic association studies of suicide risk, also in schizophrenia, have focused on genes related to the serotonin system. There are several promising findings but also some contradictory results. This may be due to limitations of association studies, mainly too small samples, diagnostic heterogeneity, and suicide attempt or ideation as phenotype rather than suicide per se.
The purpose of this study is to identify genetic risk markers for suicide in schizophrenia. We use genetic association, comparing schizophrenic patients who have died from suicide with living schizophrenic patients, and also with a population-based control group. By linkage of diagnosis from the Patient Register with the cause of death from the Swedish Forensic database, 216 cases from Stockholm County have been identified. The cases have a clinical schizophrenia diagnosis, have died from suicide and there is tissue available from the forensic autopsy. The control group consists of patients with schizophrenia, and blood donor population controls, all from Stockholm County.
We have focused on SNPs in genes of the serotonin pathway. This study will in a favorable way address previous problems with identifying genetic markers for increased suicide risk in schizophrenia.

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» NR3-035

GENE X ENVIRONMENT INTERACTION: THE SEROTONIN TRANSPORTER GENE POLYMORPHISM AND ABUSE HISTORY INFLUENCING THE CHARACTERISTICS OF DEPRESSED INPATIENT

Gen Shinozaki M.D., Victoria Passov, M.D., Magdalena Romanowicz, M.D., Simon Kung, M.D., Renato D. Alarcon, M.D., M.P.H, David A. Mrazek, M.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize that the interaction between long alleles of serotonin transporter gene polymorphism (5HTTLPR) and the child abuse history impacts the characteristics of depressed inpatients with selected psychiatric co-morbidities, and how it might differ in the inpatient psychiatric setting compared to other reports.

SUMMARY:

Introduction: The serotonin transporter gene polymorphism (5HTTLPR) has been associated with individual stress response as well as to mental illnesses including anxiety, bipolar disorder, alcoholism, and personality disorder (1). Caspi et al. showed that individuals maltreated in childhood have higher rates of depression in later life if they are homozygous short (s/s) compared to homozygous long (l/l) (2). We examined if these findings would similarly extend to an inpatient psychiatric setting.
Methods: Retrospective chart review of 283 patients hospitalized for depression from 2005-2007. Those who had serotonin transporter genotyping were included. Subjects with each genotype were subcategorized into 2 groups with/without history of child abuse. The characteristics of each group (psychiatric co-morbidities) were compared.
Results: Of the 283 patients genotyped, 44 were s/s, 142 were heterozygous (s/l), and 97 were l/l. Among those, the history of child abuse was found as follows: 21 out of 44 s/s (47.7%), 62 out of 142 s/l (43.7%), and 45 out of 97 l/l (46.4%). An interaction was found between 5HTTLPR and child abuse history influencing the prevalence of suicidal attempt and cluster B personality trait. Contrary to our prediction, l/l was significantly associated with the largest increase of the rate of suicide attempt (from 25% to 71%; $p<0.01$) and cluster B trait among depressed inpatients with the presence of abuse history.
Conclusions: Our findings showed an opposite direction of interaction between 5HTTLPR and stressful life event. This may be because of our special population of very sick depressed inpatients. While other studies have reported the importance of the short allele of the serotonin transporter gene as one of the many risk factors affecting individual differences of vulnerability to psychiatric illnesses against stressful life event, our findings suggest that there may be a quite different and complex mechanism in an inpatient depression setting.

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NR3-036

FUNCTIONAL EFFECTS OF POLYMORPHISMS IN THE HUMAN CORTICOTROPIN-RELEASING HORMONE RECEPTOR 1 (CRHR1) GENE

Kirstin Thode M.D., Consuelo Walss-Bass, Ph.D., Karen Munoz, M.S., Ahmad Hariri, Ph.D., Rene Olvera, M.D., Douglas E. Williamson, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to explain how polymorphisms in the corticotropin-releasing hormore receptor 1 (CRHR1) gene moderate HPA axis activation, neural systems subserving affect regulation and response to reward, & baseline gene expression levels.

SUMMARY:

The role of the hypothalamic-pituitary-adrenal (HPA) axis in stress-related psychiatric disorders (i.e. depression and anxiety) has been well-established. Recent data indicate that corticotropin-releasing hormone (CRH), the principal neuroregulator of the HPA axis, plays a key role in alcohol dependence and that a gene-environment interaction between a SNP (rs1876831) in the CRH receptor 1 (CRHR1) gene and stressful life events predicts heavy alcohol use patterns in adolescents. Our group previously identified a CRHR1 promoter SNP (rs12938031) that predicted a more robust HPA axis response to CRH stimulation. The aims of our current study were to examine rs12938031's relationship to rs1876831 as well as the effects of rs12938031 on HPA brain system reactivity and CRHR1 gene expression levels. Data were available from the Teen Alcohol Outcomes Study (TAOS), an ongoing cohort study of the long-term outcome of early risk factors. Subjects included adolescents aged 12 to 15 years. DNA was obtained from saliva (n=340), and a subset (n=57) had an fMRI. Lymphoblastoid cell lines of 12 homozygotes for rs12938031 were selected (6 AA and 6 GG) to determine CRHR1 mRNA levels. Linkage disequilibrium (LD) analyses were carried out using Haploview 4.1, imaging analyses were done using GLM in SPM5, and for baseline mRNA levels, unpaired t-tests were used. SNPs rs12938031 and rs1876831 were found to be in high LD (D'0.951, LOD 35.6, $p<0.0001$). rs12938031 GG homozygotes were associated with less bilateral amygdala reactivity (left $p<0.001$, right $p<0.05$) and greater left ventral striatum reactivity ($p=0.039$) and trended toward lower expression of CRHR1 ($p=0.055$) as compared to AA homozygotes. These results provide additional evidence for genetic moderation of the stress response directly involving a SNP rs12938031 in the promoter of CRHR1. Our ongoing work is examining whether this moderation stems from baseline and/or stress-induced differences in CRHR1 expression.

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NR3-037

THE MITOCHONDRIAL A3243G MUTATION: SAME GENOTYPE, DIFFERENT PHENOTYPE - A MOTHER AND HER DAUGHTER WITH PSYCHIATRIC MANIFESTATION OF MELAS

Maarten Van Den Bossche M.D., Ann T. Van Vre, M.D., Manuel Morrens, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the possible psychiatric presentation of the A3243G mitochondrial mutation and understand some of the mechanisms resonsible for its broad range of clinical presentations.

SUMMARY:

BACKGROUND: The tRNA(Leu) A3243G mutation is one of the most frequently observed mutations of the mitochondrial genome. Nevertheless, the same point mutation can cause a broad range of phenotypes ranging from mitochondrial myopathy, encephalopathy and stroke like episodes (MELAS) to asymptomatic carriership. Psychiatric abnormalities with the exception of dementia are rare.
AIM: To demonstrate the considerable intrafamiliar variability of the A3243G mutation by presenting the case of a mother and her daughter who both displayed striking psychiatric symptomatology.
METHODS: Clinico-anamnestic, neuropychiatric, endocrinologic, histopathologic and genetic profiles of both patients were assessed. A subsequent systematic search of the literature on intrafamiliar variability of the A3243G mutation was conducted.
RESULTS: The mother presented herself at 46years of age with anorexia, epilepsy, different episodes of pychosis, mutism and visual abnormalities; that quickly evolved to a dementia with severe outbursts of physical aggression. Her daughter at the age of 19 suffered from epilepsy, migraines, disorientation and severe mood swings. In both patients, cerebrospinal fluid and blood showed elevated lactate; MRI spectrometry showed large ischaemic areas and lactate peaks. Muscular biopsy and genetic blood analyses confirmed the diagnosis of MELAS caused by the A3243G mutation in both mother and daughter.
CONCLUSIONS: The A3243G mutation can cause a broad range of phenotypical presentations characterized by significant inter- and intrafamiliar variability. Due to the unique mitochondrial inheritance patterns, mutation loads can vary from subject to subject. Nevertheless, variability in mutation load alone has proven to be insufficient to explain the broad range of clinical presentations caused by this mutation. It is suggested that mechanisms of relaxed replication and nuclear background interactions are responsible for the complex genotype-phenotype association.

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NR3-038

INCREASED INCIDENCE OF SCHIZOPHRENIA IN MIGRANTS: ARE DRUGS TO BLAME?

Maarten Van Den Bossche M.D., Jean-Paul Selten, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the possible role of drug abuse in the excess of schizophrenia in migrants.

SUMMARY:

Introduction: A large amount of studies in multiple countries have shown that migrants have an increased risk of developing schizophrenia when compared to the native-born population. Substance abuse has been suggested as a possible explanation. We looked at the different studies to see if substance abuse had been taken into account. Furthermore we provide some arguments on whether or not this hypothesis is plausible.
Methods: A sytematic search of MEDLINE was conducted using the key words "migration", "ethnicity", "psychosis" and/or "schizophrenia" for population-based incidence studies concerning migrants in English-language publications appearing between January 1977 and November 2008. Bibliographies from identified articles were cross-referenced. Relevant studies were further investigated to determine whether use of alcohol and drugs were determined and by what method.
Results: 26 population-based studies were found, only 5 of which

contained information on substance abuse. One study did not mention the method used to determine abuse, 2 studies relied on patient history taking, One study used information of the medical file, including lab test results if present. The remaining study used data from history taking of the patient, family members, responsible physician and of the medical file including urine drug screens. All 5 studies found an equal or lower substance abuse in migrants compared to non-migrants.
Conclusions: Few studies have examined substance abuse, and most researchers have relied on methods not fully reliable. Consequently, there is a lack of research in this area. Recent animal studies have shown that repeated exposure to social defeat stress can disturb the dopaminergic circuit in the brain, resulting in an increased sensitivity to illicit drugs. Thus, it is possible that members of immigrant groups are more sensitive to the psychotogenic effects of drug abuse than natives.

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» NR3-039

EFFECT OF THE DYSBINDIN GENE ON ANTIMANIC AGENTS IN PATIENTS WITH BIPOLAR I DISORDER

Dong Hwan Yoon M.D., Chi-Un Pae, MD, PhD, Jung-Jin Kim, MD, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that the dysbindin gene does not seem to be involved in acute antimanic efficacy.

SUMMARY:

Objective: Recently the association between dysbindin gene (DTNBP1)variants and bipolar I disorder (BID)has been reported. This paper expands upon previous findings suggesting that DTNBP1 variants may play a role in the response to acute mood stabilizer treatment.
Methods: A total of 45 BID patients were treated with antimanic agents (lithium, valproate,or carbamazepine) for an average of 36.52 (±19.87) days. After treatment, the patients were evaluated using the Clinical Global Impression (CGI) scale and the Young Mania Rating Scale (YMRS) and genotyped for their DTNBP1 variants (rs3213207 A/G, rs1011313 C/T, rs2005976 G/A, rs760761 C/T and rs2619522 A/C).
Results: There was no association between the variants investigated and response to mood stabilizer treatment, even after considering possible stratification factors.
Conclusion: Although the small number of subjects is an important limitation in our study, DTNBP1 does not seem to be involved in acute antimanic efficacy.

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» NR3-040

A SIB-PAIR STUDY OF PERSONALITY TRAITS IN BIPOLAR DISORDER

Karla Almeida M.D., Beny Lafer, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that euthymic patients with bipolar disorder have higher scores on Harm Avoidance (HA) and Self-transcendence, and lower scores on Self-directedness (SD) than healthy controls, their siblings have higher scores on HA and lower scores on SD than controls, and that patients have higher scores on impulsivity than healthy controls, and their siblings do not show any differences from patients and healthy controls.

SUMMARY:

Introduction: Recent studies have shown that patients with bipolar disorder have higher scores on Impulsivity, Harm Avoidance (HA), Novelty Seeking and Self-transcendence (ST) and lower scores on Persistence, Self-directedness (SD) and Cooperativeness than healthy controls. The results suggest that these personality traits are associated with bipolar disorder in a state independent manner. However, it is unclear whether this association reflects a "scarring effect" of the affective episodes or is a risk factor for the illness.
Objective: To assess the relationship between personality traits and bipolar disorder by comparing temperament, character, and impulsivity traits among patients with bipolar disorder, their siblings and healthy controls.
Methods: Twenty-four euthymic patients with bipolar I disorder, 24 siblings without a bipolar disorder diagnosis and 24 controls were interviewed. Instruments: the SCID Axis I, the Hamilton Depression Rating Scale – 17 items, the Young Mania Rating Scale, the Temperament and Character Inventory, the Barratt Impulsiveness Scale (BIS) and the Family History Screen by Weissman.
Results: Patients have higher scores on HA and ST, and lower scores on SD than healthy controls. Siblings have higher scores on HA and lower scores on SD than controls. When siblings are divided into affected and non-affected, these differences remain significant only for the affected group. Patients have higher scores on impulsivity than healthy controls, and siblings do not show any differences from patients and healthy controls.
Conclusion: Our results suggest that these personality traits may be influenced by the presence of a psychiatric disorder rather than being of familial or genetic origin.

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» NR3-041

MEDICAL CO MORBIDITIES IN BIPOLAR PATIENTS INCREASE THE RISK FOR SUICIDAL ATTEMPTS

Mahboob Aslam M.D., Gulam Noorani,M.D., D.Korya, J.Bibawy, C.Charoonbara.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand correlation of medical co morbid illnesses with risk of suicide in adult Bipolar patient population.

SUMMARY:

Although recent studies have shown a high association between bipolar disorders (BP) and increased suicide risk, little is known about the medical comorbidities and the associated increase of suicidal attempts. In this study we investigate the prevalence of suicidal attempts among adults with BP, and compare the rate of suicidal attempts in bipolar patients with and without medical co morbidities. Subjects were 208 adults aged 21-75 years, who fulfilled the DSM-IV criteria for either BPI (n=89), BPII (n=10) or BP not otherwise specified (BP NOS; n=109). An extensive review of inpatient medical records was conducted in search of suicidal attempts and the number of medical comorbidities that these attempters suffered from. Other factors that have been implicated in prior studies were also looked at and listed in order

to fully assess the data collected. 56% (n=116) of the inpatients with BP had attempted suicide in some manner, and 46% (n=54) of those required some form of emergency care. Compared with non-attempters, suicide attempters were more likely to have at least one comorbid medical condition. Of the 120 patients with comorbid medical conditions 67 (56%) attempted suicide. That is compared to only 39 of the 88 (44%) of the patients without co morbid medical conditions. Furthermore, we found that the percentage of BP patients attempting suicide increased as the number of comorbid medical conditions increased. For example, those patients with two or more comorbid medical conditions attempted suicide at a rate of 61% (30 of 49) compared to 44 %(39 of 88) who were non attempters. We also found several psychosocial factors to have a role in the increased likelihood of suicidality in this population. Of the 208 patients, 54 reported sexual or physical abuse; 38 attempted suicide in this group (70%). Homeless and living alone were also at higher risk comparing to those living with families. We also found that of the 44 patients who had either borderline or antisocial personality traits, 26 (59%) had attempted suicide. These findings demonstrate that adult inpatients diagnosed with BP have extremely high rates of suicide attempts. In addition, the findings specify that medical co morbidities may increase the likelihood of suicidal attempts in this population. The factors that emerged as correlates to the increased likelihood of suicide attempts should be considered while assessing and treating patients.

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» NR3-042

RAPID CYCLING MOODS: MEDIATED BY ANTIBODIES?

Ajay Bhatia, M.D., and Hossam H. Guirgis, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to:
1. Recognize the similarities between Hashimoto's Encephalopathy (HE) and rapid cycling bipolar affective disorder (rcBPAD).
2. Understand HE's favorable response to steroids or plasmapheresis and rcBPAD's poor response to psychotropic treatment.
3. Consider tests for HE in all rcBPAD patients and modify treatment approaches appropriately.

SUMMARY:

Introduction: Rapid cycling bipolar affective disorder (rcBPAD) is a relapse-remitting mood illness, and Hashimoto's Encephalopathy (HE) is a relapse-remitting neurological illness. Certain cases of rcBPAD may be variants of HE, changing ways which psychotropic-resistant rcBPAD is treated. Hypothesis: An association exists between rcBPAD and HE.
Methods: Literature analysis and case report.
Results: HE and rcBPAD are similar clinically: both may occur with psychosis, poor self-care, sleep disorder, or cognitive disorder. High titers of anti-thyroid peroxidase (anti-TPO) antibodies and anti-thyroglobulin (anti-TG) antibodies aid in HE diagnosis. EEG, MRI, CSF are non-specific; serum thyroid hormones (TSH, free T4, T3) are usually normal. In one study (total n=3756), Oomen, et al., concluded that high titers of anti-TPO antibodies occur in rcBPAD with normal serum thyroid hormones. Anti-TG antibody levels were not done. L.M, a 49 year-old South American woman with a past history of psychotropic-resistant rcBPAD, has high titers of anti-TPO and anti-TG antibodies, and is preliminarily diagnosed with a psychiatric variant of HE.
Discussion: High anti-TPO and anti-TG antibodies (HE hallmarks) generally are not tested for when routine thyroid labs are normal. In all cases of rcBPAD, anti-TPO and anti-TG antibody testing should be considered. HE and rcBPAD are similar clinically, and some rcBPAD cases may be psychiatric variants of HE. HE responds readily to steroid or plasmapheresis treatment, the latter having few risks and many benefits. Some rcBPAD patients could respond to HE treatments.
Conclusion: Clinicians should consider testing anti-TPO and anti-TG levels in all rcBPAD patients. HE treatments may prove helpful for some psychotropic refractory rcBPAD patients. Further study is needed. We declare no conflict of interest. The research for this project was unfunded.

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» NR3-043

DEVELOPMENT OF THE KOREAN AFFECTIVE WORDS

Bo Ra Kim MD, Jin Young Park MD, Jee In Kang MD, Eun Lee MD, PhD, Suk Kyoon An MD, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that the various types of emotional stimuli have been used as materials for emotional research in the country, but the Korean Affective Words, which eliciting emotional reactions was not still to be developed. Therefore development of the Korean Affective Words are expected to be possibly applied widely as the emotion-induction stimuli domestically to an emotional research in the future.

SUMMARY:

Objective: As the interest in field of emotional and affective science is recently getting higher, emotional research of using facial stimuli, event pictures, and words stimuli have been performed actively. The purpose of this study was to develop the Korean Affective Words, which eliciting emotional reactions. Method: From 'Korean-language dictionary according to vocabulary frequency.', we selected the preliminary affective words, which included 93 words for happiness, 43 words for sadness, 87 words for fear, 23 words for anger, and 41 words for disgust. These words were presented to normal young subjects (n=50). Subjects were allowed to categorize their emotional reactions into one of happiness, sadness, fear(threat), anger, surprise, and disgust. Results: Given enumerating the affective words, which caused the intended-emotional response with the consistent ratio in more than 70%, those are as follows. Namely, those were extracted love, smile, hope, and friend in case of happiness; silence, despair, disorder, unemployed person, and funeral in case of sadness; bullet, invasion, menace, hostility, and massacre in case of fear(threat); fishy smell, maggot, nausea, body wastes, and bad smell in case of disgust. Conclusions: These Korean affective words are expected to be possibly applied widely as the emotion-induction stimuli domestically to an emotional research in the future. Key Words: Emotion, Korean words, Happiness, Sadness, Fear, Threat, Disgust

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NR3-044

PREDICTIVE VALUE BIPOLAR-SPECTRUM CLINICAL FEATURES IN A LARGE COHORT OF FLUOXETINE TREATED PATIENTS WITH MAJOR DEPRESSIVE DISORDER

Francesco Casamassima M.D., Fava M., M.D., Clain A., Ph.D., Jonathan P. Stange, B.A., Roy H. Perlis, M.D., M.Sc

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize clinical characteristics pertaining to Bipolar Spectrum Disorders, and their prognostic role in patients affected by major depression

SUMMARY:

Objective: The presence of unrecognized bipolar disorder or "bipolar spectrum" features has been suggested to contribute to poor treatment response in major depressive disorder (Akiskal and Mallya, 1987; Fagiolini and Kupfer, 2003).We aimed to investigate the association between putative bipolar spectrum features and clinical outcomes in a cohort of fluoxetine-treated patients with MDD.
Method: N= 570 outpatients aged 18-65 years with major depressive disorder recruited at 2 academic medical centers first entered a 12-week phase of open-label treatment with fluoxetine titrated up to 60mg/day. Patients who met the response criteria by week 12 entered the second phase of the study during which they were double-blindly randomized either to continue the same fluoxetine doses to which they had responded or to take placebo, for 52 weeks or until the occurrence of a relapse. The following clinical features suggestive of bipolar illness were selected for analysis: a history of early onset and recurrent depression, baseline atypical depressive features, irritability, psychoticism, suicidality, interpersonal sensitivity, comorbid anxiety disorders, and substance abuse/dependence. These measures were condensed into a "Bipolar Index" score ranging from 0 to 10 points. We considered as primary outcomes time to response, remission, and discontinuation during acute treatment and time to relapse in the second phase of the study, utilizing survival analyses.
Results: Higher scores on the Bipolarity Index were not associated with differential acute treatment outcomes. They were significantly associated with a shorter time to relapse ($p = 0.002$). The mean time until first recurrence was 31.1 weeks in the group with lower scores vs. 25.3 wk in the group with higher scores ($p = 0.02$).
Conclusion: Bipolar spectrum features may be associated with shorter time to recurrence in MDD patients after recovery, suggesting some predictive validity for this measure.

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NR3-045

INTERNET ADDICTION AS A SYMPTOM OF DEPRESSIVE MOOD DISORDERS IN A SAMPLE OF KOREAN ADOLESCENTS

Jung Eun-Jung M.D., Hyun-Jae Woo, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that there were significant positive correlations among Internet addiction and depression in adolescents and that it is crucial to include questions about Internet usage in psychiatric examination taking.

SUMMARY:

OBJECTIVE: The purpose of this study was to evaluate the relationship between depression and Internet addiction among Korean adolescents.
METHOD: Fifty three adolescents(22 boys and 31 girls; mean age, 16.0 ± 1.0)were included in this study. They were diagnosed with a depressive mood disorder by thorough clinical examination and structured interviews. We assessed the level of Internet addiction using rating scale (ARS; Korean version, K-ARS). Beck's depression inventory (BDI) and Barratt impulsiveness scale(BIS) were also self-rated.
RESULTS: Among 53 depressive mood disorder patients with significant psychological strain, 36 (67.8%) were diagnosed as Internet addiction by K-ARS. There was no significant correlation between internet addiction scale score and BDI severity. The prevalence of Internet addiction did not vary with gender.
CONCLUSION: There were significant positive correlations among Internet addiction and depression in adolescents. It seems to be crucial to include questions about Internet usage in psychiatric examination taking. Future studies should investigate the direct relationship between psychological health problems and Internet dependency.

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NR3-046

BIPOLAR DISORDER IMPAIRS PHYSICAL HEALTH AS MUCH AS SCHIZOPHRENIA

Maria Garcia-Portilla M.D., Susana Santamarina, M.D., Pilar A. Saiz, M.D.Ph.D., Maria T. Bascaran, M.D., Celso Iglesias, M.D., Ph.D., Julio Bobes, M.D.,Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify and diganose metabolic syndrome in its patients with schizophrenia and bipolar disorder.

SUMMARY:

Background: Several studies have reported increased rates of metabolic syndrome (MetS) in patients with schizophrenia and bipolar disorders compared to general population.
Objective: We compared patients with schizophrenia and bipolar disorder from the same geographical area to determine whether there are differences in the prevalence of MetS according to the diagnosis.
Methods: Naturalistic, one-year longitudinal study conducted in Asturias, Northern Spain. A total of 172 patients with schizophrenia or bipolar disorder (ICD-10 criteria) were included. Prevalence of MetS was determined according to 2 sets of criteria: 1) NHANES 1999-2000 study, and 2) AHA-NHLBI.
Results: Patients with schizophrenia were significantly younger (41.7 versus 53.3, p .000) and were men in greater proportion (65.2% versus 42.1%, p .004) than patients with bipolar disorder. At baseline, there were not statistically significant differences in body mass index (30.0 versus 30.3 kg/m2, p 0.723), nor in MetS (NHANES criteria: 28.7% versus 21.4%, p 0.315; AHA-NHLBI criteria: 37.4% versus 42.9%, p 0.497). According to both set of criteria patients with bipolar disorder showed significantly greater rates of hypertension than patients with schizophrenia (NHANES criterion: 35.7% versus 13.8%, p .001; AHA-NHLBI criterion: 64.3% versus 40.4%, p .004). In the logistic regression model the unique variable significantly associated with MetS was obesity (NHANES: adjusted OR= 10.21, 95% CI= 2.2-47.3, p .003; AHA-NHLBI: adjusted OR= 24.03, 95% CI= 5.1-112.5, p <.001).
Conclusion: Patients with bipolar disorder and schizophrenia have nearly identical rates of metabolic syndrome.

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2) Birkenaes AB, Opjordsmoen S, Brunborg C, Engh JA, Jonsdottir H, Ringen PA, Simonsen C, Vaskinn A, Birkeland KI, Friis S, Sundet K, Andreassen OA. The level of cardiovascular risk factors in bipolar disorder equals that of schizophrenia: a comparative study. J. Clin. Psyhiatry 2007;68:917-923.

» NR3-047

WHAT'S IN THE PIPELINE FOR MAJOR DEPRESSIVE DISORDER?

Aarti Gupta M.B.B.S, Rajnish Mago, M.D, Michelle Shwarz, M.S.Ed.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the: 1)Novel mechanisms for medications currently in clinical trials for Major Depressive Disorder, both as primary treatments and for augmentation of conventional antidepressants. 2)Proportions of clinical trials in children vs. adults and medications vs. psychotherapy. 3)Patterns of funding of clinical trials and their association with characteristics of the trials.

SUMMARY:

Introduction: We aimed to describe the types of treatments currently in clinical trials for major depressive disorder along with characteristics of these trials.

Methods: Since registration of clinical trials is now mandatory, we searched clinicaltrials.gov for ongoing treatment trials in MDD. Data about each trial was extracted based on predefined variables of interest.

Results: 155 ongoing treatment trials were found, with sample sizes varying markedly from 5 to 1200. 19.4% trials were uncontrolled, 23.9% had an active comparator, and 56.8% were placebo-controlled. 69.1% trials involved medications, 17.8% used psychotherapy, and 11.2% used TMS. 10.5% trials were in children/adolescents. Comparing trials in adults vs. in children, 69.9% and 43.8% respectively used a medication, 14.7% and 43.8% used psychotherapy (Fisher's exact test p=.01). 74.8% trials were for primary treatment of MDD including novel treatments including triple reuptake inhibitors, a norepinephrine reuptake inhibitor, a nicotinic receptor antagonist, a CRF-1 antagonist, a 5HT-7 antagonist, vilazodone, riluzole, etc. 23.2% were augmentation studies using compounds like antipsychotics, and novel ones like D-cycloserine, cysteamine, cimicoxib, creatine monohydrate, aerobic exercise, and magnetic seizure therapy. Only 16.6% of trials were funded by NIH/ other federal agencies. The median sample size by funding source was 374.5 for industry, 152 for federal agencies, and 50 for a university/organization (Kruskal Wallis test, p=.0001).

Conclusion: A robust pipeline of potential medications with novel mechanisms exists. Consistent with the importance of MDD with inadequate response, various augmentation strategies, including novel ones, are being studied. However, psychotherapy trials, trials in children (especially of medication), and NIH funding of trials continue to be neglected. Also, studies not funded by industry are significantly smaller.

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1) clinical trials.gov: registry of federally and privately supported clinical trials conducted in the United States and around the world. http://clinicaltrials.gov/

2) Baghai TC, Volz HP, Möller HJ: Drug treatment of depression in the 2000s: An overview of achievements in the last 10 years and future possibilities. World J Biol Psychiatry 2006;7(4):198-222.

» NR3-048

PERSONALITY DIFFERENCES IN DEPRESSED POPULATION ACROSS NINE CENTRES IN EUROPE

Bhanu Gupta M.B.B.S, Robert Keers, B.Sc., Anne Farmer M.D., Peter McGuffin Ph.D., Rudolph Uher Ph.D.,Wolfgang Maier M.D.,Joanna Hauser Ph.D., Ole Mors Ph.D.,Ann S Kristensen Ph.D., Marcella Rietschel M.D., Astrid W Zobel M.D., J Perez Ph.D.,Caterina Giovannini, Andrej Marusic Ph.D., Dejan Kozel B.Sc. , Julien Mendlewicz M.D., Neven Henigsberg Ph.D., Katherine J Aitchison Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to develop greater understanding of the link between personality and depression and appreciate the variation in personality dimensions in depressed population by cultural and demographic variables.

SUMMARY:

Personality differences in depressed population across nine centres in Europe

Background: Personality traits are known to be determined by both environmental and genetic influences. GENDEP is a large multicentre pharmacogenomic study that was conducted across 9 centres in Europe, which aimed to identify clinical and genetic predictors of antidepressant response.

Aim: To examine differences in personality traits as measured by the Temperament and Character Inventory- Revised (TCI-R) in moderate to severely depressed subjects across nine European centres.

Method: 555 participants were recruited for GENDEP study in nine centres in eight European countries: Aarhus (Denmark, n=66), Brescia (Italy, n=30), Brussels (Belgium, n=37), Bonn (Germany, n=94), Ljubljana (Slovenia, n=58), London (UK, n=69), Mannheim (Germany, n=69), Poznan (Poland, n=87), and Zagreb (Croatia, n=45). Inclusion criterion: at least 18 years of age and suffering from a depressive episode established using the Schedules for Clinical Assessment in Neuropsychiatry interview (SCAN version 2.1, WHO, 1999). TCI-R was administered at baseline prior to commencement of treatment.

Results: Geographically and culturally similar countries had closely correlated scores; otherwise there was a significant difference in personality traits across the eight countries. Interestingly, the scores of the participants in the two German centres were highly correlated. ($r > 0.99$, 95% CI 0.997 to 0.999) German subjects scored highest in novelty seeking (NS) and self-transcendence (ST) but lowest in harm avoidance (HA), reward dependence (RD), and cooperativeness (CO). The subjects from the Denmark and Belgian centres scored highest in CO. Denmark and UK participants scored lowest in ST. Overall there was a significant difference in personality dimensions by centre on non parametric testing with Kruskal Wallis one way analysis of variance ($p = 0.0001$ df=8).

Conclusions: This suggests that there are regional differences in personality dimensions in depressed subjects across different European countries that participated in the GENDEP study. These are unlikely to be artefactual owing to the close correlation between the two German centres, and may reflect underlying genetic and environmental differences.

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2) Uher R, Farmer A, Maier W, Rietschel M, Hauser J, Marusic A, Mors O, Elkin A, Williamson RJ, Schmael C, Henigsberg N, Perez J, Mendlewicz J, Janzing JGE, Zobel A, Skibinska M, Kozel D, Stamp AS, Bajs M, Placentino A, Barreto M, McGuffin P, Aitchison, KJ Measuring depression: comparison and integration of three scales in the GENDEP study. Psychological Medicine 38, 289-300 (online first 09 Oct 2007, doi: 10.1017/S0033291707001730)

» NR3-049

DEPRESSION AND ATTENTION DEFICIT HYPERACTIVITY DISORDER: RESULTS FROM AN EXPERIMENTAL STUDY

Désirée Harnic M.D., Marianna Mazza, M.D., Ph.D., Valeria Catalano, Giuseppe Marano, Marco Di Nicola, M.D., Giovanni Martinotti, M.D., Luigi Janiri, M.D., Pietro Bria, M.D.

EDUCATIONAL OBJECTIVES:

[no data]

SUMMARY:

Introduction: The present study investigates Attention Deficit Hyperactivity Disorder (ADHD) in order to evaluate a possible predisposition in adult age to particular psychopathologic case history and to find differences in symptomatology of ADHD between Bipolar and Unipolar Depression.
Methods: The sample was composed of 67 patients, of which 35 were affected by Bipolar Depression and 32 by Unipolar Depression, according to DSM-IV criteria. All patients were submitted to psychometric assessment through Neo Personality Inventory (NEO-PI-R), Brown Attention Deficit Disorder Scale (Brown ADD-Scale), Adult ADHD Self-Report Scale (ASRS-v1.1).
Resuls: 42% of the sample, during infancy, was accorded to DSM-IV criteria for ADHD, with prevalence of the masculine sex on the female one. Besides, during their infancy patients affected by Bipolar Depression satisfied ADHD criteria with greater frequency in comparison with patients affected by Unipolar Depression.
Conclusions: The study showed that a significant percentage of the sample had satisfied ADHD criteria during infancy. In particular, it seems that such criteria predispose to the development in adult age of Bipolar Depression rather than Unipolar Depression. Further studies on larger sample will be necessary in order to confirm these results.

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1) Semiz UB, Basoglu C et al, Effects of diagnostic comorbidity and dimensional symptoms of attention-deficit-hyperactivity disorder in men with antisocial personality disorder, The Australian ad New Zealand Journal of Psychiatry, May; 42(5):405-13, 2008.

2) Spencer T.J., Treatment of adult ADHD and comorbid depression, CNS Spectrum. 2008 May;13(5 Suppl 8):14-6.

» NR3-050

MANIC PATIENTS SHOW MOOD-CONGRUENT BIAS IN AFFECTIVE GO/NO-GO TASK USING SCENERY PICTURES BUT NOT WORDS OR FACIAL PICTURES

Seung Jun Kim MD, Jee In Kang MD, Ji Hyun Lee MA, Suk Kyoon An MD, PhD, Hyun-Sang Cho MD, PhD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that patients with mania display a mood congruent bias toward affective stimuli and that it is important which type of affective stimuli is adopted in performance tasks in that the scenery picture-based affective Go/No-Go task may produce the mood congruent bias of patients with mania more effectively than word or facial picture-based affective Go/No-Go task.

SUMMARY:

Objective: Patients with bipolar mania have a mood-congruent bias for recognizing or attending to negatively affective stimuli. However, previous reports have adopted words or facial pictures, not scenery pictures as affective stimuli. This study investigated performance of patients with mania on the word, face picture and scenery picture-based affective Go/No-Go tasks. Method: Twenty patients with bipolar mania and 20 healthy comparison subjects, matched for age, gender and education, performed three types of affective Go/No-Go tasks as well as a non-affective Go/No-Go task. Three affective Go/No-Go tasks contained happy/sad words, facial pictures, and scenery pictures respectively. The non-affective Go/No-Go task comprised neutral male/female facial pictures. Results: On the scenery picture-based affective Go/No-Go task, manic patients required significantly more time to respond to happy than to sad stimuli, but healthy subjects did not differ in time to respond to happy or sad stimuli($F=8.157$, $p<0.05$). On the word and facial picture-based affective Go/No-Go tasks, patients with mania as well as healthy subjects statistically did not differ in time to respond to happy or sad stimuli($F=0.385$, $p=0.539$; $F=2.171$, $p=0.149$). On the non-affective Go/No-Go task, there is no difference in time to response to male or female picture not only in healthy subjects but also in patients with mania($F=0.595$, $p=0.445$). On the affective and non-affective Go/No-Go tasks, there was no significant difference in the number of omission and commission error to happy or sad stimuli in patients with mania as well as healthy subjects. Conclusions: Manic patients displayed a mood-congruent bias toward affective scenery pictures, but not toward affective word or facial pictures. This finding suggests that complex and scenery stimuli may influence more the affective arousal state, and therefore increase the mood-congruent bias in manic patients.

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1) Murphy FC, Sahakian BJ, Rubinsztein JS, Michael A, Rogers RD, Robbins TW, Paykel ES: Emotional bias and inhibitory control processes in mania and depression. Psychol Med 1999; 29: 1307–1321

2) Erickson K, Drevets WC, Clark L, Cannon DM, Bain EE, Zarate CA Jr, Charney DS, Sahakian BJ: Mood-Congruent Bias in Affective Go/No-Go Performance of Unmedicated Patients With Major Depressive Disorder. Am J Psychiatry 2005; 162: 2171–2173

» NR3-051

THE RELATIONSHIP BETWEEN STIGMA, MOOD, AND QUALITY OF LIFE IN BIPOLAR PATIENTS AND THEIR FAMILIES PRESENTING FOR FAMILY TREATMENT

Allison Lee M.D., Annie Steele, Jena Bobish, Ashley Kronen, Lisa Cohen Ph.D., Igor I. Galynker, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, participants should be familiar with Family-Inclusive treatment as it is conducted at the Family Center for Bipolar Disorder at Beth Israel Medical Center, and with characteristics of a population seeking family-involved treatment.

SUMMARY:

Introduction: Including family in the treatment of bipolar disorder can improve both patient and family outcomes, as shown in prior studies. However, little is known about the particular population that seeks family-inclusive treatment. In order characterize this new treatment population, baseline data from patients and caregivers seeking Family-Inclusive Treatment (FIT) were examined.
Methods: Participants were either recruited from the outpatient psychiatric clinic at Beth Israel Medical Center, recruited from the practices of BIMC's Family Center for Bipolar Disorder (FCBD) faculty, or self-referred for consultation at FCBD. FIT consisted of medication management and supportive psychotherapy for bipolar patients along with open communication between psychiatrists and families about patient medications and symptoms. Families were included in sessions regularly, as needed. Data were collected on patient and family Depression (CES-D), Anxiety (STAI), Quality of Life (QLES-Q), Bipolar Knowledge, Doctor-Patient Communication (MD Comm), and Stigma.
Results: Patient depression and anxiety were positively correlated with patient stigma. Patient quality of life (QOL) was negatively correlated with patient MD Comm. Caregiver QOL was negatively correlated with caregiver stigma but positively correlated with patient stigma. Patient and caregiver QOL were positively correlated with one another. Caregiver knowledge was positively correlated with caregiver anxiety. There was a trend towards a negative correlation between caregiver MD Comm and patient anxiety.
Conclusions: Stigma plays a significant role in both patient and caregiver distress and therefore should be a major focus of psychosocial treatment in bipolar disorder. However, the nature and

source of stigma in patients and caregivers may be different and may therefore benefit from differing treatment approaches. The relationship between MD Comm, bipolar knowledge, and other variables warrants further study.

REFERENCES:

1) Gonzalez JM, Perlick DA, Miklowitz DJ, Kaczynski R, Hernandez M, Rosenheck RA, Culver JL, Ostacher MJ, Bowden CL: Factors associated with stigma among caregivers of patients with bipolar disorder in the STEP-BD study. Psychiatr Serv 2007; 58:41-8

2) Reinares M, Colom F, Martinez-Aran A, Vieta E: Therapeutic interventions focused on the family of bipolar patients. Psychother Psychosom 2001; 71:2-10

» NR3-052

DIFFERENTIAL EXPRESSION OF ATYPICAL DEPRESSION IN AFRICAN AMERICANS AND ITS ASSOCIATION WITH CARDIOVASCULAR RISK FACTORS AND DISEASES

Oreisa O'Neil M.P.H., Yu Dong, M.D., Ph.D (Co-First Author), William B. Lawson, M.D., Ph.D, Douglas Levinson, M.D., Evaristus Nwulia, M.D., MHS, NIMH Genetics of Recurrent Early-Onset Depression.

EDUCATIONAL OBJECTIVES:

At the end of this presentation, a participant should be able to identify: some atypical features of major depression; the differential expression of these atypical symptoms in African Americans with early-onset depression compared to their Caucasian counterparts; and the association of these features with cardiovascular risk factors and diseases.

SUMMARY:

Objective: Atypical depression, featured by overeating and oversleeping, is generally under-recognized, especially in African Americans (AA) and may be correlated with obesity and cardiovascular diseases. We hypothesized that AA have a higher prevalence of atypical features of depression than their Caucasian counterparts, and these features will correlate with higher prevalence of obesity and comorbid cardiovascular diseases.

Method: Symptoms of atypical depression were compared between AA (N=158) and non-Hispanic Caucasians (CA) (N=775) based on two major depression episodes recorded in the structured Diagnostic Interview for Genetic Studies (DIGS). Ethnicity, anthropometric measures and medical histories were obtained through self-report and medical records.

Results: AA's have significantly higher prevalence of reactive moods; disturbances in sleep, eating and body weight; and lower rate of anhedonia in both recorded episodes, more significant in the less severe episode. Average body mass index (BMI) (± S.D.) in the study sample is 27.1 (6.7). AA ethnicity is associated with a 2-point increase in the mean BMI ($P<0.005$). Adjusting separately for increased appetite and increased weight gain during less severe depression significantly decreased the association between AA and BMI. Similarly, significant association between AA and higher prevalence of reported angina/MI, hypertension, and diabetes diminished after adjusting for increased appetite and weight gain during less severe depression.

Conclusion: Since the less severe episode of depression more likely reflects the life-time depression history, these results indicate that greater expression of atypical features of depression may underlie some of the health disparity consistently observed in national surveys.

REFERENCES:

1) Uebelacker LA, Strong D, Weinstock LM, Miller IW. Use of item response theory to understand differential functioning of DSM-IV major depression symptoms by race, ethnicity and gender. Psychol Med. 2008 Jun 30:1-11.

2) Posternak MA, Zimmerman M. Symptoms of atypical depression. Psychiatry Res. 2001 Nov 1;104(2):175-81.

» NR3-053

MISDIAGNOSIS OF BIPOLAR DISORDER AMONG PATIENTS WITH SUBSTANCE ABUSE

Anoosh Salman, M.D., Mahboob Aslam, M.D., Steven Kwoh, Amir Aryaie, Alisha Oelke, M.S., Javed Iqbal, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should demonstrate background knowledge of bipolar disorder, recognize the difference between a substance induced mood disorder and bipolar mood disorder, and correctly diagnose and treat the bipolar disorder. Readers should learn to look for comorbid factors of substance abuse indicated by a positive urine toxicology or blood alcohol level in the bipolar patient. Treatment should be planned on the basis of evidence of clear diagnosis.

SUMMARY:

Bipolar disorder, which causes significant psychosocial morbidity and increased mortality, has been reported to be overdiagnosed, underdiagnosed, and misdiagnosed. Accurate diagnosis of bipolar disorder is imperative for determination and optimization of the most effective and benign treatment plan. When substance comorbidities are present, the diagnosis of bipolar disorder is more difficult to determine due to similar symptomology of the mood states. Differentiation of mood disorders in substance abusers was the purpose of the study. Methodology included a retrospective analysis of 198 patient charts from Bergen Regional Medical Center in the setting of Adult Inpatient Psychiatric Unit during 2007 and 2008 that were diagnosed with bipolar disorder. If a bipolar disorder was diagnosed, then charts were further assessed for comorbidities of substance abuse. Patients underwent a structured interview with a psychiatrist using a standardized 10 point form. Age, gender, race, dates of admission and discharge, duration of bipolar diagnosis, duration of substance abuse, substances abused, Axis I, Axis II, Axis IV, Blood Alcohol Level (BAL), and Urine Toxicology (UTOX) were recorded at the time of admission. In congruence with DSM IV criteria, a diagnosis of bipolar disorder with concurrent active substance use, or a diagnosis of bipolar disorder with a history of continuous substance use that surpasses the duration of bipolar disorder were considered overdiagnosed. Results indicated 69/134 (51.5%) patients were overdiagnosed with bipolar disorder, 46/134 (34.3%) were correctly diagnosed, and 19/134 (14.2%) could not be determined. This study concluded that over 50% of bipolar disorder patients were overdiagnosed due the presence of substance abuse. Further study between dual diagnoses of bipolar disorder and substance induced mood disorder is necessary in order for a correct treatment course to be identified.

REFERENCES:

1) Hasin D, Samet S, Nunes E, Meydan J, Matseoane K, Waxman R. Diagnosis of comorbid psychiatric disorders in substance users assessed with the Psychiatric Research Interview for Substance and Mental Disorders for DSM-IV. Am J Psychiatry. 2006 Apr;163(4):689-96.

2) Zimmerman M, Ruggero CJ, Chelminski I, Young D. Is bipolar disorder overdiagnosed? J Clin Psychiatry. 2008 Jun;69(6):935-40.

» NR3-054

CO-OCCURRENCE OF BIPOLAR AND ATTENTION-DEFICIT HYPERACTIVITY DISORDERS IN CHILDREN: A CASE REPORT

Anoosh Salman, M.D., Abderrahmane Richane, M.D., Khaja Faisal, M.D., Javed Iqbal, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the importance of early recognition of atypical presentation of bipolar disorder in children with rapid fluctuations in mood and behavior, often associated with comorbid ADHD and the treatment challenges in these children.

SUMMARY:
The number of children and adolescent receiving a diagnosis of bipolar disorder has increased markedly during the past decade in the U.S. The patterns of illness and symptoms are atypical in children characterized by irritability, outburst of mood lability, reckless behavior, high rates of rapid cycling and low rates of interepisode recovery and children are often associated with comorbid attention-deficit hyperactivity disorder. At this time, it is not clear whether the atypical forms of juvenile mania and the classic adult form of the disorder represent the same illness.
Several investigators have tried to discern which symptoms are the most helpful in distinguishing ADHD from Bipolar disorder. Five symptoms: elation, grandiosity, flight of ideas/racing thoughts, decreased need for sleep and hypersexuality, best discriminated children who have Bipolar disorder from children who have ADHD. The following case report describes a 12 year old Caucasian male with 6 year history of ADHD and 4 year history of bipolar disorder. He presented with disruptive behavior, increased energy level, impulsivity, restlessness, constant racing thoughts, disruptive sleep with frequent awakening, often running or climbing in inappropriate situations, excessive involvement in risky activities, and sense of entitlement. Therefore the diagnosis and treatment of patients suffering from ADHD and bipolar disorder is very challenging. The etiology of comorbid Bipolar disorder and ADHD is likely multifactorial. Additional longitudinal and biological studies are warranted to clarify the relationships between Bipolar disorder and ADHD since they may have important diagnostic and treatment implications.

REFERENCES:

1) SINGH Manpreet K. ; DELBELLO Melissa P. ; KOWATCH Robert A. ; STRAKOWSKI Stephen M. ;Bipolar Disord. 2006 Dec;8(6).

2) Rebecca Tillman & Barbara Geller Development and Psychopathology 18(2006).

» NR3-055

EFFECT OF LONG-TERM ANTIDEPRESSANT TREATMENT TO SERUM BRAIN-DERIVED NEUROTROPHIC FACTOR

Lee Seungyoun, Doh Kwan Kim,M.D, Jae-Won Chung,M.D, Shinn-Won Lim,M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to predict effect of change of BDNF concentration after long term antidepressant treatment

SUMMARY:
Object: BDNF is a prosurvival factor induced by cortical neurons that is necessary for survival of striatal neurons in the brain. Circulating BDNF in the serum reflect neuroplastic change. Neuroplastic change may play a role prognostic factor. Our study aims at elucidating the serum BDNF level be predictible marker after chronic antidepressant treatment.
Method: BDNF level was quantified via Emax ImmunoAssay system from 84 depressed patients at 0, 1, 6, 24th week during antidepressant treatment. Drug response was quantified as HAM-D score at 0,1,6,24th week. The correlations between alterations of serum BDNF level and drug response during drug treatment were analyzed by Pearson or Spearman's rho correlation using SPSS 11.0.
Result: During 24 weeks of antidepressant treatment, antidepressant responsiveness was associated with the change of serum BDNF level during 1 week. There were positive correlation between change of BDNF concentration at 1 week and antidepressant responsiveness during 0_24week (r=0.098, p=0.000, Pearson correlation). And after 24 weeks of antidepressant treatment, There were positive correlation between change of serum BDNF level during 1 week and antidepressant responsiveness at 24week (r=-0.975, p=0.005, Spearmann's correlation).
Conclusion: These results represent that the BDNF concentration in seum of depressed patients is potential to a marker of response status during antidepressant treatment. Significant correlations of the change between 1week serum BDNF level and antidepressant responsiveness from 0 to 24week during antidepressant administration represent that the change of BDNF concentration for 1 week may predict antidepressant responsiveness after 24 week.

REFERENCES:

1) Pezawas L, Meyer-Lindenberg A, Goldman AL, Verchinski BA, Chen G, Kolachana BS, Egan MF, Mattay VS, Hariri AR, Weinberger DR. Evidence of biologic epistasis between BDNF and SLC6A4 and implications for depression. Mol Psychiatry. 2008 Jul:13(7):709-16.Epub 2008 Mar 18

2) Yuan TF. BDNF signaling during olfactory bulb neurogenesis. J Neurosci.2008 May 14;28(20):5139-40

» NR3-056

ALTERATIONS OF EXPRESSION AND FUNCTION OF CREB IN LYMPHOCYTE OF DEPRESSED PATIENTS DURING SSRI TREATMENT

Lee Seungyoun, Doh Kwan Kim,M.D., Jae-Won Chung,M.D., Shinn-Won Lim,Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to predict alterations of expression of CREB

SUMMARY:
Object: The therapeutic procedure of several antidepressants develop a time lag of 2 to 6 weeks. Such a time lag is known as contain the several signal transduction pathway in post-synapse after targeting antidepressant to monoamine transporter, primary target of most antidepressant. Our study aims at elucidating the alterations and adaptable changes of signaling pathway in post synapse after chronic antidepressant treatment
Design: We studied the changes between drug responsive and the expression and function of transcription factor, CREB in peripheral lymphocytes of depressed patients at 0 and 6weeks, during SSRI antidepressant treatment
Methods: CREB-expression and phosphrylation was quantified via immunoblot, and binding activity between transcription factor and DNA via electrophoretic mobility shift assay(EMSA) in nuclear extracts from 65 depressed patients at 0 and 6th week during antidepressant treatment. Drug response was quantified as HAM-D score. The correlations between alterations of CREB characteristics and drug response during drug treatment were analyzed by Pearson or Spearman's rho correlation using SPSS 11.0.
Result: During 6 weeks of antidepressant treatment, antidepressant responsiveness is associated with the change of CREB expression, phosphorylation, and CRE-DNA binding(p=0.001, p=0.001, p=0.068, respectively by Mann-Whitney). During 0-6weeks, CREB expression, pCREB expression and CRE-DNA binding were positively correlated each other(CREB-pCREB r=0.700, p=0.0000; pCREB-CRE-DNA binding, r=0587, p=0.0000 by Spearmann's rho).
Conclusion: These results represent that the CREB in peripheral lymphocyte of depressed patients is potential to a marker of response status during antidepressant treatment. Significant correlations of the change between CREB and pCREB immunoreactivity, and pCREB and DNA-CRD binding from 0 to 6week during fluoxetine administration represent that the action mechanism of antidepressants involves CREB-transcription.

REFERENCES:

1) Tardito D, Perez J, Tiraboschi E, Musazzi L, Racagni G, Poppli M. Sinaling pathways regulating gene expression, neuroplasticity, and neurotrophic mechanisms in the action of antidepressants: a critical overview. Pharmacol Rev. 2006 Mar;58(1):115-34.

2) Tiraboschi E, Tardito D, Kasahara J, Moraschi S, Pruneri P, Gennarelli M, Racaqni G, Popoli M. Selective phosphorylation of nuclear CREB

by fluoxetine is linked to activation of CaM kinase IV and MAP kinase casecades. Neuropsychopharmacology. 2004 Oct;29(10):1831-40

» NR3-057

ETHNICITY AND PREVALENCE OF BIPOLAR DISORDER: A REVIEW

Jacqueline Shafiroff, B.A., Sophia Haeri, B.S., Alexis Newmark, B.A., Jamie Johnson, B.A., Igor Galynker, M.D., PhD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should have an understanding of the prevalence of bipolar disorder worldwide. Participants should also be able to recognize trends regarding common diagnoses among specific ethnic groups.

SUMMARY:

The prevalence of bipolar disorder throughout the world and the ethnic groups it most affects has not been well-defined. There has not, to date, been any systematic review of the impact of race, ethnicity, or culture on that diagnosis. The current investigation examines existing research on the impact of ethnic and cultural factors on the prevalence of bipolar disorder.

It is important to review the literature that explores rates of diagnoses according to both geographical location and ethnicity so that these individuals can be identified and properly treated. In addition to this, knowledge of bipolar disorder prevalence can help us to better understand what factors, whether environmental or biological, may influence this disorder.

METHODS: We conducted searches on Medline and PsychINFO using the keywords "prevalence" "ethnicity", "race", "ethnic", and "culture", in combination with "bipolar", "bipolar disorder", "mania", and "manic depression". This search was completed in December 2007. 38 articles were included in the evaluation. Papers focusing on Bipolar Disorder and comorbid conditions, and papers not directly related to prevalence, were excluded.

RESULTS: Bipolar disorder has a prevalence rate ranging from 0.3% to 6.5% even in isolated communities. Technologically advanced communities seem to have higher rates of BD (rate of 1.9% vs 6.5%). There have been findings that show both increased and decreased rates of bipolar disorder according to ethnicity. 28 articles found that certain ethnic groups have increased rates, 4 articles found that certain ethnic groups had decreased rates, and 6 articles found no difference in rates according to ethnicity. Nine articles found increased rates of bipolar disorder, mania, and schizophrenia among those of African descent.

CONCLUSION: Though there appears to be a relationship between ethnicity and the prevalence of bipolar disorder, the current literature is inconclusive. Future research should investigate biological and environmental influences.

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» NR3-058

THE ROLE OF ANTIDEPRESSANTS FOR BIPOLAR-DEPRESSION: AN UPDATED AND EXPANDED META-ANALYSIS

Michelle Sidor M.S.C., Glenda M. MacQueen, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that antidepressants may not be an effective treatment option for the acute treatment of bipolar-depression.

SUMMARY:

Objective: The role of antidepressants for the acute treatment of bipolar depression (BD) remains a contentious issue. A previous meta-analysis of randomized controlled trials (RCTs) concluded that antidepressants were both effective and safe for BD. Several trials published since then suggest that antidepressants may not be as beneficial as previously concluded. The current analyses re-examine the efficacy and safety of antidepressant use for the acute treatment of BD. Methods: A systematic review and meta-analysis was performed. Electronic databases were searched for double-blind RCTs published between 2003-2008. Trials that compared acute (<16 wks) antidepressant treatment with either an active or placebo comparator in adult bipolar patients, depressive phase were eligible for inclusion. Main outcome measures were clinical response, remission, and affective switch. Results: Six RCTs (N=1034) published since the original meta-analysis by Gijsman et al. (2004) were identified. These studies were combined with earlier studies for a total of fifteen studies containing 2373 patients. Antidepressants were not statistically superior to placebo or other current standard treatment for BD. Antidepressants were not associated with an increased risk of switch. The overall switch rate was 7.7% for antidepressants and 7.2% for placebo. Studies that employed more sensitive diagnostic switch criterion reported elevated switch rates for antidepressants (24%) versus placebo (4%). Amongst the antidepressants, bupropion was associated with a significantly reduced risk of affective switch (RR=0.34, 95% CI=0.13-0.88, p=0.03) but was no more efficacious than other pharmacological treatment. Conclusions: Overall the results suggest that the risk-benefit ratio for antidepressant use in patients with BD may not be favourable. Further studies are required to address the existing limitations in order to resolve the seemingly contradictory evidence provided in the literature.

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» NR3-059

INTUITION-CREATIVITY RELATIONSHIPS IN MOOD DISORDER PATIENTS, HEALTHY CONTROLS AND HIGHLY CREATIVE INDIVIDUALS

Shefali Srivastava M.D., Meredith Childers, M.A., Connie M. Strong, Ph.D., Kimberley Warsett, M.A., Jenifer L. Culver, Ph.D., Po W. Wang, M.D., Terence A. Ketter, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to evaluate the relationships between Intuition (as assessed by the Myers-Briggs Type Inventory) and Creativity (as assessed by the Barron-Welsh Art Scale) in mood disorder patients, healthy controls and highly creative individuals.

SUMMARY:

Objective: Although Myers-Briggs Type Inventory (MBTI) Intuition preference (MBTI-N) has been related to creativity in the general population, there are limited data regarding the MBTI and its relationship to creativity in mood disorder patients.

Methods: We assessed MBTI, Barron-Welsh Art Scale (BWAS), and Revised NEO Personality Inventory (NEO) scores in 32 euthymic bipolar (BP) and 21 unipolar major depressive disorder (MDD) patients, 22 creative discipline controls (CC), and 42 healthy controls (HC). MBTI preference types, continuous scores, and Creativity Index scores were compared across groups, and correlations were assessed with BWAS and NEO scores.

Results: BP and CC (but not MDD) compared to HC had higher rates of MBTI-N type (78.1% and 95.5% vs. 50.0%, p < 0.001) and higher MBTI-N continuous scores (116 and 114 vs. 102, p < 0.04). In the entire sample, MBTI-N type was associated with 37.8% higher BWAS scores (p = 0.0026), and MBTI-N continuous scores correlated with BWAS scores (r = 0.31, p = 0.0007). Also, in the entire sample, MBTI-N type was associated with 23.5% higher NEO-Openness (NEO-O) scores (p < 0.0001), and MBTI-N continuous scores correlated with NEO-O scores (r = 0.61, p < 0.0001). MBTI-N also had significant but less robust relationships with NEO-N. The MBTI Creativity Index (to which MBTI-N is the largest contributor) but not the other MBTI preferences (Extroversion-Introversion, Thinking-Feeling, Judging-Perceiving) had a similar pattern of relationships to diagnostic subgroups, BWAS, and NEO.
Conclusion: MBTI-N (but not other MBTI preferences) was increased in BP and CC and related to BWAS creativity. MBTI-N correlated with NEO-O and NEO-N, personality constructs that have also been related to creativity and BP. Further studies are needed to explore relationships between MBTI-N and clinical features of BP.
Supported by National Alliance for Research in Schizophrenia And Depression, and Stanley Foundation Research Awards Program.

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» NR3-060

SATISFACTION WITH MEDICATION AND RESPONSE TO TREATMENT WITH ESCITALOPRAM COMPARED TO PLACEBO AND SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITORS

Malcolm Lader,M.D.,PhD., Elin Heldbo Reines,M.D., Sara Larsson Lönn, Koen Demyttenaere,Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand that satisfaction with medication is correlated with a higher patient response to placebo.

SUMMARY:

Background: To test whether satisfaction with taking medication, assessed at baseline using item 15 of the Q-LES-Q (satisfaction with medication) predicts outcome or time to withdrawal.
Methods: Four placebo-controlled studies of MDD patients treated with escitalopram assessed the Q-LES-Q (650 patients on escitalopram and 534 on placebo), together with two comparisons of escitalopram vs venlafaxine (1), or duloxetine (235 patients on escitalopram and 233 on an SNRI) (2). The Q-LES-Q was assessed at baseline and week-8.
Results: At baseline, the mean MADRS total score was 30.0?4.5, and mean Q-LES-Q item 15 score was 2.9?0.9. At week 8, the mean MADRS score of placebo-treated patients with low satisfaction with medication at baseline decreased 9.9 points, vs 11.4 points for patients with moderate satisfaction and 13.6 points for patients with high satisfaction (MMRM). This differentiating effect of baseline satisfaction with medication the MADRS was not found in the active treatment group. In escitalopram-treated patients in the placebo-controlled studies, the improvement for patients with a low, moderate, or high satisfaction at baseline was 14.8, 14.9, and 15.2, respectively. Remission rates (LOCF) were higher in patients with high baseline satisfaction with medication than with low baseline satisfaction [placebo remission rates of 42% vs 19% (p<0.01), 48% vs 37% for escitalopram; SNRI remission rates of 51% vs 43%, and 66% vs 40% (p<0.01) for escitalopram in the head-to-head studies]. The change in satisfaction with medication from baseline to endpoint was significantly correlated with symptomatic improvement. Baseline satisfaction with medication was not significantly correlated with time to withdrawal (all reasons) for escitalopram vs placebo.
Conclusion: Higher baseline satisfaction is correlated with a higher patient response to placebo, but does not influence overall or AE withdrawal rates, or response to active treatment. Funded by Lundbeck.

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» NR3-061

NEUROTOXICITY RELATED TO TRACE ELEMENTS IN BIPOLAR DISORDER:A HIPOTHESIS ABOUT COGNITIVE IMPAIRMENT

Kazuhiro Tajima Pozo M.D., Rafael Fernandez Garcia-Andrade MD, Javier Fernandez Aurrecoechea MD, Virginia Vidal Martinez MD, Diana Zambrano-Enrriquez Gandolfo MD, Ana Montes Montero MD, Helena Fernandez Garcimartin MD, Jose Luis Carrasco Perera MD, Marina Diaz Marsa MD.

EDUCATIONAL OBJECTIVES:

Conclusions: in the bipolar patients group, superior lead and cadmium concentrations in blood and urine, zinc in serum and thallium in urine have been observed. Lead and thallium are two well-known neurotoxics, lacking a safe threshold, so more research is required to determine their role in the ethiopathogenia or aggravation of the bipolar-disorder cognitive dysfunction.

SUMMARY:

Introduction: The cognitive dysfunctions in bipolar disorder are currently creating a great interest, despite the small attention that has been paid to it in the pass, just because the therapeutic efforts have been focusing on the clinical and treatment aspects of the illness. However, a large number of bipolar patients show persistent cognitive impairment, even if they are in euthimia. Lithium, a exogenous trace element in humans, has been one of the cornerstones of the bipolar-disorder's treatment for 50 years. Some studies suggest the involvement of trace elements in the origin of this disorder, many of which are potentially neurotoxic. Thus, we propose that these elements should be considered as potentially implied factors in the cognitive dysfunctions of these patients, as neurotoxic agents.
Objective: Lead and cadmium blood concentrations have been measured by electrothermal atomic absorption spectrometry and Zeeman background correction in the PerkinElmer AAnalyst 800 Spectrometer. The blood levels of copper and zinc have been determined by flame atomic absorption spectroscopy (ICP-MS) (PerkinElmer ELAN 6100-DRC). The data processing has been made by the statistical package SPSS 12.0.
Methodology: the tests that have been applied are the median and the Mann-Whitney U, obtaining a statistically significant difference in the serum lead concentration (p = 0,024), urine lead (p < 0,01), serum cadmium (p < 0,001), urine cadmium (p < 0,001) and serum zinc (p = 0,020) between the bipolar patients and the control group. Although the bipolar patients that were hospitalized during the maniac phase had zinc concentrations slightly superior (median (RIC) = 100 (94-120)) than had the patients that were hospitalized in the depressive phase, statistically significant differences have not been observed.

Results:	Bipolar Group		Control Group	
	n	median (RIC)	n	median (RIC)
LEAD blood (µg/dL)	25	3,0 (1,4-4,2)	29	2,2 (0,9-3,0)
CADMIUM blood (µg/L)	25	0,39 (0,06-1,15)	29	0,2 (0,05-0,4)
COPPER serum (µg/dL)	25	112 (91-130)	29	103 (93-131)
Zinc serum (µg/dL)	25	100 (93-120)	29	85 (77-98)
LEAD urine (µg/L)	25	1,50 (0,60-2,45)	29	0,80 (0,10-1,70)
CADMIUM urine (µg/L)	25	0,25 (0,16-0,57)	29	0,11 (0,0-0,19)
THALLIUM urine (µg/L)	25	0,14 (0,12-0,22)	29	0,08 (0,07-0,13)

Conclusions: in the bipolar patients group, superior lead and cadmium concentrations in blood and urine, zinc in serum and thallium in urine have been observed. Lead and thallium are

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» NR3-062

SEASONAL DEPRESSION SEVERITY AS A PREDICTOR OF HEALTH SERVICE UTILIZATION IN A COMMUNITY-BASED SAMPLE

Simone N Vigod M.D., Anthony J Levitt, MBBS, FRCPC

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to
a) describe the extent of seasonality in depressive symptoms in a community based sample in Ontario, Canada
b) describe the relationship between seasonality of depressive symptoms and help-seeking, use of psychotropic medication and psychiatric hospitalization
c) describe the relationship between seasonality of depressive symptoms and health service utilization after controlling for potential confounding factors.

SUMMARY:

Objective: Patients with depression tend to make more primary care visits than non-depressed patients with the excess due to somatic complaints, not depression. Seasonality has been associated with even greater service use for somatic complaints. However, whether seasonality has an impact on depression-specific health service utilization is unknown. Methods: This community-based cross-sectional telephone study in Ontario, Canada was designed to evaluate mood-related symptom changes across seasons in individuals over age 20. Seasonality was measured using the 6-item global severity of seasonality scale (GSS) from the Seasonal Pattern Assessment Questionnaire (SPAQ) combined with five additional seasonality items to form the seasonal depression severity scale (SDS). SDS was examined as a predictor of four self-reported outcomes: seeking help from a medical doctor, seeking help from a therapist, psychotropic medication use and psychiatric hospitalization. Results: 619 participants who screened positive for depressive symptoms and therefore completed the health service utilization section were analyzed. The mean SDS scores for subjects who sought help from a medical physician (mean=11.5 vs. 9.70,p=0.001), therapist (mean=11.2 vs. 9.73,p=0.006) or who took psychotropic medication (mean=11.9 vs. 9.99,p=0.003)were significantly higher than those who did not. The mean SDS scores did not differ significantly between individuals who were and were not hospitalized. For every 1 point increase in SDS score, the ORs for seeking help from a medical doctor, therapist or psychotropic medication were 1.048 (95%CI 1.018-1.078), 1.034 (95%CI 1.004-1.065) and 1.046 (95%CI 1.015-1.077) respectively after controlling for covariates. Conclusions: Seasonality significantly increased help-seeking for depression even after controlling for important confounding variables. Clinicians should be alert to the possibility of seasonality in help-seekers and modify treatment regimens appropriately.

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» NR3-063

TYPE OF RESIDUAL SYMPTOM AND RISK OF RELAPSE DURING THE CONTINUATION/ MAINTENANCE PHASE TREATMENT OF MAJOR DEPRESSIVE DISORDER WITH THE SELECTIVE SEROT

Huaiyu Yang M.D., Sarah Chuzi, B.A., Lara Sinicropi-Yao, B.A., Dan Johnson, B.A., Ying Chen, M.D., M.S., Alisabet Clain, M.S., Lee Baer, Ph.D., Patrick J. McGrath, M.D., Jonathan W. Stewart, M.D., Maurizio Fava, M.D., George I. Papakostas, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that there may be a specific pattern of residual symptoms associated with depressive relapse during antidepressant continuation/maintenance, which is unrelated to treatment assignment; to identify the importance of treating residual symptoms, specifically residual phobic-anxiety symptoms, and residual obsessive-compulsive symptoms among antidepressant responders/remitters in order to decrease relapse risk.

SUMMARY:

Background: Relapse of major depression among responders during continuation and maintenance treatment is a common clinical problem. Identify predictors of relapse will help develop strategies to prevent relapse. This study is an exploratory analysis to determine whether type of residual symptoms of depression (mood, anxiety, hostility, somatic) predicts relapse in major depression. Method: 570 patients with major depression were treated with fluoxetine (mean dose=45.8mg/d, SD=15.1) for 12 weeks. Treatment response was rated on the 17-Item Hamilton Depression Rating Scale and the Clinical Global Impression Scale. Under double blind conditions, all responders (N=292) were randomly assigned to continue fluoxetine or to switch to placebo for 52-week or until relapse. Residual symptoms were captured by the Symptom Checklist-90 (SCL-90) and the Symptom Questionnaire (SQ) during randomization. Descriptive analysis and survival analysis were utilized to determine the effect of covariates on relapse. Results: Without adjusting for overall residual symptom severity measured by 17-item Hamilton Depression Scale, a greater severity of residual obsessive-compulsive and phobic-anxiety symptoms were found to predict a greater risk of relapse during continuation/maintenance treatment. After adjusting for overall residual

symptom severity, severity of phobic-anxiety but not obsessive-compulsive symptoms predicted risk of relapse. The predictive value of severity of phobic-anxiety symptoms with respect to risk of relapse was equivalent regardless of treatment assignment (fluoxetine or placebo).
Conclusion: There may be a specific pattern of residual symptoms associated with depressive relapse during antidepressant continuation/maintenance, which is unrelated to treatment assignment. Future studies are needed to replicate and further explore the relationship between residual symptoms and risk of relapse in MDD.

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» NR3-064

CHANGES IN REGIONAL CEREBRAL BLOOD FLOW AND CLINICAL EFFECTS IN PATIENTS WITH PANIC DISORDER TREATED BY GROUP COGNITIVE BEHAVIORAL THERAPY

Jung-Ah Min, MD, Eun-Jin Jahng, MD, Ho-Jun Seo, MD, Young-Eun Jung, MD,Won-Myong Bahk, MD, PhD, Tae-Youn Jun, MD, PhD, Jeong-Ho Chae, MD, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to have some evidence about neurobiological basis of cognitive-behavioral therapy in panic disorder. And further understanding about pathophysiological mechanism of panic disorder is also able to get.

SUMMARY:

It is hypothesized that patients with panic disorder have a sensitive central nervous system fear mechanism. In these hypotheses, while medications may reduce panic attacks by decreasing the activity of the amygdala, cognitive behavior therapy (CBT) may reduce phobic avoidance by deconditioning contextual fear learned at the level of the hippocampus and decrease cognitive misattributions by strengthening the ability of the medial prefrontal cortex to inhibit the amygdala. The present study was performed to examine the change of brain function associated with anxiety alleviation by successful completion of CBT in patients with panic disorder.
Nineteen subjects with panic disorder were enrolled into the present study, but finally fourteen subjects underwent both brain SPECT evaluations before and after CBT. The CBT was given in a manual-guided group format with 8-12 patients, with 2 hours weekly sessions for 3 months. The CBT protocol was consisted of several components, which were psychoeducation, breathing retraining and muscle relaxation training, cognitive restructuring, interoceptive and in vivo exposure. In this study, we compared regional cerebral blood flow (rCBF) with Tc-99m-ECD SPECT before and after completion of CBT and also inspected the correlation with some clinical measures applied to assess the change of symptoms during the CBT.
When compared the rCBF of subjects between before and after CBT, significant increase of rCBF were detected in left postcentral gyrus (Brodmann's area 43), left precentral gyrus (BA 4) and inferior frontal gyrus (BA 9, BA 47) and significant decrease was detected in left pons and subgyral white matter in left limbic lobe. In present study, we could find changes of rCBF of various regions associated with anxiety alleviation by successful completion of CBT in patients with panic disorder.

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» NR3-065

CHANGES IN NEUROIMAGING EVOKED BY MASKED TRAUMATIC STIMULI IN POSTTRAUMATIC STRESS DISORDER: A FUNCTIONAL MRI STUDY

Jung-Ah Min, MD, Eun-Jin Jahng, MD, Young-Eun Jung, MD, Ho-Jun Seo, MD, Won-Myong Bahk, MD, PhD, Tae-Youn Jun, MD, PhD, Jeong-Ho Chae, MD, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to get a preliminary data about dysfunctional areas of Posttraumatic stress disorder (PTSD). And Hopefuly, these data can be applied to early diagnosis of PTSD and to therapeutic modalities such as site-specific neuromodulation using repetitive transcranial magnetic stimulation.

SUMMARY:

The purpose of our study is to detect dysfunctional areas to post-traumatic stress disorder (PTSD), especially related to the major symptoms of marked fear associated with traumatic experiences. The result will provide the preliminary data for investigation of the pathology of PTSD, the establishment of objective parameter of early diagnosis and the recommendation of specific, early intervention.
Participants are composed of eight patients with PTSD and nine subjects of control. Masked images were presented for a very short period, which was below the cognition threshold, and measurements were performed by functional MR employing the method visual stimulation (Hideshi Sakamoto et. al). We analyzed differences in brain activation between the PSTD and control groups. In control group, activation associated with the masked stimuli was observed in the right inferior frontal gyrus and the left cerebellum. In the PTSD group, significant activation was not observed in these areas, but significant deactivation was observed in the right ventromedial prefrontal cortex (vmPFC) and the right anterior cingulated gyrus (ACC). In analyzing the differences in activation between the PTSD and control groups, the PTSD group also showed marked deactivation in the right vmPFC and the right ACC.
In PTSD, ACC with adjacent medial and ventral frontal cortical areas show to play a critical role in extinction of learned associations to aversive stimuli, therefore hyper-reactivity in PTSD patients is accentuated by deactivated and insufficient inhibition by these areas. We suggest that these findings can be applied therapeutically, such as site-specific neuromodulation using repetitive transcranial magnetic stimulation (rTMS), and also diagnostically in clinical situations.

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» NR3-066

A NEUROCOGNITIVE ASSESSMENT OF MOTOR INHIBITION AND COGNITIVE FLEXIBILITY IN PATHOLOGICAL SKIN PICKING

Brian Odlaug B.A., Samuel R. Chamberlain, M.D., Ph.D., Jon E. Grant, M.D., J.D., M.P.H.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able

to, i) talk about the cognitive differences between patients with pathological skin picking versus healthy controls; and ii) discuss how these results may contribute to treatment approaches used for pathological skin picking.

SUMMARY:
Introduction: Individuals with pathological skin picking (PSP) often report significant difficulty in resisting the urges and drive to engage in picking behavior. Studies have shown significant inhibitory deficiencies (impulsiveness) in the motor responses of subjects with other obsessive-compulsive spectrum disorders such as trichotillomania. This study sought to assess cognitive flexibility and motor inhibitory control in a sample of individuals with PSP.
Methods: A total of 20 subjects with PSP (mean age 33.7 years; 85% female) and 20 healthy controls (mean age 31.4 years; 80% female) underwent a single session of cognitive testing. Motor inhibition was measured using the Stop-Signal Task, and cognitive flexibility was measured using the Intradimensional/Extradimensional Shift Task. Subjects were matched for age, gender, and education. A sub-group analysis was also conducted on clinical characteristic data (e.g., age of onset, disease severity, psychiatric comorbidity) to assess cognitive differences within the PSP sample.
Results: PSP was associated with significantly worse motor inhibitory control (p=.037) while no differences were found in cognitive flexibility compared to healthy controls. No clinical characteristics of PSP were associated with response on the Stop-Signal Task.
Discussion: The finding of impaired inhibition of motor responses but not cognitive flexibility is consistent with studies of trichotillomania and differs from studies of obsessive compulsive disorder. These findings should allow for proper characterization of PSP and assist in developing effective treatment options.

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» NR3-067

DOES COGNITIVE PERFORMANCE CORRELATE WITH SUBJECT AND INJURY CHARACTERISTICS IN SURVIVORS OF COMBAT-RELATED TRAUMATIC BRAIN INJURY: A PILOT STUDY

Brian Writer D.O., Jason Schillerstrom, M.D.,Heather Regwan, D.O., Brent Harlan, M.D., Jackie L. Reeves, MSN, RN, Melissa Keough, M.Ed., Brian Waters, M.D., Manuel Nunez, M.D., Jan Kennedy, Ph.D, Mark Shapiro PA-C

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to describe why traumatic brain injury (TBI) is important. Describe how combat-related TBI differs from civilian TBI. State the common cognitive domains impacted after TBI. Describe why cognitive impairment is important. State which cognitive domain correlates with demographics in combat-related TBI and describe why that's important to the U.S. military.

SUMMARY:
Background: Traumatic Brain Injury (TBI), the signature wound of the Iraq War, is characterized by cognitive impairment in multiple domains.
Objective: Determine the relationship between executive function, memory, visuospatial ability, and global cognition with demographic and injury characteristics in combat-related TBI survivors. We hypothesized that each cognitive domain would correlate with age and time since injury and that blast TBI survivors would have worse cognitive performance than those suffering from non-blast TBI.
Methods: In a cross sectional design, n=45 adult ambulatory military active duty and veteran subjects with combat-related mild to severe TBI during Operation Iraqi Freedom (OIF) were recruited during routine outpatient clinical care for their TBI. Cognition was assessed using the Executive Interview, Executive Clock Drawing Task (CLOX1 and 2), Memory Impairment Screen (MIS), and Mini-Mental State Exam. Pearson correlation coefficients were calculated for each domain with age and time since injury. Mean cognitive performance was compared between those suffering blast and non-blast TBI.
Results: n=12 were consented. Mean sample age was 35 years (SD 9.3) and mean time since injury was 27.4 months (SD 15.5). All subjects were male OIF veterans (7 active duty) with closed TBI. 92% suffered a mild TBI. Only memory performance correlated with age (r=-0.59, p=0.04) with older subjects having worse performance. There was no correlation between time since injury and cognitive performance. Subjects sustaining a non-blast TBI had worse mean performance on the MIS [4.75 (SD 0.96) versus 6.75 (SD 1.39)] compared to those surviving a blast TBI (t=-2.92, p=0.02).
Conclusions: Memory is more affected by age and type of TBI sustained than other cognitive domains with older patients and those surviving non-blast TBI demonstrating worse memory.

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» NR3-068

CLINICAL AND SOCIODEMOGRAPHIC PROFILE OF PERSONALITY DISORDERS IN AN ACUTE PSYCHIATRIC UNIT

Eva Román Mazuecos, M.D., David López Gómez, M.D., Jesús J. Marín Lozano, M.D., Ainoa Muñoz San José, M.D., Belén Bardón Rivera, M.D., Mª Fe Bravo Ortiz, M.D. Ph.D

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize which are the most common clinical (including psychiatric comorbidities) and sociodemographic aspects of patients who suffer of Personality Disorders.

SUMMARY:
Objective: The aim of this study is to find out which characteristics define the patients diagnosed of a Personality Disorder that were admitted to an Acute Psychiatric Unit. Methods: The sample was comprised by 466 patients with Personality Disorders diagnosis admitted to an Acute Psychiatric Unit at a General Hospital in Madrid, Spain, between February 2006 and October 2008. The data of this descriptive retrospective case-series study were analyzed with SPSS-PC. Eleven variables have been analyzed: gender, age, nationality, marital status, diagnosis in axes I and II (according to the APA Diagnostic Classification DSM-IV TR), type of admission, reason for admission, treatment, prior existence of psychiatric disorder, alcohol or substance abuse and previous history of suicide attempts. Results: There was a higher proportion of women (60.9%) than men (39.1%). Mean age was 38 years, with a majority of Spanish nationality (90.8%). Most patients were single (61.2%). Regarding specific Personality Disorders, the great majority was diagnosed of Personality Disorder NOS (62.2%), Borderline Personality Disorder (20.6%) came second, and paranoid (5.8%) was third. Environmental or psychosocial problems were detected in 68% patients. Nine of ten patients had prior psychiatric history, highlighting Mood Disorders (44.2%), Alcohol or Substance Abuse (39.3%) and history of suicide attempts (22.5%). Regarding psychotropic drugs prescription, anxiolytics showed highest prevalence (79.4%), followed by antidepressants (71%)

and antipsychotics (65%). These findings could be related to Mood Disorder (33.3%) and Substances Abuse Disorder (17.6%) comorbidity. Conclusion: Personality disorder is a common diagnosis in Psychiatric Units. Sociodemographic and clinical data, including assessment of comorbidity, may be very useful in the management of this population in psychiatric units. More investigations may help to define the profile of these patients with the aim of improving their care.

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» NR3-069

A CASE STUDY: LITHIUM TOXICITY AND ACE INHIBITORS

Patricia Bauza M.D., Gabrielle Melin, M.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize symptoms associated with lithium toxcicity and be aware of the possible interaction between lithium and angiotensin-converting enzyme inhibitors. In addition, participants should be mindful that even patients who have been maintained for many years on the combination of these two medications are at risk for significant lithium toxicity if dose of ACE inhibitor is increased.

SUMMARY:

Purpose: Due to its narrow therapeutic index even small increments in lithium levels may lead to toxicity. Drugs that affect renal function may have clinically important effects on lithium levels. Methodology: RT is a 60 year old male who had been maintained on lithium 600 mg BID for 10 plus years with good control of his manic symptoms. His lithium levels consistently ranged between 0.5 mmol/L and 0.7 mmol/L. Treatment with lisinopril had been initiated at 10 mg 3 years ago with no significant change in his lithium level. In July of 2007, his lisinopril dose was increased from 10 mg to 20 mg for better control of blood pressure. Six months later his lithium level was 1.4 mmol/L with no symptoms consistent with lithium toxicity. In April of 2008, he was brought to the ER after a fall that occurred secondary to lightheadedness. The fall did not result in any significant injuries but he was noted to have confusion and bilateral coarse tremor. His wife reported a 4 week history of fatigue and dizziness. A lithium level drawn in the ER was 3.0 mmol/L. He was admitted to the ICU and received IV hydration and supportive care. Serial lithium levels were drawn until, 30 hours after admission, he was discharged from the hospital with a lithium level of 1.1 mmol/L. While in the hospital, he denied any history of diarrhea, vomiting, decreased fluid intake, or changes in diet. Lithium was reinitiated at 300 mg daily as no other medication had been efficacious for his bipolar disorder. A blood level drawn 1 week later was 0.6 mmol/L and he was maintained on this dose for 2 months. Ultimately dose was increased to 300 mg BID secondary to the development of manic symptoms. His level has been stable at 0.7 mmol/L as have his manic symptoms for 5 months. Conclusion: Even small changes in dosage of an ACE inhibitor can cause up to a 4-fold increase in lithium levels. Frequent monitoring of lithium levels is recommended in patients taking these agents concurrently.

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» NR3-070

THE EFFECT OF ANTIPSYCHOTIC POLIPHARMACY WITH HALOPERIDOL ON QTC INTERVAL IN ACUTE PSYCHIATRIC SETTING

Salvatore Calò M.D.,Gianfranco Amodio, MD.,Guido Di Sciascio, Psy.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the potential differences between antipsychotics and their associations in affecting QTc interval, in order to clarify which drug and which association can be considered safe especially in acute setting.

SUMMARY:

Objective: The association of different antipsychotics, a common practice especially in acute psychiatric setting, has not been explored in detail with regard to its effect on the QTc. The aim of this study is to investigate whether the polytherapy and the association with haloperidol can increase the risk of QTc prolongation regardless other socio-demographic and clinical variables. Methods: We assessed 94 schizophrenic patients, according to DSM-IV criteria, admitted to our acute psychiatric Unit. The ECG, the serum electrolytes, the fasting glucose and the thyroid hormones levels were obtained for all patients during the first day of admission. The patients enrolled in this study, after screening phase (N=52), were divided into 2 groups: monotherapy group (patients treated with one antipsychotic, N=29) and polytherapy group (group of patients treated with more than one antipsychotic, N=23). The daily chlorpromazine equivalent was calculated for the two groups and the QTc duration was assessed in DII leads and calculated with the Bazett's formula by a cardiologist. Statistical analysis will be carried out with the Statistica software using parametric and non-parametric test. Results: The QTc interval in the polipharmacy group resulted significantly longer (p=.00001) than in the monotherapy group (QTc mean±SD, 361.7±23.2 ms vs 329.6 ± 23 ms). The daily chlorpromazine equivalent dose was significantly greater in the polytherapy group than in the monotherapy groups (dose mean±SD, 569.5±310.5 mg/die vs 362.9±306.5 mg/die) but we didn't find a significant correlation between QTc and the daily chlorpromazine equivalents. The patients who were treated with this drug had a QTc interval significantly (p=.0001) longer than patients treated with other antipsychotics (362 ± 23.3 ms vs 332.5 ± 24.7 ms). Conclusions: Our finding calls for caution when using haloperidol in acute setting especially in association with other antipsychotics.

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» NR3-071

LITHIUM-INDUCED NEUROLEPTIC MALIGNANT SYNDROME WITHOUT ANTIPSYCOTICS: A CASE REPORT

AYA HOJO M.D., TAKAFUMI SHIMADA, M.D., KOJI KASANUKI, M.D., HOZUMI KYONO, M.D., TAKAO NISHIMURA, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to remind that lithium may cause neuroleptic malignant syndrome independent of other antipsychotics.

SUMMARY:

OBJECTIVE: To report a case of lithium-induced neuroleptic

malignant syndrome (NMS). METHOD: A case report and the theoretical and clinical deliberations are described. CASE SUMMARY: A 42-year old Japanese male with a history of schizoaffective disorder was admitted to our hospital due to high fever and severe muscle rigidity. He had been prescribed lithium 800mg/day and flunitrazepam 1mg/day, but he had been taking lithium much more than prescribed at his disposal. He had stopped taking lithium 3 days before admission because of muscle rigidity. He had not been taking any antipsychotics at least for a year before admission because he was stable without psychotic symptoms for five years. When he was admitted, he had a high fever of 103 degrees F (39.2 degrees C), hypertension (200/118 mmHg), tachycardia (110 /min), akinetic mutism, and muscle rigidity. Laboratory tests showed an elevation of creatine phosphokinase (14,249 IU/L) and leukocyte levels (12,100*10^9 /L). His serum lithium level was 0.42 mEq/L. A cerebrospinal fluid examination and a brain computerized tomography scan showed no remarkable change. NMS was diagnosed and he received dantrolene treatment. His clinical response was good. On the 4th day of admission, his fever was back to normal, and muscle rigidity was resolved. On the 18th day, his serum creatine phosphokinase level returned to normal range (106 IU/L). He was discharged in a stable condition on the 29th day. DISCUSSION: This case is notable in that NMS occurred because of lithium alone without antipsychotics. Although his serum lithium level was lower than the therapeutic range (0.42 mEq/L) when admitted, he had not been taking lithium 3 days prior to admission. This could indicate that his serum lithium level was in the toxic range prior to admission, and his presentation of NMS was caused by lithium intoxication. CONCLUSION: Clinicians should be aware that lithium may cause NMS independent of antipsychotics.

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» NR3-072

PSYCHOPHARMACOLOGY INTERACTIVE TRAINING ALGORITHM

Nicole Hraniotis M.D., Anthony Tobia, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to appreciate the complexity of drug interactions, increase their learning and understanding, and retain the knowledge of the P450 system and drug interactions.

SUMMARY:

The purpose of this study is to develop an effective method of teaching the cytochrome P450 system and drug interactions to enhance learning and retention among psychiatric residents. A psychopharmacology program was developed to promote understanding, retention, and future teaching of the material. Isoenzymes 1A2, 2A6, 3A4, 3A5-7, 2B6, 2C8, 2C9, 2C18, 2C19, 2D6, 2E1 were presented using analogies and visual mnemonics to enhance recall and retention. Eleven residents participated in the study and completed baseline quizzes and questionnaires. The five-item quiz was also administered after presentation of the teaching material and at the completion of the study. A likert scale was used in the pre-questionnaire to explore the views of the residents regarding learning, knowledge, and retention. The presentation was then placed on the internet (psychiatric residents' forum). At the end of the study, residents will complete a quiz and post-questionnaire, reflecting the extent to which the residents used the program. At baseline, both groups exhibited low scores overall, each obtaining an average of one question correct. First- and second-year residents scored higher on the follow-up quiz (3.6 % and 3.2 % of the questions correct, respectively). Preliminary end-point results demonstrate that the residents scored intermediary between the scores received before and after the material was presented. The psychopharmacology program is an interactive method used to promote recall and retention of this challenging topic. Placing the material in this format on the internet forum allows the psychiatric residents to have the material available to them in various settings of their training to promote reinforcement. The preferred learning styles of the residents as well as the effectiveness of the psychopharmacology program as a future learning style was also assessed.

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» NR3-073

THE LONG TERM EFFECTIVENESS OF QUETIAPINE PLUS LAMOTRIGINE THERAPY IN BIPOLAR PATIENTS

Kaja Johnson, Meredith Childers, M.A., Shefali Srivastava, M.D., John O. Brooks, M.D., Jennifer C. Hoblyn, M.D., Terence A. Ketter, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to evaluate the efficacy and tolerability of long-term quetiapine + lamotrigine therapy for bipolar disorder.

SUMMARY:

Objective: To investigate effectiveness of long-term quetiapine (QTP) plus lamotrigine (LTG) therapy in bipolar disorder (BD).
Methods: This was a retrospective chart review of outpatients naturalistically prescribed QTP and LTG combination treatment (QTP+LTG) who achieved at least 8 consecutive weeks of euthymia. Patients were assessed with the Systematic Treatment Program for Bipolar Disorder (STEP-BD) Affective Disorders Evaluation and followed with the STEP-BD Clinical Monitoring Form.
Results: Thirty-five patients (11 BD I, 21 BD II, 3 BD NOS; mean ± SD age 40.3±12.1 years; 77% female) had 37 QTP+LTG trials. LTG therapy preceded addition of QTP in 28/37 (75%) trials. In addition to QTP+LTG, patients were taking a mean of 2.2±1.5 other psychotropic and 1.8±1.6 non-psychotropic prescription medications. The mean duration of QTP+LTG therapy was 27±21months. Mean final doses of QTP and LTG were 177±257 and 303±117 mg/day, respectively. Most patients (21/37, 57%) continued QTP+LTG. However, in 16/37 (43%) trials, QTP+LTG was discontinued, due to physical side effects (n = 7), desire to reduce medication burden (n = 5), and inefficacy (n = 4). Subsequent psychotropic medication was added in most (21/37, 57%) trials, after a mean of 8.0±9.8 months, and included anxiolytics/hypnotics (n = 10), antipsychotics (n = 6), mood stabilizers (n = 4), and antidepressants (n = 1). No serious adverse events were reported and there was no significant change in mean weight. Syndromal depressive (n = 11), elevated (n = 4), or mixed (n = 1) episodes occurred in 43% of trials, after a mean of 6.3±7.6 months. However, GAF scores did not differ significantly from baseline (68±7) to last evaluation (64±8).
Conclusion: QTP+LTG therapy may be an effective bipolar disorder maintenance treatment, with most patients continuing therapy, but commonly receiving subsequent additional psychotropic medications. This research was supported by the Investigator-Sponsored Study Program of AstraZeneca.

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» NR3-074

AUDITORY EVENT-RELATED POTENTIAL P300 IN BIOLOGICAL EQUIVALENCY STUDY:A HYPNOTIC ZOLPIDEM

Namkwon Kim, E-Jin Park, MD., Chin-Yang Kang, PhD.,and Yang-Whan Jeon, MD, PhD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that bio-equivalent hypnotic drug could have similar effect on cognitive function to zolpidem.

SUMMARY:

Objective:This study was designed to evaluate the cognitive effect of a new hypnotic drug, biologically equivalent for zolpidem with using auditory P300.
Methods:The auditory oddball paradigm was employed for university students (N=14). All subjects were double-blind randomized and assigned for two groups, who took zolpidem (N=7) or a new bio-equivalent drug (N=7). The stimuli were composed of target (20%, 2,000 Hz, 75 dB) and standard (80%, 1,000 Hz, 75 dB) tones, with 2 s inter-stimulus interval, 50 ms duration, and 10 ms rise/fall time. For all subjects, P300 was employed when the elapsed time after taking drugs was matched between the groups.
Results:There were no differences in the reaction time and the accuracy between two groups. P300 amplitude and latency in subjects taking a bio-equivalent drug were shown in similar pattern to those in subjects taking zolpidem across all electrodes.
Conclusion:These results suggested that the bio-equivalent hypnotic drug could have similar effect on cognitive function to zolpidem.

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» NR3-075

DOPAMINE PARTIAL AGONIST EFFECTS ON THE CHANGES IN PSYCHOTIC AND MOTOR SYMPTOMS IN PARKINSON'S PATIENTS WITH PSYCHOTIC SYMPTOMS

Sehee Kim M.D., Han Doug Hyun, MD, Ph.D, NA Churl, MD, Ph.D, Min Kyung Joon, MD, Ph.D, Son In Ki, MD, Ph.D, Shin Ho Cheol MD, Kim Tae Ho, MD, Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify aripiprazole, dopamine partial agonist has some benefit for the treatment of psychotic symptoms of Parkinsonian patients who developed psychotic symptoms after taking levodopa.

SUMMARY:

Objective : About 5~8% of Parkinson's patients(PKP) with dopamine treatment were thought to have psychotic symptoms. Low dose(5mg) of aripiprazole, the human dopamine D2 receptor partial agonist was reported to improve the psychotic symptoms in PKP. We compared the effect of aripiprazole, risperidone and quetiapine on the change of psychotic and motor symptoms during 4 weeks in PKP with psychotic symptoms after levodopa treatment.
Methods : Of 60 PKP with psychotic symptoms after taking levodopa, 19 patients took risperidone, 21 patients took quetiapine and 20 patients took aripiprazole. Before starting medications and after 4 weeks of treatment, psychotic symptoms and motor symptoms were assessed with Scale for the Assessment of Positive Symptoms(SAPS), Scale for the Assessment of Negative Symptoms(SANS) and motor part of Unified Parkinson's Disease Rating Scale(UPDRS).
Results : During 4 weeks antipsychotic treatment period, there was significant change in SAPS score between 3 groups; risperidone and aripiprazole showed better improvement in positive symptoms scale than quetiapine, but there was no difference between risperidone and aripiprazole. There was no significant difference in negative symptoms between 3groups. In UPDRS, quetiapine group showed less aggravation in motor symptoms than the risperidone and the aripiprazole group. The aripiprazole group showed less aggravation in motor symptom than risperidone group.
Conclusion : Comparing the effectiveness of 3 antipsychotics on the psychotic and motor symptoms in PKP with psychotic symptoms after taking levodopa, aripiprazole showed greater improvement in positive symptoms than quetiapine and similar effect with risperidone. Aripiprazole also showed greater improvement in motor symptoms than risperidone but lesser than quetiapine. Thus, aripiprazole is considered to have some benefit for the treatment of psychotic symptoms of Parkinsonian patients with psychotic symptoms after taking levodopa.

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» NR3-076

CLINICAL OUTCOMES OF SWITCHING STRATEGIES FROM PREVIOUS ANTIPSYCHOTICS TO ARIPIPRAZOLE: 1-YEAR, NATURALISTIC STUDY

Won-hyoung Kim M.D., Tae-Yeon Seo, MD., Won-Hyoung Kim, MD., Min-Hee Kang, MD,Ph.D., Jeong-Seop Lee, MD,Ph.D., Jae Nam Bae, MD, Ph.D., Chul-Eung Kim, MD,Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to decide more effective strategies of the switch to aripiprazole

SUMMARY:

Objectives: This study was aimed to investigate effective strategies of the switch to aripiprazole by analyzing clinical courses.
Methods: Patients were recruited from inpatient and outpatient of Inha hospital from March 2005 to February 2007. They were confirmed DSM-IV diagnosis of schizophrenia had been treated with atypical antipsychotics, then switched to aripiprazole. We classified patients in three switching strategies (cross tapering, abrupt switch, tapering switch) and followed up for 1 year in switching period of time.
Results: Total 48 patients(cross tapering, N=20; abrupt switches, N=23; tapering switches, N=5) were recruited, and their average age was 36.25 ± 8.58 years old. The previous antipsychotics were risperidone, olazapine, amisulpride, quetiapine, and ziprasidone. The reasons of the switch were weight gaining (26.1 %), hyperprolactinemia (23.9%), the lack of efficacy(15.2%), and oversedation (13.0%). 50% of cross tapering patients, 30.4% of the abrupt switch patients, and 20% of tapering switch patients were treated as aripiprazole monotherapy. In addition, 25% of cross tapering patients, 43.5% of the abrupt switch patients, and 80% of tapering switch patients switched to different antipsychotics. The cross tapering group had higher ratio of aripiprazole retention rate than abrupt switch group. There was, however, no statistical significance (p= 0.351). An average aripiprazole retention duration was cross tapering 10.75 ± 3.29 months, abrupt switch 10.39 ± 3.29 months, tapering switch 10.00 ± 4.47 months. Cross tapering showed a long retention period, yet no statistical significant differ-

ence (p= 0.653) were found.
Conclusion: In this study, all three switching strategies showed tolerable clinical outcomes after the switch to aripiprazole. The aripiprazole retention rate and duration of the cross tapering had higher outcomes compare to the abrupt switches. Nevertheless, this result had no statistical significance.

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» NR3-077

RELATIONSHIPS OF MENTAL DISORDERS WITH OBESITY IN THE KOREAN ADULT POPULATION

Won-hyoung Kim M.D., Young-kyung Sunwoo, MD., Jae-Nam Bae, MD, Ph.D.,Sung Man Chang, MD, Ph.D., Hong Jin Jeon, MD, PhD., Jin-Yeong Kim, MD, Ph.D., Jun-Young Lee, MD, Ph.D., Jin-Pyo Hong, MD, Ph.D., Maeng Je Cho, MD, Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to use this paper as the fundamental data for establishing mental health policies for underweight or obese adults in community.

SUMMARY:

Objectives: The purpose of this study is to examine the associations among obesity, mental disorders(ex. depressive disorder, anxiety disorder, and alcohol use disorder), and demographic variables(ex. sex, age, marital status, educations, and smoking).
Methods: A nationally representative face-to-face household survey was conducted in twelve different regions of Korea form June 2006 to August 2007. There were 6,510 subjects, aged 18 to 64, and the response rate was 81.7 %. The diagnoses of depressive disorder, anxiety disorder, and alcohol use disorder were made using the Korean version of the Composite International Diagnostic Interview(K-CIDI). Height and weight were self-reported, while waist circumference was measured using a tape measure.
Results: Obesity(defined as BMI=25) was associated with significant increase in lifetime diagnosis of panic disorder or agoraphobia(OR 2.58) and alcohol use disorder(OR 1.29). Similarly, the lifetime diagnosis of panic disorder or agoraphobia(OR 3.08) and alcohol use disorder(OR 1.25) was associated with significantly increased levels of central obesity. Moreover, the lifetime diagnosis of obsessive-compulsive disorder(OR 3.36) and major depressive disorder(OR 2.12) was significantly associated with underweight. After adjusting for sex and age, the lifetime diagnosis of depressive disorder was significantly increased in the underweight group(OR 1.68). Furthermore, risk factors for depressive disorder included any age except for the 40s, high education level, married or cohabiting, and unmarried.
Conclusion: Lifetime diagnosis of panic disorder or agoraphobia(OR 2.58) and alcohol use disorder(OR 1.29) showed significant increases in the obesity(defined as BMI=25) and central obesity. After adjusting for sex and age, the lifetime diagnosis of depressive disorder was significantly increased in the underweight group, and it was influenced by the factors of age, education level, and marital status.

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» NR3-078

CHEMOKINE (C-C MOTIF) RECEPTOR 3 (CCR3) GENE HAPLOTYPE IS ASSOCIATED WITH SCHIZOPHRENIA IN KOREAN POPULATION

Woojae Kim M.D., Jiyoung Song, Ph.D.,MD., Ahrang Cho, Ph.D.,MD., Jaejin Lee, MD., Sukang Kim, Ph.D.,MD., Jongwoo Kim, Ph.D.,MD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to CCR3 may be contributing to the susceptibility of schizophrenia in Korean population.

SUMMARY:

Objectives : Several lines of evidence have revealed that polymorphism of chemokines is associated with schizophrenia However, the genetic association between chemokine (C-C motif) receptor 3 (CCR3) and the susceptibility of schizophrenia is not yet known. Aim of the present study was determined whether single nucleotide polymorphisms (SNPs) of CCR3 gene associate with the susceptibility of schizophrenia in Korean population.
Methods : A total of 218 schizophrenic patients and 377 control subjects were recruited. Five SNPs were selected in the CCR3 gene region (intron 1; rs9853223, rs6441948, rs13326331, and rs7652290, intron 2; rs1491962) and genotyped by direct sequencing. SNPStats, Haploview, HapAnalyzer, SNPAnalyzer, and Helixtree programs were used for the analysis of genetic data. Genotype frequencies were compared between patients with schizophrenia and controls using logistic regression models adjusting age and sex as co-variables.
Results : In logistic regression models, we did not find any significant association between CCR3 SNPs and schizophrenia. However, we found two linkage disequilibrium (LD) blocks by the Gabriel method (block 1 comprised rs9853223, rs6441948, and rs13326331; block 2 consisted of rs7652290 and rs1491962). The haplotype (GAC) in block 1 and haplotype (AC) in block 2 showed significant associations between schizophrenia and control groups (haplotype GAC, frequency = 0.153, chi square = 4.828, p = 0.028; haplotype AC, frequency= 0.151, chi square = 4.129, p = 0.042, respectively).
Conclusions : These results suggest that CCR3 may be contributing to the susceptibility of schizophrenia in Korean population.

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» NR3-079

CASE STUDY OF A LATE ONSET BUPROPION ER-INDUCED SEIZURE

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EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know Bupropion ER induced seizures in Korea

SUMMARY:

Introduction: To our knowledge there were only two case reports of a seizure case with bupropion ER. Despite of increasing use of the drug since the first approval of bupropion ER in 2007, this case report represents the first bupropion ER-induced seizure case in Korea which took place within 6-month-drug medication.
Case report: A 26-year-old female patient who is a college student was diagnosed as dysthymia. From April, 2008, she started to visit neuropsychiatry clinic and received bupropion SR for medication. In June, bupropion ER was increased to 300mg. Other than that

she received etizolam 0.75mg in the evening, to treat her insomnia. On July, her depressive symptom was remitted. On September, the patient had seizures at home twice. She was immediately driven to the hospital and came to the clinic. The patient had another generalized tonic clonic seizure during her examination. She was admitted in neuropsychiatry. EEG was checked after 1 and 3 hours of the third seizure. There was a spike in the left temporal area indicating partial seizure. After bupropion had been discontinued, no seizures occurred and she was discharged 3days later. She did not go on medication again and no signs of seizers were observed until now.
Discussion: This report is the first Korean published seizures induced by bupropion ER. The patient had been administrating bupropion ER (300mg) for a long term (more than 6 months). There are two reported cases of seizures caused by Bupropion ER, which both of them occurred right after an increased dose of bupropion ER. However in this case the patient had a seizure after 6 months from the increased dose (to 300mg) was given. Clinician should be attend to bupropion ER induced-seizure even though relating low case reports of bupropion ER compared with bupropion IR.

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» NR3-080

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

Yujin Lee M.D., Han-Yong Jung, M.D.,Ph.D., Soyoung Irene Lee, M.D., Ph.D., Shin Gyeom Kim, M.D., Eun Young Shin, M.D., Joonho Park, Ph.D., Hyunil Moon, M.D., Yeonjung Lee, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that quetiapine is as effective as haloperidol in the treatment of delirium and possibly more effective in specifically reducing behavioral disturbances and cognitive impairments.

SUMMARY:

Objectives: Haloperidol has been the medication of choice in most deliriums. But due to fewer side effects atypical antipsychotics are becoming the first line drugs in various neuropsychiatric conditions, and also increasing in delirium treatment. The purpose of this study was to compare the clinical efficacy of quetiapine with haloperidol in the treatment of delirium.
Method: Seventy-seven subjects completed the study receiving a flexible-dose regimen of quetiapine(n=40,mean dosage 95mg) or haloperidol(n=37,mean dosage 1.4mg). Memorial delirium assessment scale (MDAS) was administered as a specific tool to rate the severity of delirium and Neurobehavioral rating scale (NRS) to rate psychiatric and behavioral symptoms and Mini mental state examination Korean version(MMSE-K) to access cognitive status, specifically. The symptoms were checked at baseline, on day 3 and day 7 of treatment and compared between the two groups.
Results: In both quetiapine and haloperidol groups, MDAS and NRS scores improved significantly on day 3 and day 7 compared to baseline. But in the NRS scale, drug-time interaction approached significance(p=0.074) whereas MDAS scale showed no significance. The interaction in the NRS scale is likely caused by the difference in scores between the groups on day 3 with the quetiapine group having a trend toward significantly higher(worse) score(p=0.07) than haloperidol, and not on day 7. In MMSE-K scores, compared to baseline, quetiapine group improved significantly on day 3 and day 7, whereas haloperidol group showed no improvement on neither day 3 nor day 7.
Conclusion: This study demonstrated that quetiapine is efficacious as haloperidol in the treatment of delirium. In particular, behavioral problems decreased faster with quetiapine than haloperidol and cognitive impairments improved with quetiapine and not haloperidol. Thus, it is possible that quetiapine can be used as a first-line treatment in delirium. Further prospective studies are warranted.

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» NR3-081

OPISTHOTONOS WITH LOW DOSES OF QUETIAPINE

SUSANA MARTINEZ, Jasna Raventós Simic, Psychiatry Resident.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the importance of tailored psychopharmacology in the prescription act. Our aim is to bring in new evidence of the extrapyramidal symptoms that can be observed in patients treated with quetipiane. We will try, through the analysis of an individual clinical case, to identify risk factors of acute dystonic reactions. We will focus on the role of alcohol use, sleep deprivation and familial history of dystonia.

SUMMARY:

There is enough scientific evidence to affirm that atypical antipsycotics carry minimal risk of acute dystonic reactions. Amongst all second-generation antipsychotics quetiapine is known to have a particularly benign profile of secondary extrapyramidal symptoms, this is due to its effect on the 5HT2A receptors and its low affinity to D2 receptors. Quetiapine is often chosen as one of the first line treatment for psychotic disorders in the elderly, in patients with Parkinson disease or suffering from other illnesses with the basal ganglia involved in its pathogenesis. You can find described in medical literature few individual cases of extrapyramidal symptoms caused by quetiapine.
We describe a 21-year-old male patient who was taken to the emergency room complaining of movement of his head to the side and stiffness of the neck, he also presented and oculo-gyric crisis. This symptoms developed rapidly into a severe opisthotonos that needed treatment with high doses of biperiden and diazepam.He had taken 2 hours before the symptoms appeared 200mg of quetiapine, 100mg more than his usual treatment dose. The patient the day before suffered an alcohol intoxication and had been exposed to a sleep deprivation situation.
We have identified possible risk factors of dystonic reactions in this particular case and after analyzing scientific evidence we have concluded that is cardinal to systematically look for this risk factors in precise clinical histories of patients. There are evincible risk factors that must be considered when deciding the type and dose of and antipsychotic treatment prescribed to a patient.
Furthermore we reflect on need to analyze extrapyramidal risk factors in systematic and controlled studies and we support the position of introducing in clinical practice the results obtained in pharmacogenetic studies in order to prescribe taking in account individual vulnerabilities.

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NR3-082

SODIUM VALPROATE INDUCED HYPONATREMIA

Kajal Patel M.D., Anil Meesala,M.D., Joseph Stanilla,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to 1)Identify a new side effect of Sodium Valproate 2)Recognize the side effect of hyponatremia due to Sodium Valproate from laboratory studies, the dose range at which it occurs and it's management.

SUMMARY:

We report a case of hyponatremia secondary to sodium valproate possibly due to syndrome of inappropriate anti diuretic hormone (SIADH) like syndrome during a routine follow up of a 54 year old Caucasian male with Schizoaffective disorder. The patient was on 2000mg of sodium valproate and developed hyponatremia with a sodium level of 126MMOL/L. The initial baseline sodium before sodium valproate was started was normal (139MMOL/L).Upon stopping the sodium valproate, the sodium level returned to normal (137MMOL/L).After ruling out other causes of hyponatremia such as psychogenic polydipsia and hypothyroidism, it was concluded that the hyponatremia was due to administration of high doses of sodium valproate.This was further confirmed when patient returned and was admitted again at a later date and was found to be on Sodium Valproate and having hyponatremia which resolved again on stopping the sodium valproate.

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» NR3-083

VARENICLINE INDUCED ACUTE EXACERBATION OF SCHIZOAFFECTIVE DISORDER: A CASE REPORT AND REVIEW OF THE LITERATURE

Akshat Pujara B.A., Smitha Battula, M.D., Xiangyang Zhao, M.D., M.S., Toni Johnson, M.D., Lendita Haxhiu-Erhardt, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify psychiatric patients in whom varenicline treatment for smoking cessation should be approached with particular caution. Patients maintained on low dose medication regimens may be most vulnerable to mood and affective disruptions with varenicline use. Participants should understand the psychopharmacology of varenicline and the importance of considering alternative smoking cessation aids in psychiatric patients.

SUMMARY:

Introduction: Varenicline is a partial nicotinic agonist used for smoking cessation. Recent reports raise concerns about psychiatric side effects of the drug. We report the first case of varenicline induced acute exacerbation of schizoaffective disorder.
Case: A middle-aged woman with a 19 year history of schizoaffective disorder, bipolar subtype, presented with confusion, paranoia and unstable mood. Three weeks earlier, her outpatient psychiatrist noted she was euthymic with full affect on 30mg aripiprazole and 20mg fluoxetine daily, and prescribed varenicline for smoking cessation. After one day on 0.5mg varenicline, the patient was unable to complete tasks and performed bizarre behaviors such as stuffing shoes with newspaper. Varenicline was stopped. Confusion, disorganization and affective instability prevailed for 10 days. The patient was then brought to the ED. During her 6 week hospital stay, she had recurrent paranoid delusions with themes of sexuality, pregnancy and religion. The patient improved on clozapine 100mg qam and 200mg qhs, zolpidem 10mg qhs, divalproex 1000mg ER qhs and lithium.
Discussion: Varenicline achieved higher rates of smoking cessation than placebo in phase 2 and 3 clinical trials. The drug is a high affinity partial agonist of presynaptic alpha-4 beta-2 nicotinic acetylcholine receptors. Varenicline does not exhibit nicotine-like tachyphylaxis, resulting in prolonged release of dopamine and norepinephrine. These two neurotransmitters have been implicated in the pathophysiology of mania and psychosis. Varenicline induced acute mania in bipolar disorder and worsening of schizophrenic symptoms by the drug have been reported. Evins et al reported no exacerbation in 19 schizophrenic patients treated with varenicline. However, given the increasing number of adverse psychiatric events reported, it is important that clinicians carefully weigh risks and benefits and consider alternatives before prescribing varenicline for smoking cessation.

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» NR3-084

CHRONIC IMIPRAMINE DOWNREGULATES CYCLIC AMP SIGNALING IN RAT HIPPOCAMPUS

Gillian Reierson, Claudio Mastronardi, Ph.D., Julio Licinio, M.D., Ma-Li Wong, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand that there are gaps and controversies about the role of cyclic adenosine monophosphate (cAMP) signalling in the therapeutic effects of antidepressants that warrant further investigation.

SUMMARY:

Phosphodiesterases (PDEs) are enzymes that degrade cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) while adenylate cyclase (AC) and guanylyl cyclase (GC) enzymes synthesize these intracellular signaling cascade intermediates. The action of chronic antidepressants is hypothesized to occur via increased cAMP signaling; however, PDE type IV (PDE4) expression is paradoxically increased. We assayed PDE and cyclase gene expression and cAMP levels in rat hippocampus following chronic, 8-week treatment with the antidepressant imipramine. Using quantitative real-time PCR and enzyme immunoassay we found the following gene expression changes: increased PDE3B (+21%, $p<0.01$), PDE4B (+15%, $p<0.05$), and PDE5A (+25%, $p<0.01$); decreased AC1 (-15%, $p<0.01$); increased GCa2 (+15%, $p<0.05$) and GCß1 (+19%, $p<0.01$), and correspondingly decreased cAMP levels (-46%, $p<0.001$) levels in the hippocampus of rats chronically treated with imipramine (n=10/group). Surprisingly, our results suggest that in contrast with shorter-term studies hypothesizing increases in cAMP levels, longer-term imipramine administration may cause the opposite effect. Whether decreased hippocampal cAMP levels following chronic imipramine have an impact on antidepressant treatment response remains unclear. It is possible that not all antidepressants work by chronically increasing cAMP signaling. Our data is highly suggestive that addressing the gaps and controversies in the current hypothesis of the role of intracellular cAMP in MDD and antidepressant action may lead to improved strategies in the development of more efficacious treatments.

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brain derived neurotrophic factor: molecules that modulate our mood? JBiosci. 2006; 31: 423-434

» NR3-085

JUMPING TO CONCLUSIONS OR NON-COMPREHENSION? A RE-EXAMINATION OF THE "BEADS TASK"

Ryan Balzan, Paul H. Delfabbro, PhD, Cherrie Galletly, M.D., PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognise that the "Beads Task", traditionally used to test the assumed "jumping to conclusions" cognitive bias employed by people with schizophrenia, may not be eliciting the bias itself, but that the results may be driven by a degree of non-comprehension of the task instructions. The participant should recognise that commonly used psychological tests may be subject to a range of biases and confounds.

SUMMARY:

In recent years there has been increasing recognition of the role that "cognitive biases" (i.e., irregular thinking or decision-making strategies) may play in the development and/or maintenance of delusions in schizophrenia. The most commonly investigated of these cognitive biases has been the "jumping to conclusions" (JTC) bias, traditionally elicited using the "Beads Task". This task, first used by Huq, Garety and Hemsley (1988), requires participants to choose one of two containers from which a sequence of beads is being drawn. Results typically show people with schizophrenia tend to jump to a conclusion on the very first trial, while healthy controls take a more conservative approach. However, a recent computerised replication of the task by Moritz and Woodward (2005) suggested that it may be confounded by a lack of comprehension of the instructions. This experiment aimed to determine whether this finding was unique to computerised versions of the task or could be replicated in the more traditional version using actual beads.

The sample consisted of 72 undergraduate psychology students, randomly allocated to either the computerised task or the more traditional non-computerised task. Overall, 20% of the sample showed a JTC bias. Half the sample were identified as being delusion-prone (DP) as determined by the Peters et al Delusions Inventory, and 70% of these subjects showed the JTC bias. However, approximately 60% of the non-computerised and 35% of computerised sample displayed a lack of comprehension of the task (i.e., sequence of beads strongly suggested "Container A" yet "Container B" was selected). Moreover, 80% of these non-comprehending participants showed the JTC bias. This suggests that non-comprehension could equally be driving the JTC effect as much as delusion-proneness, particularly in the traditional non-computerised version of the task. This questions the validity of the Beads Task and the previous research that has used this methodology.

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» NR3-086

ANTIPSYCHOTIC COMBINATION IN PATIENTS DIAGNOSED WITH TREATMENT-RESISTANT SCHIZOPHRENIA RECEIVING CLOZAPINE

María Benítez Alonso M.D., J.J. De Frutos Guijarro M.D., A. A. García Rosales M.D., M. B. Bardón Rivera M.D., E. Román Mazuecos M.D., S. Kassem Vargas M.D, J.J. Marín Lozano M.D., M.F. Bravo Ortiz M.D. PhD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to have a broader knowledge of antipsychotic combination with Clozapine as well as understand better the rationale behind combination treatment.

SUMMARY:

Objective: The purpose of this study is to describe prescribing practices and augmenting strategies for inpatients diagnosed with treatment-resistant schizophrenia receiving Clozapine (C) in La Paz University Hospital acute psychiatric short-term hospitalization unit.

Methods: Data was collected from the discharge summaries of inpatients treated with clozapine when discharged, between 01/01/2003 and 12/1/2008 (n=62). Data collection included patient's sex, age, length of admission, doses of all medications given at discharge and DSM-IV diagnosis. Data was processed with SPSS 16 for Mac.

Results: 84.8% of the patients receiving C at discharge were diagnosed of Schizophrenia and other Psychoses. C was combined with another antipsychotic in 43.7% of the cases. There were no statistically significant differences, using t-test analysis, in terms of age and length of stay, when comparing the C monotherapy group and the antipsychotic combination one. Oral Haloperidol (mean dose=7.5 mg/day and s.d.=5) was the most frequently used combination drug, followed by Oral Aripiprazole (mean dose=11.6 mg/day and s.d. =5.7). As far as extended-release intramuscular formulations are concerned, Fluphenazine was the most frequently used neuroleptic.

Conclusions: Although, state-of-the-art psychopharmacology, recommends only to use one antipsychotic drug and avoid combinations. In our inpatient unit, combining another neuroleptic with clozapine clearly appears to be routine practice. Patients may need 6 months of clozapine treatment, before the clinician is accurately able to assess the full effect of the drug. Until the drug actually produces a full-blown effect, an additional neuroleptic is added. We must bear in mind that bed pressure may also explain this sort of clinical practice. Be that as it may, association of C and depot medication is striking. We may speculate that the subpopulation receiving this combination presents with serious compliance and lack of insight issues.

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» NR3-087

MEDICATION CONCORDANCE AMONGST PEOPLE WITH SCHIZOPHRENIA

Lucinda Clifford

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to gain a more holistic understanding of antipsychotic medication concordance amongst people with schizophrenia.

SUMMARY:

Objective: This qualitative, pilot study aimed to improve the understanding of antipsychotic medication non-concordance amongst people with schizophrenia. Method: Consumers of antipsychotic medication with schizophrenia were recruited from community mental health centres in Adelaide, Australia. One hour, semi-structured interviews with 5 outpatients (4 male, 1 female) were undertaken from July 2008 to September 2008 to address the absence of consumer perspectives in research related to non-concordance amongst people with schizophrenia and to

explore possible strategies to help improve concordance. Interview questions initially related to the consumers' experiences with medication, but were ultimately guided by participants' responses. Interviews were recorded, transcribed and analysed according to the principles of thematic analysis. Results: A major factor which contributes to concordance is past experiences with antipsychotic medications, particularly, the subjective experience of becoming non-concordant and noticing symptoms return or become more severe. The consequences of the return of symptoms were viewed as important predictors of future concordance (ie; hospitalisation). Interview data also consistently indicated that consumers perceive the health-care services for people with schizophrenia as inadequate (e.g. high turnover of staff compromises therapeutic relationship between health worker and consumer, psychosocial problems ignored by health workers, limited services available to people with schizophrenia). Conclusion: Consumers of antipsychotic medication with schizophrenia view episodes of non-concordance as important experiences which can be reflected upon to provide motivation to remain concordant. Furthermore, adaptation to services for people with schizophrenia may help to improve consumers' experiences in addition to health workers' understanding of concordance.

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» NR3-088

MAGNETIZATION TRANSFER IN INITIAL EPISODES OF SCHIZOPHRENIA

Rafael Fernandez Garcia-Andrade M.D., Javier Fernandez Aurrecoechea MD, Virginia Vidal Martinez MD, Kazuhiro Tajima Pozo MD, Diana Zambrano-Enrriquez Gandolfo MD, Ana Montes Montero MD, Helena Fernandez Garcimartin MD, Jose Luis Carrasco Perera MD, Marina Diaz Marsa MD.

EDUCATIONAL OBJECTIVES:

Conlclusions: The usefulness of the magnetization transfer, as a cuantitative method of the desmielinization degree and tisular destruction, has been demonstrated in recent studies that have stablished a better correlation between the degree of the neurologic dysfunction and brain atrophy, and the middle value of the magnetization transfer of the whole brain parenchyma, than the value obtained with the quantification of the lesional charge measured in T2 sequences.

SUMMARY:

Introduction: Magnetization transfer is a technique of magnetic resonance that generates a form of contrast different from the classique forms, based on the longitudinal (T1) and transveral (T2) relaxation rates. Its basic mechanism is based on the transfer of magnetization from water protons to protons that belongs to big macromolecules with low mobility as, for example, myelin. This techique, that can provide quantitative and highly reproducible data, offers an indirect map of the myelin concentration in the brain parenchyma. This techinque identifies, as well as proton spectroscopy, the presence of changes in the white substance with normal appearance, attributed to microscopic desmielinizated damages.

Objectives: This technique has been recently used for the study of brain anomalies in schizophrenia and other psychosis. The knowledge of the brain white substance in the beginning of schizophrenia might be very important.

Methodology: We have maked a bibliographic compilation of the latest studies with advanced neuroimaging techniques in schizophrenia, revising a total of 37 articles.

Results: in stabilized schizophrenic patients, reductions in the RTM in temporal areas were demonstrated. A study of initial episodes of schizophrenia, showed a reduction of the RTM in right and left frontotemporal connections, corresponding to reductions in grey substance. In a study that combines difussion tensor and TM in stabilized patients, reductions were found in the RTM in cortico-cortical and cortico-subcortical tracts, including corpus callosum, fornix, fronto-occipital fascicle, right internal capsule and cingulus, although the changes in the fractional anysotropia were more generalized. A recent study on 16 patients with a first psychotic episode, finds significant reductions in the white substance adyacent to the lateral ventricles in the right and left temporal regions, in the middle temporal gyrus and in the white substance around the right frontal gyrus.

Conclusions: the usefulness of the magnetization transfer, as a cuantitative method of the desmielinization degree and tisular destruction, has been demonstrated in recent studies that have stablished a better correlation between the degree of the neurologic dysfunction and brain atrophy, and the middle value of the magnetization transfer of the whole brain parenchyma, than the value obtained with the quantification of the lesional charge measured in T2 sequences. This indicates that the magnetiz

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» NR3-089

CTLA-4 AND CD28 GENE POLYMORPHISMS AND SUSCEPTIBILITY TO SCHIZOPHRENIA AND ITS SYMPTOMATOLOGY IN POLISH LOWER SILESIA POPULATION

Dorota Frydecka M.D., Prof. Andrzej Kiejna, M.D.Ph.D., Aleksander Beszlej, M.D., Ph.D., Monika Szewczuk-Boguslawska, M.D., Ph.D., Marcin Szechinski, M.D., Ph.D., Piotr Baranowski M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the role of the CTLA-4 and CD28 molecules in the regulation of immunological activity with respect to autoimmunological hypothesis of schizophrenia and recognize the significance of symptomatology assessment in genetic association studies in psychiatry.

SUMMARY:

Purpose: Several reports indicate a possible role of the activation of the immune system in the pathogenesis of schizophrenia. Two related receptors: CTLA-4 and CD28 mediate differentially regulation of T-cell activity. CD28 is a major co-stimulator whereas CTLA-4 performs negative regulatory functions. The polymorphisms of these genes have been implied as conferring the susceptibility to many autoimmunological and neoplastic disorders. This study was carried out to investigate the association of two polymorphisms of the CTLA-4 gene (A49G and T-319C) and a polymorphism of the CD28 gene (T17int3C) with schizophrenia in the Polish population.

Material and methods: 105 patients diagnosed with schizophrenia according to ICD-10 criteria and 380 controls were included in the study. The patients were evaluated for lifetime psychotic symp-

tomatology using the Operational Criteria for Psychotic Illness (OPCRIT) checklist.
Results: There was no significant difference in distribution of alleles or genotypes in the polymorphisms of CTLA-4 and CD28 genes in patients and controls. Consideration of possible stratification factors such as sex and age of onset did not significantly influence results. However, the analysis of symptomatology showed significant differences ($p<0,05$) in A49G variants of CTLA-4 gene between patients with no co-occurrence between psychotic and affective symptoms and patients with psychotic symptoms dominating in the clinical picture although also with the occasional occurrence of affective disturbances. Distribution of genotypes and allels between the first and second group of patients was as follow: A/A 30% vs 18%, A/G 46% vs 38%, GG 24% vs 9%, A 54% vs 72%, G 46% vs 28%.
Conclusion: Our data do not support the role of CTLA-4 –319 C/T, CTLA-4 +49 A/G, and CD28 +17 C/T gene polymorphisms in the predisposition to schizophrenia; however we have shown that affective factor in schizophrenia is associated with CTLA-4 +49 A/G variants.

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» NR3-090

TEMPORAL BEHAVIOR OF BIRTHS OF SCHIZOPHRENIC PATIENTS FROM 1976 TO 1987 IN SANTA MARTA-COLOMBIA: A STUDY ABOUT SEASONALITY OF SCHIZOPHRENIA ON TROPICS

Jairo González Díaz, Beatriz Caamaño, M.D., Beatriz Gómez, Jimmy Arévalo, Harold Garizábal

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the possibility of a seasonal effect on birth of schizophrenic patients in a tropical region

SUMMARY:

OBJECTIVE: It has been documented a winter-spring “excess” of births for schizophrenia, concluding a perinatal brain injury as the cause of this phenomenon. In Brazil and Puerto Rico, investigators found association between births of patients and rain and temperature levels 3,4 and 5 months earlier. The objective of this research was to describe the temporal behavior of births of schizophrenic patients who consulted by first time due to Schizophrenia between 2006 and 2007 at Hospital Universitario Fernando Troconis. METHOD: Design: Descriptive Retrospective; method: manual revision of clinical records; selection criteria: patients born between 1976 and 1987 in Santa Marta, Colombia, with ages between 20 and 30 years at diagnosis time and who met DSM-IV-TR diagnostic criteria for Schizophrenia; variables: birth date, sex, age at diagnosis and family history for psychiatric disorders. RESULTS: 1426 patients were attended from 2006 to 2007 on the department of Mental Health; 47 clinical records met the selection criteria: 6 were born on November and 6 on September, in contrast to January with only 1 birth; this phenomenon was similar for each sex separately. Instead, February showed the higher number of births in patients without familiar history of mental disorders, while September and November showed the highest number of births for those with familiar history of mental disorders. So, investigators observed a higher number of births on the second semester of the year, which was also observed for each sex separately, but they observed a predominance of the first semester over the second for patients without family history and a predominance of the second over the first for those with family history of mental disorders. CONCLUSIONS: Researchers found a higher rate of births in the second semester, in which precipitation levels are higher. They also observed that according to the family history patients are born on the first or second semester.

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» NR3-091

DOES INSIGHT INTO DIAGNOSIS AFFECT SATISFACTION WITH CARE IN SCHIZOPHRENIA SPECTRUM PATIENTS?

Sophia Haeri BA, Jenny Williams BA, Irina Kopeykina BA, Igor Galynker MD PhD, Lisa Cohen PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, participants should gain an understanding of the relationship between insight and treatment satisfaction in schizophrenia spectrum patients, and of the utility of assessing patients’ knowledge of their diagnosis as one measure of insight.

SUMMARY:

Background: Poor insight is a common quality in schizophrenia spectrum patients. Level of insight has been linked to treatment outcome, but not to satisfaction with care. Method: Knowledge of one’s diagnosis could constitute one measure of insight. In an attempt to gain understanding of the relationship of this indication of insight to satisfaction with care, the self-reported diagnosis of 104 psychiatric outpatients who had volunteered to participate in a research study of schizophrenia spectrum patients was compared with the DSM-IV diagnosis listed in their hospital chart. Participants’ satisfaction with care was assessed using a 5 point Likert scale. Results: 75 % of the 60 patients whose clinicians diagnosed them with schizophrenia and 42% of the 33 patients whose clinicians diagnosed them with schizoaffective disorder self-reported a different diagnosis than the one listed in their chart. Of the 22 patients whose self-reported diagnosis matched that given to them by their clinician, 100% responded that their treatment had helped “somewhat”, “a lot”, or “extremely”. Of those whose diagnosis differed from that given them by their clinician, only 88% found their treatment moderately helpful or more, and 12% found their treatment “not at all” or “a little” helpful. While this difference was not statistically significant, preliminary research indicates that knowledge of diagnosis may be associated with patient satisfaction with care in an outpatient community clinic. Conclusion: Further research is needed to understand how knowledge of diagnosis affects treatment motivation and medication adherence as well as satisfaction with care. Commercial Support was provided by Bristol-Meyers Squibb.

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» NR3-092

INVESTIGATION OF HIPPOCAMPAL VOLUME AND SHAPE IN SUBJECTS AT ULTRA-HIGH RISK FOR SCHIZOPHRENIA

Chi-Won Kim M.D., Do-Hyung Kang, M.D., Jung-Seok Choi, M.D., Ji-Young Park, M.A., Wi Hoon Jung, M.S., Chi-Hoon Choi, M.D., Myung Hun Jung, M.D., Jun Hwan Jang, M.D., Sun Hyung Kim, Ph.D, Jong-Min Lee, Ph.D, Jun Soo Kwon, M.D., Ph.D

EDUCATIONAL OBJECTIVES:
We investigated hippocampal structural changes in ultra high risk group for schizophrenia, and at the conclusion of this presentation, we suggest the role of subtle structural changes of the hippocampus as a possible vulnerability marker for schizophrenia.

SUMMARY:
Introduction: Magnetic resonance imaging (MRI) studies have proposed hippocampal volume reduction in chronic schizophrenia, and first-episode psychosis. While these findings suggest the structural changes start from the onset of illness, studies in ultra-high risk (UHR) group experiencing prodromal symptoms of schizophrena have shown controversial results. In this study, we compared hippocampal volume of healthy control with that of UHR individuals. We additionally performed 3-D shape deformation analysis of the hippocampus to investigate deformity pattern in UHR groups.
Method: Hippocampal and intra-cranial volumes (ICV) were estimated using MRI scans in 29 UHR subjects (M:F=15:14) and 29 healthy controls (M:F=15:14). The mean ages of two groups were 22.24±4.33 years and 23.24±2.71 years, respectively. Prodromal symptoms were assessed using the Comprehensive Assessment of At-Risk Mental States, and all subjects of high risk group met the attenuated psychotic symptoms criterion. All hippocampal volumes were corrected using ICV and analysis of variance (ANOVA) was conducted. A deformable model that parameterizes hippocampal surface to 2562 vertexes was used for preliminary results of hippocampal shape analysis between 6 UHR members and 7 controls.
Result: In the present study, we did not find any significant volume differences in left and right hippocampus between UHR group (Left: 2245.00±418.42 mm3, Right: 2376.11±435.67 mm3; p=0.628) and healthy control (Left: 2198.45±370.20 mm3, Right: 2330.21±340.99 mm3; p=0.657). However, shape deformities in the inferior subregions of posterior body of left hippocampus were observed in UHR subjects compare to controls ($p<0.05$).
Discussion: These results provide that hippocampal volume changes would not be present before the onset of psychosis, wheares hippocampal shape analysis in UHR group to detect subtle structural brain change showed different surface shape abnormality pattern compared with healthy control. These findings suggest that subtle structural changes of the hippocampus begin before onset of psychosis, suggestive of possibility of vulnerability marker for schizophrenia. Further study using follow-up design with larger sample size will be needed.

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» NR3-093

PROGRESSIVE WHITE MATTER CHANGES IN FIRST EPISODE SCHIZOPHRENIA: A 4-YEAR LONGITUDINAL MAGNETIC RESONANCE STUDY USING VOXEL-BASED MORPHOMETRY

Anna Mane M.D., Carles Falcon , Ph.D, Guillermo Horga , M.D., Jose J. Mateos , M.D., Ph.D., Emilio Fernandez-Egea M.D., Francisco Lomeña M.D., Ph.D., Nuria Bargalló , M.D., Ph.D., Miguel Bernardo M.D., Ph.D.,Eduard Parellada M.D., Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to to have a greater understanding of mechanisms of illness progression in schizophrenia.

SUMMARY:
Schizophrenia is a disabling illness, characterized by a heterogeneous course, including clinical deterioration and poor outcome. Accumulating findings in schizophrenia suggest that it might involve two pathophysiologic processes, one early in life (neurodevelopmental), and one after onset of the illness (neurodegenerative). Longitudinal imaging studies after onset of the illness may help to clarify these pathophysiological aspects of schizophrenia, but so far, probably due to methodological differences, there have been no conclusive results. On the other hand, schizophrenia has long been considered a disorder of brain connectivity, however few studies have investigated specifically whether there is progressive white matter pathology in the disease. The present study sets out to investigate longitudinal white matter changes in patients with first-episode schizophrenia relative to healthy subjects, over the first 4 years of the illness, and the relation of white matter changes in patients with functional outcome. Methods: We included 28 neuroleptic-naive patients with DSM-IV diagnosis of schizophreniform disorder, and 17 controls. 15 patients and 11 controls completed the longitudinal study and were reevaluated after four years. White matter changes over time were measured with voxel-based morphometry using SPM5. Functional outcome was measured with the global assessment functioning scale (GAF). Results: Excessive decrease in white matter was found in patients as compared to healthy individuals in right frontal and temporal areas. Thus, white matter changes in patients in left occipital areas were inversely related to functional outcome (voxel-level $p<0.001$, uncorrected, cluster-level $p<0.05$ corrected for multiple comparisons). Conclusions: There are progressive fronto-temporal white matter changes in patients with schizophrenia during the first years of the illness as compared to healthy individuals. Some progressive white matter changes in patients are related to functional outcome.
Supported by funding from Premi Fi de Residència Hospital Clínic, beca de investigación para psiquiatras reción especializados de FEPSM-AstraZéneca, and the Instituto de Salud Carlos III, Centro de Investigación Biomédica en Red de Salud Mental, CIBERSAM.

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» NR3-094

ELECTROPHYSIOLOGICAL EVIDENCE OF MIRROR NEURON DYSFUNCTION IN SCHIZOPHRENIA

Laurie M. McCormick, M.D., Michael C. Brumm, B.S., Nancy C. Andreasen, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, participants should be able to understand how mirror neuron function has evolved in the human brain and how electroencephalography (EEG) can be used to investigate functional capabilities of this system. Participants will also learn how mirror neuron dysfunction in schizophrenia may be one of the core pathological underpinnings of “theory of mind” deficits in schizophrenia.

SUMMARY:
Background: Schizophrenia-spectrum disorders are characterized by deficits in theory of mind and empathy. Previous research has provided evidence of a dysfunctional mirror neuron system that may explain some of the pathology involved in schizophrenia. Electroencephalography (EEG) oscillations in the mu frequency range (8-13z) are known to be suppressed over the sensorimotor

cortex in response to a person's own movement and also while observing another person perform the same movement. This phenomenon, in which mu suppression occurs in response to both self and observed movement, is thought to reflect mirror neuron activity. This study investigated whether people with schizophrenia have dysfunction of the mirror neuron system when observing other people, which may account for their inability to understand the motives and social cues of others.
Methods: EEG recordings were obtained for nine schizophrenia-spectrum subjects and six age and gender-matched normal controls who completed four tasks: (1) watching their own hand move ("self hand" condition); (2) watching a video of a moving hand ("observed hand" condition); (3) watching a video of two bouncing balls ("ball" condition); and (4) watching visual white noise ("baseline" condition). The degree of mu wave suppression was determined using quantitative EEG (qEEG) and low-resolution electromagnetic tomography analysis (LORETA), which calculated the ratio of the power during the self hand, observed hand and ball conditions relative to the power during the baseline condition.
Results: Control subjects showed significant mu suppression in bilateral frontal leads during both self and observed hand movements whereas schizophrenia subjects had no mu suppression with observed hand movements as assessed by qEEG. Similar results were found with the LORETA analysis, which revealed a significant difference in mu suppression between groups for observing hand movements primarily in the left frontal cortex ($p<0.05$).
Conclusion: These results suggest that individuals with schizophrenia have a dysfunctional mirror neuron system that can be identified with EEG, which may explain some pathophysiological aspects of this disorder.

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» NR3-095

BORDERLINE PERSONALITY TRAITS AND TRANSITION TO PSYCHOSIS IN A "ULTRA HIGH RISK"(UHR)POPULATION: A CASE CONTROL STUDY

KAREN O CONNOR M.D., Nilufar Mossaheb M.D., Barnaby Nelson Ph.D., Isobel Domingues, Andreas Bechdolf M.D., Alison Yung M.D., Andrew Thompson M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognise the high rates of Borderline Personality Disorder(BPD) in the 'Ultra High Risk' (UHR) for psychosis population.

SUMMARY:

Introduction: A 15% prevalence of Borderline Personality Disorder (BPD) has previously been reported in a 'prodromal' or clinically high risk for psychosis cohort. Psychotic-like symptoms are commonly reported in BPD patients and transient paranoid ideation is part of some current diagnostic criteria. However there has been limited research in the 'Ultra high risk'(UHR) for psychosis population into BPD or BPD traits and development of a psychotic illness.
Aim: Investigate the prevalence of BPD and BPD traits in a UHR population and explore the relationship between BPD traits and Risk of transition to psychosis.
Method: Retrospective case-control study. The clinical files of all cases treated at the clinic between 2003 and 2007 that subsequently transitioned to psychosis were examined. Borderline personality traits were routinely recorded using SCID II criteria as part of the initial triage assessment prior to admission to the PACE clinic. Using these assessments, we were able to calculate the number of BPD traits and BPD score out of 27.
Results: We identified 51 cases that transitioned to psychosis in the 4 year period and matched these to 51 controls. Overall 19.2% of the cohort met DSM IV criteria for BPD. Fewer individuals who transitioned to psychosis (10.4%) had a diagnosis of BPD at entry to the service compared with those who did not (17.6%) although this difference was not statistically significant. Neither the number of BPD traits nor the trait scores were significantly different between those who made the transition to psychosis and those who did not. There was no significant difference in trait or trait scores for cases with a diagnosis of schizophrenia spectrum psychosis, affective psychosis or 'other' psychosis.
Conclusion: The rate of BPD is relatively high in this UHR sample. In this sample the presence of borderline traits does not appear to reduce the risk of transition to psychosis nor of developing a schizophrenia spectrum psychosis.

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» NR3-096

ARE YOU LOOKING AT ME? SOCIAL PHOBIA AND PSYCHOSIS A CASE SERIES AND REVIEW OF THE EPIDEMIOLOGICAL AND PSYCHOLOGICAL LITERATURE

KAREN O CONNOR M.D., Paul Scully MD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognise the high rates of social phobia in psychotic disorders, identify the value of treating both disorders concurrently and appreciate the increasingly robust cognitive literature coinnecting psychosis and neurosis.

SUMMARY:

Background: Three females in there 30s, who each had pre-existing social phobia, developed a first episode psychosis. We sought to explore the epidemiological and psychological literature on the co-occurrence of these disorders and to investigate three hypotheses to explain it, namely (1) the chance co-occurrence of two disorders with distinct aetiology; (2) two clinical presentations signifying different points on the same spectrum of illness (3) two distinct disorders representing alternate clinical outcomes resulting from the same aetiology. Results: We found no reports on social phobia pre-existing an episode of psychosis, and prevalence studies indicate that their chance co-occurrence is extremely unlikely. Three key theoretical models for the co-occurrence of social phobia and psychosis were identified. (a)Persecutory delusions and hallucinations are the result of a psychological defence. (b)Negative emotion and low self-esteem have a central, normal, direct and non-defensive role in the development of psychotic symptoms. (c) The large co-occurrence of social phobia and psychosis is a psychological reaction to psychosis itself. Conclusion: Epidemiological studies indicate that their chance occurrence as two unrelated disorders is unlikely. Most people with one of these disorders do not develop the other and the hypothesis (2), two clinical presentations signifying different points on the same spectrum of illness, is also unlikely. The greatest evidence was found to support our hypothesis (3) two distinct disorders representing alternate clinical outcomes with the same aetiology. However it seems more likely that social phobia and psychosis rather than simply being alternate outcomes, instead are implicated in a complex interaction where symptoms, which characterise social phobia and psychosis, have the capacity to affect, alter and possibly provoke each.

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» NR3-097

RESPIRATORY HEALTH IN PSYCHOTIC DISORDERS: A POPULATION STUDY

Krista Partti, Tuula Vasankari, M.D., Ph.D, Jonna Perälä, M.D., Samuli I. Saarni, M.D., Ph.D., Sami Heistaro, M.D., Ph.D., Pekka Jousilahti, M.D., Ph.D., Jouko Lönnqvist, M.D., Ph.D., Jaana Suvisaari, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that persons with schizophrenia have impaired lung function, which is not explained by the higher prevalence of cigarette smoking among individuals with schizophrenia.

SUMMARY:

Introduction: Persons with schizophrenia and other psychotic disorders suffer from increased mortality from medical disorders. Many studies have reported high standardized mortality ratios for respiratory diseases (1). However, there are only a few studies that have investigated respiratory function and the prevalence of respiratory diseases and symptoms in persons with psychotic disorders. Our study is the first general population survey of respiratory health in persons with psychotic disorder.

Methods: The study was based on a nationally representative sample of 8028 persons aged 30 or over from Finland. Psychotic disorders were screened from the general study population, and final lifetime-ever DSM-IV psychosis diagnoses were based on SCID-I interview and case note data (2). Lung function was measured by spirometry from subjects with schizophrenia (n=43), other non-affective psychosis (n=58), affective psychosis (n=33), and from 5926 controls. Respiratory diseases and symptoms were diagnosed in a physician's examination. Smoking was quantified by measuring serum cotinine levels.

Results: Subjects with schizophrenia and other non-affective psychosis had lower FEV1 (p=.006 and p=.010, respectively) and FVC (p=.010 and p=.006, respectively) as compared with the general study population; however, no significant differences were found for the FEV1/FVC ratio, suggestive of a restrictive pulmonary impairment. In the linear regression model, schizophrenia remained an independent predictor of low FEV1 (p=.001) and FVC (p=.001) after adjusting for age, sex, height, waist circumference, type 2 diabetes and serum cotinine level. In addition, schizophrenia was associated with abnormalities in breathing (p=.005) and significantly high cotinine levels (p=.019). No significant differences were found for the prevalences of the diagnosed respiratory diseases.

Conclusion: According to our study, schizophrenia is an independent risk factor for impaired lung function.

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» NR3-098

NEUROCOGNITIVE EFFICACY OF CLOZAPINE-ZIPRASIDONE COMBINATION THERAPY IN TREATMENT-RESISTANT SCHIZOPHRENIA

Seon-Jin Yim M.D., Hwang-Bin Lee, M.D., Minyoung Sim, M.D., Hae-Joo Yoon, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the possible neurocognitive efficacy of clozapine-ziprasidone combination Therapy in treatment-resistant schizophrenia.

SUMMARY:

Objectives: Neurocognitive impairment in schizophrenia is severe and it affects function and life quality of the patients. Since ziprasidone has been reported to improve cognition in schizophrenia, we aimed to investigate the efficacy of ziprazidone combining with clozapine in improving cognition of treatment-resistent schizophrenia.

Methods: 30 patients with treatment-resistent schizophrenia who has been taking clozapine of 300mg or more for at least 6 months participated in this open clinical trial and received additional regimen of ziprasidone. Clinical status, functional outcome and quality of life were assessed by BPRS, PSP and GAF and SQLS-R4 at baseline, and will be assessed at 3 and 6 months' follow-up. Neurocognitive assessment battery consisting of 4 dimensions, learning and memory, attention and vigilance, visuomotor speed, and executive function, was administered to evaluate neurocognition. Neurocognition will be evaluated again at 6 month's follow-up.

Results: All 30 patients completed baseline studies. GAF and PSP scores, the index of functional outcome, showed significant positive correlations with executive function dimension of neurocognitive assessment battery. Scores of SQLS-R4 and BPRS did not show any correlation.

Conclusion: Executive function might be a possible predictor of functional outcome of treatment-resistent schizophrenia. Follow-up assements with ziprasidone combination will be important to identify the efficacy of clozapine-ziprasidone combination therapy, and any correlation of neurocognitive change with functional outcome and life quality of the patients.

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» NR3-099

THE RELATIONSHIP BETWEEN PLASMA LEVEL OF LEPTIN, BODY MASS INDEX AND SLEEP QUALITY IN HEALTHY VOLUNTEERS

Wei Tzeng Chen M.D., Tzung Lieh Yeh, M.D., I Hui Lee, M.D., Po See Chen, Ph.D., Kao Ching Chen, M.D., Yeng Kuang Yang, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the relationship between sleep quality, body mass index, and plasma leptin level.

SUMMARY:

Objective: Leptin, an adipose tissue derived hormone, had been known to have positive correlation with body mass index (BMI). One of the recent interests is the negative relationship between sleep quality and the body mass index. Our study was designed to investigate the relationship between sleep quality, BMI, plasma leptin level, gender, lipid profile and age.

Method: 54 healthy volunteers (30 women and 24 men) were recruited through the advertising. They were all interviewed by a senior psychiatrist with the Chinease version of the Mini International Neuropsychiatric Interview (MINI) to exclude mental illness. The excluding criteria including pregnancy, with medical or neurological disorder, history of head-trauma, alcohol or substance abuse, or recent usage of hypnotics. Pittsburgh Sleep Quality Index (PSQI) is administrated to access their sleep quality.

Results: There is a significant positive correlation between sleep duration with BMI and also plasma leptin levels in female volunteers. This relationship remained after controlling age and excluding the subjects with previous hypnotics usage. However, in the male volunteers, only the correlation between sleep duration and the plasma level of cholesterol was noted.
Conclusion: Our result demonstrated hyperleptinemia correlates with poor sleep quality in healthy adult female volunteers. However, this did not exist in male gender. Whether the leptin level correlated with stressful and hyperarousal status remains unclear. Further study should be proceeded to clarify the possible causal effect of plasma leptin level and sleep duration.

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» NR3-100

EXCESSIVE DAYTIME SLEEPINESS IN DEPRESSED WOMEN

Enrique Gaspar M.D., Raffaella Calati, Ph.D., Carlos S. Cruz-Fuentes, Ph.D., Alejandro Nenclares, M.D., Alejandro Jimenez-Genchi, M.D., Diana De Ronchi, M.D., Ph.D., Alessandro Serretti, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participants should be able to appreciate the clinical differences in depressed patients with and without sleepiness and evaluate sleep features in affective patients with the aim of achieve the better possible treatment.

SUMMARY:

Introduction. Excessive daytime sleepiness (EDS) is a symptom with high public health importance, and the most widely subjective method for measure it is the Epworth Sleepiness Scale (ESS). Epidemiological data reported that depression is the most significant risk factor for EDS, however, this relationship is not clearly detailed and its elucidation has a major clinical significance. The aim of this study was to describe the sleep quality of depressed patients with and without EDS and study the possible association to severity of depressive symptoms. Methods. 78 female depressed and drug naïve outpatients (age 34.2±11.3) were included. We applied three self-administered questionnaires: ESS, Athens Insomnia Scale (AIS) and Pittsburgh Sleep Quality Index (PSQI), also BMI was calculated. Student t-test for independent samples and ANCOVA were used. Results. According to the ESS scores, patients were classified in two groups: without excessive daytime sleepiness (=10, n=44, 56.5%), and with excessive daytime sleepiness (=11, n=34, 43.5%). None of the demographic variables were different, except unemployment, that was more frequent in EDS patients. Neither the HRSD variables nor the comorbidity distribution were different, nevertheless, a trend to higher comorbidity with social phobia was observed in the with-EDS group (p= 0.07). The AIS item-8 presents marginally higher scores in with-EDS group (p= 0.025). Besides, PSQI item-8 (with higher scores for with-EDS group, p= 0.00014) and item-5-h (with higher scores for without-EDS, p= 0.026) were also different.
Conclusion. There is a frequent EDS complain in depressed women, but it is not associated with reduced sleep efficiency neither severity of depressive symptoms. These results offer valuable information to clinicians in the sense of the need to investigate on detail the etiology of the EDS before attribute it to bad sleep quality or depression severity.

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» NR3-101

T3111C CLOCK GENE POLYMORPHISM IS NOT ASSOCIATED WITH SLEEP DISTURBANCES IN DEPRESSED PATIENTS

Enrique Gaspar M.D., Raffaella Calati, Ph.D., Carlos S. Cruz-Fuentes, Ph.D., Martha P. Ontiveros-Uribe, M.D., Diana De Ronchi, M.D., Ph.D., Alessandro Serretti, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the role of the CLOCK gene in sleep disturbances in depression and recognize the potential role of these genes in affective disorders.

SUMMARY:

Introduction. Circadian alterations represent a central feature in depression. Previous studies have shown that there is an association of severity of depression (SD) and eveningness, since this has also been associated to rs1801260, we hypothesized that the SD could be associated to that clock gene variant. The aim of this study was to investigate the possible effect of rs1801260 on insomnia, daytime sleepiness, quality of sleep and SD in MDD. Methods. 100 MDD patients were included (age: 34±11.7y; female/male: 79/21). The Morningness-Eveningness Questionnaire (MEQ), the Epworth Sleepiness Scale (ESS), the Athens Insomnia Scale (AIS) and the Pittsburgh Sleep Quality Index (PSQI) were applied. Standard protocols were performed to identify rs1801260. The means of the scales according to the genotype were compared through the Student t-test for independent samples. General Linear Model was used for confounding variables control. All p values were 2-tailed, and statistical significance was conservatively set at the 0.05 level. With these parameters we had a sufficient power on the sample (0.80) to detect a medium effect size (d=0.59) between two main genotypes (TT: n=61; TC+CC: n=39). Results. The sample was homogeneous regarding socio-demographic variables. There was no significant deviation from HWE in the sample (p=1.0). No significant difference was found concerning genotypes or allele groups and the HRSD items or clusters; neither the clinical parameters “melancholic” of depression (p=0.96), “recurrent” (p=0.69) nor “psychotic symptoms” (p=0.81). We found no difference between genotypes according to the comorbidity (p=0.26), the ESS (p=0.74), the AIS (p=0.94) or the PSQI (p=0.59) total scores, nor the chronotypes distribution. Conclusion. Overall, our findings do not support the hypothesis that rs1801260 has an effect on sleep disturbances in MDD. Further analysis of clock machinery will clarify the contribution of clock genes to the maintenance of mental health.

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» NR3-102

THE ASSOCIATION BETWEEN SELF-PERCEIVED SLEEP LATENCY AND SEROTONIN TRANSPORTER AVAILABILITY IN HEALTHY VOLUNTEERS-A SPECT STUDY WITH [123I]ADAM

HUICHUN HUANG M.D., Yen-Kuang Yang, M.D., Po-See Chen, M.D., Ph.D., Tzung-Lieh Yeh, M.D., I-Hui Lee, M.D., Kao-Ching Chen, M.D., Wei-Jen Yao, M.D., Ru-Band Lu, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to get to know the role of serotonergic system in the modulation of sleep quality and the application of [123I]ADAM SPECT study in assessing the serotonin transporter availability.

SUMMARY:
Objective: Among the diverse neurochemical systems that interact to regulate wakefulness and sleep, serotonergic neurotransmission plays an important role within brain areas. The present study aimed to examine the relationship between serotonin transporter (SERT) availability in mid-brain and self-reported sleep characteristics in healthy volunteers.
Method: 33 healthy volunteers were recruited, including 19 females (mean age 33.93±13.50 years), and 14 males (mean age 28.11±8.43 years). The Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep quality and frequency of sleep symptoms. SERT availability was determined using [123I] ADAM SPECT Imaging. Pearson correlation was conducted to explore the relationship between self-reported sleep symptoms and SERT availability.
Results: The SERT availability mean ratio was 2.42±0.48(F:2 .41±0.49 , M:2.42±0.48). The mean scores of PSQI total scores was 5.39 ±2.17(F:5.85±2.03, M:5.05±2.27). Among the PSQI items, sleep latency was associated significantly with SERT availability in mid-brain (r=-.619, p=.024), but only for women.
Conclusions: The data suggested that subjective ratings of sleep latency are negatively correlated with SERT availability in the midbrain in women. These gender-specific associations may have implications to recent observations suggesting gender differences in depression and life stress perception.

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» NR3-103

COMPARISON BETWEEN BOTH WRIST ACTIGRAPHIC INDICES AND THEIR CORRELATION WITH APNEA-HYPOPNEA INDEX OF NOCTURNAL POLYSOMNOGRAPH

Hong Jun Jeon M.D., Doo-Heum Park

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to learn that there are meaningful correlation between wrist actigraphic indices and estimates of nocturnal polysomnograph by recognizing which data correlates significantly and which dose not.

SUMMARY:
The present study compared the left and right actigraphic indices during sleep in obstructive sleep apnea syndrome patients, and assessed correlation between both side actigraphic indices and apnea-hypopnea index (AHI) via wrist actigraph (WATG) and nocturnal polysomnograph (NPSG). We studied 72 right-handed subjects (mean age 43.1 ± 12.5 years, M:F = 6.2 : 1) with untreated obstructive sleep apnea syndrome (OSAS) undergone overnight both WATGs and NPSG, simultaneously. Participants with any parasomnia other than obstructive sleep apnea syndrome or on any medication were excluded. Comparison was analyzed between right and left wrist actigraphic data. Right and left WATG data were compared to each other and each WATG data was tested for their correlation with AHI of NPSG under controlling for age and sex. SPSS (version 16.0) was used for statistical analysis. Left WATG total activity score, mean activity score, fragmentation index are significantly higher than right. And our data showed positive correlation between left WATG mean activity score and AHI and also between both side WATG fragmentation indexes and AHI. We put pulse oxymetry to all subjects during whole test period, and it was applied to their third finger of left hand. Subjective discomfort caused by pulse oxymetry may have had the subjects move their left hands and arms more frequently than right. The present study demonstrated that activity of non dominant arm was significantly higher in scores during sleep in OSAS subjects and several WATG indices was positively correlated with AHI, leaving necessity of further investigation which controls possible variables like pulse oxymetry better. Key words: wrist actigraph, polysomnograph, handedness

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» NR3-104

DETRENDED FLUCTUATION ANALYSIS OF HEART RATE VARIABILITY IN OBSTRUCTIVE SLEEP APNEA

Gawon Ju M.D., Chul-Jin Shin, M.D.,Doo-Heum Park, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to explain the pathophysiology of obstructive sleep apnea syndrome and pros of detrended fluctuation analysis in the analysis of biological timeseries.

SUMMARY:
Objective : The Detrended fluctuation analysis is one of the nonlinear methods for the investigation of biological time series. It quantifies the fractal scaling properties and is known to be useful in the evaluation of long-range correlations in time series. The heart rate variability (HRV) of obstructive sleep apnea (OSAS) patients during night time was analyzed by detrended fluctuation analysis to assess their relationship with the severity of the symptoms.
Methods : Fifty nine male untreated OSAS patients with moderate to severe symptoms (mean age=45.4±11.7 years, apnea-hypopnea index, AHI=15) underwent nocturnal polysomnography. Moderate (AHI=15-30, n=22) and severe (AHI>30, n=37) OSAS patients were compared for the indices derived from detrended fluctuation analysis and frequency domain analysis of HRV.
Results : In detrended fluctuation analysis, the alpha values were 0.75±0.11 and 0.82±0.07 for the severe and the moderate OSAS groups respectively. The difference was significant ($p<0.01$). The alpha value had negative correlation with AHI (r=-0.425, p=0.001). Negative correlation coefficients were also found in the relationship between the alpha values and very low frequency (VLF) (r=-.425, p=.001), low frequency (LF) (r=-.633, p=<.0001) and the LF/HF ratio (r=-0.305, p=.019) respectively. LF/HF ratio (p=0.005) was higher in the severe OSAS group compared to that of the moderate OSAS group.
Conclusions : In this study, the detrended fluctuation analysis showed the significant difference between the two OSAS groups classified according to their severity of symptoms. The scaling exponent showed the negative correlation with AHI and indicies of frequency analysis. This result suggests that detrended fluctuation analysis can be helpful to estimate the severity of OSAS.

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» NR3-105

SLEEP PROBLEMS IN ELEMENTARY SCHOOLCHILDREN IN KOREA

Min-Ji Kim, M.D., Jong-Bum Lee, M.D., Ph.D., Bon-Hoon Koo, M.D., Ph.D., Jun-Yeob Lee M.D., Shin-Ho Song M.D., Hye-Jeong Hong, M.A., Yoon-Jung An, M.S.W.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be able to understand the characteristics of sleep problems in Korean schoolchildren.

SUMMARY:
Objectives: The aim of this study is to evaluate the prevalence and characteristics of sleep problems in elementary schoolchildren in Korea.
Methods: Four public elementary school in Daegu city which is one of the largest population cities in Korea were randomly selected and the modified version of Tucson Children's Assessment of Sleep Apnea screening questionnaire was applied to evaluate snoring, sleep bruxism, nocturnal enuresis, witnessed sleep apnea, oral breathing, daytime fatigue, morning headache, excessive sleepiness (falling asleep while watching TV before 8 P.M., falling asleep while doing homework, and falling asleep in a vehicle), nightmare and sleep terror. 3,956 schoolchildren's parents assented to join this study in 4,979 schoolchildren and completed the questionnaire. Among them 3,745 data of schoolchildren were analyzed.
Results: The most common sleep problem was 'falling asleep in a vehicle' and the prevalence rate was differed by grades. The prevalence rate of falling asleep while watching TV before 8 P.M., daytime fatigue, nocturnal enuresis for the past 6 months and bruxism were 10.3%, 21.2%, 6.5% and 14.0%, respectfully. All of them have differences by grades. Snoring over moderate degree and bruxism were more prevalent in boys. Meanwhile, more girls have daytime fatigue and morning headache.
Conclusion: This study demonstrates that many children in Korea have various sleep problems. Lower grade children have sleep problems related to neurodevelopmental aspects and higher grade children have sleep problems related to sleep deprivation and stress. This study may help to understand the differences and characteristics of sleep problems in Korean elementary schoolchildren compared with different cultural background in the future.

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» NR3-106

THE RELATION OF RESTLESS LEGS SYNDROME AND SERUM FERRITIN -COMPARISON WITH PRIMARY INSOMNIA

Younghee Kim, Seung-Chul Hong, M.D., Ph.D, Jong-Hyun Jeong, M.D., Ph.D

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize the relation of RLS and serum ferritin and understand the importance of distinguishing RLS patients from the primary insomnia patietns.

SUMMARY:
Objectives: Restless Legs Syndrome(RLS) is a sleep disorder, characterized by an irresistible urge to move the legs that worsen with inactivity, especially during evening or night and a subsequent insomnia. Low serum ferritin level is one of the most important causes of RLS. This study was designed to investigate the relation between RLS and serum ferritin level by comparing with Primary Insomnia.
Methods: From May 1, 2006 to May 31, 2008, we selected 71 patients who have been diagnosed RLS or primary insomnia at Sleep Disorders Clinic of St. Vincent's hospital, Catholic University of Korea. Patients were divided into 33 RLS group and 38 primary insomnia group. The results of serum ferritin level for all patients were investigated through chart review, and telephone interview was done for 9 RLS patients.
Results: 1) There is no significant difference in demographic data between RLS group and primary insomnia group. 2) There is no significant difference in serum ferritin between two groups. 3) There is no correlation between RLS symptom severity and serum ferritin level.
Conclusions: RLS is likely to be misdiagnosed with simple insomnia so it is important for physicians to have full understanding about RLS and make a proper diagnosis and treatment. Also a future study such as ferritin level in cerebrospinal fluid(CSF) between two groups will be needed. Key words: Restless legs syndrome(RLS), serum ferritin

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» NR3-107

THE ASSOCIATION BETWEEN CENTRAL APNEA AND ANXIETY AMONG MIDDLE AGED ADULTS

Leon Tourian M.D., Sok S. Lee, B.Sc., Brian J. Murray, M.D., M.Sc., Nancy C.P. Low, M.D., M.Sc.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to appreciate the clinical importance of central sleep apnea in mood and anxiety disorders.

SUMMARY:
Background: Sleep disordered breathing includes central (CSA) and obstructive sleep apnea (OSA). OSA is characterised by obstruction of the upper airway during sleep causing oxygen desaturation, frequent arousals and poorly restorative sleep, while CSA is triggered by hypocapnia induced by hyperventilation during sleep. Clinical and population based studies show that OSA and anxiety or depression frequently co-occur in middle aged adults, however the association between CSA and anxiety is not yet delineated. Moreover, studies demonstrate that patients suffering from anxiety present heightened sensitivity to hyperventilation supporting evidence for the investigation of hyperventilation- driven CSA and anxiety.
Objective: To examine the association between CSA and anxiety versus depression.
Method: 314 patients referred to a sleep laboratory (1) completed a questionnaire about basic medical information including the presence of depression and anxiety and (2) underwent a respiratory polysomnogram (PSG). Linear regression analyses were conducted with anxiety and depression as independent variables to predict the outcome of central apnea. Relevant confounders were also considered.
Results: A strong association between increasing episodes of central apnea and anxiety (P=0.008) but not depression (P=0.893) was found. Relevant confounders such as gender, age, BMI and alcohol use did not change this association.
Conclusion: The association between CSA and anxiety is a novel finding. It shows that patients who hyperventilate and hence experience increasing central apneic events during sleep are more likely to self report anxiety rather than depression. This finding reflects the need to increase awareness of clinicians and further investigate the impact and association of CSA on mental health especially in the aging population who are increasingly at risk to suffer from central apnea.

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» NR3-108

THE EFFECT OF SELECTIVE SEROTONIN RE-UPTAKE INHIBITORS ON PERIODIC LIMB MOVEMENTS AND RESTLESS LEG SYNDROME IN DEPRESSED PATIENTS

Fahd Zarrouf M.D., Kumaraswamy Budur,MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize the clinical picture of restless leg syndrome and periodic limb movement disorder in depressed population and the effect of antidepressants on these disorders.

SUMMARY:

Introduction: Sleep disturbance constitutes one of the most common symptoms expressed by depressed patients, yet assessment of sleep quality is frequently neglected during the initial clinical evaluation and during the follow up evaluation after starting antidepressant medications.

Limited and conflicting data are found regarding the effect of Selective Serotonin Re-uptake Inhibitors (SSRIs) on Restless Leg Syndrome (RLS) sensory symptoms and Periodic Limb Movement Indices (PLMIs). Our goal is to evaluate the effect of SSRIs on RLS diagnosis and PLMIs in depressed patients undergoing polysomnographic (PSG) evaluations (group A), when compared to these levels in depressed patients not taking antidepressant medications (group B).

Methods: Depressed patients undergone PSG evaluations in our sleep center were included. The database was reviewed for demographic data, medical and mental history, medications used at the time of the PSG evaluation, and other PSG findings. Descriptive procedures for each variable were conducted to determine measures of central tendency, variability and shape of score distributions. The presence of outliers and the violations of parametrical tests were determined using exploratory analyses. Respiratory data [apnea-hypopnea index (AHI) and minimum oxygen saturation (mSaO2)] and PLMIs were compared between group A and group B using independent T-test for continuous variables and cross tabulation using Chi-square test without imputation for missing values for categorical variables.

Results: 230 consecutive depressed patients were included, 124 (53.9%) females and 106 (46.1%) males. Mean age= 44.96/16.128, mean BMI= 35.09/9.74. Of them, 164 (71.3%) were on SSRI medications at the time of evaluations. There was no significant difference in gender, Epworth Sleepiness Scale (ESS) and BMI between the two groups. Age was significantly higher in group A when compared to group B (47.38/14.49 vs 38.49/18.13 p< 0.001). RLS was diagnosed in 34 (14.8%) subjects. Off them 25 subjects were from group A and 8 were from group B (Pearson Chi-square df=1, p=0.817). PLM index (PLMI) was significantly higher in group A when compared to group B (15.91/25.631 vs 6.81/ 15.565 p=0.011). PLM-Arousal Index (PLMAI) was not (2.840/5.1561 vs 2.137/4.2910 p=0.345). When controlling for other variables including age, mSaO2 and AHI, we found no significant differences between group A and group B in regard to PLMI, PLMAI and RLS (r= 0.086, P=0.363; r=0.032, p=0.

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» NR3-109

THE PREVALENCE OF BODY DYSMORPHIC DISORDER IN A KOREAN MEDICAL STUDENT SAMPLE

Hyun-Jin Kim, M.D., 640 Daesa-dong, Jung-gu, Daejeon, Korea, Department of Medicine, Chungnam National University; Seung-Min Cha, M.D., Tae-Kyung Lee, M.D., Jung-Lan Kim, M.D., Ph.D., Seung-Keun Wang, M.D., Ph.D., Iik-Seung Chee, M.D. Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize and understand the importance of body dysmorphic disorder.

SUMMARY:

Introduction: Body dysmorphic disorder (BDD) is significant distressing or functional impairing disorder characterized by a preoccupation with imagined or slight physical defects in appearance. There has been little previous research about BDD in Korea. Therefore, this study aimed to investigate the prevalence rate and dissatisfied body parts of BDD in a Korea medical student sample. Method: The 386 medical students enrolled in a medical school of Chungnam National University in Daejeon, Korea filled out the Body Dysmorphic disorder Examination-self report; Korean version (BDDE-SR; Korean version) which assess BDD. Result: Out of the 386 students, 72.0%(N = 278) were male and 28%(N = 108) were female. Subjects satisfying BDD diagnostic criteria of BDDE-SR; Korean version was 1.3% (N = 5). The most dissatisfied body part of participants were waist-abdomen (16.8%, N = 65), head hair (10.9% N = 42), thigh (8.3%, N = 32). The gender difference in dissatisfied body parts, the most frequently reported body part in male student were waist-abdomen (19.1%, N = 53), head hair (14.4%, N=40) and nose (7.9%, N = 22). Whereas, Females were concerned about thigh (20.4%, N = 22), waist-abdomen (11.1%, N = 12) and calf (8.3% N = 9). Conclusion: Our study indicates that self-reported BDD is relatively common in medical student population. Future researches should be directed to patients with BDD.

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» NR3-110

PREVALENCE AND ETHNIC DIFFERENCES OF SOMATIZATION DISORDERS IN A RURAL CALIFORNIA COMMUNITY

Bernardo Ng M.D., Lianne M Tomfohr,.B.S., Alvaro Camacho, M.D., Joel E. Dimsdale M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to the participant should be able to: identify sociodemographic, ethnic and clinical features associated with somatization disorders in rural patient.

SUMMARY:

Somatization refers to mild to disabling medically unexplained symptoms. A higher prevalence is proposed in minority and rural patients. We studied the prevalence of somatization in a predominantly Latino rural outpatient clinic, and their course compared to patients without somatization.

METHODOLOGY: retrospective chart review at a clinic located in a rural underserved community in the southeast quadrant of California.

RESULTS: 37 out of 737 records had the disorder. The somatization group (SG) was older than the rest of the sample (p <0.001). There were no differences in ethnicity, gender, marital status, or education level. The most common AXIS I diagnosis in the SG

was MDD (p=0.007) followed by GAD. The SG was more likely to have a chronic axis III illness (p=0.002), hypertension was the most common (p=0.005), followed by arthritis (p=0.034). SG patients had more surgeries (p=0.043). SG's response to treatment was less favorable compared to the rest of the sample (p= 0.01). CONCLUSION: In conclusion, our findings suggest that somatization patients may not be common in a rural, general outpatient psychiatric clinic, but do include patients with depression, with more medical and surgical conditions, and who respond less favorably to treatment.

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» NR3-111

SALIVARY MHPG LEVELS AFTER VIDEO CHALLENGE PREDICT PERITRAUMATIC DISTRESS AND PTSD SYMPTOMS IN A PROSPECTIVE STUDY OF URBAN POLICE OFFICERS

Brigitte Apfel M.D., Sabra S. Inslicht, Ph.D., Shannon E. McCaslin, Ph.D., Thomas Metzler, M.A., Thomas C. Neylan, M.D., Charles R. Marmar, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the predicitve role of adrenergic activity as measured by salivary norepinephrine for the development of PTSD symptoms.

SUMMARY:

Introduction: Increased adrenergic activity (AA) during and immediately after a traumatic event predicts PTSD symptoms and patients with PTSD have increased AA. It is unclear if increased AA is a reaction to the trauma or a pre-existing risk factor for developing PTSD symptoms. The purpose of this study was to examine this relationship by a video challenge test (VChT) in a prospective cohort study of newly recruited urban police officers. Methods: 209 police recruits were assessed during academy training and after 12 months of active duty. At baseline, salivary MHPG was measured before, immediately after and 20 minutes following a VChT. After 12 months of active duty peritraumatic distress (PDI) and PTSD symptoms (PCL-S) were assessed. Correlations between the variables were analyzed using SPSS, and a path analysis was performed using AMOS.
Results: The mean MHPG level increased in response to the VChT. Greater PTSD symptoms at 12 months of duty were associated with higher peritraumatic distress and with higher MHPG levels 20 minutes after the VChT. Salivary MHPG levels immediately after the VChT were not correlated with PTSD symptoms. In the path analysis higher MHPG levels 20 minutes after the VChT predicted higher peritraumatic distress during the trauma experience which in turn predicted higher levels of PTSD symptoms. The direct path from MHPG to PTSD symptoms was no longer significant. Discussion: AA measured by salivary MHPG levels in a VChT prior to trauma exposure predicted the later development of PTSD symptoms, and this relationship was mediated by peritraumatic distress. These findings indicate that pre-existing high AA may be a risk factor for increased distress at the time of trauma and the subsequent development of PTSD. The MHPG value 20 minutes after the VChT best predicted peritraumatic reactions and PTSD symptoms. Therefore, it appears that sustained AA with a lack of recovery following a challenge places individuals at heightened risk for PTSD.

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» NR3-112 – WITHDRAWN

» NR3-113

INCREASING CRF EXPRESSION IN AMYGDALA BY VISCERAL PAIN IN RATS

Hoseon Lee M.D., Seok Hyeon Kim, M.D., PH.D., Younghwa Oh, M.D., Hyoin Park, M.D., Sangwon Jeon, M.D.

EDUCATIONAL OBJECTIVES:

[no data]

SUMMARY:

Objective: Previous animal studies observed increases of CRF in amygdale by various stresses. The studies also observed symptoms of depression, posttraumatic stress disorder, anxiety disorder. This psychiatric diseases are induced by pain as well as stress. This study tried to observe if visceral pain increases CRF expression in amygdala as previous studies and to test possibility of CRD as animal model of depression, posttraumatic stress disorder, anxiety disorder. Etc.
Methods: Nine week-old male Sprague-Dawley white rats were used as experimental subjects to induce visceral pain by ballooning with 80mmHg for 5 minutes. Such procedure was repeated 3 times with 1 minute resting between each ballooning without anesthetizing the rats. Visceral pains were induced for 1 day for the first experimental group and 5 days for the second experimental group. For the control group only tube was inserted without ballooning. In order to compare the CRF immune responses, serial sections of amygdala were photographed by fluorescence microscope and an image analysis program was used to measure the surface area(?2) of CRF immune response.
Results: CRF expression of amygdala increased both in control group and experimental groups and more CRF was expressed in experimental groups than control group. Variation of CRF expression between individual subjects in same group was larger in experimental groups than control group and the experimental group with 5 days of stimulus showed larger variation between individual subjects than other groups.
Conclusions: CRF expression was continuously increased by CRD. We supposed that CRD for 5 days developed acute stress and no habituation. Variation of CRF expression between individual was probably caused by individual factor. It is important to consider individual factor in animal study. In future, it is expected that CRD is used in animal model for psychiatric disease.

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» NR3-114

STRESS RELATED SLEEP DISTURBANCES: RISK FACTOR OF ABDOMINAL OBESITY

Mehdi A, Calhoun SL, Vgontzas AN, Bixler EO, Asad Mehdi M.D., Susan L. Calahoun, PhD, Alexandros N. Vgontzas, MD, Edward O. Bixler, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation the participant should be able to identify the link of increase prevalence of abdominal obesity with stress and/or stress related sleep disturbance. Therefore

identifying stress as a marker for cardiometabolic disorders. Also recognize the association of hypothalamic-pituitary-adrenal axis in stress and abdominal obesity.

SUMMARY:

Stress Related Sleep Disturbances are Significant Risk Factors of Abdominal Obesity in a General Random Sample of Men and Women: Asad Mehdi MD, Susan L. Calhoun PhD, Alexandros N. Vgontzas MD, Edward O. Bixler PhD.
Abdominal obesity is linked to greater risk of cardiometabolic disease. The activation of the stress system, particularly the hypothalamic-pituitary-adrenal axis, has been associated with abdominal obesity. In this study, we investigate the association between stress related sleep disturbance and/or emotional stress and abdominal obesity in a large population sample of men and women.
Method: Subjects included 642 research participants (318 men and 324 women) from the Penn State Cohort in which we obtained waist measurement. Waist circumference, full night polysomnography and the Multiphasic Minnesota Personality Inventory-2 (MMPI-2) were collected. This sample was divided into two groups by gender and further subdivided by level of stress. Stress was considered present if stress related sleep disturbance was reported and/or an MMPI-2 average T score > 60 across indices on Hypochondriasis(Hs), Depression (D),and Hysteria (Hy) was obtained.
Results: Due to gender differences, the analyses were run separately for men and women. The mean waist circumference was higher for both stressed men (103.0 vs 100.4 cm; p <.06) and women (102.6 vs 96.5 cm; p<.002). This difference was maintained even when controlling for AHI and age in men and AHI, age, menopausal status and HRT therapy in women.
Conclusions: Stress related sleep disturbances and/or self-reported emotional stress are significant risk factors for abdominal obesity in a large population sample of men and women. The detection and management of sleep disturbances and associated stress may lead to a reduction of abdominal obesity which is a condition linked to increase morbidity and mortality.

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» NR3-115

CLINICAL ACUITY AND CIVIL COMMITMENT OF NOT COMPETENT, NOT RESTORABLE FORENSIC PATIENTS COMPARED TO OTHER INPATIENTS IN AN ACUTE PSYCHIATRIC SETTING

Kelly Tyler M.D., Liliane Arenzon, MD, Illa Vora, MD, Gwen Levitt, DO, Gilbert Ramos, MA, David Drachman, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should have knowledge of the civil commitment process and forensic terminology including Not Competent Not Restorable (NCNR), and recognize the differences that may exist between NCNR patients and other hospitalized psychiatric patients. The participant will also be able to identify the legal standards under which patients receive court-ordered treatment, and begin to evaluate the influences behind civil commitment proceedings for NCNR patients

SUMMARY:

Objective: In some legal jurisdictions a criminal defendant found Not Competent Not Restorable (NCNR) may be involuntarily placed in an acute psychiatric setting for civil commitment proceedings. This practice implies the NCNR patient is dangerous, a characterization we hypothesize is undeserved relative to other patients on the hospital unit. To test this, we examine seclusion & restraint (S&R) episodes and forced medication orders for a sample of NCNR and control patients undergoing civil commitment. We relate these outcomes to court-ordered treatment (COT) findings to characterize the NCNR patient.
Methods: Retrospective chart review identified 293 NCNR patients at two psychiatric acute hospitals in greater Phoenix, Arizona, referred for court-ordered evaluation (COE) from 2003 to 2006. We compared them to 280 matched control patients from the same period, evaluating each group for S&R episodes, forced medication orders, proceedings with COT outcome, and the standards accepted for COT.
Results: NCNR patient S&R episodes occurred at a lower average daily rate than control patient S&R episodes (.002 episodes per day vs. .008 episodes per day; p=.004). Also, NCNR patients spent less average time in S&R than controls (.003 hours per day vs. .023 hours per day; p=.005). Additionally, 4% of the NCNR group required forced medications compared to 9% in the control group. At commitment proceedings, 84% of NCNR patients and 69% of controls received COT (p<.001). However, of the NCNR COT patients, only 6% received COT for a standard of danger to others (DTO), and 7% for a standard of danger to self (DTS), compared to 31% DTO and 31% DTS standards for COT controls. Courts gave NCNR patients COT under a standard of persistently and acutely disabled (PAD) 99% of the time.
Conclusion: Overall, NCNR patients required less seclusion & restraint and forced medications throughout their hospital stay than the average inpatient. Any perceived notion that NCNR patients are more dangerous than other hospital patients is unwarranted and further unsupported by the standards under which they receive COT. Their placement in an acute setting where they receive COT more often than others undergoing civil commitment proceedings merits closer examination as to judicial motives and the manner in which their mental health needs are being addressed.

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Tuesday, May 19, 2009

12:00 p.m. - 2:00 9.m.
Hall D, Exhibit Level,
Moscone Convention Center

NEW RESEARCH POSTER SESSION 4: ANXIETY AND MOOD DISORDER

» NR4-001 – WITHDRAWN

» NR4-002 – WITHDRAWN

» NR4-003 – WITHDRAWN

» NR4-004

COGNITIVE DEFICITS ASSOCIATED WITH POSTTRAUMATIC STRESS DISORDER

Moon yong Chung, Tae Yong Kim, M.D., Hong Shick Lee, M.D., Hae Gyung Chung, M.D., Jin Hee Choi, M.D., Han Sang Shin, M.D., Dong Ho Song, M.D., Tae Young Lee, M.D.

EDUCATIONAL OBJECTIVES:

In addition to main symptoms of posttraumatic stress disorder (PTSD), which include reexperience, avoidance and hyperarousal, many patients complain of cognitive deficits, especially in attention and memory. At the conclusion of this session, the participant should be able to: understand cognitive impairments in patients with posttraumatic stress disorder.

SUMMARY:

Objectives: In addition to main symptoms of posttraumatic stress disorder (PTSD), which include reexperience, avoidance and hyperarousal, many patients complain of cognitive deficits, especially in attention and memory. This study was conducted to evaluate cognitive deficits in survivors of a tragic shooting incident at a frontline guard post. All of the survivors experienced the same accident, and they were homogeneous in terms of age and education level, which are closely associated with cognitive performance. Methods: We recruited 12 survivors who suffered from PTSD following the same traumatic incident and 12 normal volunteers, and assessed their neurocognitive functions using a vigilance test, continuous attention test, reaction unit test, and the Corsi block tapping test in the computerized Vienna Test System, as well as an auditory verbal learning test and complex figure test in the Rey-Kim Memory Test. Standardized clinical scales, including the Clinician-Administered PTSD Scale, Hamilton Depression Rating Scale, Hamilton Anxiety Scale, and State-Trait Anxiety Scale I and II, were used to assess the areas involved and the severity of PTSD symptoms. Results: The patient group showed significant impairments in continuous attention, visual and auditory information processing time on the Vienna test when compared to the control group. The patient group also showed significant impairments in verbal memory, visual memory, and visuospatial function on the Rey-Kim Memory Test.
Conclusions: In this study, the author reports cognitive impairments in patients with PTSD measured by computerized neurocognitive tests and memory tests. Future studies are needed to determine the changes in cognitive functioning that are related to symptom improvement as well as the influence of therapeutic effects on cognitive improvement.

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1) Wolfe J, Charney DS. Use of neuropsychological assessment in post-traumatic stress disorder. Psychol Assess 1991;3:573-580.

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» NR4-005

DRIVING SAFETY IN YOUNG ADULTS DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) WITH AND WITHOUT LONG ACTING TRANSDERMAL METHYPHENIDATE

Daniel Cox Ph.D., Roger C. Burket, M.D., Margaret T. Davis, B.A., Atainyene Ibia, Amori Yee Mikami, Ph.D., Michelle Frieben, M.D., Mayin Wong, M.D., Elizabeth Gillespie, M.D., Richard Lawrence Merkel,M.D.,Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: 1) Identify adolescents with ADHD as an extremely high risk group in terms of driving safety; 2) Recognize that studies in the laboratory, and now in a real world setting have indicated that long acting stimulants may work to mitigate risk for this group; 3) Use this understanding in clinical practice and research to enhance the safety of ADHD drivers and by extension everyone on the road.

SUMMARY:

The core symptoms of ADHD: inattention, impulsivity and hyperactivity, could interfere with safe operations of a motor vehicle. In fact, adolescents with ADHD have 4 X more at-fault collisions, receive 3 X more citations and are 8 X more likely to lose their license due to multiple violations. Recent evidence suggests that, at least for males with ADHD, collision rates rise from adolescents to young adults and rise even further into middle age. While long acting oral methylphenidate has been demonstrated to improve driving safety of adolescents with ADHD in laboratory studies, we present the first evidence that long acting transdermal methylphenidate significantly reduces driving collisions during routine driving. Eighteen methylphenidate-responsive ADHD young adults (18-25 years, 4 females, 3 African American) were recruited if: they were no longer taking ADHD medication, did not have significant co-morbidity, and were active drivers with at least 2 driving mishaps (collisions +/- citations) in the previous two years. Employing a randomized cross-over, open-label design, subjects were monitored with in-car audio-video recoding for 6 months (3 months on and 3 months off medication). Medication was titrated to optimal dose, and adherence was monitored with a computerized medication dispenser. With 90% of the data collection being complete, we have documented six collisions (3 collisions while using a cell phone and one car reported unrepairable). All collisions occurred on days subjects did not take medication (Z=2.45, p=.01). Coding of audio-video data continues and will be available at the time of presentation. These data suggest that there may be real-world benefits of long-acting transdermal methylphenidate routine usage among young adult drivers.

REFERENCES:

1) Cox DJ, Merkel RL, Moore M, Thorndike F, Muller C, Kovatchev B: Relative benefits of OROS® MPH vs. se-AMPH ER in improving driving performance of ADHD adolescent drivers . Pediatrics [serial online] 2006;118(9):e704-e710.

2) Fischer M, Barkley RA, Smallish L, Fletcher K: Hyperactive children as young adults: driving abilities, safe driving behavior, and adverse driving outcomes. Accid Anal Prev 2007;39:94-105.

» NR4-006

EVALUATING CHILDHOOD EXPERIENCES AS POTENTIAL RISK FOR ADULT ANXIETY DISORDERS: PD, GAD, AND GSP

Marilla Geraci M.S.N., David Luckenbaugh MA, Karina Blair PhD , Daniel Bradford BS, Meena Vythilingam MD, Shmuel Lissek PhD, Christian Grillon PhD, James Blair PhD, Daniel Pine, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the potential benefit of retrospective assessment of childhood experiences in adults with anxiety disorders to increase understanding of anxiety disorders.

SUMMARY:

Background: Information about potential disorder specific candidate genes in depression and anxiety and possible gene-environment interactions provide renewed interest in early life experiences as risk factors for adult anxiety disorders. We examined the impact of early life experiences across 3 anxiety disorders.

Methods: Adult patients diagnosed with a primary anxiety disorder [49 panic disorder (PD), 56 generalized social phobia (GSP), 37 generalized anxiety disorder (GAD)] and 51 healthy comparison subjects were interviewed about adverse experiences that occurred before age 18. Experiences assessed included: abuse (physical, sexual, home violence), death (parent/sibling), parental substance abuse (ETOH, other substances) and LEC (events endorsed on a PTSD life events checklist were reviewed for events occurring prior to age 18), which served as a control for varied events.

Results: Chi-square tests showed significantly more abuse related events ($p<.001$) and parental substance abuse ($p<.001$) across all 3 anxiety groups compared to healthy subjects. There were no significant differences in death events ($p=.49$) or LEC events ($p=.60$) across all 4 groups. When the effect of lifetime major depression (MDD) was included in a multinomial logistic regression model, abuse related events remained a significant independent predictor of PD ($p=.005$) and GAD ($p=.01$), not GSP ($p=.058$). The same was true for substance abuse with PD ($p=.007$) and GAD ($p=.02$), not GSP ($p=.30$). However, when placing abuse, substance abuse and MDD in a single model, abuse remained a significant independent predictor of PD ($p=.03$, OR=12.0) and GAD ($p=.04$, OR=9.8), but substance abuse did not (PD: $p=.11$, OR=4.1; GAD: $p=.14$, OR=3.8).

Summary: We found abuse before age 18 was the strongest risk factor for anxiety disorders in adulthood, raising the risk 12 fold.

REFERENCES:

1) Relationship of childhood sexual and physical abuse to anxiety disorders. Mancini C, Van Ameringen M, Macmillan H: J Nerv Ment. Dis. 1995 May; 183(5):304-14.

2) Gene-environment interactions in depression research. Monroe SM,Reid MW. Psychological Science: 2008; 19(10) 947-56.

» NR4-007

A COMPARISON OF OBSESSIVE COMPULSIVE DISORDER AND PATHOLOGICAL SKIN PICKING: CLINICAL CHARACTERISTICS AND DISEASE SEVERITY

Jon Grant M.D., Brian L. Odlaug, B.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to (1) understand the significant clinical differences between OCD and PSP; and (2) consider possible treatment implications based on these differences/similarities.

SUMMARY:

Introduction: Pathological skin picking (PSP) and obsessive-compulsive disorder (OCD) are associated with significant psychosocial dysfunction and have lifetime prevalence rates of approximately 2-4% and 1-3%, respectively. PSP may share biological and phenomenological characteristics of OCD, but limited information is available regarding the clinical similarities and differences between the two disorders.

Methods: Demographic and clinical characteristic information was reviewed in a treatment-seeking sample of 104 subjects diagnosed with either PSP or OCD. Subjects included in the sample were either participants of pharmacotherapy studies or outpatients of a large Midwestern University psychiatry clinic. Severity of illness was determined by the Yale-Brown Obsessive-Compulsive Scale (YBOCS) for both groups, using a modified version for PSP.

Results: A total of 53 subjects with pathological skin picking (mean age 34.2 (±13.1); 86.8% female) and 51 subjects with obsessive compulsive disorder (mean age 36.5 (±11.7; 35.3% female) were included in this sample. Subjects with PSP were more likely to have a longer lag time between disease onset and diagnosis (mean 19.0 years; $p=.021$), have higher rates of a co-occurring grooming disorder (64.2%), and have a first-degree relative with a grooming disorder (53.8%; $p<.001$). OCD was associated with significantly higher rates of body dysmorphic disorder (17.6%), past psychiatric hospitalizations (21.6%), being unemployed or on disability due to the condition (17.6%), and having a first-degree relative with OCD (35.3%; $p=.002$). High rates of lifetime psychiatric comorbidity were noted in the PSP (77.4%) and OCD (68.6%) groups overall.

Discussion: To our knowledge, this is the first clinical comparison of PSP and OCD in a treatment-seeking sample. Our results indicate that PSP goes largely unrecognized and is associated with being female and having a family history of grooming disorders while OCD causes significantly more time spent engaging in the behavior.

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2) Arzeno Ferrão Y, Almeida VP, Bedin NR, Rosa R, D'Arrigo Busnello E: Impulsivity and compulsivity in patients with trichotillomania or skin picking compared with patients with obsessive-compulsive disorder. Compr Psychiatry 2006 Jul-Aug; 47(4):282-288.

» NR4-008

QUETIAPINE MONOTHERAPY IN CHRONIC POSTTRAUMATIC STRESS DISORDER: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Mark Hamner M.D., Jose Canive, M.D., Sophie Robert Pharm.D., Gerardo Villareal, M.D., Valerie Durkalski, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to To review mainstay treatments for PTSD,review literature regarding atypical antipsychotics in this population, and discuss the results of this controlled trial of quetiapine in PTSD.

SUMMARY:

Background: Psychotherapy and antidepressants are mainstay treatments for PTSD. Atypical antipsychotics also may be effective in reducing symptoms of PTSD in patients who are refractory to other treatments.

This study investigated the efficacy of monotherapy with quetiapine, an atypical antipsychotic, in patients with chronic PTSD.

Method: A double-blind, randomized, placebo-controlled trial was conducted. There was a one week placebo phase followed by a twelve week randomized phase. Eighty patients entered the study and 77 had as least one efficacy assessment. The primary outcome measure was the Clinician-Administered PTSD Scale (CAPS). A number of secondary rating instruments were also administered including the Positive and Negative Symptom Scale (PANSS), Clinical Global Impressions -Severity of Illness Scale (CGI-S), the CGI-Improvement Scale (CGI-I), the Hamilton Rating Scale for Depression (HRSD), the Hamilton rating Scale for Anxiety (HRSA) and other psychosocial and safety measures. Results: There was significant (threefold) decline in CAPS composite scores in quetiapine-treated patients as compared with placebo (intent-to-treat analysis, last observation carried forward, $p=0.0070$, 2-tailed) and on re-experiencing ($p=0.0019$) and hyperarousal symptom ($p=0.030$) subscales but not on the avoidance subscale ($p=0.56$). Greater improvement was observed in the

CGI-S (p=0.0030), the CGI-I (p=0.030) and the PANSS composite scores (p=0.0135). The HRSA (p= 0.020) and HDRS (p=0.0093) also declined versus placebo. The average dose of quetiapine was 258 mg daily (range: 50 to 800 mg daily).
Conclusion: These results suggest that quetiapine monotherapy is efficacious in the treatment of PTSD. Larger controlled trials are needed to better define the role of quetiapine and other atypical antipsychotics alone or as adjuncts in treating patients suffering from PTSD.

REFERENCES:

1) Hamner MB, Deitsch SE, Brodrick PS, Ulmer HG, Lorberbaum JP: Quetiapine treatment in patients with posttraumatic stress disorder: an open trial of adjunctive therapy. J Clin Psychopharmacology 2003: 23(1): 15-20.

2) Hamner MB, Robert S: Emerging roles for atypical antipsychotics in chronic posttraumatic stress disorder. Expert Rev Neurotherapeutics 2005: 5(2):267-75.

» NR4-009

COMPARISON OF SLEEP OUTCOMES IN GENERALIZED ANXIETY DISORDER FOLLOWING TREATMENT WITH PREGABALIN OR VENLAFAXINE-XR

Ashish Joshi Ph.D., Francine S. Mandel,Ph.D., Edward Schweizer, M.D., Barry Herman, M.D., M.M.M.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the types of sleep disturbances that occur in GAD, and understand the differential effects of 2 classes of medications on anxiety-related sleep disturbances.

SUMMARY:

Objectives: To evaluate the impact of pregabalin and venlafaxine-XR on sleep outcomes in non-depressed outpatients with generalized anxiety disorder (GAD).
Methods: This is an a priori secondary analysis of data from an 8-week, double-blind, randomized, flexible-dose, placebo-controlled study in DSM-IV GAD with a baseline HAM-A>20. Patients (N=374) received pregabalin (300-600mg/day), venlafaxine-XR (75-225mg/day) or placebo. Sleep was evaluated using the Medical Outcomes Study (MOS) Sleep Scale (sleep factors and sleep-problem index). Outcomes were compared between the 3 study-drug groups at weeks 4, 8, and endpoint using ANCOVA.
Results: Based on a Sleep Problems Index score <45, 64% of patients at baseline met normative community criteria for insomnia (Hays et al, 2005). Treatment with pregabalin was associated with significantly greater endpoint improvement on the sleep disturbance score compared to placebo (-22.2 vs. -12.0; P<0.001), while venlafaxine-XR did not (-11.6). Treatment with pregabalin was associated with numerically greater (non-significant) improvement in MOS-daytime sleepiness compared to both venlafaxine-XR and placebo (-9.7 vs. -5.8 and -6.6). In contrast, somnolence as a treatment-emergent adverse event occurred more frequently on pregabalin (9.1%) compared to venlafaxine-XR (4.8%) and placebo (2.3%). Treatment with pregabalin was associated with a significant reduction vs. placebo in other MOS sleep factors, as well as the MOS sleep problems index (-18.1 vs. -10.5; P<0.01); however improvement on venlafaxine-XR was not significantly different from placebo (-10.1 vs. -10.5).
Conclusions: Treatment with pregabalin was associated with significant improvement in most MOS sleep outcomes. The improvement in daytime sleepiness on pregabalin suggests that improvement in nighttime sleep disturbance, and reduction in anxiety, outweigh the transient sedating effects associated, in some patients, with initial treatment with pregabalin.
Funded by Pfizer Inc.

REFERENCES:

1) Hays RD, Martin SA, Sesti AM, Spritzer KL. Psychometric properties of the Medical Outcomes Study Sleep measure. Sleep Med. 2005;6:41-4.

2) Wittchen HU, Kessler RC, Beesdo K, Krause P, Höfler M, Hoyer J. Generalized anxiety and depression in primary care: prevalence, recognition, and management. J Clin Psychiatry. 2002;63 Suppl 8:24-34.

» NR4-010

RANDOMIZED TRIAL OF A MULTI-FAITH SPIRITUAL INTERVENTION FOR GENERALIZED ANXIETY DISORDER: A PILOT STUDY

Diana Koszycki Ph.D., Kelley Raab, Ph.D., Fahad Aldosary, M.D., Jacques Bradwejn, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the clinical utility of spiritually-focused psychotherapies
Summary:

Objective: With growing public interest in spirituality many patients are requesting spiritually-integrated care from mental health professionals. The present study evaluated the acceptability and efficacy of a spiritually-based intervention (SBI) for generalized anxiety disorder (GAD) and compared its efficacy to a first-line psychological intervention.
Method: Patients meeting DSM-IV criteria for GAD of at least moderate severity (Hamilton Anxiety Rating Scale (HAM-A) score =18) were randomized to either 12 weeks of the SBI delivered by a spiritual care counselor or 12 weeks of psychologist-administered cognitive behavior therapy (CBT). The spiritual intervention was multi-faith and focused on core spiritual principles found in many religious traditions rather than on the teachings of a specific denomination or faith group. Thus, the intervention was suitable for individuals from diverse religious and spiritual pathways. Primary efficacy measures included the HAM-A total score, Penn State Worry Questionnaire, and Beck Anxiety Inventory. Data analysis was performed on the intent-to-treat sample using the Last Observation Carried Forward method.
Results: A total of 50 participants (30 women, 20 men) were evaluated for the study. Of these 22 were randomized to the SBI (n=11) or CBT (n=11). The majority of patients (82%) completed acute treatment (n=9 SBI and n=9 CBT). Repeated measures ANOVA revealed that both treatments produced robust and clinically significant reductions in self- and clinician-rated primary efficacy measures (Time main effects ps <0.001). There was no significant Time x Treatment interactions. The percentage of patients who were rated as very much or much improved on the Clinician Global Impression-Improvement scale were 72.3% for the SBI and 72.3% for CBT. Treatment gains were maintained at the 3 month follow-up visit.
Conclusion. This pilot study indicates that a multi-faith SBI is as effective as CBT in improving core symptoms of GAD While these findings are preliminary and require replication in a larger trial the study provides additional support that promoting spiritual growth and well-being has therapeutic benefit.

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2) Pargament KI. Spiritually integrated psychotherapy: Understanding and addressing the sacred. The Guildford Press, New York, N.Y. 2007.

» NR4-011

EFFICACY OF EXTENDED RELEASE QUETIAPINE FUMARATE: POOLED ANALYSIS IN PATIENTS WITH SEVERE GENERALIZED ANXIETY DISORDER

Julie Locklear Pharm.D., Stuart A. Montgomery, M.D., Henrik Svedsäter, Ph.D., Hans Eriksson, M.D., Ph.D., M.B.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize the impact of generalized anxiety disorder, and

be able to describe the efficacy of once-daily quetiapine XR in patients with severe generalized anxiety disorder.

SUMMARY:

GAD is a highly prevalent disorder; patients (pts) experience impaired functioning1,2 that increases with symptom severity. Once-daily quetiapine XR (QTP XR) showed efficacy in 3 GAD trials; this pooled analysis evaluated efficacy in pts with severe GAD. Three previously reported positive 8-wk, randomized, placebo (PBO)-controlled studies (D1448C00009; D1448C00010; D1448C00011) evaluated efficacy of QTP XR monotherapy (50, 150, 300mg/day) in pts with GAD (HAM-A total score >=20). In this subanalysis, pts were stratified by baseline (BL) HAM-A total score (>=26 and >=28), based on mean HAM-A total score at BL (25.80, 25.70, 25.40, 24.80 in the QTP XR 50, 150, 300mg/day, and PBO groups). We report differences vs PBO (95%CI) in least squares means (LSM) change in HAM-A total score from randomization to Wk 1 and 8 (primary endpoint) (LOCF) using ANCOVA with HAM-A at BL as a covariate.

QTP XR 50, 150, and 300 mg/day significantly improved HAM-A total scores vs PBO at each timepoint in all-pt, HAM-A >=26 and >=28 groups (except QTP XR 300mg/day at Wk 8 in HAM-A >=28 group).

At Wk 1, LSM (95%CI) HAM-A total scores vs PBO in the QTP XR 50, 150, and 300mg/day groups were: -2.10 (-2.76,-1.43), -2.80 (-3.37,-2.24), and -1.80 (-2.47,-1.13) in all pts (n=2113); -2.43 (-3.48,-1.37), -3.37 (-4.30,-2.44), and -2.62 (-3.81,-1.44) in the HAM-A >=26 group (n=921); and -3.00 (-4.39,-1.61), -3.84 (-5.08,-2.60), and -3.57 (-5.17,-1.97) in the HAM-A >=28 group (n=567).

At Wk 8, LSM (95%CI) HAM-A total scores vs PBO in the QTP XR 50, 150, and 300mg/day groups were: -2.01 (-2.93,-1.10), -3.10 (-3.90,-2.31), and -1.22 (-2.15,-0.29) in all pts (n=2171); -3.16 (-4.65,-1.68), -4.57 (-5.89,-3.25), and -1.86 (-3.52,-0.20) in the HAM-A >=26 group (n=945); and -4.77 (-6.70,-2.83), -5.11 (-6.84,-3.37), and -1.75 (-3.97,0.47) in the HAM-A >=28 group (n=583).

QTP XR (50-300mg/day) significantly improves anxiety symptoms vs PBO in pts with severe GAD as early as Wk 1.

Funded by AstraZeneca Pharmaceuticals

REFERENCES:

1) Henning ER, Turk CL, Mennin DS, Fresco DM, Heimberg RG: Impairment and quality of life in individuals with generalized anxiety disorder. Depress Anxiety 2007; 24:342-349

2) Grant BF, Hasin DS, Stinson FS, Dawson DA, June RW, Goldstein RB, Smith SM, Saha TD, Huang B: Prevalence, correlates, co-morbidity, and comparative disability of DSM-IV generalized anxiety disorder in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychol Med 2005; 35(12):1747-1759

» NR4-012 - WITHDRAWN

» NR4-013

SUBJECTIVE PERCEPTIONS OF OCD

Catherine Mancini M.D., Michael Van Ameringen, M.D., F.R.C.P.C., William Simpson, B.Sc., Beth Patterson, B.ScN., B.Ed.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: 1. become familiar with the ways OCD is perceived by those afflicted by it. 2. become aware of OCD patients' perceptions of their treatment.

SUMMARY:

BACKGROUND: Although much is known about the characteristics of Obsessive Compulsive Disorder (OCD), little is known about the perceptions of those afflicted by this condition. As part of a naturalistic study of OCD, sponsored by the International College for Obsessive Compulsive Spectrum, we collected data concerning patient's perceptions of their OCD.

METHOD: Sixty-five consecutive patients with OCD, at various stages of treatment in a tertiary care anxiety disorders clinic were evaluated. Patients completed a number of self-report measures as well as a detailed clinical and structured interview. Results from the self-report measures regarding patients' views about their OCD and their treatment will be presented.

RESULTS: The mean age of participants was 37.7 years (± 13.5), 73.8% of the sample was female, and the mean Yale-Brown Obsessive Compulsive Scale score was 19.7 (± 6.5), indicating overall a moderate level of severity. The majority of the sample (=80%) see their OCD as permanent and expect to have it for the rest of their life, having major consequences on their life, and causing difficulties for those close to them. Over half feel they have power to influence their OCD, see treatment as controlling their OCD and that it affects the way others see them. Medication, as compared to exposure strategies were felt to be at least moderately effective in 72% vs 61% respectively.

Conclusion: OCD is perceived as a chronic condition with significant impact on afflicted individuals. Treatments are seen as at least moderately effective in controlling symptoms in most sufferers.

REFERENCES:

1) Masellis M, Rector NA, Richter MA: Quality of life in OCD: differential impact of obsessions, compulsions, and depression comorbidity. Can J Psychiatry 2003; 48(2):72-77

2) Besiroglu L, Cilli AS, Askiu R: The predictors of health care seeking behavior in obsessive-compulsive disorder. Compr Psychiatry 2004; 45(2):99-108

» NR4-014

EFFICACY AND TOLERABILITY OF EXTENDED RELEASE QUETIAPINE FUMARATE IN THE TREATMENT OF GENERALIZED ANXIETY DISORDER (GAD): AN ANALYSIS OF POOLED DATA

Charles Merideth, Borwin Bandelow M.D., Dan Stein M.D., Ph.D., Bengt Olausson M.D., Ph.D., Johan Szamosi M.Sc., Hans Eriksson, M.D., Ph.D., M.B.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to demonstrate a knowledge and understanding of the efficacy across patient subgroups and tolerability of once-daily quetiapine XR as monotherapy in the treatment of patients with GAD as demonstrated by the analysis of pooled data from three double-blind, placebo-controlled studies.

SUMMARY:

Objectives: GAD is a highly prevalent condition (1) and one of the most common anxiety disorders seen in primary care (2). This prospectively planned pooled analysis evaluated the efficacy and tolerability of once-daily extended release quetiapine fumarate (QTP XR) monotherapy in patients with GAD.

Methods: Data were analyzed from three previously-reported, positive, 10-week (8-week treatment; 2-week drug-discontinuation/tapering phase), double-blind, randomized, placebo (PBO)-controlled studies (D1448C00009, D1448C00010, D1448C00011). Patients received QTP XR 50mg/day (n=455), 150mg/day (n=678), 300mg/day (n=448), or PBO (n=667). Primary endpoint: Week 8 change in HAM-A total score. Other assessments: HAM-A total score by subgroup (including gender, age, disease severity), HAM-A response (>=50% total score reduction), HAM-A remission (total score <=7); AE reporting.

Results: QTP XR 50, 150, and 300mg/day significantly reduced HAM-A total scores at Week 8 (-13.3, $p<0.001$; -14.4, $p<0.001$; -12.5, $p<0.05$, respectively) vs PBO (-11.3); significant ($p<0.001$) reductions were also seen at Week 1 for all doses.

Improvement in HAM-A total scores across patient subgroups was consistent with the general pattern of results for QTP XR in the overall study population.

Response rates at Week 1 were 17.9% (p<0.001; QTP XR 50mg/day), 21.7% (p<0.001; QTP XR 150mg/day), 21.4% (p<0.01; QTP XR 300mg/day) vs 12.5% (PBO); response rates at Week 8 were 61.4% (p<0.01), 65.0% (p<0.001), 53.9% (p=0.062) vs 49.7%, respectively.
Remission rates at Week 8 were: 34.2% (p<0.05) QTP XR 50mg/day; 39.0% (p<0.001) 150mg/day; 28.5% (p=0.722) 300mg/day vs 27.4% (PBO).
AEs (>=10% for QTP XR) were dry mouth, somnolence, sedation, dizziness, nausea, constipation, headache, and fatigue.
Conclusions: In patients with GAD, QTP XR monotherapy is effective at 50, 150, and 300mg/day across patient subgroups, and AEs were consistent with the known tolerability profile of quetiapine. Funded by AstraZeneca Pharmaceuticals

REFERENCES:

1) Gale C, Davidson O: Generalised anxiety disorder. BMJ 2007; 334(7593):579-581

2) Tonks A: Treating generalised anxiety disorder. BMJ 2003; 326(7391):700-702

» NR4-015

ADJUNCTIVE PREGABALIN TREATMENT AFTER PARTIAL RESPONSE IN GENERALIZED ANXIETY DISORDER (GAD): RESULTS OF A DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Jeffrey Miceli Ph.D., Tanya Ramey, M.D.,Ph.D., Jerry Weaver, M.S., Jeffrey Gleit, B.S., Lloyd Knapp, Pharm.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant will better understand the results from a well-controlled trial involving adjunct pregabalin treatment to patients who have only partially responded to antidepressant therapy.

SUMMARY:

Objective: To investigate the efficacy and safety of adjunctive pregabalin in patients with GAD who had not optimally responded to two previous courses of adequate treatment.
Method: Patients with a primary diagnosis of GAD who did not respond to a course of SSRI/SNRI or benzodiazepine (HAM-A >22 at screen), and had only a partial response with a different SSRI/SNRI (ie, HAM-A >16, <50% decrease in HAM-A, and CGI-I<3) after 8 weeks of prospective open-label treatment, were randomized to 8 weeks of combination treatment with either pregabalin (150-600 mg/day) or placebo in addition to continuation of the existing SSRI/SNRI. The primary endpoint was the HAM-A change score averaged up to 8 weeks of double-blind treatment.
Results: A total of 353 patients met inclusion criteria and were randomized and treated with adjunctive pregabalin (N=177; mean baseline HAM-A, 20.7) or placebo (N=176; mean baseline HAM-A, 21.4). For the primary analysis, the mean (SE) change in HAM-A was significantly greater for pregabalin compared to placebo (-7.74 (0.38) vs. 6.55 (0.38); difference score, -1.19 [adjusted 95%CI: -2.14 to 0.24]; P<0.05). At Week 8, HAM-A responder rates (>50% reduction) were significantly higher on adjunctive pregabalin compared to placebo (50% vs. 37%; P=0.023). Treatment with pregabalin was associated with a significantly earlier time-to-sustained response compared to placebo (log-rank P=0.014). Adjunctive treatment with pregabalin was well tolerated relative to placebo, with the most common adverse events being dizziness (11.7% vs. 5.7%), headache (9.4% vs. 4.0%), and somnolence (7.2% vs. 3.4%). Discontinuations due to AEs were 4.4% for pregabalin and 1.7% for placebo.
Conclusions: The results indicate that adding pregabalin is a safe and efficacious treatment strategy in patients whose GAD is treatment-refractory to SSRI/SNRI monotherapy.
Funded by Pfizer Inc

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» NR4-016

A NEW TRAUMA FOCUSED PSYCHOTHERAPY FOR POST TRAUMATIC STRESS DISORDER

Nick Miller, M.D., Fabien Jeker MSc., Corneliu Feroiu, M.D., M.D., Eric Adam, MSc., Coralie Lazignac, M.D., Cristian Damsa, M. D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know the actual psychological and pharmacological expert recommendations for PTSD treatment.

SUMMARY:

Objective: Posttraumatic stress disorder (PTSD) is a common, prevalent and disabling condition. The aim of this work is to review the most recent expert recommendations for the treatment for PTSD including psychotherapy and pharmacotherapy, starting from a preliminary observational study.
Method: This is a 12 weeks open label study performed in a private psychotherapeutic center in Switzerland. We include 20 patients with severe PTSD during one year, after a screening of 400 patients. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) formed the basis for diagnostic evaluations carried out by a psychiatrist not otherwise engaged in the study. Psychiatric diagnoses, including PTSD, were established according to the DSM-IV criteria. Full PTSD diagnosis was pre-defined as the primary outcome variable and the CAPS – Clinician-Administered PTSD Scale scores as a secondary variable [1].
All patients benefited of a specific trauma-focused psychotherapy, called “Trauma and Reintegration Psychotherapy, TRP”. This is a combined psychodynamic eclectic treatment combining Ericksonian Hypnosis and EMDR techniques.
Results: The results suggest a more promising outcome (PTSD remission, CAPS scores) for patients beneficiating of the TRP than the patients of others clinical studies, inventoried by a recent meta-analysis [2], p<0.05. The drop out was of 15%. The most recent expert recommendations for the treatment for PTSD are presented focusing on the specificity of care in a private psychotherapeutic center.
Discussion: Those data suggest the interest of this new type of trauma-focused psychotherapy, even if further larger studies with a randomized design are required to confirm these preliminary results. The interest of a good knowledge of the expert recommendations in the treatment of PTSD by the psychiatrists working in private practice is emphasized.

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» NR4-017

TENSION IN GENERALIZED ANXIETY DISORDER: A RELATIVELY NEGLECTED TREATMENT TARGET

Dan Stein M.D., Francine S. Mandel, Ph.D., Piotr Szczypa, M.D., M.Sc., Edward Schwiezer, M.D., Barry Herman, M.D., M.M.M.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the contribution of psychic and somatic forms of ten-

sion to the clinical presentation of GAD, and should have a better understanding of the potential efficacy of pregabalin and benzodiazepines in treating tension as a component symptom in GAD.

SUMMARY:
Background: Tension is a DSM-IV criterion for GAD, and is rated on the HAM-A scale by a Psychic Tension item (PT; tension, inability to relax, fatigability, etc) and a Somatic-Muscular Tension item (SMT; increased muscle tone, pains and aches; stiffness, teeth grinding, etc). The goal of this exploratory analysis was to evaluate the efficacy of pregabalin and benzodiazepines in treating tension.
Methods: Data were pooled from 6 double-blind, placebo-controlled, 4-6 week trials of outpatients with DSM-IV GAD with a HAM-A total score >18. Treatment response was analyzed for three fixed-dosage groups of pregabalin, 150 mg/d (N=210; baseline HAM-A, 24.4), 300-450 mg/d (N=455; HAM-A, 25.4), and 600 mg/d (N=406; HAM-A, 25.1); a combined alprazolam and lorazepam treatment group (N=299; HAM-A, 24.4); and placebo (N=484; HAM-A, 25.0).
Results: At baseline, the proportion of patients rating PT as severe (84.7% rating a 3 of 4; max=4) was higher than for SMT (25.9%). PT was significanlty correlated with anxious mood (r=0.47; P<0.05; HAM-A item 1), the intellectual item (r=0.15; ANCOVA, P<0.05), and the SMT item (r=0.16; P<0.05). SMT was also significantly correlated with the somatic-sensory item (r=0.15; P<0.05) and the autonomic item (r=0.15; P<0.05). There was a very weak correlation between SMT and gender (r=0.11; P<0.05; more common in women). Endpoint improvement in PT and SMT, respectively, was significantly greater than placebo (-0.89; -0.78) on pregabalin 300-450 mg (-1.27 [P<0.0001]; -1.00 [P=0.0084]), 600 mg (-1.26 [P<0.0001]; -1.00 [P=0.0066]); alprazolam/lorazepam (-1.20 [P<0.001]; -0.98 [P=0.0481]); and pregabalin 150 mg, but only on the PT item (-1.16 [P=0.022]).
Conclusions: Pregabalin was effective in treating both psychic and somatic-muscular forms of tension. The improvement on somatic-muscular symptoms was comparable to the benzodiazepines, suggesting that it would be of interest to test the muscle relaxing properties of pregabalin. Funded by Pfizer Inc

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» NR4-018 - WITHDRAWN

» NR4-019

EFFECTS OF EXTENDED RELEASE QUETIAPINE FUMARATE (QUETIAPINE XR) ON PATIENT-REPORTED OUTCOMES IN PATIENTS WITH GENERALIZED ANXIETY DISORDER

Henrik Svedsäter Ph.D., Julie Locklear, Pharm.D., M.B.A., Jean Endicott, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be able to understand the prevalence of GAD, and gain knowledge of the effects of quetiapine XR on quality of life and functioning in patients with GAD.

SUMMARY:
GAD is a chronic, disabling disorder,1 with patients (pts) experiencing impaired functioning and quality of life (QoL).2 This analysis evaluated effects of once-daily quetiapine XR (QTP XR) on pt-reported outcomes in pts with GAD.
This was a pre-planned analysis of pooled data from 3 acute 8-wk, randomized, placebo (PBO)-controlled studies (D1448C00009;D1448C00010;D1448C00011) and an analysis of a 52-wk maintenance study (D1448C00012) of QTP XR monotherapy (50, 150, and 300mg/day) in pts with GAD. The analysis of HAM-A total scores and Q-LES-Q (short form [SF]) % maximum total scores in acute studies are reported. Changes in SDS total score and PSQI global score in maintenance treatment are reported. For all variables, least squares means (LSM) changes from randomization to end of treatment were analyzed using ANCOVA with baseline measurement as a covariate (p<0.05 denoted statistical significance).
In acute studies, 455, 678, 448, and 667 pts were randomized to QTP XR 50, 150, 300mg/day, and PBO, respectively. Pooled LSM changes in HAM-A total scores at Wk 8 were -13.3 (p<0.001), -14.4 (p<0.001), and -12.5 (p<0.05) for QTP XR 50, 150, and 300mg/day, respectively vs PBO (-11.3). At Wk 8, pooled LSM increases in Q-LES-Q-SF % maximum total score were 9.5, 11.9 (p<0.001 vs PBO), 8.2, and 8.8 in the QTP XR 50, 150, 300mg/day and PBO groups, respectively.
In the maintenance study, 216 pts continued on QTP XR (50, 150, or 300mg/day) and 216 patients were switched to PBO. LSM changes in SDS total scores were -0.2, and 1.0 in the QTP XR and PBO groups, respectively (p<0.05 vs PBO). LSM changes in PSQI global score were 1.6 and 0.4 in the QTP XR and PBO groups, respectively (p<0.001 vs PBO).
QTP XR 50-300mg/day improves symptoms of anxiety and is associated with maintaining long-term functioning and sleep quality in patients with GAD. QTP XR 150mg/day improved QoL. Overall tolerability and safety were consistent with the known profile of QTP. Funded by AstraZeneca Pharmaceuticals

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» NR4-020 - WITHDRAWN

» NR4-021

A PILOT STUDY OF THE POTENTIAL USE OF INTERNET-BASED SCREENING FOR ANXIETY DISORDERS

Michael Van Ameringen M.D., Catherine Mancini, M.D., F.R.C.P.C., William Simpson, B.Sc., Beth Patterson, B.ScN., B.Ed.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to: 1. become familiar with the potential role of the internet in seeking health information in anxiety disorders. 2. become aware that many people who are seeking this information have clinically significant anxiety disorders that would warrant professional assessment and treatment.

SUMMARY:
Background: The internet is a widely used resource for obtaining health information. Internet-users are able to obtain anonymous information on diagnoses and treatment, seek confirmatory information and are able to self-diagnose. We posted a self-report diagnostic screening questionnaire for DSM-IV anxiety and mood disorders (MACSCREEN) on our clinic website.
METHOD: Fifty-five individuals completed the MACSREEN. For those who qualified for a DSM-IV disorder, self-report symptom severity measures were completed for the specified disorder: Quick Inventory of Depressive Symptomatology, self-report (QUIDS-SR), Social Phobia Inventory (SPIN), GAD-7 (GAD), Davidson Trauma Scale (DTS), panic and agoraphobia scale (PAS) and Yale-Brown Obsessive Compulsive Scale-self-report (Y-

BOCS-SR). Cut-off scores for each self-report measure were used to evaluate clinically significant symptom severity.
RESULTS: Thirty met criteria for social phobia on the MAC-SCREEN, 25 (83.4%) had clinically significant scores on the SPIN; 10 met criteria for panic disorder with agoraphobia and 9 (90%) had clinically significant scores on the PAS; 26 met criteria for GAD and 25 (96.2%) had clinically significant scores on the GAD-7; 18 met criteria for OCD, 7 (38.9%) had clinically significant scores on the Y-BOCS-SR; 33 met criteria for depression and 6 (18.2%) had clinically significant scores on the QUIDS-SR; 5 met criteria for PTSD, 4 (80%) had clinically significant scores on the DTS.
CONCLUSION: Individuals with clinically significant disorder appear to be using the internet to self-diagnose. Further information as to how people will use this information and how self-diagnosis relates to treatment seeking will be presented. Data collection is ongoing.

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» NR4-022

EEG ASYMMETRY IN INFANTS OF MOTHERS WITH SOCIAL PHOBIA

Susan L. Warren, M.D., Kirsten VanMeenen, Ph.D., Jill Settle, B.A., Samuel J. Simmens, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant will have an understanding of research concerning electroencephalographic (EEG) asymmetry and will understand the results of the present study focused on infants of mothers with social phobia.

SUMMARY:

Background/Objective: Numerous studies suggest that positive and negative emotions are associated with different patterns of cerebral hemisphere activation and that specific patterns of electroencephalographic (EEG) asymmetry may indicate risk for depression and anxiety. Some research has examined patterns of EEG asymmetry in the offspring of depressed mothers and has reported associations between frontal EEG asymmetry and depression. Other research has found frontal and parietal asymmetry in adults with anxiety disorders. This study is unique in that it examines EEG asymmetries in infants of mothers with current social phobia. Method: In prescreening, infants with medical problems or a history of abuse or trauma and mothers with major psychopathology, other than anxiety disorders, were excluded. EEG measures of alpha power (4-6 Hz) in the right and left hemisphere were recorded in 180 infants (four to eight months of age) from frontal and parietal sites during a baseline period of approximately three minutes and during another similar period except for the addition of brief bursts of white noise, designed to elicit the startle reflex. The EEG was edited to remove artifact from eye blinks and movement. Mothers were diagnosed with the Structured Clinical Interview for DSM-IV Axis I Disorders. Results: Infants of mothers with current social phobia (N=51) were significantly more likely than the other infants to show increased right parietal activation during the startle burst period. No significant differences were found for the baseline period. Current maternal depression did not account for the findings. Discussion: The research is consistent with findings in adults that show increased right parietal activation in the context of anxious arousal, and suggests that increased right parietal activation in the context of anxious arousal could be an early marker for children at risk.

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» NR4-023

SUBTHERAPEUTIC DOSING AND ADHERENCE IN THE USE OF ANTIDEPRESSANT MEDICATIONS IN THE TREATMENT OF DEPRESSION OR ANXIETY

Stephen Able Ph.D., Stacey Bledsoe, M.S.N.; Steven Gelwicks, M.S.; Peter Watson, M.S.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should understand that initiation of antidepressant therapy at subtherapeutic dosing levels is associated with more frequent early discontinuation of antidepressant therapy and fewer days on therapy.

SUMMARY:

OBJECTIVE: Physician decisions regarding initial antidepressant dosing levels may impact treatment outcomes (1,2). This study examined initial dosing levels and their associations with adherence among selective serotonin and serotonin-norepinephrine reuptake inhibitors (SSRIs and SNRIs). METHODS: A total of 115,284 patients from a large managed-care claims database initiating treatment on an SSRI or SNRI during 2005 were selected for analysis. Patients were assigned to a drug cohort on the basis of their most recent prescription for 1 of the studied medications. The study included only patients with 1 or more ICD-9 coded diagnosis for depression or anxiety within +/- 3 months of initiation on drug, an initial 30 days supply of the prescribed medication, and continuous eligibility >6 months prior and 12 months following treatment initiation. Subtherapeutic dosing levels of each studied medication were determined based on label information. Outcome measures included early discontinuation (no second prescription following initiation) and days on therapy with the index medication. All reported differences were significant at the <.01 level. RESULTS: A total of 13.6% of all study patients initiated antidepressant treatment at a subtherapeutic dose. There was substantial variation across the studied medications, with paroxetine most frequently (30.1%) and escitalopram least frequently (2.7%), initially dosed subtherapeutically. Across all studied medications, subtherapeutic initial dosing was associated with higher levels of early discontinuation (29.9%) and fewer average days on therapy (164.1) than initial dosing at therapeutic doses or higher (24.3% and 176.8 days, respectively). CONCLUSION: Subtherapeutic initial dosing of antidepressants is associated with more frequent early discontinuation and fewer average days on treatment. Prescribers should be cognizant of the potential impact of initial dosing decisions on subsequent adherence to therapy. Funded by Eli Lilly.

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2) Revicki DA, Simon GE, Chan K, Katon W, Heiligenstein J: Depression, health-related quality of life, and medical cost outcomes of receiving recommended levels of antidepressant treatment. J Fam Pract 1998; 47(6):446-452

» NR4-024

FIRST DOUBLE-BLIND, RANDOMISED, PLACEBO-CONTROLLED, ACTIVE-REFERENCED STUDY OF LU AA21004 IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER (MDD)

Francesc Artigas Ph.D., Marianne Dragheim, M.D., Henrik Loft, M.Sc., Victor Perez, M.D., Enric Alvarez, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be familiar with a novel antidepressant that is a 5-HT3 receptor antagonist, 5-HT1A receptor agonist, and 5-HT enhancer, that also increases levels of noradrenaline, dopamine and acetylcholine.

SUMMARY:
Objective: To evaluate efficacy and tolerability of Lu AA21004 in patients with MDD diagnosed according to DSM-IV-TR (1), vs placebo using venlafaxine XR as active reference. Lu AA21004 is a novel 5-HT3 receptor antagonist, 5-HT1A receptor agonist, and 5-HT enhancer that increases levels of noradrenaline, dopamine and acetylcholine in nonclinical studies. Method: In this 6-week trial, patients were randomised (1:1:1:1) to one of two doses of Lu AA21004, or to placebo or venlafaxine XR. Patients randomized to Lu AA21004 received either 5 or 10mg/day for 6 weeks; patients on venlafaxine XR received 75 mg/day for 4 days, 150 mg/day for the following 3 days, and 225 mg/day for the remainder of the period. All patients had a baseline MADRS (2) total score >=30. The primary efficacy analysis was based on the MADRS total score adjusting for multiplicity using a hierarchical testing procedure starting with the highest dose versus placebo. Results: At baseline, the mean MADRS total score was 34. The primary efficacy analyses showed that both doses of Lu AA21004 were statistically significantly superior to placebo (n=105) in mean change from baseline in MADRS total score at Week 6 (p<0.0001, LOCF), with a mean treatment difference to placebo of 5.9 (5mg, n=108) and 5.7 points (10mg, n=100). Venlafaxine (n=112) was significantly superior to placebo at Week 6 (p<0.001). 30 patients withdrew due to adverse events (AEs): placebo 4 (4%), Lu AA21004 5mg: 3 (3%), Lu AA21004 10mg: 7 (7%), venlafaxine: 16 (14%). The incidence of severe AEs was 4% (placebo), 6% (each Lu AA21004 dose), and 12% (venlafaxine). The most common AEs were nausea, headache, hyperhidrosis, and dry mouth. No clinically relevant changes over time were seen in the clinical laboratory results, vital signs, weight, or ECG parameters. Conclusion: In this study, treatment with 5mg and 10mg Lu AA21004 for 6 weeks was efficacious and well tolerated in patients with MDD. Funded by Lundbeck.

REFERENCES:
1) American Psychiatric Association (APA). Diagnostic and Statistical Manual of Mental Disorders. Fourth Ed. Text Revision (DSM-IV-TR). Washington DC: American Psychiatric Association; 2000.

2) Montgomery S, Åsberg M. A new depression scale designed to be sensitive to change. Br J Psychiatry 1979; 134: 382-389.

» NR4-025

LATITUDE, CLIMATE, SEASON AND SELF-REPORTED MOOD IN BIPOLAR DISORDER

Michael Bauer M.D., Tasha Glenn, Ph.D., Paul Grof, M.D., Natalie L Rasgon, M.D., Wendy Marsh, M.D., Kemal Sagduyu, M.D., Martin Alda, M.D., Greg Murray, Ph.D., Danilo Quiroz, M.D., Yanni Malliaris, BSc (Hons), Johanna Sasse,M.D., Peter C Whybrow, M.D.

EDUCATIONAL OBJECTIVES:
The viewer should understand that no seasonal pattern was detected in the daily self-reported mood fluctuations of patients with bipolar disorder receiving treatment as usual. Also, neither climate nor latitude had a significant impact.

SUMMARY:
Objective: Many researchers have analyzed seasonality in hospital admissions for bipolar disorder but results have been inconsistent. This study investigated seasonal variation using self-reported daily mood ratings from patients living in five climate zones in the northern and southern hemispheres. Additionally, the influence of latitude and seasonal climate variables on mood was analyzed. Method: 360 patients from different geographic locations in North and South America, Europe and Australia receiving treatment as usual recorded mood daily (59,422 total days of data). The percent of days depressed and hypomanic/manic, and episodes of depression and hypomania/mania were determined. These data were analyzed for seasonality by climate zone using both a sinusoidal regression and the Gini index. Additionally, the influence of latitude and climate variables on mood was estimated using generalized linear models for each season and month.
Results: Seasonality was not found in any climate zone with either method. In spite of vastly different weather, neither latitude nor climate variables were associated with mood by season or month. Conclusion: Most patients with bipolar disorder do not show a seasonal pattern of illness. Neither climate nor latitude has a primary influence on the daily mood fluctuations of most patients receiving medication for bipolar disorder.

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» NR4-026

SSRI ENHANCES KILLER LYMPHOCYTE (NK/CD8) NON-CYTOLYTIC HIV SUPPRESSION IN HIV/AIDS IN A CHRONIC T-CELL MODEL OF HIV

Tami Benton M.D., Kevin G. Lynch, Ph.D., Steven D.Douglas, M.D., Benoit Dube, M.D., David R. Gettes, B.S., Nancy B.Tustin, MLT.,(ASCP) HEW., Jian Ping Lai, M.D., David Metzger, Ph.D., Joshua Blume,M.D., Dwight L. Evans M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, participants will be able to: 1) identify potential immune mediators for the relationships between HIV disease and depression; and 2) recognize a potential clinical role for selective serotonin reuptake inhibitors in depression/immune relationships.

SUMMARY:
Objective: Depression is prevalent among HIV+ individuals, and is a potential risk factor for morbidity and mortality. Yet the mechanisms underlying these relationships are unknown. Natural killer (NK) cells and CD8+ cells are potential mediators through cytolytic and non-cytolytic mechanisms. Evidence suggests roles for NK and CD8+T-lymphocytes in the host defense against HIV disease, depression associated alterations in killer lymphocyte subpopulations and serotonin as a potential mediator between depression and NK cell activity. The modulation of NK cytolytic activity by serotonergic agents has been demonstrated. This study examines the role of NK and CD8+ non-cytolytic activity on HIV viral replication ex vivo.
Method: HIV+ women were recruited to obtain a sample of depressed and nondepressed women. Ex-vivo experiments focused on the effects of an SSRI antagonist, citalopram, on NK cell function were performed using peripheral blood mononuclear cells incubated with SSRI or control from each HIV seropositive subject. Supernatants were incubated with cells from a latently infected T-lymphocyte cell line and viral loads were determined.
Results: Among 42 HIV+ depressed and non-depressed women, citalopram significantly decreased cytokine stimulated HIV viral replication in the latently infected T-lymphocyte cell line (ACH-2) relative to the control condition.
Conclusions: SSRI treatment (citalopram) of PBMC's ex-vivo enhances NK/CD8+ HIV suppression in latently infected T-cells stimulated to produce HIV ex vivo. This study extends previous findings that an SSRI (citalopram) enhances NK cytolytic activity in HIV infection, among depressed and non-depressed women. NK cells are important in fighting HIV infection and NK function is decreased in HIV and depression. Future studies should determine whether an SSRI could improve NK and CD8+ cell activity, and

have potential clinical utility by delaying HIV disease progression and extending survival with HIV infection.

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» NR4-027

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RESPONSE STUDY OF PALIPERIDONE ER FOR ACUTE MANIC AND MIXED EPISODES IN BIPOLAR I DISORDER

Joris Berwaerts M.D., Haiyan Xu, Ph.D., Isaac Nuamah, Ph.D., Pilar Lim, Ph.D., David Hough, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the efficacy and safety of fixed doses (3, 6 or 12 mg/day) of the oral antipsychotic paliperidone extended-release in the treatment of patients with bipolar I disorder experiencing acute manic or mixed episodes.

SUMMARY:

Introduction: Efficacy and safety of fixed doses of paliperidone extended-release (ER) vs placebo (PB) were assessed in pts with bipolar I disorder experiencing acute manic or mixed episodes (YMRS >=20) in a multicenter, international trial.

Methods: Pts were randomized to once-daily paliperidone ER 3, 6 or 12mg or PB (1:1:1:1 ratio) for 3 wks.

Results: The ITT analysis set included 465 pts (PB: n=121; paliperidone ER 3mg: n=112; 6mg: n=118; 12mg: n=114). Most recent episode was described as 'manic' for 64% of pts. 61% of 469 randomized pts completed the study; 20% of PB-treated pts discontinued due to lack of efficacy vs 11, 10 and 6% in the paliperidone ER 3, 6 and 12mg groups, respectively. Mean±SD changes in YMRS score from baseline to Wk 3 (LOCF) (primary endpoint) were –9.9±10.22, –9.6±11.30, –11.7±10.04 and –13.9±9.19 for PB, paliperidone ER 3, 6 and 12mg, respectively (p=0.992, p=0.302 and p=0.005 for paliperidone ER 3, 6 and 12mg vs PB, respectively). Least-squares mean difference (paliperidone ER–PB) for change from baseline in YMRS score was –4.0 (–6.56, –1.52) for paliperidone ER 12mg. The paliperidone ER 12mg group showed statistically significant improvement from baseline in YMRS score relative to PB from Day 2 ($p<0.05$) until study end. Mean±SD changes from baseline in GAF score were 10.1±14.28, 9.9±13.48, 12.8±13.78 and 14.0±13.69 for PB, paliperidone ER 3, 6 and 12mg, respectively (with no statistically significant between-group differences vs PB). TEAEs were reported by 70, 61, 75 and 87% of pts treated with PB, paliperidone ER 3, 6 and 12mg, respectively. Serious AEs had similar incidence across paliperidone ER groups (4%) and were more frequent in the PB group (8%).

Discussion: Paliperidone ER 12mg/day was superior to PB (LOCF change from baseline in YMRS score) from Day 2 to end point. Paliperidone ER 3, 6 and 12mg were safe and well tolerated in pts with bipolar I disorder experiencing acute manic or mixed episodes. Funded by J&J PRD.

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» NR4-028

THE EFFICACY OF QUETIAPINE MONOTHERAPY IN BIPOLAR DEPRESSION: COMBINED DATA FROM THE BOLDER AND EMBOLDEN STUDIES

Joseph Calabrese M.D., Allan H. Young, M.B., Ch.B., M.Phil., Ph.D., Urban Gustafsson, Ph.D., Björn Paulsson, M.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should better understand the depth of the evidence base supporting the use of the atypical antipsychotic, quetiapine, as monotherapy in acute bipolar depression. The data presented, pooled from 4 large, placebo-controlled studies—BOLDER I and II and EMBOLDEN I and II—also demonstrate the consistency of effect associated with quetiapine in this treatment area.

SUMMARY:

Introduction: Combined data are presented from 4 placebo-controlled, fixed-dose studies (BOLDER I and II; EMBOLDEN I and II) that evaluated the efficacy of quetiapine (QTP) in patients with bipolar depression.

Methods: All studies included an 8-week, double-blind treatment phase in which patients were randomly assigned to QTP 300 mg/d, QTP 600 mg/d, or placebo. EMBOLDEN studies also included lithium (EMBOLDEN I) or paroxetine (EMBOLDEN II) as active comparators. The primary outcome measure was change from baseline in Montgomery-Åsberg Depression Rating Scale (MADRS) score at Week 8. Secondary efficacy measures included MADRS response (=50% reduction in MADRS score) and remission (MADRS score =12) rates, MADRS item scores, and Hamilton Rating Scale for Depression (HAM-D) and Hamilton Rating Scale for Anxiety (HAM-A) scores.

Results: The mean change in MADRS total score at Week 8 was statistically significantly greater in both QTP treatment groups versus placebo (-15.99 [n=811] and -16.17 [n=816] vs -11.43 [n=580] for QTP 300 mg/d, QTP 600 mg/d and placebo; $P<0.001$ for both doses). Improvement was evident as early as Week 1 and continued through Week 8. The overall effect size for QTP was 0.45 (ITT, LOCF). A significantly greater proportion of QTP- than placebo-treated patients met response or remission criteria at Week 8 (response: 64.1%, 64.5% vs 46.4% for QTP 300 mg/d, QTP 600 mg/d vs placebo [$P<0.001$ for both doses]; remission: 61.3%, 62.9% vs 42.4%, respectively [$P<0.001$ for both doses]). QTP-treated patients showed significant improvement ($P<0.001$) in HAM-A and HAM-D total scores compared with placebo. Tolerability was in line with previous reports for QTP.

Conclusions: Collectively, the BOLDER and EMBOLDEN trials—4 of the largest placebo-controlled studies of QTP monotherapy to date—confirm the efficacy of QTP (300 or 600 mg/d) in acute bipolar depression. QTP was generally well tolerated in all studies. Supported by funding from AstraZeneca Pharmaceuticals LP.

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» NR4-029

COMMON MENTAL DISORDERS IN COLOMBIAN WOMEN: PREVALENCE AND SOME ASSOCIATED FACTORS

Adalberto Campo-Arias M.D., Edwin Herazo, MD, MSc, Jaider Alfonso Barros-Bermudez, MD, German Eduardo Rueda-Jaimes, MD, Luis Alfonso Diaz-Martinez, MD, MSc.

EDUCATIONAL OBJECTIVES:
At the end of this poster presentation, the participants should be able to know the prevalence and associated factors with common mental disorders in Colombia women.

SUMMARY:
Background: Common mental disorders are more frequent among women than men. These mental health problems impact negatively on life quality of many women. However, its prevalence and associated variables have not been studied in Colombian population.
Objective: To explore the prevalence and associated factors with mental common disorders among Colombia women from Bucaramanga, Colombia.
Method: A cross-sectional study was carried out. A multi-stage probability sample of women was taken from the general population. Common mental disorders were explored with the General Health Questionnaire (GHQ-12). Non conditional logistic regression was computed to adjust associated variables.
Results: A total of 1,740 women participated in this survey. The mean age was 38.3 years (SD=13.3) and mean years of education, 8.8 years (SD=3.9), 59.5% were married, 37.0% were employed, 1.4% reported abusive alcohol consumption, 6.3% daily cigarette smoking, 44.5% daily coffee intake, 17.5% medical condition and 15.7% (95%CI 14.0-17.4) scored for common mental disorders. Abusive alcohol consumption (OR=6.4, 95%CI 2.7-15.2), daily cigarette smoking (OR=3.3, 95%CI 2.1-5.0), medical condition (OR=2.0, 95%CI 1.4-2.8) and daily coffee intake (OR=1.3, 95%CI 1.0-1.8) were statistically associated with common mental disorders, adjusted for age and education.
Conclusions: Common mental disorders are frequent in Colombian women. Health risk behaviors (abusive alcohol consumption, daily smoking, and daily coffee drink) and stressing events (medical condition) are strongly related to common mental disorders. It is necessary to identify and treat early these mental disorders in women to reduce health risk behaviors. More researches are needed.

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» NR4-030

ADJUNCTIVE ARIPIPRAZOLE TREATS SYMPTOMS OF CORE DEPRESSION, ANXIETY, AND INSOMNIA IN PATIENTS WITH ANXIOUS OR NON-ANXIOUS MDD (CN138-139/163/165)

Berit Carlson Ph.D., Michael Nashat, Pharm.D., James Eudicone, M.S., Quynh-Van Tran, Pharm.D., Andrei Pikalov M.D., Ph.D., Ronald N Marcus, M.D., Robert M Berman, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand the role of adjunctive aripiprazole in the reduction of anxiety, insomnia and core depressive symptoms in anxious and non-anxious major depressive disorder (MDD).

SUMMARY:
Objective: To evaluate the efficacy and safety of adjunctive aripiprazole in reducing symptoms of anxiety, insomnia, and core depression (Bech6) in major depressive disorder (MDD) patients with anxious or non-anxious features.
Methods: Data were pooled from two identical studies consisting of an 8-week prospective antidepressant treatment (ADT) phase and a 6-week, randomized, controlled trial phase using adjunctive placebo or aripiprazole (2-20 mg/day) in MDD patients with an inadequate response to ADT. Similar to the Sequenced Treatment Alternative to Relieve Depression Study (STAR-D), anxious depression was defined by the Hamilton Rating Scale for Depression 17 (HAMD-17) criteria. The efficacy endpoints were the mean change from baseline to endpoint (LOCF) in the HAMD17 score total as well as subscales of anxiety (items 9-11), insomnia (items 4-6) and core depression (Bech6) for both subpopulations. Response rates (>=50% reduction on Bech6) at endpoint were also examined.
Results: In anxious patients, adjunctive aripiprazole (n=185) had greater reductions than ADT alone (n=191) in the Bech6 subscale: -4.03 vs. -2.77, p=0.001; Anxiety subscale: -1.51 versus -1.18, p=0.04; and Insomnia subscale: -1.07 versus -0.69, p=0.03. In non-anxious patients, adjunctive aripiprazole (n=138) also had significant improvements versus ADT alone (n=118) in all HAM-D17 subscales and the HAMD-17 score total (p<=0.01). Response rates favored adjunctive aripiprazole in both anxious (38% vs. 26%; p<0.02) and nonanxious (39% vs. 25%; p<0.03) populations. The adverse event profiles of adjunctive aripiprazole in these two subpopulations were not different.
Conclusions: In this pooled post-hoc analysis, adjunctive aripiprazole improved symptoms of anxiety, insomnia and depression in MDD patients with both anxious and non-anxious features.
Supported by Bristol-Myers Squibb and Otsuka Pharmaceutical Co., Ltd.

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» NR4-031

LONG-ACTING RISPERIDONE IN THE PREVENTION OF RE-HOSPITALIZATION IN SCHIZOAFFECTIVE AND BIPOLAR DISORDER

Piero Castro-Loli M.D., Andrea Murru, M.D., Antoni Benabarre, Ph.D., Alessandra Nivoli, M.D., Jose Sánchez-Moreno, Psy. D., Anabel Martínez-Arán, Ph.D., Manuel Salamero, Ph.D., Maria Reinares, Ph.D., Eduard Vieta, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to know that long-acting risperidone treatment could be a useful tool in handling drug therapy specifically in complex bipolar and schizoaffective patients, characterized by lack of compliance to treatment.

SUMMARY:
INTRODUCTION: A good number of bipolar and schizoaffective patients need a long-term therapy with antipsychotic drugs. A possible strategy in maintenance therapy could be the use of a long term atypical antipsychotic as risperidone long-acting injectable (RLAI), which could grant a better compliance, thus reducing frequency of relapses.
OBJECTIVE: To evaluate tolerability, adherence and effectiveness of RLAI as a maintenance add-on therapy in bipolar and schizoaffective disorders relapse prophylaxis.
METHODS: We included 22 patients (14 bipolar and 8 schizoaffective). 18 received 25mg of RLAI as initial dose treatment and 4 received 37.5 mg continuing all of them in addition to a mood stabilizer. Every patient was evaluated with following scales in scheduled visits along 40 weeks: YMRS and HAM-D scales, CGI scale and UKU (adverse effects). A mirror evaluation on the number of hospitalizations before and after treatment with RLAI was done.
RESULTS: YMRS scores were significantly reduced from 10,19±7,34 at baseline to 3,23±2,17 at 9 months follow-up

($p<0.001$), whereas HAM-D scores remained stably low, (4,91±4,76 at week 0 vs. 4,43±2,37 at week 40) with no significant difference ($p=0.779$). Statistical differences were observed between baseline and final visits on CGI-S (3.8±1.2 versus 1.5±0.6, respectively at week 0 and at week 40, with $p<0.0001$). Similar findings were found in CGI-E. A trend towards a lower number of side effects was identified through the UKU ($p=0.056$). Mean hospitalization rate lowered from 1.14±0.921 to 0.61±0.982 per year. CONCLUSIONS: The use of RLAI as maintenance add-on therapy appears to be efficacious and well tolerated in bipolar and schizoaffective patients. During the follow-up, manic symptoms were reduced without switch to a depressive episode or increased depressive symptoms. Moreover, clinical improvement occurred since week 8 and was sustained over time. Hospitalizations were significantly decreased by the use of RLAI.

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» NR4-032

A PROSPECTIVE FOLLOW-UP STUDY OF MOOD SYMPTOMS IN PATIENTS WITH PARKINSON'S DISEASE REFERRED FOR DEEP BRAIN STIMULATION

Amit Chopra MBBS, Sarah Lageman PhD, Shirlene Sampson MD, Joseph Matsumoto MD, Andrea Adams MD, S. Matt Stead MD PhD, Kendall Lee MD PhD,Alexis Sharp, MBA, and Mark Frye MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the need for evaluation of prevalence of syndromal (depression and mania) and sub-syndromal symptoms in PD patients post-DBS surgery and importance of evaluation of safety in terms of risk of suicide associated with DBS surgery in PD patients.

SUMMARY:

Parkinson's disease (PD) affects as many as 1 million people in the United States alone, with approximately 40,000 Americans diagnosed with the disease annually. There is no known cure for the disease, and patients are typically treated symptomatically with medications. There is a high degree of psychiatric co-morbidity in PD, including major depression (20-38%), chronic dysthymia (20%), dementia (30%), anxiety disorders (40%), and sleep disorders (94%). Deep brain stimulation (DBS) is FDA-approved for the treatment of PD and essential tremor and has humanitarian device exemption status for treatment of primary dystonia. While DBS has been surgically refined and studies have documented improvements in motor symptoms and quality of life in patients with PD, there are few well-controlled studies that have examined the effects of DBS on mood, behavior, and cognition.

The suicide rate in PD patients has been reported to be 10 times lower than in the general population. Current research evidence suggests that DBS surgery has been associated with induction of mood disorders including mania and increased risk of suicide despite favorable clinical outcomes in PD patients. These findings emphasize the need for comprehensive pre- and post-DBS surgery psychiatric evaluations for monitoring mood disorders and risk of suicide in this population group.

This study "Deep Brain Stimulation and Mood: A Prospective Follow-Up Study" (Mayo IRB 07-004602, PI: Frye and Lageman) follows PD patients who have been approved for DBS surgery by Mayo Clinic DBS Clinical Committee to monitor their mood with a focus on mania induction and evaluation of risk of suicide, and to see how mood changes over time in PD patients in relation to DBS surgery.

This study aims to assess underlying risk factors that predispose PD patients to be at greater risk of psychiatric morbidity and mortality related to DBS surgery, improve our understanding of underlying neuropsychiatric aspects of mood disorders and suicide, and ensure safety of DBS surgery in PD patients from a psychiatric perspective.

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» NR4-033

DETECTING CINGULATE ABNORMALITIES IN MAJOR DEPRESSION WITH PREFRONTAL MIDLINE EEG

Ian Cook M.D., Aimee M. Hunter, Ph.D., Haleh Farahbod, Ph.D., Alexander Korb, B.S., Andrew F. Leuchter, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to (a) describe the context of cingulate dysfunction in major depression and (b) discuss clinically-practical methods to monitor anterior cingulate activity.

SUMMARY:

Background: Abnormalities of perfusion and metabolism in the anterior cingulate cortex (ACC) have been reported in Major Depressive Disorder (MDD). We examined healthy and depressed adults using two surface quantitative electroencephalographic (QEEG) measures, theta-band relative power and cordance, to evaluate physiologic differences in EEG signals overlying anterior, central, and posterior cingulate regions

Methods: Awake EEGs were recorded from 120 subjects: 44 healthy, never-depressed adults and 76 subjects with MDD and 17-item Hamilton Depression Rating Scale (HAM-D17) scores >= 16, who had been enrolled in treatment trials. EEGs recorded prior to initiating treatment were examined using individual midline electrodes (Fpz, Fz, Cz, Pz, and Oz) with both EEG relative power and cordance in the theta band (4-8 Hz).

Results: MDD subjects exhibited significantly higher values of cordance ($p<0.001$) at the Fpz electrode than controls; other locations did not show differences between subject groups. Relative power did not differ significantly between groups at any location. Using cordance at Fpz as a single parameter classifier (MDD vs control), 67% of subjects were correctly classified in the training sample, and replication in a testing sample correctly classified 65% of subjects.

Conclusions: In our subjects, adults with depression showed higher midline prefrontal (Fpz) cordance values than did never-depressed healthy control subjects, suggesting that functional ACC abnormalities in MDD may be detected by monitoring Fpz activity. Physiologic monitoring focused on this region may be integrated into clinical care more practically than assessments of the entire brain.

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» NR4-034

A NEW DIAGNOSTIC CRITERIA FOR DEPRESSION

(THE CDAD/IDASD SYSTEM)

AMELIA CORDERO, Cordero A, Psy.D., Ramos J, Psy.D., Gutierrez R, Psy.D., Zamarro ML, Psy.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to diagnose depression using a new diagnostic criteria for the depression (CDAD)made up of seven nuclear symptoms: mood, motivation/interest, impulse, pleasure, daily work, energy and different quality. The system offers a procedure to diagnose depression valid and reliable. It also possesses an excellent internal architecture, a good validity of construct and a good internal consistency.

SUMMARY:

Introduction: Few studies exist that have examined the psychometric properties of the criteria diagnoses for the depression at the moment in use1. The authors develop a new diagnostic criteria for the depression (in Spanish: CDAD) made up of seven nuclear symptoms: mood, motivation/interest, impulse/drive, pleasure, daily work, energy and different quality. Other items less relevant for the diagnosis was not included. They analyze its predictive validity, psychometric properties, reliability and its constructive validity.
Material and Method: They interview 111 psychiatric outpatients attended consecutively in ambulatory care. Sixty completed the criteria for depressive episode of the ICD-10 and fifty one were part of the group of control: psychiatric outpatients not depressed. The authors use for it a brief self-questionnaire (in Spanish: IDASD) in which patients indicate how they feel. Each item has a Visual Analogical Scale so that the subjects quantify their answers. The CDAD's predictive validity has been analyzed by means of the calculation of its sensitivity, specificity, the coefficient of agreement kappa and the probability of guessing right, pi. The determination of the most discriminant items was made by means of a Stepped Analysis Discriminant, with criteria of inclusion and exclusion for F of 0.05 and 0.10 respectively. The analysis of the dimensions of the items of the CDAD was made by means of Factorial Analysis using the method of the Principal Components, stopped when the eigenvalues were inferior to unit. The Factorial Analysis is also the procedure of greater power for analyze the construct validity of an instrument or a criterion diagnosis2. For the calculation of the internal consistency and the reliability has been selected the alpha intraclass correlation coefficient (for each item individually and for the global criterion). The authors have also analyzed the internal consistency by means of the methods of correlation item/total, and the correlation of two halves with the Spearman-Brown correction has been analyzed, in addition to the test of temporal stability test-retest.

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» NR4-035

THE PREVALENCE AND IMPLICATIONS OF RESIDUAL INSOMNIA IN EUTHYMIC BIPOLAR PATIENTS

Colleen Cowperthwait B.A., Aleena C. Hay, B.A., Michael J. Ostacher, M.D., M.P.H., Gary S. Sachs, M.D., Andrew A. Nierenberg, M.D., Roy H. Perlis, M.D., M.Sc.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be familiar with the association between mood episode recurrence and insomnia and current comorbid axis I anxiety disorders in bipolar disorder.

SUMMARY:

OBJECTIVE: Evidence suggests that sleep disturbance could be both a predictor of and cause of mood episodes in bipolar patients. In order to test the hypothesis that euthymic bipolar patients who are experiencing symptoms of sleep disturbance are at risk for mood episode recurrence, we examined the prevalence and implications of residual insomnia in euthymic bipolar patients.
METHODS: A cohort of bipolar I and II subjects participating in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) who were euthymic for at least 8 weeks on entering STEP-BD and for whom MADRS was available were evaluated for presence of insomnia. Evaluations were completed using structured and semi-structured assessments and clinical interviews.
RESULTS: 199 subjects of 673 bipolar I and II subjects (29.6%) reported at least mild insomnia (MADRS sleep item>0) for the week prior to study entry. Presence of insomnia was associated with older age at study entry and presence of a current comorbid axis I anxiety disorder, but not with gender, bipolar I versus II status, or rapid cycling in the prior year. Likewise, it was not associated with presence or absence of treatment with lithium, valproate, atypical antipsychotics, or benzodiazepines. In Cox regression, severity of insomnia at study entry was significantly associated with risk for mood episode recurrence after adjustment for overall depression, severity, age, and comorbid anxiety (hazard ratio (HR) = 1.15, 95% CI 1.06-1.25).
CONCLUSION: Insomnia among euthymic bipolar subjects was common and associated with older age at study entry and the presence of comorbid axis I anxiety disorders. Severity of insomnia was associated with risk for mood episode recurrence. This suggests that insomnia may be a prodromal symptom, which, in the presence of comorbid anxiety disorders, could indicate a poorer illness course, but could also represent a target of maintenance treatment.

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» NR4-036

WHICH CLINICAL AND SOCIODEMOGRAPHICS FACTORS ARE ASSOCIATED TO THE PRESENCE OF SUBSYNDROMIC SYMPTOMS IN BIPOLAR DISORDER?

Consuelo De Dios M.D., Elena Ezquiaga, M.D. Ph.D., Aurelio García, M.D. Ph.D., Agustín Madoz-Gúrpide M.D. Ph.D., Begoña Soler, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to confirm or reject the importance of some clinical and sociodemographic variables as predictors to the presence of subsyndromal symptoms in the bipolar disorder.

SUMMARY:

Introduction. No clear factors to predict the onset or persistence of subsyndromal symptoms are evident in the literature. Differences by gender, age at onset, time of evolution, or type of the most recent mood disorder don't seem to be present; and the role of the previous use of mood stabiliser and the comorbidity with substance misuse is dubious. More previous episodes, shorter time since resolution of the last episode, higher baseline scores in the scales of affective symptoms, worse social disability, and longer time of duration of the primary episode seem to be predictors of subsyndromal symptoms. Objective. To analyse the role of sociodemographic and clinical variables in the prediction of subsyndromal symptoms. Methods: 296 bipolar I, II and schizoaffective outpatients (diagnosed according to the Mini International Neuropsychiatric Interview) were included in a longitudinal follow-up study. Data used in this analysis are from the baseline cross-sectional data at the moment of inclusion in the

study. Logistic regression was used. Results. 32.7% of the patients have subsyndromal symptoms at the moment of inclusion in the study (majority subdepressive symptoms, 61.7%). More affective episodes in the last year (p=0.031) and higher baseline social disability (p<0.001) are associated with the presence of sybsyndromal symptoms. Gender, age at inclusion, employment status, time of evolution, current use of alcohol or other illicit drugs, the presence of rapid cycling or seasonal pattern don't seem to predict such symptomatology. Conclusion. As in previous studies in the literature, the number of affective episodes in the last year and the social disability are predictors of the presence of subsyndromal symptoms in bipolar disorder, but not the comorbidity with alcohol or other drug current misuse. They do confirm that gender, age at the inclusion in the study and time of evolution of the disorder are not associated with this type of symptoms.

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» NR4-037

PATTERNS OF PSYCHIATRIC COMORBIDITY IN RELATION TO AGE IN PATIENTS WITH BIPOLAR DISORDER: A CROSS-SECTIONAL ANALYSIS

Bernardo Dell'Osso M.D., Massimiliano Buoli, M.D., Sara Bortolussi, M.D., Maria Carlotta Palazzo, M.D., Giulia Camuri, M.D., Carlo A. Altamura, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize most frequent patterns of comorbid diagnoses and substance abuse, including alcohol and psychotropic compounds, in patients with Bipolar Disorder according to their age.

SUMMARY:

Purpose of the study: Several data indicate that clinical course and treatment response in bipolar patients (BPs) is complicated by comorbid psychiatric disorders and substance abuse (1, 2). The aim of this study was to detect differences in terms of psychiatric comorbidity between young (< 30 years), adult (> 30 and < 45 years) and senior BPs (> 45 years).
Methods: Study sample included 508 BPs, subdivided into 3 groups of age: < 30 years (n=52), > 30 and < 45 years (n=186) and > 45 years (n=270). Diagnoses of Bipolar Disorder and comorbid conditions were assessed by the administration of the SCID-I. Demographic and clinical variables were compared across the different groups using chi-square tests.
Results: The 3 groups were homogenous for the type of diagnosis (Bipolar Disorder type 1 or 2) (?2=1.28, df=2, p=0.518) and gender (?2=4.39, df=2, p=0.112), but they were different for psychiatric comorbidity (?2=39.93, df=18, p=0.004) with a higher frequency of Anorexia in young and adult BPs compared to senior BPs, and a higher frequency of Obsessive Compulsive Disorder in adult BPs in comparison to the other subgroups. Young BPs showed more frequently the presence of a third comorbid psychiatric condition compared to the other subgroups (?2=8.10, df=2, p=0.017). In addition, young BPs reported more frequently substance abuse (?2=13.91, df=2, p=0.002) in comparison to the other sub-groups and, with regard to the type of abuse, they were more frequently cannabis abusers, whereas adult BPs were more often alcohol abusers and senior BPs were abusers of both benzodiazepines and alcohol (?2=85.87, df=16, p< 0.0001).
Conclusions: Results from the present study suggest different profiles of psychiatric comorbidity and abuse in BPs in relation to age and this aspect should be taken into account for the choice of pharmacological treatments and global management of these patients (2).

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» NR4-038

TRANSCRANIAL MAGNETIC STIMULATION (TMS) IN THE TREATMENT OF PHARMACORESISTANT DEPRESSION: EXAMINATION OF COGNITIVE FUNCTION DURING ACUTE TREATMENT

Mark Demitrack M.D., Colleen Loo, MD, Daniel Maixner, MD, David Avery, MD, Keith Isenberg, MD, Sheila Dowd, PhD, John P. O'Reardon, MD, Pilar Cristancho, MD, Harold A. Sackeim, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: 1) Understand the evidence for the safety and efficacy of TMS in the treatment of patients with pharmacoresistant major depression, 2) Understand the evidence for the effects of TMS on cognitive function during acute treatment of patients with pharmacoresistant major depression.

SUMMARY:

Objective: TMS is safe and effective in patients with major depression (MDD) who have failed to receive benefit from initial pharmacotherapy. In this report, we provide additional evidence of the effect of TMS on cognitive function during acute treatment.
Methods: Cognitive function was examined in a multisite, randomized controlled trial of NeuroStar TMS therapy in patients with pharmacoresistant MDD (O'Reardon, 2007) (N=155 active TMS, N=146 sham TMS). Specific measures of global cognition (Mini Mental Status Examination), short-term (Buschke Selective Reminding Test) and long-term (Autobiographical Memory Interview-Short Form) memory were obtained prior to first treatment, and at 4 and 6 weeks during an acute treatment course of daily, left prefrontal TMS.
Results: There was no deterioration within or between treatment groups on any measure of cognition during acute treatment. Additionally, each treatment group was stratified by clinical outcome (HAMD24 responder) at the end of 6 weeks. Within the TMS group only, there was a statistically significant improvement on the BSRT in the TMS responders compared to TMS non-responders for both short-term recall (P = 0.0116 at 4 weeks; P = 0.0038 at 6 weeks) and delayed recall (P = 0.0463 at 4 weeks; P = 0.0012 at 6 weeks). This improvement in cognitive function was not seen in sham treated patients (P = NS at both 4 and 6 weeks).
Conclusions: These results suggest that clinical recovery with active TMS is associated with an improvement in short-term verbal memory that cannot be fully accounted for by improvement in mood.

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» NR4-039

COURSE OF SEXUAL FUNCTIONING DURING LONG-TERM DULOXETINE TREATMENT IN PATIENTS WITH RECURRENT MAJOR DEPRESSIVE DISORDER

Michael Detke M.D., David G. S. Perahia, M.D., M.R.C. Psych., Melissa E. Spann, Ph.D., Fujun Wang, Ph.D., Daniel J. Walker, Ph.D., Charles R. Yang, Ph.D, Montejo A.L., M.D. Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participants should be aware of the effects of long-term (up to 86 weeks) duloxetine treatment on sexual functioning in patients with recurrent Major Depressive Disorder.

SUMMARY:
OBJECTIVE: Sexual dysfunction is frequently associated with major depressive disorder (MDD) in the untreated state and may be worsened by antidepressant treatment. We evaluated sexual functioning in patients with recurrent MDD treated with duloxetine (DLX).
METHODS: Data were from the open-label (OL) and placebo-controlled maintenance phases of an MDD recurrence prevention study. Patients (N=514) received OL DLX 60-120 mg/d for up to 34 weeks. Response criteria were a HAMD17 Total Score =9; CGI-S =2; and not meeting DSM-IV MDD criteria. Responders (N=288) were randomized to DLX or placebo in the 52-week maintenance phase. Sexual dysfunction was assessed using the Arizona Sexual Experience Scale (ASEX). Treatment-emergent sexual dysfunction (TESD), defined as total ASEX score =19, =5 on any item or =4 on any 3 items, was evaluated at end-point.
RESULTS: At study entry, 65% of MDD patients met ASEX criteria for sexual dysfunction (SD).
With OL DLX treatment in these patients, 78% of nonresponders and 58% of responders still experienced SD at the end of the OL phases. For patients without SD at entry, 43% of nonresponders and 32% of responders experienced TESD. In the maintenance phase, there was insignificant difference (p=.08) in TESD incidence between placebo-treated (49%) and DLX-treated (25%) patients and no gender difference. Patients with MDD recurrence showed no difference (p=.48) in TESD incidence between the placebo (71%) and DLX (83%) groups. However, in patients with no recurrence of MDD, placebo patients (40%) had a significantly higher (p=.046) TESD incidence than DLX (7%) patients.
CONCLUSIONS: There was no significant difference between DLX and placebo in the incidence of TESD overall, although in patients not experiencing a recurrence of MDD, a significantly lower incidence of TESD was found in DLX-treated patients compared with placebo-treated patients. The high rate of TESD with placebo suggests that depression itself is playing a major role.
Research supported by Eli Lilly and Company and Boehringer Ingelheim GmbH.

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» NR4-040

CIGARETTE SMOKING ENHANCES DEPRESSION TREATMENT OUTCOME

Dale D'Mello M.D., Alric Hawkins, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to: Appreciate the prevalence and clinical correlates of cigarette smoking in patients with depression. Understand how apparent therapeutic benefits of cigarette smoking on the outcome of antidepressant treatment may interfere with attempts at smoking cessation.

SUMMARY:
The prevalence of cigarette smoking is disproportionately high in patients with depression. Among smokers with depression, some studies have reported a linear relationship between the severity of depression and the number of cigarettes smoked. Objective: The purpose of the present study was to examine the impact of smoking and other concurrent cardiovascular risk factors on depression treatment outcome. Methods: Patients who were hospitalized with depression on the adult psychiatry unit of a general hospital in mid-Michigan during calendar years 2006-2008 were invited to participate in the study. Following informed consent the patients completed a brief cardiovascular risk questionnaire. The cohort of patients who received electroconvulsive therapy (ECT) following failure to respond to drug treatment was compared to those who responded to antidepressant medications. Results: Two hundred and twenty five patients participated in the study. They included 142 women and 83 men, who ranged in age from 18 to 75 years. Forty-nine percent of the patients smoked cigarettes, 40% had hypertension, 16% had diabetes mellitus, 34% had dyslipidemia, and 40% were obese (BMI>30). Forty-nine (22%) of the 225 patients received ECT following non-response to antidepressants. Patients with comorbid cardiovascular risk factors responded less well to drug therapy and received a greater number of antidepressant trials. However, cigarette smoking was more prevalent in the drug responders (51% vs 45%; Pearson chi-square t=0.493, df=1, p=0.295). Smokers required fewer trials of antidepressants to achieve an antidepressant response (2.8; SD=2.3 vs 3.5; SD= 3.8, ANOVA df=1, F=2.98, p=0.086). Conclusions: While some concurrent cardiovascular risk factors appear to predict non-response to antidepressant medications, cigarette smoking appears to convey a beneficial effect. This is consistent with the observation that depressed patients have more difficulty quitting smoking than others and are susceptible to relapse when they do quit smoking. The elucidation of specific brain nicotinic receptor subtypes that convey the apparent antidepressant effects of nicotine may in the future lead to the development of novel psychotherapeutic tools.

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2) Bronisch, T., Höfler M, Liebet R: Smoking predicts suicidality: Findings from a prospective community study, Journal of Affective Disorders 2007;108:135-145.

» NR4-041

DOPAMINE FUNCTION AND CORTISOL SECRETION IN DEPRESSION

Fabrice Duval M.D., Marie-Claude Mokrani, Felix Gonzalez Lopera, Thanh Son Diep, Hassen Rabia

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand that, in depressed patients, chronic elevation of cortisol and consequently desensitization of corticotropes can lead to increased DA release and to D2-receptor-like dysfunction at the hypothalamic level.

SUMMARY:
Background: Several lines of evidence suggest that hypothalamic-pituitary adrenal (HPA) axis hormones stimulate the activity of dopamine (DA) systems. The aim of this study was to investigate the relationship between HPA axis and DA activity in depressed patients.
Methods: Cortisol and adrenocorticotropic hormone (ACTH) reponse to apomorphine (APO, a dopamine receptor agonist), circadian rhythm of cortisol and cortisol response to dexamethasone suppression test (DST) were determined in 107 drug-free DSM-IV major depressed inpatients, and 21 healthy hospitalized controls.
Results: Mesor and post-DST cortisol values were significantly

higher in patients (p<0.02 and p<0.03 respectively) than in controls, while ACTH responses to APO (? ACTH), but not cortisol, were significantly reduced (p<0.01). In patients, mesor and post-DST cortisol values were positively correlated (r=0.58; p<0.00001). DST nonsuppressors (n=31) showed 1) higher mesor and amplitude of cortisol values (p<0.00001 and p<0.05 respectively), and 2) lower ? ACTH values (p<0.006) than DST suppressors (n=76).
Conclusions: Our results suggest that blunted ACTH response to APO (which may reflect decreased D2-receptor-like function at the hypothalamic level secondary to increased DA release) is associated with chronic elevation of cortisol in depressed patients. However, further studies are needed to determine the influence of other factors such as CRH receptor desensitization of corticotropes (secondary to chronic CRH hypersecretion), altered processing and storage of ACTH precursors, and alternative processing of propiomelanocortin in the blunting of ACTH response to APO in depressed patients.

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» NR4-042

DOPAMINERGIC, NORADRENERGIC, ADRENAL AND THYROID ABNORMALITIES IN AFFECTIVE AND PSYCHOTIC DISORDERS

Fabrice Duval M.D., Marie-Claude Mokrani, Ph.D., Felix Gonzalez Lopera, M.D., Thahn Son Diep, M.D., Hassen Rabia, M.D., Said Fattah, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand that the neuroendocrine characteristics are comparable between schizoaffective patients and bipolar patients but different in schizophrenic patients. These results may be of great interest in devising appropriate therapeutic strategies.

SUMMARY:

Background: The aim of this study was to assess hypothalamic-pituitary dopaminergic (DA), noradrenergic (NA), thyroid (HPT) and adrenal (HPA) activity in bipolar disorder, in schizoaffective disorder, and in schizophrenia.
Method: Hormonal responses to 8 AM and 11 PM TRH tests, dexamethasone suppression test (DST), apomorphine test (APO; a DA receptor agonist) and clonidine test (CLO; an alpha 2-adrenoreceptor agonist) were evaluated in 13 hospitalized healthy male controls and in 39 untreated male inpatients: 13 with DSM-IV bipolar disorder (depressed), 13 with DSM-IV schizoaffective disorder (bipolar subtype), and 13 with DSM-IV paranoid schizophrenia.
Results: Compared to controls, schizoaffective and bipolar patients showed 1) lower ??TSH values [i.e. difference between 11 PM-?TSH and 8 AM-?TSH], p<0.0005 and p<0.00002, respectively); 2) lower APO-induced PRL suppression (p<0.05 and p<0.002, respectively); 3) lower CLO-induced growth hormone stimulation (p<0.001 and p<0.02, respectively); and 4) higher post-dexamethasone cortisol values (p<0.02 and p<0.01, respectively). Compared to controls, paranoid schizophrenic patients showed 1) lower APO-induced adrenocorticotropin (ACTH) and cortisol stimulation (p<0.04 and p<0.01 respectively); 2) higher post-dexamethasone cortisol values (p<0.02); and 3) higher rate of blunted prolactin (PRL) suppression to APO (p<0.01).
Conclusions: Our results suggest that decreased pituitary TRH and DA-D2 receptor function (possibly secondary to increased TRH and DA release, respectively), together with increased HPA axis activity and decreased alpha 2-noradrenergic function (possibly secondary to erratic NA release) characterize bipolar and schizoaffective patients; while decreased hypothalamic DA receptor activity (possibly secondary to increased DA release) associated with increased HPA axis activity characterize paranoid schizophrenic patients.

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» NR4-043

EXTENDED RELEASE QUETIAPINE FUMARATE ADJUNCT TO ANTIDEPRESSANTS FOR MDD: POOLED ANALYSIS OF SUSTAINED RESPONSE (STUDIES D1448C00006 AND D1448C00007)

Willie Earley M.D., Michael Bauer, M.D., Ph.D., Eduard Vieta, M.D., Ph.D., Johan Szamosi, M.Sc., Helena Schiöler M.Sc., Hans Eriksson, M.D., Ph.D., M.B.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the importance of an early onset of action and a sustained response to treatment in patients with MDD and be able to describe the early onset of action, and the time-to-first- and time-to-sustained-response with quetiapine XR as adjunct to ongoing antidepressant.

SUMMARY:

Objectives: Early improvements in symptoms of MDD are predictive of short- and long-term response (1); onset of action occurs along a continuum between fully symptomatic and asymptomatic states (sustained response) (2). This post hoc analysis evaluated sustained response with quetiapine fumarate (QTP XR) as adjunct therapy in patients with MDD showing an inadequate response to ongoing antidepressant (AD).
Methods: Efficacy and tolerability data from two similar 6-week, multicenter, double-blind, placebo (PBO)-controlled studies (D1448C00006, D1448C00007) have previously been reported. The present analysis was conducted using pooled data. Eligible patients (HAM-D: total score >=20; Item 1 score >=2) received QTP XR (150 or 300mg/day) or PBO as adjunct to ongoing AD. Study outcomes: change in MADRS total scores at Weeks 1, 2, 4, and 6. Post hoc Cochran-Mantel-Haenszel analysis: sustained response rate (>=50% reduction in MADRS total score at specific visit assessed and at all subsequent visits until Week 6).
Results: Data from 919 patients were included: 309 QTP XR 150mg/day; 307 QTP XR 300mg/day; 303 PBO. MADRS total scores were significantly reduced with QTP XR 150mg/day and QTP XR 300mg/day vs PBO (-7.8, -7.3 vs -5.1, respectively; both p<0.001) at Week 1 and through the study to Week 6 (-14.5, -14.8 vs -12.0, respectively; both p<0.001).The proportion of patients at each visit achieving a response that was sustained at all subsequent visits until Week 6 was: 13.0% (p=0.050), 14.2% (p<0.05) vs 8.1% at Week 1; 32.7% (p<0.001), 34.9% (p<0.001) vs 17.5% at Week 2; and 43.4% (p<0.05), 48.5% (p<0.001) vs 35.0% at Week 4, for QTP XR 150 and 300mg/day vs PBO, respectively.
Conclusions: In patients with MDD who had an inadequate response to ongoing AD treatment, adjunctive QTP XR (150 and 300mg/day) is associated with statistically significant reductions in MADRS total score from Week 1 and with greater sustained response rates vs PBO from Week 1. Funded by AstraZeneca

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research and treatment of major depressive disorder. J Clin Psychiatry 2008; 69(6):946-958

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» NR4-044

EFFECTIVENESS OF PSYCHOTROPIC MEDICATIONS IN THE MAINTENANCE PHASE OF BIPOLAR DISORDER: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Mattias Ekman Ph.D., Eduard Vieta, M.D., Ph.D., Julie Locklear, Pharm.D., M.B.A., Carolin Miltenburger, Ph.D., Mary Lou Chatterton, Pharm.D., Mikael Åström, M.Sc., Ph.L.,Björn Paulsson, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should gain familiarity with the range of maintenance treatment options available for patients with bipolar disorder as well as an understanding of the analyses used to acquire these clinical data.

SUMMARY:

Introduction: The purpose of this meta-analysis was to examine the efficacy and tolerability of maintenance treatments for bipolar disorder.
Methods: Placebo-controlled or active comparator bipolar maintenance clinical trials of planned duration =6 months and with =15 patients per treatment arm were identified using MEDLINE, EMBASE, clinicaltrials.gov, and Cochrane databases (period, 1993 to July 2008). Outcomes included relative risk for relapse for patients in remission. Tolerability outcomes were also assessed.
Results: 20 trials were identified, including a total of 6168 patients. The most trials were identified for lithium (9 trials) and quetiapine (5 trials). The mean period of follow up was 70 weeks. In general, the relative risk of relapse into any mood event was more homogenous across the treatments investigated than if manic/mixed or depressive events were considered separately. All medications (mono- and combination therapy) showed a relative risk for manic/mixed relapse that was below 1, although significance versus placebo varied among treatments. Of the combination treatments, only quetiapine+lithium/divalproex had a relative risk for manic/mixed relapse that was significantly below 1 (0.39; 95% CI: 0.30-0.52). The risk for depressive relapse was below 1 for all monotherapy studies identified, although only divalproex, lithium and quetiapine showed significance versus placebo. Of the combination therapies, only quetiapine+lithium/divalproex had a risk of depressive relapse that was significantly below 1 (0.38; 95% CI: 0.29-0.49). Tolerability profiles varied according to the individual medication.
Conclusions: This analysis identified considerable variation in efficacy among bipolar maintenance therapies. Quetiapine+lithium/divalproex was the only combination treatment to show significant reduction in the risk for both manic/mixed and depressive relapse. Supported by funding from AstraZeneca Pharmaceuticals LP.

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» NR4-045

COST-EFFECTIVENESS OF QUETIAPINE IN PATIENTS WITH ACUTE BIPOLAR DEPRESSION AND IN MAINTENANCE TREATMENT AFTER AN ACUTE DEPRESSIVE EPISODE

Mattias Ekman Ph.D.,Peter Lindgren, Ph.D., Carolin Miltenburger, Ph.D., Genevieve Meier, B.Pharm., M.Sc., Julie C. Locklear, Pharm.D., M.B.A., Mary Lou Chatterton, Pharm.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the direct medical costs and impact on quality of life for patients with acute bipolar depression and those receiving maintenance treatment for bipolar disorder. Participants should also be able to recognize that quetiapine represents a cost-effective treatment option for acute bipolar depression and as maintenance treatment following an acute depressive episode.

SUMMARY:

Background: Clinical trials in bipolar disorder have shown that quetiapine is an effective treatment for acute episodes of mania and depression, and as maintenance treatment. This study assessed the cost-effectiveness of quetiapine versus olanzapine in a UK health care setting by predicting mood events based on the observed probability of remission and relapse in clinical trials.
Methods: The cost-effectiveness of quetiapine in bipolar disorder was estimated using a newly developed simulation model. The probability of remission and relapse for different medications was modeled through relative risks versus placebo obtained either from published meta-analyses or from a meta-analytic review performed in parallel with this study. The baseline probabilities for remission and relapse were taken from the placebo arms in pivotal quetiapine trials. Costs included pharmacological therapy and resource use associated with the treatment of mood events and selected adverse events (weight gain and extrapyramidal symptoms), and health effects were measured in terms of quality-adjusted life years (QALYs). The study had a time horizon of 5 years and was conducted from a health care payer's perspective. A sensitivity analysis was undertaken to establish the robustness of the findings.
Results: For a patient starting with acute depression or in remission at 40 years of age, quetiapine 300 mg/d was a dominant strategy (better health effects at lower costs), compared with olanzapine 15 mg/d, over a 5-year time frame. For patients starting with acute bipolar depression as an index episode, total medical costs over 5 years were £180 lower and QALYs were 0.06 greater for quetiapine compared with olanzapine. The results were stable for variations in key variables.
Conclusions: The results of the model indicate that quetiapine is cost-effective compared with olanzapine for bipolar depression and bipolar maintenance therapy. Supported by funding from AstraZeneca Pharmaceuticals LP.

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» NR4-046

ANTIDEPRESSANT-ASSOCIATED MANIA OR HYPOMANIA: A COMPARISON WITH PERSONALITY AND BIPOLARITY FEATURES OF BIPOLAR I DISORDER

Rahsan Erim M.D., Omer Saatcioglu, M.D., Nesrin Tomruk, M.D., Timucin Oral, M.D., Nihat Alpay, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize, identify and diagnose in types of bipolar disorder.

SUMMARY:

Introduction: Although hypomania/mania during antidepressant treatment is not rare, it is often neglected by clinicians. As a result of the recent developments in this topic, bipolarity is now accepted

as a wide spectrum. There are no specific diagnostic criteria for hypomania and mania in bipolar spectrum caused by taking antidepressants. Method: In this study, 84 consecutive mood disorder patients who met DSM-IV criteria for "Bipolar Disorder-Type I in remission of mania or depression (group 1; N=44)" and patients with major depression in remission who had manic/hypomanic response to antidepressant treatment (group 2; N=40)" were admitted. All patients were given SCID-I, SCID-II, Bipolar Disorder Functioning Questionnaire (BDFQ) and Bipolarity Index (BI). First-degree relatives of all patients were evaluated using Mood Disorder Questionnaire (MDQ) which screens for bipolar spectrum disorder. Results: Sociodemographic, clinical features of group 1 and group 2 were similar. The majority of patients in both groups were female. Intensity of personality disorders was higher in group 2, but there was no significant difference between two groups (x2 =4.89, sd=2, p=0.09). The mean of functioning score according to BDFQ was 98.80±22.54 and 101.34±16.05 for group 1and group 2 respectively (t =0.55, sd=74, p=0.59). First-degree relatives of patients in group 1 had higher positive answers on MDQ (x2 =6.12, sd=2, p=0.05). In the comparison of the two groups with BI, a statistically significant difference was found in all dimensions' scores except family history (d1; t=15.55, sd=74, p=0.0001, d2; t =4.31, sd=74, p=0.0001, d3; t =7.55, sd=74, p=0.0001, d4; t =4.31, sd=74, p=0.0001, d5; t =-1.837, sd=74, p=0.070). Conclusion: Our results suggest that group 2 patients should not be categorized in the clinical spectrum of depressive disorders according to DSM IV and ICD 10 classification. Comparative studies between these patients may provide valuable information.

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2) Mitchell PB, Wilhelm K, Parker G, Austin MP, Rutgers P, Malhi GS: The clinical features of bipolar depression: a comparison with matched major depressive disorder patients. J Clin Psychiatry 2001; 62:212-216.

» NR4-047

IS EUTHYMIA AN UTOPIA IN BIPOLAR DISORDER PATIENTS? THE IMPORTANCE OF SUBSYNDROMAL SYMPTOMS

Elena Ezquiaga M.D., Consuelo de Dios, M.D., Aurelio García, Ph.D., Agustín Madoz-Gúrpide, Ph.D., Begoña Soler, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to consider the importance of identifying non-euthymic patients among bipolar patients who don't meet criteria for a major affective episode in an outpatient, a non tertiary hospital setting. Knowing the probability of euthymia and the prevalence and clinical characteristics of subsyndromal symptoms may be useful to improve treatment and outcome of bipolar patients.

SUMMARY:

Introduction and objectives. The high prevalence of subsyndromal symptoms has been emphasized in the last few years, even when patients were properly treated. Subsyndromal symptoms have been associated with a worse clinical and psychosocial outcome. Data are generally limited to tertiary research medical settings. Objective. To determine the percentage of bipolar outpatients treated according to clinical guidelines that are not euthymic, and to know the clinical characteristics of subsyndromal symptoms. Methods: Bipolar I, II, cyclothymic and schizoaffective outpatients (diagnosed according to the Mini International Neuropsychiatric Interview), cared for in two Mental Health Centers and a Hospital outpatient clinic, were included with a 2-year longitudinal follow-up. We present initial cross-sectional data.
Euthymia was defined as HDRS-21<7 and YMRS <5 scores. Subsyndromal symptoms when patients scored 7-17 in HDRS and 5-10 in YMRS.
Results: 296 patients were recruited. 65.2% BD-I, 56.8% females, 48.8 years old as average. 49.8% were euthymic, 32.7% had subsyndromal symptoms, most of them (20.2%) depressive symptoms, and 17.5% suffered a depressive, hypomanic, manic or mixed episode. Bipolar diagnostic subtypes, gender and age were not associated to euthymia.
Conclusion. Half of the patients were not euthymic at a cross-sectional analysis. Most of non-euthymic patients had subsyndromal depressive symptoms. Clinical diagnosis is not related to euthymia. For an optimal management of this insidious and severe disease, clinicians have to be in mind not only episodes but subsyndromal symptoms.

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2) Vieta E, Sánchez-Moreno J, Lahuerta J, Zaragoza S; Subsyndromal depressive symptoms in patients with bipolar and unipolar disorder during clinical remission. J Affect Disord 2008;107: 169-174.

» NR4-048

10-YEAR COURSE OF SOCIAL ADJUSTMENT OF MAJOR DEPRESSION

Toshiaki A. Furukawa M.D., Hiroshi Takeuchi, M.D., Ph.D, Hideki Azuma, M.D., Ph.D., Toshiaki Imaizumi, M.D., Hirofumi Ueki, M.D., Ph.D., Kazuhira Miki, M.D., Ph.D., Toshinori Kitamura, FRCPsych, Kiyohisa Takahashi, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:
1) Describe the fluctuating course of social adjustment of patients with major depression over 10 years,
2) And recognize its clinical implications and discuss possible means to ameliorate it.

SUMMARY:

Objective: It is well known that major depression is accompanied by grave social dysfunction (1) and that its recovery lags behind that of symptoms. Moreover, previous follow-up studies have shown that it cannot attain the level of the general population not only after the acute phase treatment but even after 2-5 years of follow-up (2).
Method: A multi-center prospective follow-up study of an inception cohort of heretofore untreated DSM-IV unipolar major depressive episodes (n=44) for 10 years. The social adjustment was measured with the Social Adjustment Scale Self-Report (SAS-SR) every 6 months up to 2-year follow-up and every year up to 10-year follow-up, three quarters of which time was spent in euthymia. Missing values were imputed by multiple imputation method.
Results: There were 28 women (64%) and the average age was 41.7 (SD=16.6). The SAS-SR total score was 2.36 at baseline, went down to 1.96 at 6 months but then hovered between 1.7 and 2.0 throughout the 10 year follow-up. In comparison with the general population mean, the effect size was 0.68 at baseline and 0.31 on the average through 2-10 years of follow-up. Among the various domains of social function, work was particularly affected, with an effect size of 1.36 at baseline and 0.72 through 2-10 years of follow-up.
Conclusions: This is the longest prospective study of social adjustment of major depression to date. It revealed that major depression is accompanied with persistent social dysfunction of small to large magnitude for up to 10 years. Whether this represents sequelae of major depressive episodes or trait dysfunction of the patients remains to be researched.
Acknowledgments: This paper was prepared on behalf of the Group for Longitudinal Affective Disorders Study (GLADS).

This study was supported by Research Grants 3A-6, 6A-4, 8B-2, 11A-5, 14A-3, 17A-5 and 20A-1 for Nervous and Mental Disorders from the Ministry of Health, Labour and Welfare, Japan.

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» NR4-049

DEPRESSIVE SYMPTOMS IN BIPOLAR PATIENTS ADMITTED INTO A PSYCHIATRIC UNIT DUE TO AN ACUTE MANIC EPISODE

Jaime Galan M.D., Ana Gonzalez-Pinto, M.D., Ph.D., Eduard Vieta, M.D., Ph.D., Manuel Martin, M.D.

EDUCATIONAL OBJECTIVES:

[no data]

SUMMARY:

Objective: The purpose of this study was to assess depressive symptoms in bipolar patients with acute mania.
Methodology: This was a multicenter, cross-sectional, observational study. Bipolar patients admitted into a psychiatric unit due to an acute manic episode were assessed in the 24 hours previous to be discharged.
The primary outcome was total score in MADRS (Montgomey-Asberg Depression Rating Scale). Secondary outcomes included evaluation of the relationship between depressive symptoms and the clinical global impression, manic symptoms and length of admission.
Results: 242 patients were included, and 45 psychiatrist were involved. 42,7% of patients were male. Average age was 43,14. Average length of evaluated admission was 19.47 days (IC95%: 17.98,20.96). Average of MADRS total score was 14,92 (IC95%: 14.02,15.82).
A statistically significant correlation was shown between MADRS total score and general status of the Clinical Global Impression-Bipolar (CGI-BP) (Spearman:0,49; p<0,0001), length of admission (Spearman: 0,19; p=0,005), and insight, assessed by the Scale Awareness of Mental Disorder (SUMD) (Spearman: -0,17; p<0,001).
Average of total score of Young Mania Rating Scale (YMRS) and CGI-BP were statistically significant higher in the group of patients with MADRS score >20 and >7 than in the group with MADRS<7.
Conclusion: This study showed that depressive symptoms are frequent in patients with acute manic episode; and those symptoms had a relationship with clinical global impression, length of admission and insight. This study was sponsored by AstraZeneca Farmaceutica Spain, S.A.

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» NR4-050

THE SENSITIVITY AND TOLERABILITY OF QUETIAPINE-XR IN THE TREATMENT OF BIPOLAR DEPRESSION, MAJOR DEPRESSIVE DISORDER, AND GENERALIZED ANXIETY DISORDER

Keming Gao M.D., David E. Kemp, M.D., Stephen J. Ganocy, Ph.D., Joseph R. Calabrese, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the differences and similarities of the sensitivity and tolerability of quetiapine-XR monotherapy in the treatment of bipolar depression, major depressive disorder, and generalized anxiety disorder.

SUMMARY:

Objectives: Quetiapine extended release (XR) monotherapy have been tested in the treatment of bipolar depression, major depressive disorder (MDD), and generalized anxiety disorder (GAD). This study explored the sensitivity (incidence of somnolence and sedation) and tolerability (discontinuation due to adverse events) of quetiapine-XR in the treatment of these conditions.
Methods: Studies of Quetiapine-XR monotherapy in the treatment of bipolar depression, MDD, and GAD that have been published or presented in major scientific meetings were examined. The rates of premature discontinuation due to adverse events, reported somnolence and sedation of quetiapine-XR 300 mg/d were compared with the rates of these variables of their respective placebo. The number need to treat to harm (NNTH) was calculated with 95% confidence interval (CI) to reflect the magnitude of variance.
Results: Data of 1 study in bipolar depression (quetiapine-XR n=140, placebo n=140),1 1 study of quetiapine-XR in MDD (quetiapine-XR n=152; placebo n=157),2 and 2 studies of quetiapine-XR in GAD (quetiapine-XR n= 444, placebo n=428)3,4 are available. The NNTH for the discontinuations due to adverse events were 9 (95% CI 6 to 20) in bipolar depression, 15 (95% CI 7 to 347) in MDD, and 5 (95% CI 4 to 7) in GAD, respectively. The NNTH for somnolence was 4 (95% 3 to 7) in bipolar depression, 5 (95% 4 to 9) in MDD, and 5 (95% CI 4 to 7) in GAD, respectively. The NNTH for sedation was 6 (95% CI 4 to 13) in bipolar depression, 3 (95% CI 2 to 4) in MDD, and 5 (95% CI 4 to 6) in GAD.
Conclusion: Patients with bipolar depression, MDD, or GAD had comparable sensitivity to quetiapine-XR 300 mg/d treatment, but patients with GAD had lower tolerability to quetiapine compared to those with MDD or bipolar depression.

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» NR4-051

A PROSPECTIVE COHORT STUDY TO ASSESS SUBSYNDROMAL AFFECTIVE SYMPTOMS IN BIPOLAR PATIENTS: DESCRIPTION OF THE SAMPLE

Aurelio García-López M.D.,Ph.D.Consuelo de Dios, M.D., Elena Ezquiaga, M.D. Ph.D., Agustín Madoz M.D. Ph.D., Begoña Soler, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know sociodemographic and clinical characteristics of patients treated in specialized psychiatric consultations in a public sanitary system, and to considere some of the difficulties in diagnosis and treatment of bipolar patients. The great delay for bipolar patients to be diagnosed and then to be treated with stabilizing treatment must be taken into account in clinical practice.

SUMMARY:

In the last years, several studies on patients with bipolar disorder revealed that a substantial proportion suffers a chronic course with frequent relapses, but also subsyndromal symptoms which have an impact on outcome. Objective: Description of a sample of bipolar outpatients under naturalistic follow-up in a Madrid (Spain) Methods:Initial sociodemographic and clinical features from a sample due to long-term follow-up are presented. Diagnosis relied

upon clinical judgement and semi-structured MINI Interview. Results: N=296. 56.8% females; 48.8 yrs old. TBI: 65.2%, TBII: 23.3%, cyclothymic: 2%, schizoaffective: 4.4%. 31.8% had comorbidiy in Axis I, 23.3% in Axis II, 47.6% in Axis III. Patients suffered a delay to be diagnosed of 9.2 yrs and 13 months more to initiate stabilizing treatment. Overall, patients had 12.7 prior episodes and 69.1% hospital admissions. 54% suffered psychotic symptoms. BDII patient diagnosis had a greater delay, they suffered more major depression and hypomanic episodes than BDI patients and were much older at their first hospital admission. Depression is the most common first episode in all BD subtypes. Number of episodes correlated with longer time to start stabilizers. Shorter time course of illness, was associated with more episodes and higher prevalence of current psychotic symptoms.
Conclusions: Patients suffered many episodes and a long delay to be diagnosed and to start stabilizing treatment. Greater severity of illness seems to be present in the first years of the illness. As most patients start with a depressive episode in all diagnosis subtypes, an accurate diagnosis of depressive episodes appears important to try to decrease the malignity of the illness.

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» NR4-052

PREDICTORS OF DULOXETINE TREATMENT PERSISTENCE FOR PATIENTS WITH MAJOR DEPRESSIVE DISORDER

Steven Gelwicks M.S., Douglas E. Faries, Ph.D.; Wenyu Ye, Ph.D.; Xianchen Liu, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to gain an understanding of the factors associated with persistence of duloxetine treatment for patients with major depressive disorder, including the effects of demographics, initial dose, previous medications, and comorbidities.

SUMMARY:

Objective: Treatment of depression is often accompanied by discontinuation and switching of antidepressant medications (1). Information on factors predicting persistence (and avoidance of switching) would thus be of value to medical decision makers (2). We assess the impact of demographics, initial dose, prior medications, and comorbidities on duloxetine treatment persistence for patients with major depressive disorder (MDD) using retrospective claims data.
Methods: Using the PharMetrics Database, we studied individuals aged 18-64 who initiated duloxetine treatment between April 2005 and March 2006, had =1 prior MDD diagnosis, and had continuous insurance coverage 6 months before and 12 months after initiation. Persistence was defined as =3 months' continuous duloxetine treatment. Stepwise logistic regression and tree analyses of demographics, initial dose, prior medications, and comorbidities assessed predictors of persistence. Sensitivity analysis was done by analyzing factors associated with switching to venlafaxine XR or a selective serotonin reuptake inhibitor (SSRI) within a year of initiating duloxetine.
Results: Among 9,148 patients (74.1% female; mean age=45.6, SD=11.1) who initiated duloxetine treatment, 63.5% had persistence of duloxetine treatment for = 3 months. Regression results showed the most significant factors for persistence to be initial dose of =60 mg QD (OR=1.38), age group of 46-64 yrs (OR vs. age 18-25 yrs=1.63), and venlafaxine XR/SSRI use in the prior 3 months (OR=1.64) (all p-values <.001). Sensitivity analysis showed initial dose of <60 mg QD was associated with switching from duloxetine (OR=1.22), although other factors showed differences from the persistence analysis.
Conclusion: The results suggest that for MDD patients, initial dose, age group, and recent venlafaxine XR/SSRI use predict persistence on duloxetine treatment. Sensitivity analysis on switching showed a consistent effect of initial dose. Funded by Eli Lilly and Company.

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» NR4-053

24 MONTH OUTCOMES FROM THE FRENCH COHORT OF THE EUROPEAN MANIA IN BIPOLAR LONGITUDINAL EVALUATION OF MEDICATION (EMBLEM) STUDY

Stephanie Gerard Pharm.D., Jean-Michel Azorin, M.D., Ph.D., Elodie Aubrun, Jordan Bertsch, Catherine Reed Pharm.D., Michael Lukasiewicz,MD

EDUCATIONAL OBJECTIVES:

Poster. No oral communication.

SUMMARY:

OBJECTIVES: To describe and compare clinical course and treatment patterns over 24 months of French patients of the EMBLEM cohort experiencing pure mania or mixed episode.
METHODS: EMBLEM is a 2-year European prospective, observational study on outcomes following a manic/mixed episode. Adult in/outpatients with bipolar disorder were enrolled within the standard course of care if they initiated or changed oral medication for treatment of acute mania. 24 month data of the French cohort are presented, with subgroup analysis for mixed states (MS) and pure mania (PM).
RESULTS: In France, 771 patients were eligible for the maintenance phase (766 eligible for analysis). 69% of patients completed the follow-up period. At baseline, 504 (66%) patients were experiencing pure mania and 262 (34%) mixed state. Mean age was 45.5 years (±13.6) and 57% were women. The main relevant differences in MS (vs. PM) were at baseline: higher rate of women (69% vs. 51%, p<0.001), and in the last 12 months: more previous episodes (manic/mixed and depressive), more suicide attempts (19% vs. 6%, p<0.001), more rapid cycling (26% vs. 11%, p<0.001), less social activities (p<0.05) and more work impairment (89% vs. 81% p=0.003). Over the 24 months follow-up period: MS presented more suicide attempts (26% vs. 13%, p<0,001), more work impairment (65% vs. 46%, p<0,001) and a recovery rate significantly lower than PM (36% vs. 46%, p=0.006). A monotherapy were initiated in 42% of patients and a combination therapy in 58%. At baseline, 36% were treated with an antidepressant, especially in MS (53% vs. 28%, p<0,001).
CONCLUSION: In this large sample of bipolar patients, MS is frequent (34%), are more severe at baseline and have a worse functional prognosis than PM. Although antidepressants are not recommended in MS and PM, they were frequently prescribed at baseline and remained stable during the 24 month of follow-up. These results must be investigated to better understand this pattern of prescriptions.

REFERENCES:

1) No Literature Reference because it is a poster on results of an observational study.

2) No Literature Reference because it is a poster on results of an observational study.

» NR4-054

RESPIRATORY FUNCTION AND DEPRESSIVE SYMPTOMS IN LATER LIFE IN ITALIAN AND FINNISH MEN

Erik Giltay M.D., Aulikki Nissinen, MD, PhD, Simona Giampaoli, MD, Frans G. Zitman, MD, PhD, Daan Kromhout4, MPH, PhD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know the association between repiratory function measured through spirometry and depressive symptoms later in life. This supports the hypothesis that poor lung function per se is a risk factor of geriatric depression. A better understanding of the risk factors for geriatric depression may help to improve prevention and to develop new treatment options.

SUMMARY:

Context: Chronic obstructive pulmonary disease (COPD) is associated with a high prevalence of depression, but the association of poor respiratory function with depressive symptoms has not been established in prospective population-based cohort studies.
Objective: To test the association of poor respiratory function with depressive symptoms.Design: Prospective population-based cohort study with up to 30 years of follow-up.Setting: Men from the general community living in Finland and Italy.
Participants: 1,205 men, 663 men in Finland and 542 men in Italy, aged 50-69 years from rural populations.
Main Outcome Measures: Through spirometry, forced vital capacity (FVC) and forced expiratory flow in 0.75 sec (FEV0.75) were measured in 1970. FVC and FEV0.75 were analyzed in relation to depressive symptoms (by Zung self-rating depression scale [SDS]) in 1985, 1990, 1995 and 2000 using multilevel regression models. Subsequent analyses were done separately in the strata with (n=469) and without (n=367) chronic disease in 1970 (i.e., COPD, cardiovascular disease and/or diabetes mellitus), because depressive symptoms are often found in case of physical comorbidity while the causal pathway may be bidirectional.
Results: Poor respiratory function was independently associated with steeper increases in depressive symptoms over time, both for FVC (P<0.001) and FEV0.75 (P=0.003). In participants without chronic disease, a standard deviation (SD) increase in FVC was associated with a 0.9 (SE 0.4) point decrease in Zung SDS (P=0.02) versus a 1.6 (SE 0.4) point decrease (P<0.001) in participants with chronic disease at baseline (P=0.045 for interaction). Low FEV0.75 was associated with more depressive symptoms in participants with chronic disease (1.7 SE 0.4 decrease per SD; P<0.001), but not in participants without chronic disease (0.6 SE 0.4 decrease per SD; P=0.13; P=0.02 for interaction).
Conclusions: The present prospective cohort study demonstrates that there is a strong relationship between low respiratory function and subsequent depressive symptoms at old age, which is consistent in two European countries. The association was stronger in the subgroup of men with COPD, cardiovascular disease and diabetes at baseline than in those participants free of chronic disease. Chronic hypoxaemia may be a causal factor for geriatric depression, or there may be an indirect pathway linking poor respiratory function to depression, secondary to impaired fetal an

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» NR4-055

SUBSYNDROMAL DEPRESSIVE SYMPTOMS AFTER SYMPTOMATIC RECOVERY FROM MANIA ARE ASSOCIATED WITH DELAYED FUNCTIONAL RECOVERY

Michael Gitlin M.D., Jim Mintz, Ph.D., Kenneth Sokolski, M.D., Connie Hammen, Ph.D., Lori L. Altshuler, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the relationship between subsyndromal depression and the delay in functional recovery after a manic episode in bipolar individuals.

SUMMARY:

Objective: This study examined the role of subsyndromal depressive symptoms as a predictor of functional recovery after an acute manic episode. Method: Bipolar I subjects who at the time of symptomatic recovery from an acute manic or hypomanic episode had a concomitant functional recovery (n=52) were compared on demographic variables and mood symptoms to those who had symptomatically recovered but not functionally recovered (n=33). Demographic and mood variables were examined in the non-functionally recovered group to assess predictors of time to functional recovery. Result: Depressive symptoms, even at a subsyndromal level were associated with functional nonrecovery after a manic episode. Subsyndromal depressive symptoms also predicted a slower time to recovery over the next nine months (p=.026). Conclusions: The presence of even mild, subsyndromal depressive symptoms may interfere with functional recovery in bipolar patients after symptomatic recovery from a manic or hypomanic episode.
Funding for this study was provided by the National Institute of Mental Health (1R01MH057762). Abbott Laboratories (LLA) provided funding to obtain divalproex sodium levels at the UCLA laboratory and provided divalproex sodium for some study subjects.

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» NR4-056 - WITHDRAWN

» NR4-057

MIND THEIR HEARTS: PREVALENCE AND CORRELATES OF CORONARY HEART DISEASE AND HYPERTENSION IN BIPOLAR I DISORDER

Benjamin Goldstein M.D., Patricia Houck, MSH, Andrea Fagiolini, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:
1. Appreciate that bipolar disorder is associated with markedly increased risk of coronary heart disease and hypertension.
2. Recognize that these conditions occur at least a decade early among persons with bipolar disorder.

SUMMARY:

Objective: Excess cardiovascular mortality in bipolar disorder (BD) has been documented for over 70 years. Few studies, mainly based on treatment-seeking samples, have shown that BD is associated with increased prevalence of CHD or HTN. We therefore examined this topic in a representative epidemiologic sample.
Methods: The 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a nationally representative sample of the U.S. adult population, was used to determine whether 1) prevalence of physician-diagnosed CHD (angina, arteriosclerosis, or myocardial infarction) and HTN is greater among

subjects with (N=1,411) versus without (N=41,682) lifetime BD, and 2) BD characteristics (age of onset, number of episodes, and history of hospitalization), are associated with CHD and HTN among persons with BD.
Results: Controlling for between-group differences in demographics, obesity, smoking, anxiety, and substance use disorders, the prevalence of CHD was significantly greater among subjects with versus without BD (odds ratio (OR) 3.86, 95% confidence interval (CI) 3.32-4.48; p<0.0001). The prevalence of HTN was also significantly greater (OR 2.15, 95% CI 1.95-2.36; p<0.0001). Hospitalization for depression was associated with lower prevalence of CHD and HTN, whereas hospitalization for mania was associated with greater prevalence of CHD and HTN. Number of depressive episodes was positively associated with prevalence of CHD and HTN. The mean age of BD subjects with CHD (50.4±0.7 years) and HTN (48.±0.6 years) was approximately 11 years younger than non-BD subjects with CHD (62.1±0.1 years) and HTN (59.9±0.1 years; p<0.0001).
Conclusions: Subjects with BD have quadruple the risk of CHD and double the risk of HTN compared to those without BD. Adults with BD manifest CHD and HTN more than a decade earlier than non-BD adults. There is an urgent need for preventive strategies to mitigate the impact of BD on excessive and premature CHD and HTN.

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» NR4-058

OMEGA-3 FATTY ACIDS AS ADJUNCTIVE OF ANTIDEPRESSANT THERAPY AND ITS EFFECTS ON BRAIN-DERIVED NEUROTROPHIC FACTOR IN SERUM AND LYMPHOCYTES

Alfonso Gonzalez Ph.D., Paul Sánchez, MD., Dacia González, MD., Salvador Mata, MD., Ph. D., Mary Urbina BSc., Fili Fazzino BSc, MSc., Lucimey Lima MD., Ph. D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the usefulness of omega-3 fatty acids as adjunctive of antidepressant therapy and its possible effects on brain-derived neurotrophic factor (BDNF)

SUMMARY:

Introduction: Stress is associated with a decreased expression of brain-derived neurotrophic factor (BDNF) in the hippocampus. Antidepressants and omega-3 fatty acids might increase circulating BDNF. This research was done to evaluate in major depression patients the possible differences in clinical response to an antidepressant alone or in combination with eicosapentaenoic acid (EPA), and their influence on BDNF levels. Methods: 19 patients were included, aged 18-60, diagnosed according to DSM-IV-TR criteria; severity and response was evaluated by Hamilton Depression Rating Scale (HAM-D). Control group was composed of 15 apparently healthy subjects. Patients were randomized on a double-blind basis in two groups: one received fluoxetine 20 mg/day and EPA 3,000 mg/day, and the other one fluoxetine 20 mg/day and placebo, during 8 weeks. Blood samples were taken for obtained serum and for isolating lymphocytes (85-90% T cells) at weeks 0 and 8. BDNF levels were measured in serum by immunoassay, and its presence in specific lymphocytes was determined by indirect immunocytochemistry with a second antibody conjugated with fluorescein. Results: 10 patients dropped out for different causes. Of the remaining 9 subjects, 4 received EPA and 5 got placebo. There was a significant decrease in absolute values of HAM-D in the EPA group. However, in both groups there was a reduction > 50% in the HAM-D, with the exception of one patient in each group. Serum BDNF before treatment was significantly lower in patients than in controls. Serum BNDF was lower after treatment in EPA group .The percentage of lymphocytes expressing BDNF was lower in patients, and it increased significantly after the treatments. Conclusions: EPA seems to augment the clinical response. In depressed there was a lower content of serum BDNF and EPA seems to lower it. Moreover, lymphocytes with BDNF, which were lower in this group of depressed, increased after the treatments, indicating that in cells the modulation of BDNF by antidepressants is more evident

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» NR4-059

EVERYDAY PRACTICE OF FRENCH PSYCHIATRISTS IN THE DRUG TREATMENT OF BIPOLAR DISORDERS

Sebastien Guillaume M.D., Ludovic. Samalin, M.D., Pierre-michel. Llorca, M.D. Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the influence of characteristics of physicians on the the drug choice for patients with bipolar disorder.

SUMMARY:

Objective : The aim of our study was to describe the every day drug prescription in patients with bipolar disorder in a sample of French psychiatrists.
Method : In October 2007, self-administered questionnaires were sent to all the French psychiatrists of the Auvergne region. It included 7 questions addressing the therapeutic drug choice for a patient with a bipolar manic episode.
Results : The questionnaires have been completed by 111 of the 210 psychiatrist contacted (53% rate). Among them, 47.5% proposed Valproate in mania without psychotic symptoms and 57.5% proposed Olanzapine in mania with psychotic symptoms. Lithium was considered as a second-line therapy for 54.5% of psychiatrists. Finally most of the time (44%) Valproate had been chosen as prophylactic treatment with a systematic introduction after 1st manic episode in 60% of cases.
Our multi-variate analysis revealed different prescribing profiles. Thus the doctors with less than 10 years of practice seemed more familiar with the use of newer therapeutic (i.e. Olanzapine). Physicians with a private practice, and more experienced, more frequently used lithium.
Conclusions: The French psychiatrists' habits of prescription appear specifically related to the number of years of practice and the type of activity rather than on evidence-based medicine. Research of factors involved in clinical decision making and quality management in bipolar disorders are needed.

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» NR4-060

RECURRENT MANIA REVISITED: A STUDY FROM NORTH INDIA

Nitin Gupta M.D., M Phani Prasant, M.D., Savita Malhotra,M.D.,Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to [1] understand the concept of unipolar recurrent mania, and [2] appreciate the need for further research into unipolar affective (mania) disorders in order to help in appropriate validation, classification and management of this entity.

SUMMARY:
Objective: To evaluate and compare Unipolar Recurrent Mania patients with Bipolar Affective Disorder patients.
Methods: A retrospective cross-sectional study was carried out, using chart-review methodology, in a tertiary care teaching hospital in North India. Case records were reviewed over a 13-year period for the diagnosis of Recurrent Unipolar Mania-RM (defined 'a priori' as- presence of at least 3 distinct episodes of mania with no episode of depression at time of assessment). A comparison group of Bipolar Affective Disorder-BPAD patients (having experienced at least 1 episode each of depression and mania/hypomania) was identified. ICD-10 diagnostic criteria were used. Any patient with diagnosis of organic or substance-induced mania was excluded.
Results: A total of 82 cases of RM and 50 cases of BPAD were taken up for study. The RM and BPAD group was similar on all socio-demographic variables except that more RM patients were from a rural background (40.2% vs 22%, X2=4.65). Amongst various clinical variables, frequency of episodes was higher in the BPAD group (1.70+1.34 vs 0.81+0.81; t=12.63); though seasonal pattern (34.4% vs 18%, X2=4.57) and positive family h/o non-affective illness (47.1% vs 18.7%, X2=6.28) was more in the RM group. In terms of treatment related variables, more patients received prophylactic treatment in BPAD group (94% vs 53.7%, X2=23.07); though number of episodes (8.09+13.24 vs 5.72+3.85, t=5.60) and Duration of Illness (133.90+109.23 vs 73.17+74.90, t=6.32) prior to the start of prophylaxis was more in RM group.
Conclusions: There were a few clinical and treatment related differences between RM and BPAD. However, the similarities far outweigh the differences between the two groups. We conclude that RM is a variant of BPAD, and does not warrant a separate and distinct nosological status.

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» NR4-061

FEASIBILITY OF A STRUCTURAL NEUROIMAGING STUDY IN MAJOR DEPRESSION USING LEGACY MRI DATA

Dan Iosifescu M.D., Wouter S. Hoogenboom, MS, Roy H. Perlis, MD, Jordan W. Smoller, MD, Qing Zeng-Treitler, PhD, Vivian S. Gainer, MS, Shawn N. Murphy, MD, PhD, Susanne E. Churchill, PhD, Isaac Kohane, MD, PhD, Martha E. Shenton, PhD

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to:
1. Understand the advantages of using existing clinical and imaging data (i.e., legacy data) in the study of long-term brain changes related to psychiatric disorders
2. Recognize the changes in brain morphology associated with chronic unremitted depression (particularly in the hippocampus)

SUMMARY:
Background: Prior work has suggested that in major depressive disorder (MDD) longer durations of untreated depression are associated with reductions in hippocampal volume. We used existing clinical and neuroimaging (MRI) data collected as part of routine clinical treatment to test whether chronic unremitted MDD is associated with changes in specific brain structures compared to MDD subjects responding to treatment.
Method: Using billing codes and automated systems (based on Natural Language Processing) for examining electronic clinical notes we assembled a cohort of MDD subjects who were either in long-term remission or with chronic unremitted MDD and who also had structural MRIs with no significant pathological findings collected as part of clinical treatment. We used FreeSurfer 4.0.5 to analyze structural MRI data from the first 18 MDD subjects (mean age = 46.4 + 19.3 yrs, 5 females, 28%).
Results: 13 MDD subjects (72%) were in remission while 5 subjects had chronic unremitted MDD for more than 2 years. Numerically, compared with subjects with remitted depression, subjects with unremitted depression had lower volumes in several gray matter areas; the % reduction was 6.4% in total gray matter volume, 2.3% in left hippocampus, 3.2% in the right hippocampus, 6.2% in left amygdala, 7.1% in right amygdala and 17.4% in the right rostral anterior cingulate. None of these differences was statistically significant in this small group of MDD subjects ($p>0.05$ for all comparisons).
Conclusion: It is possible to use legacy clinical and MRI data to investigate brain structure in psychiatric populations. Additional data (which will be available at the time of this presentation) will be needed to establish whether the observed trend towards volumetric reductions in specific brain areas in unremitted MDD subjects has statistical significance.
Funding: This study was supported by a subcontract (PI: Dan Iosifescu) to NIH grant U54 LM008748 (PI: Isaac Kohane)

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» NR4-062

THE PREVALENCE AND IMPACT OF COMORBID MIGRAINE ON INDIVIDUALS WITH BIPOLAR DISORDER

Christine I. Kansky, BA, Rebecca M. Ametrano, BA, Michael J. Ostacher, MD, MPH, Roy H. Perlis, MD, MSc, Gary S. Sachs, MD, Andrew A. Nierenberg, MD.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand the prevalence of comorbid migraine in bipolar disorder, and how the presence of comorbid migraine affects the course of bipolar disorder.

SUMMARY:
Objective: Migraine has been associated with impaired functioning and lower quality of life in individuals with a physical or mental health condition. Despite the established pattern of association between migraine and mood disorders, the impact of comorbidity of migraine and bipolar disorder (BD) is not well characterized. Therefore, we investigated the prevalence of comorbid migraine in subjects with BD, and the impact of this association on their course of illness. We hypothesized that the presence of comorbid migraine is associated with a more morbid course of illness compared to BD without migraine.
Methods: The Systematic Treatment Enhancement for Bipolar Disorder (STEP-BD) is a multicenter prospective cohort study of bipolar disorder (BD) conducted in the United States between 1999 and 2005. All 4,107 subjects were assessed at study entry with a structured diagnostic evaluation, including the SCID and MINI. Interviewers also collected subjects' medical history, including presence or absence of migraine.
Results: Of the 3,845 subjects for whom migraine data was available, 1049 (27.3%) reported comorbid migraine (BDM). Subjects with BDM were more likely to be female, to be younger at study

entry, to have bipolar II or NOS, and to have a lifetime history of rapid cycling ($p<0.01$). The BDM subjects were less likely to be euthymic at study entry and more likely to have a lifetime history of suicide attempt ($p<0.01$); these differences persisted after adjusting for baseline clinical and sociodemographic differences in multiple logistic regression.
Conclusions: These results suggest that migraines are prevalent and associated with greater lifetime morbidity in BD. Limitations include absence of data about current migraine or migraine severity, and absence of a non-migraine headache comparator group.

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» NR4-063

PREDICTIVE EFFECT OF METABOLIC SYNDROME ON ARIPIPRAZOLE TREATMENT RESPONSE (CN138-010)

David Kemp M.D., James M Eudicone, M.S., Andrei Pikalov, M.D., Ph.D., Richard Whitehead, B.S., Ross A Baker Ph.D., M.B.A., Jessie S Chambers, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the predictive value of metabolic syndrome on stabilization in patients with acute episodes of bipolar I disorder and understand the impact of aripiprazole on metabolic syndrome.

SUMMARY:

Background: Patients with bipolar disorder suffer from a high burden of comorbid medical problems including metabolic syndrome (MetSyn)(1). As obesity and illnesses of the endocrine/metabolic system have been correlated with poorer outcome, we conducted a post-hoc evaluation of the effects of MetSyn on stabilization during aripiprazole treatment in patients with bipolar I disorder.
Methods: Patients with bipolar I disorder with a recent manic or mixed episode received open-label aripiprazole treatment 15 or 30 mg/day (starting dose of 30 mg/day) for 6-18 weeks during a stabilization phase. Patients achieving stabilization criteria (YMRS <=10 and MADRS <=13 for 6 consecutive weeks) entered a double-blind maintenance phase. Prevalence of MetSyn, defined according to modified NCEP III criteria (2), was calculated at stabilization phase baseline and endpoint. The predictive effect of MetSyn on stabilization during aripiprazole treatment was evaluated using LOCF with Fisher's exact test.
Results: At stabilization baseline, 45% (62/139) of patients met criteria for MetSyn, while 55% (77/139) did not. Of evaluable patients at stabilization endpoint, 33% (46/138) met criteria for MetSyn, while 67% (93/138) did not. There was a significant reduction in MetSyn for patients after aripiprazole treatment ($p<0.0001$). Presence or lack of MetSyn at baseline did not predict stabilization at endpoint (both $p>0.999$). Furthermore, rates of MetSyn did not differ between patients who were, or were not, stabilized at endpoint ($p>0.99$).
Conclusions: MetSyn status had no predictive effect on stabilization during aripiprazole treatment, either for patients who no longer met criteria for MetSyn after aripiprazole treatment or for those who continued to meet MetSyn criteria even after aripiprazole treatment. The rate of MetSyn significantly decreased for patients on aripiprazole treatment. Supported by Bristol-Myers Squibb and Otsuka Pharmaceutical Co., Ltd.

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» NR4-064

ACUTE EVENTS RISK PREDICTION AMONG ANTIPSYCHOTIC AGENTS IN THE MAINTENANCE TREATMENT OF BIPOLAR I DISORDER

Jennifer Kim Pharm.D., Arthur Lazarus, M.D., MBA

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize the efficacy of adjunct treatment of quetiapine with lithium or divalproex in maintenance therapy of bipolar I disorder.

SUMMARY:

Introduction: Bipolar I disorder (BPD) is a chronic, recurrent mood disorder associated with severe morbidity. Among stabilized patients, the prevention of episode recurrence is a critical treatment goal. This analysis examines the relative risk of acute events associated with antipsychotic agents in patients with BPD receiving maintenance treatment over 1 year.
Methods: A Markov model simulated cohorts of 1000 stabilized patients, each assigned to one of the following FDA-approved therapies for maintenance treatment of BPD: quetiapine (QTP) in combination with lithium (Li) or divalproex (DVP), olanzapine, or aripiprazole. Each cohort was followed for 1 year in the Markov model and quarterly risk of an acute event (euthymia, mania, and depression) and dropouts were derived from randomized clinical trials. Patients with mixed episodes were reclassified as manic or depressed based upon the predominant nature of their symptoms. The model took into account mortality including suicide. Primary endpoint was number of acute mood episodes (depression or mania). One-way and probabilistic sensitivity analyses were conducted to evaluate uncertainty. For each cohort, incidence rates were calculated based on the number of acute events projected and person-year of follow up. Relative risks and confidence intervals were determined for the 3 cohorts.
Results: Compared with the QTP+Li/DVP cohort, patients treated with aripiprazole or olanzapine were 2.65 (95% CI, 2.39-2.94) or 2.32 (95% CI, 2.07-2.59) times more likely to have an acute depression event during the first year of treatment, respectively. At the same time, these patients were 2.36 (95% CI, 2.21-2.51) or 2.59 (95% CI, 2.51-2.62) times more likely to have an acute mania event. Conclusion: This risk prediction model suggests that treatment with QTP+Li/DVP is associated with significantly fewer acute mood events compared with aripiprazole and olanzapine.
Supported by funding from AstraZeneca Pharmaceuticals LP

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» NR4-065

ANGER EXPERIENCE IN PATIENTS WITH DEPRESSIVE DISORDERS

Jeong-Lan Kim, Byung-Hun Ahn,M.D., Jin-Gu Lee,M.D., Seung-Kun Wang,M.D.,Ik-Seung Chee,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the importance of anger experience in the depressive

patients

SUMMARY:
Objective : This study was conducted to evaluate the degree and type of anger experienced by patients with depressive disorder and to determine which type of anger is correlated with symptom severity.
Method : 106 psychiatric outpatients with depressive disorders and 90 normal control subjects completed the Korean version of Aggression Questionnaire (AQ) and Korean version of Depression, Anxiety, and Stress Scale (DASS). Comparison between two groups was conducted to evaluate which type of anger are prominent in the depressed group. Therefore, correlation and partial correlation between the scores of 4 subscale (Anger, Hostility, Verbal aggression, and Physical aggression) of AQ and the scores of 3 subscales (Depression, Anxiety, and Stress) of DASS were assessed. A multiple regression analysis was performed to determine which type of anger predicted symptom severity.
Result : Total AQ score, hostility, anger and physical aggression scores were significantly higher in patients with depressive disorders. After the score of Stress and Anxiety subscale of DASS were controlled; the depression score was significantly correlated with total AQ score, physical aggression and hostility score. The Hostility score was a major predictor of the depressive symptom severity. In addition, the Anger score was a major predictor of the anxiety and stress symptom severity.
Conclusion : Anger is frequently found symptom in patients with depressive disorders. Therefore, it is important that clinicians routinely evaluate the degree and type of anger in patients with depressive disorders.

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» NR4-066

THE EFFECT OF COGNITIVE BEHAVIOR THERAPY PERFORMED IN FOREST ENVIRONMENT ON REMISSION AND PHYSIOLOGIC RESPONSE IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

Won Kim M.D., Jong-Min Woo, M.D.,Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to indentify the effect of CBT performed in urban forest environment on remission of major depressive disorder. In our study, the urban forest environment is more helpful to restore the function of patients with remnant depressive symptoms than the hospital environment.

SUMMARY:
Major depressive disorder is a chronic health problem with significant limitations in functioning and well-being. The treatment of major depressive disorder usually focused acute treatment and its response. However, the remission of residual depressive symptoms and full recovery of pre-morbid function is considered as the new goal of treatment of depression. For achieving remission, psychotherapeutic intervention is helpful when combined with pharmacotherapy. Therefore, we developed and tested the cognitive behavior therapy (CBT) - based psychotherapy applied in forest environment for maximizing treatment effect.
We performed 4 sessions during 4 weeks (3 hours/session) in patients with major depressive disorder during pharmacotherapy. For forest group, the sessions were performed in forest, and for hospital group, in hospital. The control group was treated with usual management for outpatient. The scales for depression such as Hamilton Rating Scales for Depression (HRSD) and Montgomery-Asberg Depression Rating Scales (MADRS), and the physiologic measurements such as heart rate variability and salivary cortisol level were applied before and after 4 sessions.
Twenty-three patients in forest group, 19 in hospital group and 21 in controls completed all the process of study. HRSD scores of the forest group were significantly decreased after 4 sessions, compared with controls. MADRS scores of forest group were significantly decreased compared with both the hospital group and controls. The remission rate (7 and below in HRSD) of the forest group was 61%(14/23), significantly higher than both the hospital group(21%, 4/19) and controls (5%, 1/21). In HRV analysis, SDNN, RMSSD, TP, HF in forest group were increased after 4 sessions. The salivary cortisol level of forest group were significantly decreased.
This CBT-based psychotherapy applied in forest environment was helpful in the achievement of remission of depression, and this effect was superior to the psychotherapy performed in hospital and the usual outpatients management. Good environment such as forest is helpful to maximize the effect of psychotherapeutic intervention because it include various natural instrument and facilitator for treatment of depression. Key Word: Major depressive disorder, Remission, Forest, Cognitive Behavior Therapy (CBT).

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» NR4-067 - WITHDRAWN

» NR4-068

A NEW CLINICAL RATING SCALE FOR WORK PRODUCTIVITY: VALIDATION STUDIES IN PATIENTS WITH DEPRESSION

Raymond Lam M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to: 1) identify barriers and limitations to the assessment of work function and productivity, 2) discuss validation data for a new self-rated scale to assess work productivity in workers with depression, 3) review methods of incorporating routine assessments of work function into clinical practice

SUMMARY:
Objective: The prevalence of major depressive disorder (MDD) is highest in working age people and depression causes significant impairment in occupational function. Work productivity and work absence should be incorporated into clinical assessments but currently available scales may not be optimized for clinical use. We developed a productivity rating scale based on data about the depressive symptoms that most impair work function and the work consequences of those symptoms. This study seeks to validate the Lam Work Absence and Productivity Scale (LWAPS), a 10-item self-report questionnaire that takes 3-5 minutes to complete.
Methods: Consecutive patients meeting DSM-IV criteria for MDD attending a Mood Disorders outpatient clinic completed the LWAPS as part of their intake assessment. In addition, patients completed the self-rated version of the Quick Inventory for Depressive Symptomatology (QIDS-SR), the Sheehan Disability Scale (SDS) and the Health and Work Performance Questionnaire (HPQ). Standard statistical analysis for scale validation was conducted.
Results: 164 patients with MDD completed the assessment. The LWAPS displayed excellent internal consistency as assessed by Cronbach's alpha of 0.89. External validity was assessed by comparing the LWAPS to the other clinical and work function

scales. The LWAPS overall score was significantly correlated with the SDS work disability score (r=0.44, p<0.01) and the global productivity score from the HPQ (r=-0.69, p<0.01). In addition, the LWAPS overall score was significantly correlated with the total score on the QIDS-SR (r=0.68, p<0.01); however, the magnitude of the correlation was not too high, indicating that the LWAPS is not simply duplicating a symptom rating scale.
Conclusions: The LWAPS displays good internal and external validity in a population of patients with MDD attending an outpatient clinic and should be a clinically useful tool to assess and monitor work productivity.

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» NR4-069

THE ASSOCIATION BETWEEN BRAIN-DERIVED NEUROTROPHIC FACTOR GENE POLYMORPHISM(VAL66MET) AND SERUM BRAIN-DERIVED NEUROTROPHIC FACTOR LEVELS

Youngmin Lee M.D., M.P.H.,Jm Park,Ph.D.,CJ Kang,Ph.D.,BD Lee,M.P.H.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the association between brain-derived neurotrophic factor gene polymorphism(val66met) and serum brain-derived neurotrophic factor levels in major depressive disorder

SUMMARY:

background: there is strong evidence demonstrating that gene polymorphism and biochemical changes are associated with higher susceptibility to major depressive disorder(mdd), but the interaction between gene polymorphism and biochemical changes remains largely unknown. The aim of this study was to investigate whether val66met polymorphism in the brain-derived neurotrophic factor(bdnf) gene is associated with changes in serum bdnf levels in mdd patients and normal control
methods: sixty patients with mdd and 33 normal controls were recruited and analyzed for this study. psychiatric diagnoses were carried out using the korean version of the structured clinical interview for dsm-iv axis-i disorder(scid-iv), and the severity of depression was measured using the 17-item hamilton rating scale for depression(ham-d-17). The genotypes of bdnf val66met polymorphism in all subject were determined using polymerase chain reaction(pcr), and serum bdnf levels was also measured from the peripheral blood
results: there were no significant deviations of patients and control groups from hardy-weinberg equilibrium(?2 test, p>0.05). no significant differences were found in the frequency of the bdnf val66met polymorphism or allele distribution between patients and controls(?2 test, p>0.05). we have found no significant interaction between bdnf polymorphism and diagnostic status(mdd and controls) on serum bdnf levels(factorial analysis of variance, f=0.688, p=0.409)
conclusions: this founding shows that the bdnf val66met polymorphism does not affect serum bdnf levels in mdd patients and normal controls.

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» NR4-070

SEROTONIN 5-HT7 RECEPTORS, PROLIFERATION, AND CAMP IN LYMPHOCYTES OF MAJOR DEPRESSION PATIENTS

Lucimey Lima M.D., Fili Fazzino, M.Sc.; Humberto Spinetti, M.D., Ph.D.; Rafael Arciniegas, M.D.; Isabel Carreira, M.D.; Salvador Mata, M.D. Ph.D.; Alfonso González, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: 1) to support the compromise of immune cell function in major depression; 2) to evaluate the relatively unknown role of 5-HT7 receptors in lymphocytes; 3) to document the relevance of 5-HT receptors interaction in depression and its probable relation to treatment; and 4) to introduce the discussion of immune modifications in the study of affective disorders by psychiatrists.

SUMMARY:

Introduction. Serotonin 5-HT7 receptors, present in the brain, are positively coupled to adenylate cyclase. Lymphocytes express these receptors, although their functional role during depression is unknown. The purpose of this research was to evaluate the possible effect of 5-HT7 receptors on lymphocyte proliferation of depressed patients. Methods. This study included 20 controls and 20 patients, 18-60 years, diagnosed with DSM-IV criteria, and severity evaluated by Hamilton Scale of Depression. Lymphocytes from blood were isolated by density gradients with Ficoll/Hypaque, cultured in RPMI medium for 72 h with or without the T-cell mitogen concanavalin A, and exposed to 5-HT7 agonist, oleamide (1-1000 nM), and antagonist, pimozide (0.01-1 ?M) or SB-269970 (0.01-1 ?M). Proliferation was measured with tetrazolium salts. cAMP was determined by radioassay. Results. Oleamide decreased proliferation in resting and in activated lymphocytes of controls, but not of patients. On the other hand, pimozide increased proliferation in resting lymphocytes of controls, and patients. The more selective antagonist, SB269970, elevated proliferation of resting lymphocytes of controls only at the higher concentration, but not in patients. The increase in proliferation produced by pimozide is impaired by oleamide more efficiently in controls than in patients. Oleamide elevated cAMP in resting lymphocytes of controls and patients, and had less effect in concanavalin A-activated lymphocytes from the two groups, which had lower levels of cAMP. Conclusions. The stimulation of 5-HT7 receptors diminished lymphocyte proliferation, in relation to the elevation of cAMP. However, in lymphocytes from this group of depressed patients there was a resistance, probably indicating a reduction in the function of these receptors and an increase in activating factors. Basal proliferation was higher and cAMP was lower in depressed than in controls, which might indicate 5-HT7 receptors dysfunction.

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» NR4-071

CHRONIC PAIN ASSOCIATED WITH INCREASED USE OF HYPNOTICS AND ANXIOLYTICS IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

Xianchen Liu M.D., Wenyu Ye, Ph.D.; Madelaine M. Wohlreich, M.D.; James M. Martinez, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participants should have learned that chronic pain is associated with increased use of hypnotics and anxiolytics in patients with major depressive disorder.

SUMMARY:
Objective: Chronic pain, sleep disturbances, and anxiety coexist in many patients with major depressive disorder (MDD) (1,2). Concomitant hypnotics, anxiolytics, and antidepressants are common in the treatment of depression. This study examined if chronic pain is associated with increased use of hypnotics or anxiolytics in patients with MDD.
Method: A total of 153,913 patients in a large administrative insured claims database, who had at least 1 diagnosis of MDD between January and December of 2006, were included in the analysis. The sample consisted of 47,109 (30.6%) males and 106,804 (69.4%) females. The mean age of the subjects was 43.6 (SD = 12.7) years. In accordance with ICD-9-CM, chronic pain was defined as any pain of the following 5 categories: headache, rheumatoid arthritis (RA)/osteoarthritis (OA), low back pain (LBP), fibromyalgia, and neuropathic pain. Hypnotics, anxiolytics, and antidepressants were identified by the National Drug Code (NDC).
Results: Of the 153,913 patients, 17.1% had been prescribed hypnotics; 35.7%, anxiolytics; and 69.0%, antidepressants during the 1-year study period. Depressed patients with chronic pain were more likely than MDD patients without pain to use hypnotics (22.0% vs. 13.4%, $p < .0001$), anxiolytics (44.0% vs. 29.5%, $p < .0001$), and antidepressants (71.9% vs. 66.8%, $p < .0001$). Although the use of hypnotics and anxiolytics significantly increased with age, the association between chronic pain and use of hypnotics and anxiolytics remained consistent across all age groups and was independent of sex, sleep disorders, and antidepressants.
Conclusions: Hypnotics and anxiolytics are commonly used in patients with MDD in the managed-care settings. Chronic pain is associated with increased use of hypnotics and anxioloytics in depressed patients. Clinical research is needed to examine the role of hypnotics and anxiolytics in the treatment of depression with and without comorbid chronic pain. Funded by Eli Lilly and Company.

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» NR4-072

CORRELATION OF LEVELS OF DEPRESSIVENESS AND CHOICE OF ELECTIVE SUBJECTS IN MEDICAL STUDENTS

Rudolf Ljubicic M.D., Ivana Ljubicic Bistrovic M.D.,MSc, Ivana Balic M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize the possibility of protective role of psycho-educative component provided to the students attending elective subject on depression within medical school environment, that has repeatedly been shown to be stressful and demanding and is beneficial for the onset of depressive disorders.

SUMMARY:
The aim of this work was to test the correlation of choice of elective subjects, namely subjects ”Depression” and “Diabetes”, and level of depressiveness in medical students. Three groups of third year medical students attending School of medicine, University of Rijeka, were tested for the level of depression using Beck’s self-evaluation scale. The groups consisted of non-randomly selected students that had enrolled elective subjects «Depression», «Diabetes», and the third group that had enrolled none of the previous subjects. The results showed no statistically significant difference in overall level of depressiveness among the groups. By testing for the difference between group pairs, there was statistically significant difference between depressiveness in students attending “Depression” and “Diabetes”, the latter being significantly more depressed. Gender difference was also tested, and there was no statistically significant difference between sexes among groups. The difference was found only within the group of students attending “Depression” elective subjects, where females scored significantly higher on Beck’s questionnaire. The analysis of difference between items of the Beck’s questionnaire showed statistically significant difference in the item “Sense of rejection”, where students attending elective subjects other then “Depression” scored significantly higher; differences in the items “Urge for punishment” and “Suicidal tendencies” were also found between “Diabetes” and “other elective subjects” group, in favor of “Diabetes” group; in the item “Weight loss” students attending “Diabetes” elective subject scored significantly higher then their peers in both other groups.

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» NR4-073

VALIDATION OF A BRIEF VERSION OF THE CENTER FOR EPIDEMIOLOGIC STUDIES DEPRESSION SCALE (CES-D) IN COLOMBIAN ADULTS

Maria Teresa Lopez-Carmargo M.D., German Eduardo Rueda-Jaimes, MD, Luis Alfonso Díaz-Martínez, MD, MSc, Adalberto Campo-Arias, MD.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to know the psychometric properties of a brief version scale CES-D in Colombian adults.

SUMMARY:
Objective: The aim of this study is to establish de criterion validity and internal consistency of a brief version of the Center for Epidemiologic Studies Depression Scale (CES-D) in adults from Bucaramanga, Colombia.
Methods: A validation study with a cross sectional sampling was designed. 266 adults were evaluated independently and blindly with the CES-D scale and the Composite International Diagnostic Interview for axis I disorders from the DSM-IV. The items with a lower association with the clinic diagnostic of major depressive disorder were excluded from the scale. A brief version of 7 items was there obtained; Cronbach’s alpha, factor analysis, ROC curve analysis, best cutoff point, sensitivity, specificity and concordance were computed.
Results: Cronbach’s alpha was 0.79 and the area under the ROC curve was 0.92. For a cutoff point of 8 the sensitivity was 93.2%, specificity was 77.5%, Cohen’s kappa was 0.5, and a single factor explained the 77.5% of the variance.
Conclusion: The brief version of the CES-D Scale is as useful as the original, moreover, it has a better psychometric properties. It is necessary to study the reproducibility and validity of this brief version in other Colombian populations.

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» NR4-074

FIBROMYALGIA AND COMORBID MAJOR DEPRESSIVE DISORDER: ASSESSMENT OF MOOD AND PAIN RESPONSE TO DULOXETINE HYDROCHLORIDE COMPARED TO PLACEBO

Lauren Marangell M.D., Laurence Bradley, Ph.D., Ernest Choy, M.D., Daniel Clauw, M.D., Philip Mease, M.D., Scarlett Shoemaker, M.S.N., Fujun Wang Ph.D, Madelaine Wohlreich, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to better understand the clinical course of patients with both fibromyalgia and comorbid Major Depressive Disorder (MDD) who were treated with duloxetine. The poster will also assess whether the clinical improvement in this cohort was dependent on baseline MDD and/ or pain severity, and whether mood and pain improved independently of one another.

SUMMARY:
Objective: To better understand the clinical course of patients with fibromyalgia (FM) and comorbid Major Depressive Disorder (MDD) who were treated with duloxetine. hydrochloride (DLX), a dual reuptake inhibitor of serotonin and norepinephrine, shown to have independent effects on both mood and pain. Method: Data pooled from 4 double-blind, placebo-controlled, randomized trials of DLX 60-120 mg in patients with FM. Of 1332 patients in pooled population, 350 (26% [147 placebo, 203 DLX]) had comorbid MDD (per DSM-IV) and were included in these analyses. Measures included Brief Pain Inventory (BPI) average pain; Hamilton Depression Rating Scale (HAMD) or Beck Depression Inventory (BDI). Pain and mood responses defined as at least 30% reduction in BPI average pain from baseline, and 50% reduction in HAMD17 or BDI total scores from baseline. Logistic regressions tested consistency of treatment effect across subgroups. Path analysis evaluated how improvement in one variable was mediated through improvement of the other. Results: No difference was found in pain response across baseline MDD severities (treatment-by-severity interaction p>0.1) or MDD response across baseline pain severities (interaction p>0.1). Path analysis indicated 69% of improvement in pain was direct effect (p=0.09), with improvement in mood accounting for 31%. For mood improvement, 60% was direct effect (p=0.2), and 40% was due to pain improvement. Conclusion: In patients with FM and comorbid MDD, response in pain (or mood) was similar regardless of baseline MDD (or pain) severities. Improvement in pain reflected greater direct treatment effect with an indirect effect of improved mood. Similarly, improvement in mood was found to reflect greater direct effect on mood, with improvements in pain also contributing to mood improvement. Hence, direct and indirect analgesic and antidepressant properties appear to be relevant to treatment of these comorbid patients with DLX. Funded by Eli Lilly and Company

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» NR4-075

USE OF TRADITIONAL AND ALTERNATIVE MEDICINES IN PEOPLE WHO SUFFER BIPOLAR DISORDERS: IMPACT ON COMPLIANCE

Eliana Marengo M.D., Maria Jose Sarmiento M.D., Maria Scapola Psy.D., Laura M.D.; Diego Martino M.D.; Ana Igoa M.D., Carlos Gomez M.D.; Sergio Strejilevich M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand tne impact of alternative therapies in compliance among bipolar patients

SUMMARY:
Introduction: While the use of Alternative Therapies (AT) has been reported in people who suffer from chronic pathologies, the rates of use of AT in people who suffer bipolar disorders is unknown. We report the results of an anonymous survey conducted among people affected by BD in Argentina and Colombia. We investigated the use of AT and its impact on the level of compliance in this population. Results: 110 people were surveyed (66,4% female; 46,6 ± 14,7 years old; first episode: 28 ± 13,5 years old; first contact: 30, 6 ± 13,6 years old). The level of compliance was rated as good for 72%, partial to 19%, bad to 5,5% and non-compliance for 3,5% of the sample.
Thirty percent of the sample reported having used AT prior to their first contact with the health system (HS) and 37% to be using them concurrently to the standard treatment. Thirty seven percent of those who had used AM before their first contact with the HS reported that this could have been a cause for delays in consultation to HS but this was not confirmed by the number of years of diagnostic delay. The use of AT prior to first contact with the mental health system was associated with less compliance, but concurrently-use was not. 57, 5% reported not having informed to their psychiatrist about the use of alternative medicine.
The use of AT did not correlate with education, social level, religion, level of improvement or gender. Concurrent use of AM was rated as useful or very useful by 68 % of the users.

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» NR4-076

INCREASED DEPRESSIVE SYMPTOMS IN PERIMENOPAUSAL AGE WOMEN WITH BIPOLAR DISORDER: AGE AND GENDER COMPARISON

Wendy K. Marsh M.D., Terence A. Ketter M.D., Natalie L. Rasgon M.D., Ph.D.

EDUCATIONAL OBJECTIVES:
After reading this poster, the participant should be able to recognize that in this study perimenopausal age women with bipolar disorder experience a higher proportion of clinic visits in the depressed state than do comparison age and gender groups with bipolar disorder.

SUMMARY:
Objective: Emerging data suggest the perimenopausal may be a time of increased risk for depression. This study examines the course of bipolar disorder focusing on depressive symptoms in perimenopausal age women, compared to similar-aged men as well as younger adult women and men.
Methods: Outpatients with bipolar disorder were assessed with the systematic treatment enhancement program for bipolar disorder (STEP-BD) affective disorders evaluation and longitudinally monitored during naturalistic treatment with the STEP-BD clinical monitoring form. Clinical status (syndromal/subsyndromal depressive symptoms, syndromal/subsyndromal elevation or mixed symptoms, and euthymia) was compared between perimenopausal age women (n = 47) and pooled similar-aged men(n = 30) 45–55 years old, younger women (n = 48) and men (n = 39) 30–40 years old.
Results: Subjects included 164 bipolar disorder patients (67 type I, 82 type II, and 15 not otherwise specified), 34% were rapid cycling and 58% women. Bipolar II disorder/bipolar NOS was more common in women. Monitoring averaged 30 ± 22 months, with an average of 0.9 ± 0.5 clinic visits/month. Perimenopausal age women had a significantly greater proportion of visits with depressive symptoms ($p < 0.05$), significantly fewer euthymic visits ($p < 0.05$) and no difference in proportion of visits with elevated/mixed symptoms compared to pooled comparison group.
Conclusions: Perimenopausal age women with bipolar disorder experience a greater proportion of clinic visits with depressive

symptoms compared to similarly aged men, and younger women and men with bipolar disorder. Further systematic assessment of the influence of the menopausal transition and reproductive hormones upon mood is needed to better inform clinical practice in treating women with bipolar disorder.

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1) Marsh WK, Templeton A, Ketter TA, Rasgon NL. Increased frequency of depressive episodes during the menopausal transition in women with bipolar disorder: preliminary report. Journal of Psychiatric Research 2008;42:247–51.

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» NR4-077

ADJUNCTIVE ARIPIPRAZOLE IMPROVES CORE DEPRESSIVE SYMPTOMS ON CLINICIAN AND PATIENT MEASURES: A POOLED MADRS/IDS CROSS CORRELATION LINE-ITEM ANALYSIS

Michael Martin M.D., Fred W Reimherr, M.D., James M Eudicone, M.S., Barrie K Marchant, M.S., Quynh-Van Tran, Pharm.D., Andrei Pikalov, M.D., Ph.D., Berit X Carlson, Ph.D., Ronald N Marcus, M.D., Robert M Berman, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session the participant should be able to demonstrate the patterns of improvement of core depressive symptoms with adjunctive aripiprazole versus adjunctive placebo added to standard antidepressant therapy (ADT) using clinician and patient rating scales.

SUMMARY:

Objective: Previous reports examined Montgomery-Åsberg Depression Rating Scale (MADRS) line-items for patterns of symptom improvement with adjunctive aripiprazole. The present analysis looks at correlations between the previous reports and data from the patient-rated Inventory of Depressive Symptoms (IDS-SR) scale.

Methods: Data were pooled from two identical aripiprazole studies1,2 that included an 8-week prospective ADT phase followed by a 6-week double-blind randomization phase. Among the 724 subjects (n=356, placebo; n=368 aripiprazole), Pearson Correlation Coefficients [r] were calculated between changes for the MADRS line-items and selected IDS-SR line-items using last observation carried forward (LOCF).

Results: At endpoint, adjunctive aripiprazole demonstrated significant improvement versus ADT alone in 8/10 MADRS items ($p<0.0001$) and 12/30 IDS-SR items ($p<0.0001$). Changes on MADRS line-items and similar IDS-SR items were highly correlated for 5 MADRS-defined symptoms: Reported Sadness:Feeling Sad (Mean [r]=0.42); Lassitude:Pleasure/Enjoyment (Mean [r]=0.40); Inability to Feel:Responsive Mood (Mean [r]=0.38); Pessimistic Thoughts:View of Future (Mean [r]=0.35); and Suicidal Thoughts:Thoughts of Suicide (Mean [r]=0.43). These symptoms showed significant treatment responses to adjunctive aripiprazole within 2 weeks and maintained until the end of the study on both scales. IDS-SR items assessing mood quality, libido, self-worth and interpersonal sensitivity showed a similar pattern of response to aripiprazole.

Conclusions: The IDS-SR identified an additional four key depression-related symptoms (mood quality, libido, self-worth and interpersonal sensitivity) which responded significantly to adjunctive aripiprazole. This cross-correlation analysis confirmed that improvement in depressive symptoms with adjunctive aripiprazole was identified by both clinicians and patients. Supported by Bristol-Myers Squibb and Otsuka Pharmaceutical Co., Ltd.

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1) Berman RM, Marcus RN, Swanink R, McQuade RD, Carson WH, Corey-Lisle PK, Khan A: The efficacy and safety of aripiprazole as adjunctive therapy in major depressive disorder: a multicenter, randomized, double-blind, placebo-controlled study. J Clin Psychiatry. 2007; 68:843-853

2) Marcus RN, McQuade RD, Carson WH, Hennicken D, Fava M, Simon JS, Trivedi MH, Thase ME, Berman RM: The efficacy and safety of aripiprazole as adjunctive therapy in major depressive disorder: a second multicenter, randomized, double-blind, placebo-controlled study. J Clin Psychopharmacol. 2008; 28:156-165

» NR4-078

INTERVENTIONS FOR THE FAMILIES OF BIPOLAR PATIENTS: IMPACT ON FAMILIES

Nancy Maruyama M.D., Allison M.R. Lee, M.D., Igor I. Galynker, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, participants should be aware of the effect of family interventions for bipolar disorder on caregivers, how such interventions may best be carried out, and potential future research topics in this area.

SUMMARY:

Background: While accumulating evidence suggests that interventions which include caregivers in the treatment of bipolar disorder impact positively on patient outcomes, few studies have examined the impact of such interventions on family members themselves. This review details what is currently known about the impact of bipolar family interventions on caregivers of bipolar patients.

Methods: Journals@Ovid Full Text, All EBM Reviews, Science Citation Index, Ovid MEDLINE® 1985 to present, and PsycINFO 1985 to present were searched, using keywords “bipolar disorder,” “manic depressive,” “family,” “partner,” “spouse,” “intervention,” and “burden.” Studies were excluded if they did not focus on an intervention that included caregivers of bipolar patients or if they did not report family outcomes.

Results: Nine studies of family interventions were analyzed for research design and intervention format and content. Many studies had design limitations; nevertheless, psychoeducation emerged as particularly beneficial, and may increase caregivers’ knowledge of bipolar disorder, improve attitudes towards treatment, and reduce burden and Expressed Emotion (EE). Family interventions may alter interactions between bipolar patients and caregivers. Multiple types of interventions appear effective and acceptable to families.

Conclusions: Group family psychoeducation appears to be a useful clinical intervention, but more research is needed to assess specifics of how it should be carried out. Recommendations for format, duration, and content of interventions are discussed.

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2) Simoneau TL, Miklowitz DJ, Richards JA, Saleem R, George EL: Bipolar disorder and family communication: effects of a psychoeducational treatment program. J Abnorm Psychol 1999; 108:588-597

» NR4-079

SEROTONIN SYNTHESIS AND PRESENCE OF TRYPTOPHAN HYDROXYLASE IN LYMPHOCYTES OF MAJOR DEPRESSION PATIENTS TREATED WITH FLUOXETINE AND FOLIC ACID

Salvador Mata M.D., Mary Urbina BSc., Renée Lavie MD., Gustavo Resler MD., Julio Campos MD., Ph. D., Lucimey Lima MD., Ph. D., Alfonso González MD., Ph. D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the capacity for serotonin production and the presence of tryptophan hydroxylase in lymphocytes of major depression patients treated with fluoxetine and folic acid

SUMMARY:

Introduction: Folic acid has been used as a coadjuvant of antide-

pressant treatment, and low levels have been reported in depressed patients. Due to the role of folic acid and the relevance of serotonergic system in lymphocytes during depression, the aim of this study is to explore the capacity for serotonin production and the presence of tryptophan hydroxylase in lymphocytes of patients treated with fluoxetine and folic acid. Methods: Patients were diagnosed by the criteria of Diagnostic and Statistical Manual of the American Psychiatric Association, the severity of the depressive episode was evaluated by Hamilton Scale for Depression. Twenty seven patients (21-58 years) selected did not present other disorder neither risk of suicide. They were randomly distributed, some (14) received 20 mg/d of fluoxetine plus 10 mg/d folic acid, and others (13) fluoxetine and placebo. Control group was composed by 15 apparently healthy subjects (26-49 years). Blood samples were taken prior and six weeks after treatment. Lymphocytes were isolated by density gradients with Ficoll/Hypaque and differential adhesion to plastic. Results: Ten patients from each experimental group finished the study. Plasma homocysteine decreased with folic acid. Serotonin concentration was not different between the two groups and neither respecting controls, but it was low in those that received treatment. Serotonin synthesis from tryptophan was lower in patients than in controls and decreased in patients after the treatments. The number of lymphocytes with the enzyme was lower in patients and decreased after folic acid. Conclusions: The results could be in agreement with the monoaminergic hypothesis of depression, in which modifications of central and peripheral serotonin systems take place. Decreases of serotonin concentration after treatments and of its synthesis before treatment might indicate modulations in relation to lymphocyte function in depressed

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1) Abou-Saleh MT, Coppen A. Folic acid and the treatment of depression. J Psychosom Res 2006; 61:285-287

2) Young SN: Folate and depression - a neglected problem. J Psychiatry Neurosci 2007; 32:80-82

» NR4-080

A RETROSPECTIVE STUDY OF FASTING BLOOD GLUCOSE LEVELS IN PSYCHIATRIC INPATIENTS WITH PSYCHOTIC VS NON-PSYCHOTIC MAJOR DEPRESSIVE DISORDER

John Matthews M.D., Elizabeth A. Davis, M.D., Caleb J. Siefert, Ph.D., Sarah Stone, M.P.H., Nelson Tauro, Adrienne O. van Nieuwenhuizen, B.A., Lawrence T. Park, M.D., Kaloyan Tanev, M.D., David W. Abramson, M.D., Maurizio Fava, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, participants should be able to recognize that patients with major depressive disorder with psychotic features may be at increased risk of developing insulin resistance or diabetes mellitus compared with major depressive disorder without psychotic features.

SUMMARY:

Background: There is growing concern that patients with major depressive disorder with and without psychotic features may be at greater risk of developing diabetes mellitus type II, cardiovascular disease, and metabolic syndrome.
Objective: To compare fasting glucose and lipid (total cholesterol, HDL, LDL, triglycerides) blood levels in patients with major depressive disorder with (MD-Psy) and without psychotic features (MD-Non-Psy).
Methods: A retrospective chart review was conducted on patients admitted to the inpatient psychiatric unit at Massachusetts General Hospital from April 2007 through May 2008 with diagnoses of MD-Psy (N=29, 12 Males and 17 Females) or MD-Non-Psy(N=53, 24 Males and 29 Females). Fasting glucose and lipid (total cholesterol, HDL, LDL, and triglycerides) blood levels measured at the time of admission were compared between the two groups.
Results: Mean fasting blood glucose levels for MD-Psy and MD-Non-Psy were 130.28 ± 54.05 and 111.00 ± 35.94 respectively ($t = 1.94$, $p = 0.057$). Regression analysis was also conducted with age, gender, and use of anti-psychotic medications on admission entered on the first block and MD-Psy status (i.e. yes/no) entered on the second. Inclusion of MD-Psy status made a significant contribution to the prediction of blood glucose levels (R2 change = .07; F change = 3.06, $p = 0.05$) beyond that predicted by age, gender, and use of anti-psychotic medications alone. Psychotic symptoms did not predict differences in the two groups with regards to fasting total cholesterol, HDL, LDL, or triglycerides. Contributing factors, including serum cortisol, will be discussed.
Conclusions: Patients with a diagnosis of MD-Psy had significantly higher fasting blood glucose levels than patients with a diagnosis of MD-Non-Psy. There were no significant differences in fasting lipids between the two groups.

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2) Eaton WW, Armenian H, Gallo J, et al. "Depression and Risk for Onset of Type Two Diabetes: A Prospective Population-Based Study," Diabetes Care 1996; 19: 1097-1102.

» NR4-081

ASENAPINE EFFICACY IN PATIENT SUBPOPULATIONS EXPERIENCING MANIC OR MIXED EPISODES OF BIPOLAR I DISORDER: A POOLED ANALYSIS

Roger McIntyre, Miriam Cohen, Jun Zhao, John Panagides

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:
1) Describe the clinical diagnoses and prevalence of manic and mixed episodes in patients with bipolar I disorder.
2) Describe the clinical efficacy of asenapine in the treatment of manic and mixed episodes in patients with bipolar I disorder.

SUMMARY:

Objective: Asenapine is being developed for the treatment of bipolar disorder and schizophrenia. We describe the efficacy of asenapine in treating acute mania or mixed states in patient subpopulations with bipolar I disorder using pooled data from two pivotal registration trials.
Methods: In two similarly designed 3-week trials (Ares 7501004 and 7501005), patients were randomized to sublingual asenapine (10 mg BID on day 1, flexible 5 or 10 mg BID thereafter; n=379), oral olanzapine (given to verify assay sensitivity; 15 mg QD on day 1, flexible 5–20 mg QD thereafter; n=395), or placebo (sublingual and oral; n=202). Change from baseline to day 21 on the Young Mania Rating Scale (YMRS) and the Clinical Global Impression for Bipolar Disorder severity score (CGI-BP-S) was assessed for asenapine vs placebo in patient subpopulations diagnosed with either manic or mixed episodes (exploratory post hoc ANCOVA with LOCF for missing data using pooled data from both trials).
Results: After pooling the data (N=976), more than twice as many patients were diagnosed with a manic episode (69.1%) vs a mixed episode (30.9%). Mean ± SD changes from baseline to day 21 in YMRS total score were greater with asenapine (manic: –11.4±11.3, n=265, $P<0.0001$; mixed: –10.4±11.1, n=107, $P<0.071$) and olanzapine (manic: –14.3±10.8, n=269, $P<0.0001$; mixed: –12.3±8.2, n=122, $P<0.003$) than with placebo (manic: –6.1±11.5, n=131; mixed: –7.7±10.2, n=66). Mean ± SD changes from baseline to day 21 in CGI-BP-S score were also greater with asenapine (manic: –1.2±1.5, $P=0.0009$; mixed: –1.4±1.5, $P=0.009$) and olanzapine (manic: –1.5±1.3, $P<0.0001$; mixed: –1.3±1.1, $P=0.003$) than with placebo (manic: –0.8±1.4; mixed: –0.8±1.1).
Conclusions: This exploratory analysis indicates that asenapine

and olanzapine reduce the severity of acute manic symptoms in patient subpopulations with bipolar I disorder diagnosed with either manic or mixed episodes. This research was supported by Schering-Plough and Pfizer Inc.

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1) Fountoulakis KN: The contemporary face of bipolar illness: complex diagnostic and therapeutic challenges. CNS Spectr. 2008; 13:763-774, 777-769

2) Lieberman DZ, Peele R, Razavi M: Combinations of DSM-IV-TR criteria sets for bipolar disorders. Psychopathology. 2008; 41:35-38

» NR4-082

EFFECTS OF QUETIAPINE FUMARATE ON SLEEP ARCHITECTURE IN PATIENTS WITH DEPRESSION – AN OPEN LABEL STUDY

Roumen Milev M.D., Lauren Lazowski, B.Sc., Ruzica Jokic, M.D., FRCP(C), Alan Lowe, M.D., FRCP(C), Regina du Toit, M.D., FRCP(C).

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation the participant should be able to understand sleep disturbances in major depressive episodes and recognized potential treatments.

SUMMARY:

Background: Sleep continuity disturbances, diminished slow wave sleep (SWS), shortened rapid eye movement (REM) latency, and an alteration in the temporal distribution of REM sleep are common in depression (1). Quetiapine has been shown to increase the percentage of stage 2 and decrease latencies to stage 1 and 2, and the percentage of time awake in healthy volunteers. The antidopaminergic and antiadrenergic properties of quetiapine are suggested to have a role in its effects on sleep (2). Our aim was to characterize the effects of quetiapine augmentation on sleep quality, sleep architecture and depressive symptoms in people with depression. Methods: Patients with bipolar disorder and major depressive disorder who were experiencing a major depressive episode were included. Quetiapine was added to their current medication regime, which must have been at stable dosing for 4 weeks prior to entry and throughout the study. Illness severity, sleep quality and polysomnographic data was collected at baseline, 2-4 days and 21-28 days after starting the medication, with an optional visit at 42-54 days after baseline. Results: 10 patients (8 female, 2 male) concluded the study so far. Sleep quality (total sleep time, latency to sleep, sleep efficiency and number of awakenings) did not significantly differ from baseline with treatment. Sleep architecture (latency to and percent of time in stage 1,2, SWS, and REM) did not significantly differ with the addition of quetiapine, however the latency to REM sleep did non-significantly decrease. Subjective sleep quality improved non-significantly. Illness severity significantly improved with the addition of quetiapine as measured by the HDRS, MADRS and CGI-S. Half of the participants had a 50% reduction in depressive symptoms. Conclusions: Quetiapine augmentation did not improve sleep quality or sleep architecture in patients with depression, but improved depressive symptoms and overall illness severity after 2-3 weeks of treatment.

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1) Kupfer DJ: Depression and Associated Sleep Disturbances Patient Benefits with Agomelatine. 2006 Eur Neuropsychopharm 16: S639-S643.

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» NR4-083

ACUPUNCTURE AUGMENTATION THERAPY IN ANTIDEPRESSANT PARTIAL AND NON-RESPONDERS WITH MAJOR DEPRESSIVE DISORDER: INTERIM ANALYSIS

David Mischoulon M.D., Albert S. Yeung, M.D., Sc.D., Sarah E. Chuzi, B.A., Victoria E. Ameral, B.A., Maurizio Fava, M.D., David Mischoulon, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the efficacy and tolerability of a standardized acupuncture treatment protocol used as augmentative therapy in patients with major depressive disorder who are partial responders to antidepressants.

SUMMARY:

We sought to determine the efficacy and safety of a standardized acupuncture protocol as augmentation therapy in major depressive disorder (MDD). Results for the first fourteen evaluable subjects (43% female, mean age 42+/-12 yrs) of a projected sample of 40 with SCID-diagnosed MDD and partial or non-response after 8 or more weeks of standard antidepressant treatment are examined in an interim analysis. All subjects received 8 weeks of open acupuncture augmentation therapy using 5 specific body points (on the arms and legs bilaterally) with manual tonification every 10 mins and electroacupuncture with a 2 Hz current applied to two points along the midline of the head. Treatment lasted 30 mins. Subjects were assigned once-weekly (n=9) or twice-weekly (n=5) acupuncture sessions, based on their preference. The change in Hamilton-D-17 (HAM-D-17) score was the primary outcome measure. Six subjects (43%; 5 in weekly and 1 in twice-weekly treatment) completed the study and 13 (8 in weekly and 5 in twice-weekly treatment) met criteria for intent-to-treat (ITT) analysis. Among completers, HAM-D-17 scores decreased from 17.8+/-3.6 to 12.0+/-5.7 in the once-weekly group ($p>0.05$), and from 15.0+/-0.0 to 11.0+/-0.0 in the twice-weekly group (one patient). In the ITT sample, HAM-D-17 scores decreased from 17.6+/-2.9 to 13.9+/-5.2 in the once-weekly group ($p>0.05$), and from 18.2+/-3.6 to 13.0+/-4.3 in the twice-weekly group ($p=0.042$). Degree of improvement did not differ significantly between treatment arms ($p>0.05$). Side effects were minimal; one subject reported mild bleeding at the needle site, two reported mild dizziness and three reported mild site-specific pain or paresthesia following treatment. Acupuncture was a well-tolerated and effective augmentation therapy in antidepressant partial responders, with no additional benefit from twice-weekly versus once-weekly sessions thus far. These preliminary findings will be expanded in a larger sample currently under recruitment.

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1) Allen JJ, Schnyer RN, Chambers AS, Hitt SK, Moreno FA, Manber R: Acupuncture for depression: a randomized controlled trial. J Clin Psychiatry 2006; 67:1665-1673

2) Leo RJ, Ligot JS, Jr.: A systematic review of randomized controlled trials of acupuncture in the treatment of depression. J Affect Disord 2007; 97:13-22.

» NR4-084

QUALITY OF LIFE AND EATING DISTURBANCES IN PATIENTS DIAGNOSED WITH BIPOLAR DISEASE TYPE I WITH SYNDROMIC REMISSION (REMFYS STUDY)

Alonso Montoya M.D., Vieta E, Montoya A, Casillas M, Polavieja P, Chacón F, Gilaberte I and Tohen M of the study REMFYS researchers

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: • Understand the importance of syndromic, symptomatic, and functional remission. • Identify the factors involved in the quality of life of patients with bipolar I disorder according to their remission status. • Ascertain the role of eating disturbances in bipolar disorder patients with syndromic remission.

SUMMARY:

Objective: To describe the influence of different types of remission on quality of life (QoL) and on eating habits in patients with Bipolar Disorder Type I which are syndromic remission .

Method: REMFYS is an epidemiological, observational, and prospective 12 months study. Patients were classified in a group with functional and symptomatic remission (group A), with symptomatic remission but not functional (group B) and with no symptomatic remission (group C). QoL was measured using the SF-12 health survey providing the physical component summary measure (PCS-12) and mental component summary measure (MCS-12). Eating habits were measured using the Bipolar Eating Disorder Scale (BEDS). The groups were compared regarding SF-12 and BEDS scores by mixed model repeated measures.
Results: Out of 398 patients 208 (52.3%) were in group A, 143 (35.9%) in group B and 47 (11.8%) in group C. Group A showed statistically better PCS-12 (45.3, 95% CI, 44.3-46.3) and MCS-12 (28.9, 27.8-30.0) means over time compared to group C (PCS-12: 43.6, 42.7-44.6) and MCS-12: (26.7, 15.6-27.8)). According to BEDS, all groups improved along the study. Patients on group A had less significant eating disturbances than patients on groups B and C at baseline (7.7% vs 15.4% and 24.4%). There were no statistically significant differences on weight changes over time between groups.
Conclusions: The type of remission at baseline was found to be associated with the QoL over time. Patients reached a higher QoL when they met all remission criteria at baseline. In this population mental aspects of QoL deviated more from the norm than psychical ones. Also the presence of the three remissions was associated with fewer eating disturbances.

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2) Tohen M, Strakowski SM, Zarate C Jr, Hennen J, Stoll AL, Suppes T, Faedda GL, Cohen BM, Gebre-Medhin P, Baldessarini RJ. The McLean-Harvard first-episode project: 6-month symptomatic and functional outcome in affective and nonaffective psychosis.

» NR4-085

RANDOMIZED PLACEBO-CONTROLLED TRIAL OF RAMELTEON FOR DEPRESSIVE SYMPTOMS IN PATIENTS WITH SEASONAL AFFECTIVE DISORDER

Edward R Norris M.D., Karen Burke, R.N., Carol Foltz, Ph.D., Emily Bates, B.A., Kenneth J. Zemanek, M.D., Michael Kaufmann, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to apply this new finding about ramelteon to the treatment of their patients with seasonal affective disorder.

SUMMARY:

Introduction: One major theory regarding the etiology of seasonal affective disorder (SAD) suggests that the lack of natural light accompanying the winter season is the central cause of a misalignment of the circadian rhythm. This study assessed if ramelteon, a novel sleep-promoting agent with high selectivity for the MT1/MT2 receptors in the brain's SCN, could resynchronize the circadian rhythm and decrease depressive symptoms associated with SAD.
Methods: In this single-site, single-blind, parallel-group study, participants with a DSM-IV diagnosis of SAD were randomly assigned to receive either ramelteon 8 mg or placebo in addition to their usual care by a Psychiatrist and assessed monthly for four months. The mean change from baseline in the Zung depression scale and the Structured Interview Guide for the Hamilton Depression Rating Scale, SAD version (SIGH-SAD) were used to assess depressive symptoms. This investigator initiated clinical trial was sponsored by Takeda Pharmaceuticals North America, Inc.
Results: Fifty participants were enrolled, 49 were randomized to receive ramelteon (n=25) or placebo (n=24). Allowing for drop-outs, the efficacy sample included 45 participants who had at least 1 follow-up (ramelteon, n=24; placebo, n=21). At baseline, there were no significant demographic differences between the 2 treatment groups, with a mean age of 46.6 years and predominantly female (74%). The ramelteon group had significantly lower Zung scores at month 2 (ramelteon 52, placebo 59, p<.05), month 3 (ramelteon 48, placebo 58, p<.01), and month 4 (ramelteon 45, placebo 62, p<.01) than the placebo group. The ramelteon group also had significantly lower SIGH-SAD scores at months 2 (p<.05), 3 and 4 (p<.01). There were few treatment emergent side effects for both groups.
Conclusions: The present study shows that ramelteon was effective at reducing the depressive symptoms of SAD. This study suggests that ramelteon is another option for those who suffer from SAD.

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» NR4-086

SOCIAL ANXIETY AS A CONSEQUENCE OF SELF-STIGMATIZATION AND LOW SELF-ESTEEM IN REMITTED BIPOLAR PATIENTS

Aydemir Omer M.D., Cengiz Akkaya, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize social anxiety in remitted bipolar patients, to list the psychosocial causes of social anxiety, and to identify low self-esteem and sense of stigmatizaion related to social anxiety in remitted bipolar patients.

SUMMARY:

INTRODUCTION: Stigmatization of mental disorders is one of the leading problems in the adaptation of psychiatric patients. It is reported that concerns about the stigma predicted poorer social adjustment. It is shown that the stigma associated with mental illness harms the self-esteem of the patients.
In this study, it is aimed to demonstrate the association between bipolar disorder and social anxiety with the hypothesis that self-stigmatization causes low self-esteem in remitted bipolar patients leading to social anxiety.
METHOD: The study was carried out with 150 remitted patients consecutively admitted to the mood disorder units. All subjects had been asymptomatic for at least 6 months based on the clinician notes and the SCID-CV interview.
In the assessment of the patients, Liebowitz Social Anxiety Scale (LSAS), Rosenberg Self-Esteem Scale (RSES), and the self-stigmatization subscale of the Bipolar Disorder Functioning Questionnaire (BDFQ-Stigma) were used. In the statistical analyses, beside demographic data, multiple linear regression analysis was performed.
RESULTS: The mean age of the patients was 39.5+/-12.7, and 52.7% (n=79) were female. Ninety percent (90.0%) of the patients had bipolar I disorder. The mean duration of the illness was 13.4+/-9.9 years and the mean number of episodes was 7.8+/-7.1. The mean LSAS anxiety subscale score was 39.7+/-10.9 and the mean LSAS avoidance/withdrawal subscale score was 38.3+/-12.1. The mean LSAS total score was calculated to be 78.1+/-21.7, and 91.3% (n=137) of the patients were above the cutoff point of 50. In the regression analysis, the LSAS anxiety subscale was associated with RSES self-esteem subscale, "difficulties in finding a job because of the illness", and BDFQ sense of stigmatization subscale. The LSAS avoidance/withdrawal subscale was associated with RSES self-esteem subscale, and "difficulties in getting married because of the illness". The LSAS total score was associated with RSES self-esteem subscale, and "difficulties in getting

married because of the illness".
CONCLUSION: In bipolar disorder, social anxiety is found to be a significant problem in patients even in remission. The major causes of the social anxiety and social avoidance/withdrawal in remitted bipolar patients are low self-esteem and sense of stigmatization.

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» NR4-087

IMPACT OF CHILDHOOD TRAUMA ON THE CLINICAL COURSE OF BIPOLAR I DISORDER

Ilker Özyildirim M.D., Sibel Çakir, M.D., Olcay Yazici, M.D.

EDUCATIONAL OBJECTIVES:

The objectives of this presentation will be to highlight the importance of taking history on childhood traumatic experiences in patients with Bipolar Disorder. A positive history may need different treatment modalities.

SUMMARY:

Objective: Only a few studies investigated the impact of childhood traumatic experiences on clinical outcome in patients with Bipolar Disorder. Additionally, reports from outside of USA on this issue are very limited. In this study we aimed 1) to show the prevalence of childhood abuse and neglect, and 2) to identify their effects on clinical features in a group of patients with Bipolar I Disorder.
Method: Ninety four patients who had a diagnosis of Bipolar I Disorder according to DSM-IV criteria from Istanbul University Faculty of Medicine, Mood Disorders Unit were included to the study. All patients underwent a Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) assessment and the presence of childhood abuse was measured using a self-report; Childhood Trauma Questionnaire (CTQ) which is composed of 53 items and 5 subscales (emotional abuse, physical abuse, sexual abuse, emotional neglect and physical neglect).
Results: Seventeen (18%) patients reported at least one kind of childhood abuse or neglect. The total (p=0.039) and emotional abuse subscale scores (p=0.041) were higher in patients with a history of psychotic features in at least one episode. The patients with more severe episodes reported higher physical neglect score (p=0.011) and who had comorbid anxiety disorder reported higher total (p=0.012), emotional (p=0.001), physical (p=0.046), and sexual (p=0.02) abuse scores.
Conclusions: Although the causality cannot be ascertained, the results of this study implies that childhood traumatic experiences may be associated with psychotic features, severe episodes and comorbid anxiety disorder in bipolar patients. These findings suggest that childhood trauma may alter the outcome of bipolar disorder.

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» NR4-088

BILATERAL VERSUS MONOLATERAL LOW-FREQUENCY REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION AS ADD-ON TREATMENT IN RESISTANT DEPRESSION

Stefano Pallanti M.D., Leonardo Quercioli, MD., Andrea DiRollo, MD., Silvia Bernardi, MD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize in which category of patients with a diagnosis of mood disorder repetitive transcranial magnetic stimulation may be of help. Further, participants will be able to understand the diversity of effects for the different application modality.

SUMMARY:

Repetitive transcranial magnetic stimulation (rTMS) has been recently FDA approved for the treatment of resistant depression. No accordance exists on which are the involved mechanisms of action and on which stimulation parameters, frequency and side are optimal. To compare these different procedures the authors studied 39 patients with unipolar recurrent resistant major depressive disorder in a double-blind, controlled trial randomized to either sequential bilaterally on the right and left dorsolateral prefrontal cortex (DLPFC) or monolaterally on the right DLPFC. Patients were randomized to receive sequentially low-frequency rTMS at 1 Hz to the right DLPFC and high-frequency rTMS at 10 Hz rTMS to the left DLPFC, or to receive low-frequency rTMS at 1 Hz to the right DLPFC. Significant antidepressant effect as expressed by a reduction of Hamilton Depression Scale score was observed in both the groups of patients with a slight superior number of remitted patients in the unilateral group (25% vs 12.5%). Results suggest that unilateral right low-frequency rTMS is at least as effective as bilateral rTMS in resistant depression.

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» NR4-089

LONG-TERM SAFETY OF DULOXETINE IN THE OPEN-LABEL COMPASSIONATE TREATMENT OF PATIENTS WHO COMPLETED PREVIOUS DULOXETINE CLINICAL TRIALS

Beth Pangallo R.N., Durisala Desaiah, Ph.D., Qi Zhang, Ph.D., David G. S. Perahia, M.D., MRCPsych, Michael J. Detke, M.D., Ph.D., Sidney H. Kennedy, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the long-term safety of duloxetine in compassionate use in patients who had previously participated in clinical trials in the treatment of major depressive disorder, general anxiety disorder, diabetic peripheral neuropathic pain, or fibromyalgia.

SUMMARY:

Purpose: To provide duloxetine, a dual reuptake inhibitor of serotonin and norepinephrine effective in the treatment of depression, anxiety, and pain1-3, to patients who had previously completed a duloxetine clinical study and for whom in the opinion of the investigator no effective alternative therapy was available.
Methods: This was an open-label compassionate use study for adult outpatients who had previously completed a duloxetine clinical study for the treatment of major depressive disorder (MDD), diabetic peripheral neuropathic pain, generalized anxiety disorder, or fibromyalgia. The study was conducted between July 2003 and July 2008 in 12 countries. The patients received duloxetine 30 mg to 120 mg daily up until local approval and launch of the drug. Safety data analyzed included treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), AEs reported as reason for discontinuation, and change in vital signs.

Results: Of 667 patients enrolled, 282 (42.3%) were still participating at the time the drug was made commercially available in their countries. The most common reasons for early discontinuation were patient decision (25.3%), adverse event (8.4%), and lack of efficacy (8.4%). Most patients in this study had previously participated in a duloxetine MDD study (76.2%); were female (68.1%) and Caucasian (94.9%); the mean age was 50.9 years at enrolment. Of the 86 SAEs experienced by 46 patients, most (including one death) were considered by the investigators to be unrelated to duloxetine treatment. The most common TEAEs reported were classified in the gastrointestinal (28.3%), nervous system (28.0%), and psychiatric (25.8%) categories and were mild or moderate in severity. A small increase of systolic blood pressure (1.8 mm Hg) and pulse rate (2.2 bpm) was reported.
Conclusion: Data from this long-term compassionate use study of duloxetine were consistent with previous experience, and revealed no new safety signals.

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» NR4-090

THE IMPACT OF GALANTAMINE HBR ON COGNITION AND MOOD DURING ELECTROCONVULSIVE THERAPY

Lawrence Park M.D., John D. Matthews, M.D., Caleb J. Siefert, Ph.D., Mark Blais, Psy.D., Adrienne O. van Nieuwenhuizen, B.A., Kathryn Rooney, B.A., Nelson Tauro, Charles Welch, M.D., Kaloyan Tanev, M.D., Maurizio Fava, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation the participant should understand the typical cognitive side effects associated with electroconvulsive therapy (ECT). Furthermore, the participant should understand that one method for preventing ECT-induced cognitive side effects is to administer galantamine, which demonstrated protective effects on delayed memory in this trial.

SUMMARY:

The purpose of this prospective, double-blind, placebo-controlled study was to assess the effectiveness of galantamine in the prevention of ECT-associated cognitive impairment. Patients receiving ECT for depression were eligible for the study. Subjects were randomized to active treatment or placebo. 30 of 39 subjects completed the trial (12 in the active treatment group and 18 in the placebo group). Active treatment subjects received galantamine 4 mg bid (titrated by 5 mg every 5 days as tolerated by the subject to a target dose of 8 mg bid). Objective measures of cognitive functioning (Repeatable Battery for the Assessment of Neuropsychological Status [RBANS], Wechsler Abbreviated Intelligence Scale, and Trails A & B) and depression (Hamilton Depression Rating Scale [HAM-D-17] and Beck Depression Inventory [BDI]) were performed pre- and post-ECT. Subjective ratings of depression, confusion and side effects were obtained weekly over the course of ECT. Categorical analysis, using ?2 analysis, indicated that the two groups did not differ significantly with regard to age, estimated IQ, or level of depression; independent t-tests indicated that the two groups did not differ significantly on baseline RBANS indices. Hierarchical regression analysis showed that subjects in the active treatment group scored significantly higher on the delayed memory index of the RBANS compared with the placebo group. Examination of these scores suggested that the placebo group experienced a significant decline in delayed memory over the course of ECT, while the active treatment group demonstrated little decline compared with baseline measures. No significant difference was noted in response to ECT between groups. This study demonstrated that the administration of galantamine prior to and over the course of ECT may be a safe and effective treatment for ECT-induced delayed memory dysfunction. This research was supported by Janssen, the makers of galantamine.

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2) Prakash J, Kotwal A, Prabhu H: Therapeutic and prophylactic utility of the memory-enhancing drug donezepil hydrochloride on cognition of patients undergoing electroconvulsive therapy: A randomized controlled trial. J ECT 2006; 22(2):163-168

» NR4-091

BRIEF DEPRESSIVE EPISODES' IMPACT IN THE OUTCOME OF MOOD DISORDERS: A NATURALISTIC STUDY

Sara Pozzoli, Francesca Colombo, M.D., Alessandra Albano, M.D., Sara Bortolussi, M.D., Ilaria Balossi, M.D., Lucio Oldani, M.D., Massimiliano Buoli, M.D., Bernardo Dell'Osso, M.D., A. Carlo Altamura, M.D.

EDUCATIONAL OBJECTIVES:

The aim of this study is to show clinical differences between patients affected by Major Depressive Disorder (MDD) or Bipolar Disorder (BD) with or without comorbidity with Brief Depressive Episodes (BDEs) .

SUMMARY:

Background: Recurrent Brief Depression (RBD) is a Mood Disorder defined by Brief Depressive Episodes (BDEs) occurring monthly for at least 12 months and lasting less than 2 weeks. In this study, we analysed the occurrence of BDES, and the relationship with work and social impairment or subjective distress in patient with Major Depressive Disorder (MDD) or Bipolar Disorder (BD). The present results refer to 6 months of follow-up.
Methods: The study sample included 28 patients with a lifetime diagnosis of MDD or BD (17 subjects with MDD and 11 with BD) according to DSM-IV-TR criteria, divided in two sub-groups on the basis of the presence of BDES (present: n=12, absent: n=16). Diagnoses were assessed by the SCID-I. Patients were assessed at baseline and monthly for BDEs, substance/alcool abuse, suicidal ideation and behaviour by means of the Mini-International Neuropsychiatric Interview, for depressive symptoms by means of the HAM-D, and by means of the YMRS for manic symptoms, and for quality of life (SF-36).
Results: The two groups were homogenous in terms of clinical and demographic variables at baseline. Subjects with BDES showed an age at onset and age at the first treatment significantly lower than patients without BDES. Moreover subjects with BDES showed a more frequent presence of death ideation (?2=3.187,df=1;p=0,074) and suicidal ideation (?2=1.867; df=1; p=0,172), than subjects without BDES, in the 6 months of follow-up.
Conclusions: At the conclusion of this presentation preliminary results would suggest that the occurrence of BDEs might worsen the outcome in patients with MDD or BD.

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NR4-092

RANDOMIZED, PLACEBO-CONTROLLED, LONG-TERM STUDY OF RISPERIDONE LONG-ACTING INJECTABLE IN RELAPSE PREVENTION IN BIPOLAR I DISORDER PATIENTS

Jorge A. Quiroz M.D., Lakshmi N. Yatham M.D., Joseph M. Palumbo, M.D., Keith Karcher, M.S., Stuart Kushner, M.D., Vivek Kusumakar, M.D., F.R.C.P.C.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should have an understanding of the efficacy and safety of risperidone long-acting injectable (12.5–50 mg) in the prevention of mood episodes in patients with bipolar I disorder.

SUMMARY:

Introduction: To evaluate the investigational use of risperidone long-acting injectable (LAI) monotherapy vs placebo for prevention of mood episodes in patients with bipolar I disorder.

Methods: Patients aged 18–65 years diagnosed as acutely manic, mixed, or stabilized on risperidone or another medication entered the screening period. The study consisted of a 3-week open-label oral risperidone treatment period (for patients not already stabilized on risperidone), a 26-week open-label stabilization period with risperidone LAI and a double-blind treatment period (placebo or risperidone LAI 12.5, 25, 37.5 and 50 mg every 2 weeks, for up to 24 months). Primary efficacy variable was time-to-relapse to any mood episode during the double-blind period.

Results: Of the 501 patients who received open-label risperidone LAI, 303 (60%) maintained symptom remission throughout the 26-week stabilization period. They were randomized 1:1 to continue their maintenance dose (n=154) or placebo (n=149); 77% of patients received a dose of 25 mg. Time-to-relapse to any mood episode was significantly longer in the risperidone LAI group compared with the placebo group ($p<0.001$). The time by which 25% of the patients relapsed to any mood episode was 173 days in the risperidone LAI group ($p<0.001$ vs placebo) and 82 days in the placebo group. Adverse events that occurred more frequently with risperidone LAI than placebo (>=3% difference) were depression (6 vs 2%) and weight increase (5 vs 1%).

Discussion: This is the first controlled study of a long-acting atypical antipsychotic to demonstrate efficacy as monotherapy in relapse prevention of mood episodes in patients with bipolar I disorder. Risperidone LAI was associated with a significant reduction in the rate of relapse and a delay in the time to relapse, and had a tolerable safety profile. Funded by J&J PRD.

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NR4-093

EARLY RESPONSE AS PREDICTOR OF GOOD OUTCOME IN THE PROGNOSIS OF A DEPRESSIVE EPISODE: RESULTS FROM A 1-YEAR FOLLOW-UP LARGE EPIDEMIOLOGICAL STUDY

Miquel Roca, M.D., Ph.D., Antonio Ciudad, M.D., Ph.D., Enrique Álvarez, M.D., Ph.D., Enrique Baca, M.D., Ph.D., Luis Caballero, M.D., Ph.D., Marta Casillas, Ph.D., Pepa García de Polavieja, BsSci , Amparo Valladares PharmD., Belén Yruretagoyena, Ph.D., Inmaculada Gilaberte, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to to recognize clinical variables as an early response to antidepressant treatment that should be considered when evaluating the long-term outcome of a depressive episode."

SUMMARY:

Objective: The goals of the study were to evaluate in a cohort of depressed patients if response within the first 6 weeks of antidepressant treatment is associated with a long-term good outcome and whether there are other clinically useful predictors of their course of illness.

Method: This is a longitudinal, prospective and multicenter study of a cohort of outpatients with major depression (DSM-IV-TR). Patients were included in the study when they started an antidepressant treatment (based on clinical criteria) for index episode, and were followed for 1 year. Early response was defined as a 50% improvement on the 17-Item Hamilton Depression Rating Scale total score (HAM-D17) within the first 6 weeks, and good outcome when the patient achieved remission (HAM-D17 = 7) in the first 6 months and remained in remission until end of follow-up. For statistical purposes, patients lost to follow-up were considered not to have a good outcome. A multivariate logistic regression model was used with good outcome as the dependent variable and early response and various baseline demographic and clinical variables as the independent variables.

Results: 930 patients were included in the study. Mean age was 47.1 years (SD, 13.5); 67.9% were female. 413 patients (44.4%) had no previous depressive episodes. Mean HAM-D17 score was 24.2 (SD, 5.5). 355 patients (38.2%) showed early response, and of those 76.1% had a good outcome (achieved remission and remained well after 1-year follow-up), versus 43% of those patients without early response. Factors associated with good outcome included early response (Odds ratio, [OR], 4.14 (95% Confidence Interval, [CI], 3.07-5.57), presence of physical comorbidities (OR, 0.71; 95% CI, 0.54-0, 95) and working (including students and housewives) (OR, 1.45; CI, 1.09-1.93).

Conclusions: Early response was strongly associated with the course of the illness at 12-months follow-up; other factors associated were working status and physical comorbidities. This study was supported by Eli Lilly & Company, Spain

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NR4-094

CORTISOL METABOLISM IN DEPRESSED PATIENTS AND HEALTHY CONTROLS

Benedikt Römer, Sabina Lewicka, Dr., Michael Deuschle, Prof. Dr.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize how changes in intracellular steroid metabolism may increase cortisol bioavailability in depressed patients. Two important enzymes show alteres function in depressed patients. First the enzyme 11beta-Hydroxylase, what may contribute to renal hypertension. Second 5alpha Reductase, what leads to reduced steroid deactivation. The participant gets insight in disturbed neuroendocrine functions during major depression.

SUMMARY:

BACKGROUND: Chronic stress as well as major depressive disorder are associated with hypercortisolemia and a dysregulation of hypothalamic-pituitary-adrenocorticol (HPA) system functioning. Aim of this study was to find out whether in major depression changes in the activity patterns of local modulators of glucocorticoid action occur, if they contribute to an increase of cortisol bioavailability within tissues and if they change during antidepres-

sant treatment and clinical response.
METHODS: Concentrations of urinary free cortisol (UFF), urinary free cortisone (UFE), allo-THF (5a-THF), THF and THE were measured in a 10 h nocturnal urine sample of 19 depressed patients and 15 healthy controls. The activity of 11 ß-hydroxysteroid dehydrogenases (11 ß-HSD) as well as 5a-and 5ß-reductase was assessed by calculating the ratios of glucocorticoid metabolites. Patients were treated for 28 days with either mirtazapine or venlafaxine. Enzyme activity was observed during the course of treatment and compared to healthy controls. Responders to treatment were selected for this analysis.
RESULTS: Depressed patients showed reduced 5a-reductase activity manifested as a significantly lower amount of 5a-THF (99.8 ± 162.7 vs. 194.6 ± 165.8 µg, P = 0.015). The observed increased UFF-to-UFE ratio (0.729 ± 0.317 vs. 0.289 ± 0.131, P < 0.0001) indicates reduced activity of renal 11 ß-HSD Type 2. During pharmacological treatment 5a-reductase activity in patients returned to the level of the control group, while the decrease of 11 ß-HSD Type 2 activity persisted until day 28.
CONCLUSIONS: Our results show changes in activity of intracellular modulators of steroid action in major depressive illness, particularly a reduced activity of the intracellular cortisol deactivating enzymes 5a-reductase and 11 ß-HSD Type 2. These changes suggest an increase of cortisol bioavailability within tissues.

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» NR4-095

AN ADJUNCTIVE MANAGEMENT OF DEPRESSION PROGRAM FOR PATIENTS WITH DIFFICULT-TO-TREAT DEPRESSION AND THEIR FAMILIES - RESULTS AT 48 WEEKS

Christine Ryan Ph.D., Gabor I. Keitner,M.D., Stephen Bishop,Ph.D, Michaela F. Jamiel, Anna Eng, Joan Kelley

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to see how growth curve analysis shows individual variation in the rate of change and the speed of change in depression and psychosocial functioning, suggesting that there are several pathways to improvement for patients with difficult-to-treat depression – including a depression management program.

SUMMARY:

Introduction: 25-40% of depressed patients have depressions resistant to currently available treatments. These patients report persistent symptoms and impaired functioning in family, interpersonal, social, and work domains. Method: The Management of Depression (MoD) Program is an adjunctive intervention designed to help depressed patients and their family members learn to deal with a persisting illness. 19 depressed patients and their family members participated in a 16-week open label intervention followed by a 32-week maintenance period. Completers of the intervention showed significant improvement in quality of life, psychological well-being, family functioning, and depression scores (all p-values <.05). Change scores and growth curve analysis were used to track the 10 patients who completed the 32 week follow-up phase to see if improvement was maintained and to examine the pattern of change throughout the entire study. Results: Mean change scores of the 10 completers were 9.4 (±4.4) and 16.6 (±5.6) on the Montgomery-Asberg Depression Rating Scale from baseline to end of intervention and end of study respectively; 14.9 (±3.1) and 18.7 (±5.5) on the Beck Depression Inventory from baseline to end of intervention and end of study; and 9.0 (±2.6) and 14.1(±4.4) on the Quality of Life Enjoyment and Satisfaction Scale from baseline to end of intervention and end of study. All scores at the end of the study were in the expected direction and the p-values were <.02. Growth curves suggest that gains made during the MoD Program continued during the follow-up period for improvement in mood, coping abilities, and quality of life. 1/3 of the patients responded early, 1/3 did not respond, and 1/3 demonstrated a fluctuating course. Conclusion: Most completers showed a variable, but sustained, improvement through the end of the study. A depression management program for those with difficult-to-treat depression may help patients learn how to deal with ongoing symptoms.

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» NR4-096

ILLNESS EXPERIENCE AND REASONS FOR NON-ADHERENCE AMONG INDIVIDUALS WITH BIPOLAR DISORDER WHO ARE POORLY ADHERENT WITH MEDICATION

Martha Sajatovic M.D., Jennifer Levin, Ph.D., Edna Fuentes-Casiano, BSW, Janis Jenkins, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to gain understanding in relevant issues regarding treatment non-adherence among populations with bipolar disorder.

SUMMARY:

Objective: Characterization of factors underlying poor adherence in bipolar disorder (BD) is essential in order to develop appropriate interventions. This mixed-methods analysis evaluated illness experience in relation to adherence among 20 poorly adherent Community Mental Health Clinic patients with BD.
Methods: A qualitative instrument (SEMI TAD BD) evaluated selected patient, social/environmental, and provider-relationship factors likely to affect adherence. Quantitative assessments measured symptoms (HAMD, YMRS), psychopathology (BPRS), adherence (Tablets Routine Questionnaire/TRQ and pill counts) and attitudes (Attitude toward Mood Stabilizers Questionnaire (AMSQ), the Drug Attitude Inventory (DAI), and the Rating of Medication Influences (ROMI). Poor adherence was defined as missing 30% or more of medication.
Results: Minorities (80%), unmarried individuals (95%), and those with substance abuse (60%) predominated. Individuals were substantially depressed (mean HAMD 19.2, range 12-28), had at least some manic symptoms (YMRS mean 13.6, range 12-28) and moderate global psychopathology (Mean BPRS 41.2, range 29-60). Rates of missing prescribed medications were in the order of 41%. Standardized attitudinal scales (AMSQ, DAI, ROMI) found generally negative attitudes towards medication and limited insight into illness. Forgetting to take medications was the top reason for non-adherence (55%), followed by side effects (20%). Half of individuals had difficulty paying for medications at times, while 35% (N=7) felt they had insufficient information about BD. Interestingly, all individuals reported good relationships with their providers.
Conclusions: Poorly adherent BD patients report that forgetting medication and side effects are primary drivers of non-adherence. Access to medications, insufficient illness knowledge, and limited insight may likewise affect overall adherence.

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» NR4-097

USE OF BIPOLAR DISORDER TREATMENT GUIDELINES BY FRENCH PSYCHIATRISTS FOR CLINICAL DECISION MAKING

Ludovic SAMALIN, Sebastien Guillaume, M.D., Pierre-Michel Llorca, M.D. Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to aware of the lack of adherence of physicians to clinical guidelines in bipolar disorder and therefore the need to strengthen clinical education in guideline use.

SUMMARY:

Objective : According to the published medical literature, tools based on medical evidence such as guidelines have been developed over the past twenty years. These tools are designed to assist the clinician to provide appropriate care in specific clinical situations. The purpose of this study was to assess the practical implementation of guidelines for the treatment of bipolar disorder.
Method : A self-administered questionnaire was sent to all the French psychiatrists of the region Auvergne. They were asked 5 questions relevant to clinical usage of, and attitudes toward existing guidelines. These questions were adapted from the study by Perlis et al and adapted to the French care system after the approval of a reviewing committee of 5 experts.
Results : Our self questionnaire has been completed by 111 of the 210 psychiatrists contacted (53%). Of these, 51% said they regularly refer to guidelines in their every day clinical practice including 75% using the American Psychiatric Association treatment guidelines. Of those who did not use bipolar guidelines, the most frequently cited reason given by respondents (56,7%) was that such guidelines were unadapted to the French health system.On the other hand, the main factor in the decision to use a molecule was personal experience (41%), the guidelines were identified in last place (12%). By comparison, in their study, Perlis et al found that for 42.5% of clinicians the primary factor guiding decision making was published clinical study literature, and only 7,6% viewed published treatment guidelines as their primary source in the selection of appropriate therapy.
Conclusions: Whatever the continent, there is a real gap between theory and practice in clinical care for bipolar patients. The guidelines are therefore interesting tools for clinical practice but are still little used. Strengthening education and establishing French guidelines should favour adhesion of French psychiatrists to their use.

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» NR4-098

BIPOLAR DISORDER IMPAIRS PHYSICAL HEALTH AS MUCH AS SCHIZOPHRENIA

Susana Santamarina, Garcia Portilla MP, Saiz PA, Bascaran MT, Iglesias C, Bobes J

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to conclude that patients with bipolar disorder suffers significant reductions in several domains of quality of life as much as patients with schizophrenia

SUMMARY:

Background: Several studies have reported lower levels of quality of life in patients with schizophrenia and bipolar disorders compared to general population.
Objective: We compared patients with schizophrenia and bipolar disorder from the same geographical area to determine whether there are differences in the level of quality of life according to the diagnosis.
Methods: Naturalistic, one-year longitudinal study conducted in Asturias, Northern Spain. A total of 172 patients with schizophrenia or bipolar disorder (ICD-10 criteria) were included. Quality of life was assessed using the SF36.
Results: Patients with schizophrenia were significantly younger (41.7 versus 53.3, p .000), and were men (65.2% versus 42.1%, p .004) and never married (73.0% versus 14.0%, p<.001) in a greater proportion than patients with bipolar disorder. At baseline, both groups of patients obtained scores below the norm in all SF36 scales but bodily pain. Patients with bipolar disorder scored significantly lower in the physical health scale than patients with schizophrenia (78.89 versus 86.11, p .045). Not statistically significant differences were found in the other seven SF36 scales nor in the summary component scores. When using standardized scores patients with schizophrenia scored significantly lower than bipolar patients in general health (-.83 versus -.27, p .003) and vitality (-.71 versus -.31, p.045).
Conclusion: Patients with bipolar disorder and schizophrenia have lower levels of quality of life than the normative Spanish population. Patients with schizophrenia showed lower levels of quality of life in the areas of general health and vitality than patients with bipolar disorder.

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2) Yen CF, Cheng CP, Huang CF, Yen JY, Ko CH, Chen CS. Quality of life and its association with insight, adverse effects of medication and use of atypical antipsychotics in patients with bipolar disorder and schizophrenia in remission. Bipolar Disord. 2008;10:617-24.

» NR4-099

BIPOLAR DISORDER IMPAIRS QUALITY OF LIFE LESS THAN SCHIZOPHRENIA

Susana Santamarina, Garcia-Portilla MP, Saiz PA, Bascaran MT, Iglesias C, Bobes J

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to conclude that patients with bipolar disorder show better quality of life than patients affetd from schizophrenia

SUMMARY:

Background: Several studies have reported lower levels of quality of life in patients with schizophrenia and bipolar disorders compared to general population.
Objective: We compared patients with schizophrenia and bipolar disorder from the same geographical area to determine whether there are differences in the level of quality of life according to the diagnosis.
Methods: Naturalistic, one-year longitudinal study conducted in Asturias, Northern Spain. A total of 172 patients with schizophrenia or bipolar disorder (ICD-10 criteria) were included. Quality of life was assessed using the SF36.
Results: Patients with schizophrenia were significantly younger (41.7 versus 53.3, p .000), and were men (65.2% versus 42.1%, p .004) and never married (73.0% versus 14.0%, p<.001) in a greater proportion than patients with bipolar disorder. At baseline, both groups of patients obtained scores below the norm in all SF36 scales but bodily pain. Patients with bipolar disorder scored significantly lower in the physical health scale than patients with

schizophrenia (78.89 versus 86.11, p .045). Not statistically significant differences were found in the other seven SF36 scales nor in the summary component scores. When using standardized scores patients with schizophrenia scored significantly lower than bipolar patients in general health (-.83 versus -.27, p .003) and vitality (-.71 versus -.31, p.045).
Conclusion: Patients with bipolar disorder and schizophrenia have lower levels of quality of life than the normative Spanish population. Patients with schizophrenia showed lower levels of quality of life in the areas of general health and vitality than patients with bipolar disorder.

REFERENCES:

1) Gutiérrez-Rojas L, Gurpegui M, Ayuso-Mateos JL, Gutiérrez-Ariza JA, Ruiz-Veguilla M, Jurado D. Quality of life in bipolar disorder patients: a comparison with a general population sample. Bipolar Disord. 2008;10:625-34.

2) Yen CF, Cheng CP, Huang CF, Yen JY, Ko CH, Chen CS. Quality of life and its association with insight, adverse effects of medication and use of atypical antipsychotics in patients with bipolar disorder and schizophrenia in remission. Bipolar Disord. 2008;10:617-24.

» NR4-100

COMPARISON OF DIFFERENT TREATMENT OPTIONS FOLLOWING INITIATION DOSE OF 10MG ESCITALOPRAM

Delphine Saragoussi,M.D.,M.P.H.,Thibaut Sanglier, M.Sc., Dominique Milea,Pharm.D.,M.Sc.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to (a) envision increasing the dose in patient treated with Escitalopram 10 mg in the case of non optimal response instead of switching or combining antidepressants; (b) consider that epidemiological analyses of claims databases can provide unique insight into real life actual practices and allow the evaluation of different treatment strategies.

SUMMARY:
OBJECTIVES: If patients do not respond to their initial treatment, the physician can increase the initial dose, switch to another treatment or add another treatment (1). Our study aims at comparing the different strategies after initiation of escitalopram 10mg.
METHODS: Adult patients initiated on escitalopram 10mg, who increased to 20mg (dose-increased patients) or switched to (switchers) or were added another antidepressant (combination patients), were identified in the PharMetrics US claims Database (2003-2006). Patients' characteristics at first treatment change and outcomes 3 months after were compared as well as treatment persistence (no drops and no further change) and healthcare costs. Multivariate regression analyses were performed to adjust for patient characteristics and baseline healthcare costs.
RESULTS: 12,830 patients started with escitalopram 10 mg of which 56% increased to 20mg, 26% switched and 18% had a combination. Mean time to treatment change was 107 days for dose increase, 82 days for switch (p<0.001) and 81 days for combination (p<0.001). Three months after treatment change, dose-increased patients had higher 3-month persistence compared with switchers or combination patients. Switch and combination were associated to a higher risk of non persistence (respectively: OR=1.8, 95%CI=[1.7-2.0]; and OR=14.66, 95%CI=[12.6-17.0]) compared to dose increase. Costs of both switchers and combination patients were higher than those of dose-increased patients (respectively: +US$214, adjusted RR=1.0, 95%CI=[0.9-1.1]; and +US$1038, adjusted RR=1.3, 95%CI=[1.2-1.4]).
CONCLUSIONS: Increasing escitalopram dose from 10 to 20mg was associated with fewer further changes in treatment and with lower healthcare costs than switching or combining with another antidepressant. For patients who do not respond well to their initial dose, dose increase should be considered before any other strategy (2). The study was funded by H.Lundbeck A/S.

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» NR4-101

A POPULATION-BASED COMPARISON OF SUICIDALITY AMONG BIPOLAR DISORDER AND MAJOR DEPRESSIVE DISORDER SUBJECTS

Ayal Schaffer, MD, John Cairney, PhD, Scott Veldhuizen, BA, Amy Cheung, MD, Paul Kurdyak, MD, Anthony Levitt, MD

Educational Objectives:

At the conclusion of this session, the participant should be able to appreciate the level of suicidality present among people with mood disorders in the community

SUMMARY:
Objective: Most studies that compare suicidality between subjects with bipolar disorder (BD) and major depressive disorder (MDD) use data derived from tertiary-care clinical samples. Due to selection bias, these results may not be generalizable to the larger group of people with mood disorders in the community. There are limited population-level data on differences in suicidality between these diagnostic groups. The aim of this report was to examine differences in suicidality between subjects with BD and MDD using data from a large epidemiological sample.
Method: This study utilized data from the Canadian Community Health Survey - Mental Health and Well-Being. This nationally representative survey was conducted by Statistics Canada and included 36,984 respondents aged 15 or older. The CIDI-based interview identified respondents with BD (N = 789) and MDD (N = 3952). Data was collected on presence of a lifetime suicide attempt as well as suicidal ideation (SI) during periods of depression.
Results: Subjects with BD were significantly more likely than subjects with MDD to report the presence of SI during periods of depression (OR = 1.77, 95% CI = 1.14-2.75, p = 0.01). A significantly higher percentage of subjects with BD reported making a lifetime suicide attempt (18.5% vs. 10.9%; ?2=39.5, df = 1, p < 0.001), and this difference remained significant after controlling for sociodemographic and clinical covariates using logistic regression (OR = 1.89, 95% CI = 1.36-2.62, p < 0.001).
Conclusions: At a population level, individuals with BD report higher rates of SI and suicide attempts than individuals with MDD. These results contribute to our understanding of the morbidity and mortality risks associated with mood disorders in the community.

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» NR4-102

COGNITIVE FUNCTIONING IN DEPRESSED PSYCHIATRIC INPATIENTS: A PILOT STUDY PREDICTING LENGTH OF STAY (LOS) ON AN ACUTE MEDICAL PSYCHIATRIC UNIT

Caleb Siefert Ph.D., Larry Park, M.D., Katherine O. Rooney, B. S., Adrienne O. van Nieuwenhuizen, B.S., Nelson Prakash Tauro, M.D., Kaloyan Tanev, M.D., John D. Matthews, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation participants will be familiar with prior research on depression and cognitive functioning, will understand the relationship between cognitive difficulties and length of stay for psychiatric inpatients, and will understand what additional research is necessary to better understand how assessment of cognitive difficulties can aid in the prediction of inpatient length of stay for individuals with depression.

SUMMARY:
Background: Severe depression has been associated with mild impairments in memory, attention, and processing speed. However, since impairment varies greatly across individuals it was hypothesized that impairment in cognitive functioning would be related to length of stay (LOS) for inpatients. Methods: This study is part of a larger study examining cognitive functioning in inpatients with mood disorders. Participants were 17 inpatients who were not abusing substances prior to admission, had no known history of neurological/cognitive disorder, and were not receiving ECT. Participants met SCID-II criteria for a major depressive episode. After providing informed consent, participants completed a 45 minute battery of neuropsychological tests that included the Wechsler Adult Intelligence Scale – III Processing Speed Index subtests; a story recall, word list recall, and digit span subtests of the Wechsler Memory Scale – III, trails A and B, a word production task, and a finger tapping task. Neuropsychological testing was conducted within 48 hours of admission to the unit. Patients also completed a brief battery of self-report measures assessing the severity of their depression.
Results: Statistically significant correlations were found between LOS and age corrected standard scores for an immediate memory story recall task (r = -0.62), an immediate word recall task (r = -0.50), a delayed word recall task (r = 0.67), a word recognition task (r = -0.60), and Trails A (r = -0.49). Regression analysis indicated that a composite memory score for the WMS-III auditory memory recall tasks (mean of standard scores across memory tasks) significantly improved prediction of LOS beyond that predicted by demographic variables alone (F Change = 7.62, p = .02).
Conclusions: Brief auditory measures of memory may be useful in identifying inpatients at risk for extended lengths of stay. Limitations of the current data set and implications for further research are discussed.

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» NR4-103

AGE OF ONSET AND SUICIDE RISK IN BIPOLAR DISORDER

Jonathan Stange B.A., Michael J. Ostacher, M.D., M.P.H., Andrew A. Nierenberg, M.D., Roy H. Perlis, M.D., MSc, Gary S. Sachs, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation the participant will be aware of data relating length of time from onset of mood symptoms to a first suicide attempt in bipolar disorder, and clinical features which may be associated with suicide attempts earlier in the illness course.

SUMMARY:
Objective: People with bipolar disorder (BP) are at substantially elevated risk for suicide attempts in comparison with the general population. While prior reports suggest a high frequency of initial suicide attempts during the first year after onset of BP symptomatology, little is known about the clinical features associated with earlier versus later suicide attempts.
Methods: 4,107 subjects with BD were evaluated as part of the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). STEP-BD was a multicenter prospective cohort study of bipolar disorder conducted in the United States. All subjects were assessed at study entry with the Affective Disorders Evaluation and Mini International Neuropsychiatric Interview. As part of this evaluation, all subjects were interviewed about age at onset of bipolar mood symptoms and age at first suicide attempt. Survival analysis was used to examine clinical features associated with interval between symptom onset and first suicide attempt.
Results: 1,495 subjects (36%) reported at least one lifetime suicide attempt. 322 (22%) of attempters made their first attempt within one year of onset of BP symptomatology, and 964 (65%) made a first attempt within the first 10 years of BP onset. Features associated with earlier attempts included being female, being bipolar I, history of rapid cycling, and history of psychotic symptoms (log-rank $p<0.001$ for all comparisons).
Conclusions: A substantial subset of subjects with BP made suicide attempts early in their illness course. However, about one third of lifetime attempters made their initial attempt after the first ten years of BP onset, indicating that suicide risk in BP remains considerable beyond initial onset of BP symptomatology. Clinical features may help to distinguish those who make earlier versus later attempts.

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» NR4-104

PSYCHIATRIC SYMPTOMS IN CAREGIVERS OF PATIENTS WITH BIPOLAR DISORDER

Annie Steele B.A., Nancy C. Maruyama, M.D., Igor I. Galynker, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to (1) recognize that caregivers may be at risk for psychiatric morbidity and (2) identify caregivers of patients with bipolar disorder who may be particularly vulnerable.

SUMMARY:
Objectives: The burden experienced by caregivers of patients with bipolar disorder is associated with increased caregiver depression, anxiety and mental health service use. As burden is also associated with poor patient outcome, these findings may indicate a source of distress for both caregivers and patients. This review presents what is currently known about psychiatric symptoms in this population and suggests directions for future research.
Methods: Databases Medline, Pubmed, PsychINFO and Google Scholar were searched using the keywords 'bipolar disorder', 'caregiver', 'caregiver burden', 'family', 'couple', 'spouse' and 'partner.' Publications reporting psychiatric symptoms or mental health service use in adult caregivers were included.
Results: Twenty four (24) papers were analyzed. Thirteen (13) of these measured general psychiatric distress, 2 measured anxiety symptoms, 9 reported mood symptoms and 8 reported increased mental health service use. Twenty one (21) papers reported clinical significance of least one category of psychiatric distress. Significant findings include up to 46% of caregivers reporting depression and up to 32.4% reporting mental health service use. Data suggests that caregiver psychiatric symptoms depend on the nature

of the caregiving relationship. Common methodological problems included: lack of control groups, small sample sizes and non-standardized caregiver and patient criteria.
Conclusions: While data is inconsistent, the majority of papers report the presence of psychiatric symptoms, such as depression, anxiety and increased mental health service use, in caregivers of patients with bipolar disorder. Future research is needed to address focus on distinguishing symptoms and identifying mediators such as caregiver-patient relationship, coping styles and stigma. Interventions tailored towards the psychiatric needs of bipolar families may result in improved caregiver and patient outcomes and decreased health care costs.

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» NR4-105

FREQUENCY EXPOSURE TO ANTIDEPRESSANTS AND MOOD STABILIZER IN THE LONG-TERM BIPOLAR DISORDER TREATMENT

Sergio Strejilevich M.D., Diego Martino MD, Ana Igoa M.D., Eliana Marengo MD, Guillermo Fassi MD, S. Nassir Ghaemi PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the impact of antidepressants in the long term course of bipolar disorder

SUMMARY:

Stability and full euthymia should be the main target in a rational treatment to bipolar disorders. Paradoxically, there are limited empirical data to guide treatment decisions taking in account this concepts, specifically, is yet controversial the risk-benefit ratio to use antidepressants. In fact, some points remain unexplored. Does the frequency and intensity to antidepressant exposure have a correlation with the impact on the stability? Is enough the simple presence of a mood stabilizer to ensure a positive effect on the stability or there should be a quantitative relationship with respect to the frequency and intensity of their exposure relative to antidepressants? Fifty three Bipolar I or II outpatients in naturalistic conditions of treatment were selected. The course of illness was documented prospectively for each participant by his/her psychiatrist using a modified life charting technique based on the NIMH life-charting method and anchored with scores from both the Ham-D and YMRS. The exposition to AD, and MS was assessed by the Scale of Intensity, Frequency, and Duration of Psychopharmacological Treatment (IFD). This scale provides a quantitative measure in a 0-5 point's range of exposure to different groups of psychotropic medications during a period. Data analysis: Spearman bivariate correlations were computed to assess relationship between measures of follow-up and pharmacological variables. A regression analysis was used. This sample was follow-up for a period of 86.38 (34.32) weeks. The only three variables that independently predicted the time asymptomatic during follow up were length of illness (ß=-0.57, p<0.001), current treatment with AD (ß=-0.28, p=0.027), and years to exposure to MS (ß=0.35, p=0.019) accounting around 36% of variance (adjusted R^2=0.356; p<0.001). Intensity of previous exposure to AD was the only independent predictor of polarity change (adjusted R^2=0.277; p<0.001; ß=0.54, p<0.001) and mixed symptomatology (ß=0.35, p=0.015; adjusted R^2=0.105; p=0.015).The main results of this study were that AD exposure was a major predictor of mood instability in the long-term outcome of bipolar disorders while exposure to MS determined the opposite. This relation could be dependent of the intensity of their exposure. The relationship between AD and MS exposure may be understood in quantitative terms to explain their impact on bipolar disorder's evolution.

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» NR4-106

EXTENDED RELEASE QUETIAPINE FUMARATE MONOTHERAPY FOR THE TREATMENT OF MDD: POOLED ANALYSIS OF SUSTAINED RESPONSE (STUDIES D1448C00001 AND D1448C00002)

Johan Szamosi M.S.C., Roger S. McIntyre M.D., Stuart Montgomery M.D., Helena Schiöler M.Sc., Hans Eriksson M.D., Ph.D., M.B.A., Willie Earley M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should understand the importance of an early onset of action and a sustained response to treatment in patients with MDD and be able to describe the early onset of action, and time-to-first- and time-to-sustained-response with quetiapine XR

SUMMARY:

Objectives: Achieving an early onset of action and a sustained response are key challenges in the development of new treatments for MDD (1). One method of determining time to onset of action is to assess maintenance of initial response (2). This post hoc analysis evaluated sustained response with once-daily extended release quetiapine fumarate (QTP XR) monotherapy in patients with MDD.
Methods: Efficacy and tolerability data from two similar 6-week, multicenter, double-blind, placebo (PBO)-controlled studies (D1448C00001, D1448C00002) have previously been reported. The present analysis was conducted using pooled data. Study outcomes included: change from randomization in MADRS total scores at Weeks 1, 2, 4, and 6; response rates (>=50% reduction in MADRS total score). Post hoc Cochran-Mantel-Haenszel analysis: sustained response rate (defined as a >=50% reduction in MADRS total score at the specific timepoint assessed and at all subsequent visits until Week 6).
Results: Data from 968 patients were included: 315 QTP XR 150mg/day, 323 QTP XR 300mg/day, 330 PBO. QTP XR 150 and 300mg/day significantly reduced MADRS total scores vs PBO at Week 1 (-8.4, -8.6 vs -6.3; both p<0.001) and throughout the study until Week 6 (both -14.7 vs -11.1; p<0.001).
The proportion of patients at each time point experiencing a response that was sustained at all subsequent visits until Week 6 was: 10.0% (p=0.187), 12.2% (p<0.05) vs 7.1% at Week 1; 27.3% (p<0.001), 26.4% (p<0.001) vs 14.5% at Week 2; 41.3% (p<0.001), 39.0% (p<0.001) vs 25.5% at Week 4 for QTP XR 150 and 300mg/day vs PBO, respectively. At Week 6, response rates were 52.7% (p<0.001), 49.5% (p<0.001) vs 33.0% for QTP XR 150 and 300mg/day vs PBO, respectively.
Conclusions: QTP XR monotherapy (150 and 300mg/day) is effective from Week 1 in patients with MDD. Based on stringent criteria for sustained response, a greater proportion of patients receiving QTP XR maintained a response to study end vs PBO.
Funded by AstraZeneca

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» NR4-107

THE COST-EFFECTIVENESS OF QUETIAPINE AS AN ADJUNCT TO A MOOD STABILIZER IN THE MAINTENANCE TREATMENT OF BIPOLAR I DISORDER

Eskinder Tafesse Ph.D., Arthur Lazarus, M.D., MBA

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant will understand the cost-effectiveness of adjunct treatment with quetiapine versus other treatment options in maintenance therapy of bipolar I disorder.

SUMMARY:

Introduction: Bipolar I disorder has a lifetime prevalence of 1% in the US.1 The maintenance phase of the disease constitutes the time period during which the most health care is provided to the patient.2

Methods: The cost-effectiveness of maintenance treatment with QTP+Li/DVP, placebo (PBO)+Li/DVP, no maintenance treatment, and Li, lamotrigine, olanzapine, or aripiprazole monotherapy was compared using a Markov model, consistent with FDA-approved indication. The model simulated a cohort of 1000 stabilized patients in each treatment arm and estimated the quarterly risk in mania and depression, based on randomized, double-blind trials. Other inputs into the model were obtained from published literature. Drug costs, hospitalizations, and physician visits were included. Benefits and costs were discounted at 3%; the reference year was 2007. Endpoints included number of acute mood episodes, hospitalizations due to an acute mood event, and costs per quality-adjusted life-years (QALYs). Probabilistic sensitivity analysis (PSA) was conducted to evaluate uncertainty.

Results: Lamotrigine was the most costly treatment option, with total direct costs of $19,709 per patient over 2 years, while Li monotherapy was the least costly treatment option, with total direct costs of $11,998 per patient over 2 years. The results of the base-case analysis found that compared with Li monotherapy, QTP+Li/DVP was associated with an incremental cost-effectiveness ratio of $17,764 per QALY gained. QTP+Li/DVP dominated all other maintenance treatment options. PSA showed these results to be robust.

Conclusion: Maintenance treatment with QTP+Li/DVP is a cost-effective treatment option compared with Li/DVP alone, no maintenance treatment option, or lamotrigine, olanzapine, or aripiprazole. Supported by funding from AstraZeneca Pharmaceuticals LP

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» NR4-108

A STUDY OF COGNITION IN UNAFFECTED FULL BIOLOGICAL SIBLINGS OF PATIENTS WITH BIPOLAR DISORDER TYPE I

Jitendra Trivedi M.D., Himanshu Sareen, MBBS, P.K. Dalal, MD, P.K. Sinha,DSQ, Mohan Dhyani, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to appreciate the importance of neurocognition studies in bipolar disorders.

SUMMARY:

Introduction: Cognitive deficits have been presupposed to be the endophenotypic markers in bipolar disorder, but few studies have actually tried to ascertain the cognitive deficits in healthy relatives of bipolar disorder. The present study is aimed to assess the cognitive functions of unaffected full biological siblings of patients with bipolar I disorder and compare them with healthy controls.

Methods: Twenty-five first degree apparently healthy siblings of patients with bipolar disorder were compared with twenty-five age, gender and education matched controlled subjects on computer based cognitive tests (Continuous Performance Test, Spatial Working Memory Test and Wisconsin Card Sorting Test). I.Q. assessment of all the subjects was done prior to administrating the neurocognitive tests and only the subjects having IQ more than 90 were included in the study. Only healthy volunteers with no past history of any psychiatric illness as well absent psychiatric illness (schizophrenia, Bipolar Disorder, psychosis) in the first degree relatives were included in the study.

Results: As compared to the control group, the sibling group performed significantly poorly on the tests for executive functions (set shifting, planning, problem solving, understanding of the problem, concept formation and trial and error learning), vigilance (higher impulsivity) and working memory.

Conclusions: The results suggest that executive functioning and vigilance could be the potential markers of endophenotype in bipolar patients. Cognitive deficits may serve as markers for familial vulnerability for bipolar disorder in future.

Study of the relatives of bipolar patients represents one unique opportunity to the further understanding of early prodromal forms of bipolar disorder, which ultimately may lead to early identification and attenuation or prevention of the full disorder.

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» NR4-109

USE OF A RELAPSE MONITORING BOARD FOR INDEPENDENT ASSESSMENT OF THE PRIMARY ENDPOINT IN AN INTERNATIONAL CLINICAL TRIAL OF BIPOLAR DISORDER

Norris Turner Pharm.D., Wayne Macfadden, M.D., Mark Hyman Rapaport, M.D., Ravi Anand, M.D., Sumant Khanna, M.D., Ph.D., M.A.M.S., M.R.C.Psych., J. Thomas Haskins, Ph.D., Ibrahim Turkoz, M.S., Larry Alphs, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant will be able to recognize the value of an independent relapse monitoring board in determining relapse to a mood episode by examining its use in an international, randomized, double- blind, placebo-controlled study of a long-acting atypical antipsychotic for patients with bipolar disorder with a recent history of frequent relapse.

SUMMARY:

Background: Review and monitoring boards may provide an independent, objective method for reviewing clinical trial data. This study introduced the concept of an independent relapse monitoring board (RMB) that determined relapse to a mood episode in an international, randomized, double-blind, placebo-controlled study of adjunctive risperidone long-acting therapy (RLAT) in patients with bipolar disorder (BD).

Methods: Principal investigators (PIs) conducted a blinded assessment of patients to determine if a relapse occurred based on predefined protocol criteria. The RMB included 3 psychiatrists

from different regions with expertise in diagnostic, clinical and therapeutic management of BD. Blinded to study drug, the RMB reviewed relevant data in all patients from the 52-week double-blind phase, discussed the case with each other, then attained consensus for whether a relapse occurred. Date of relapse was determined by the RMB using predefined protocol criteria. Study ID: CR004693.
Results: The RMB met 6 times during the study. PIs identified 42 relapses: 20.8% with RLAT, 40.3% with placebo; the RMB identified 48 relapses: 22.2% with RLAT, 47.8% with placebo. 8 patients were determined to have relapsed by the RMB but not by PIs, whereas 2 patients were determined to have relapsed by PIs but not by the RMB. Adjunctive RLAT significantly delayed onset of a mood episode compared with placebo using RMB- (P=0.004, log-rank test) or PI- (P=0.023) identified relapses. Relative relapse risk was 2.4-fold (P=0.004 chi-square [Cox regression]) and 2.1-fold (P=0.022) higher with placebo than with adjunctive RLAT using RMB- or PI-identified relapses, respectively.
Conclusion: RMBs for clinical trials may provide more comprehensive, sensitive and standardized evaluation of relapse. This may be particularly important in complex, large international trials where clinically meaningful outcomes may be difficult to discern.
Supported by Ortho-McNeil Janssen Scientific Affairs, LLC

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» NR4-110

GENDER DIFFERENCES IN SYMPTOMS AND COMORBIDITY IN A NATURALISTIC SAMPLE OF DEPRESSIVE OUTPATIENTS: THE LEIDEN ROUTINE OUTCOME MONITORING STUDY

Martijn Van Noorden M.D., Erik J. Giltay, M.D. Ph.D., Margien E. den Hollander-Gijsman, M.Sc., Nic J.A. van der Wee, M.D. Ph.D., Yanda R. van Rood, Ph.D., Rosalind van der Lem, M.D., Frans G. Zitman, M.D. Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the importance of studying gender differences in depression in order to increase the understanding of the gender gap in depression. In addition, the participant should be able to identify gender differences in symptoms and comorbidity patterns in the presented cohort and place these differences in the context of the existing hypotheses.

SUMMARY:

Gender differences in prevalence, comorbidity and symptom patterns of major depressive disorder (MDD) have been reported. Most observations are based on epidemiological samples or patients who participated in clinical trials. The aim of this study was to describe gender differences in demographic variables, comorbidity and symptoms in a naturalistic sample of outpatients with MDD.
We used a sample of 3798 patients who had been assessed with Routine Outcome Monitoring (ROM) by specially trained nurses, as part of a routine diagnostic procedure. 1637 fulfilled the DSM-IV criteria of current MDD on the MINI-Plus diagnostic interview, of whom 1131 (69%) patients had complete data. We evaluated gender differences in demographic variables, comorbidity, symptoms and social functioning.
We performed analyses in 395 men (34.9%) and 736 women (65.1%). On average, women were younger than men. No differences were found in severity of depression, measured with the Montgomery Äsberg Depression Rating Scale (MADRS). However, depression severity measured with the Beck Depression Inventory (BDI-II) was significantly higher in women. In addition, the following statistically significant differences were found: in women the reported age of onset of MDD was lower, the number of prior suicide attempts higher, the prevalence of atypical depression and comorbid posttraumatic stress disorder higher and the prevalence of comorbid social phobia, drug, alcohol abuse and attention deficit hyperactivity disorder lower than in men. Finally, reported social functioning was lower in women than in men.
The key finding of this study is that depression severity in women was higher compared to men when measured on a self-report scale (BDI-II), whereas no difference was found on an observational scale (MADRS). In addition, reported social functioning was lower in women than in men. These findings may be an explanation for the higher preponderance of women with MDD that attend psychiatric specialty care.

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» NR4-111

EFFECT OF ESCITALOPRAM ON DEPRESSED PATIENTS WITH CROHN'S DISEASE: A PLACEBO – CONTROLLED PILOT STUDY

Indu Varia M.D., Jennifer B. Reese, Ph.D., Margatha N. Kuchibhatla, Ph. D., Prakash Masand, M.D., Kenneth Gersing, M.D., Audrey Broome, N.P., Jane Onken, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand response to escitalopram on depressed patients with Crohn's Disease.

SUMMARY:

Objective: Despite a high prevalence of depression in inflammatory bowel disease (IBD), there are few placebo-controlled studies of antidepressants in IBD. The objective of this pilot study was to assess the effectiveness of escitalopram in the treatment of depression in patients with Crohn's disease.
Methods: We conducted a 12 week, double-blind trial of escitalopram in 21 adult subjects with Crohn's disease (38% male; 71% white) meeting DSM-IV criteria for Major Depressive Disorder. Dosing was initiated at 10 mg once daily increasing to 20 mg daily as indicated. The intent-to-treat method with the last observation carried forward was used. Measures included the Hamilton Depression Rating Scale (HAM-D), Short-Form McGill Pain Questionnaire, St Marks Index, Clinician's Global Index of Symptom Severity and Improvement (CGI), and SF-36.
Results: Five patients dropped out of the study; two due to hospitalization from Crohn's disease flare, two were lost to follow up and one discontinued medicine after the first dose. Drop-out did not differ by treatment arm (p=.33). HAM-D scores decreased more in escitalopram group (M=11.3; SD=7.1) than the placebo group (M=4.3; SD=5.2; p=.025). In the escitalopram group 71% of the patients experienced 50% or greater reduction in HAM-D score compared with 25% of the placebo group. Change in CGI Severity and Improvement also differed significantly by treatment group (p<.04). SF-36 Mental Health Scale scores increased an average of 10 points for the escitalopram group and 4 points for the placebo group, but the difference was not statistically significant. No significant differences were noted in change in St. Marks, or McGill.

Conclusions: Escitalopram was well tolerated. It improved clinician's ratings of depression Severity and Improvement in patients with Crohn's disease. Larger studies should be conducted to examine whether antidepressants improve quality of life in patients with IBD. Funding: Forest Laboratories, Inc.

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2) Mikocka-Walus AA, Turnbull DA, Moulding NT, Wilson IG, Andrews JM, Holtmann GJ: Controversies surrounding the comorbidity of depression and anxiety in inflammatory bowel disease patients: A literature review. Inflamm Bowel Dis 2007; 13: 225-234.

» NR4-112

GENDER-RELATED LIPID ABNORMALITIES IN OUTPATIENTS WITH BIPOLAR DISORDER

Mytilee Vemuri, M.D.,M.B.A., Terence A. Ketter, M.D., Heather A. Kenna, M.A., Uma Saha, M.D., Anna Morenkova, M.D., Po W.Wang, M.D., and Natalie L. Rasgon M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize dyslipidemia and insulin resistance based on laboratory values, and describe gender differences in specific measures of dyslipidemia and insulin resistance observed in an outpatient bipolar clinic setting.

SUMMARY:

BACKGROUND: High rates of dyslipidemia and insulin resistance (IR) have been reported in patients with bipolar disorder (BD). In the general population, men are known to have worse lipid profiles than women. We assessed gender effects upon rates of dyslipidemia/IR in outpatients with BD.
METHODS: Records of 491 outpatients (ages 18-75) seen in the Stanford Bipolar Disorders clinic between 2000 and 2007 were reviewed. Patients were systematically assessed and followed longitudinally, received naturalistic treatment according to model practice procedures, received lipid panels at clinicians' discretion. Patients were encouraged to fast prior to venipuncture. BD patients (n = 231; 42% Type I, 46% Type II, 11% Not Otherwise Specified) with a mean age of 39.6 ± 13.0 years, 62% female, and 81% Caucasian, who had one of four lipid measures (total cholesterol, LDL, HDL, Triglycerides (TG)), a psychiatry clinic visit within 2 months of laboratory, and were not taking medications for dyslipidemia were included. IR was imputed from TG/HDL ratio >3.5.
RESULTS: Men, compared with women, had significantly higher mean LDL cholesterol (124.4±36.1 vs 110.6±33.7 mg/dl, p=0.003), lower mean HDL cholesterol (93.3±26.6 vs 60.0±17.6 mg/dl, p<0.001), and TG/HDL ratio (3.6±3.6 vs 2.0±1.8, p<0.001). There were no statistically significant differences between genders in mean age, BMI, total cholesterol, TG, percentage with abnormal TSH levels or smoking, use of weight-gain liable second generation antipsychotics, bipolar subtype, race or education level.
CONCLUSIONS: In outpatients with BD, men had significantly worse lipid profiles and IR than do women despite similar demographic variables including age and BMI. Gender specific influences on glucose and lipid metabolism, such as weight distribution, or sex hormones may be important modulators of metabolic disorders in bipolar disorder.

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» NR4-113

TEMPERAMENTS AND TREATMENT OUTCOMES IN MOOD DISORDERS: PROSPECTIVE DATA

Elizabeth Whitham B.A., Sairah Thommi, B.A., SN Ghaemi, M.D., M.P.H.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should understand the distribution of different temperaments in mood disorders and appreciate the predictive value of temperaments in treatment response. The participant should also be able to replicate or refute the association of specific temperaments with antidepressant-induced mania.

SUMMARY:

Objective: Temperament is increasingly noted to be related to mood disorders, and may be a relevant modulator of treatment outcome. For instance, some studies suggest an association between cyclothymic or hyperthymic temperament and antidepressant-induced mania. We seek to replicate or refute the available studies, and to add more prospective data regarding associations with treatment response to mood stabilizers.
Method: We provided the self-report TEMPS-A (Temperament Evaluation of Memphis Pisa Paris and San Diego Auto- questionnaire) to all patients seen in the Mood Disorders Program of Tufts Medical Center. Diagnoses of cyclothymia, dysthymia, irritable, and hyperthymia temperaments were made. Treatment outcomes were assessed using clinician-rated instruments (Montgomery Asberg
Depression Rating Scale, the Mania Rating Scale for the SADS-C), and self-rated scales (the Quick Inventory of Depression Scale, and the Work Productivity and Activity Impairment Questionnaire). A sample size of about 100 subjects is expected.
Results: Associations between specific temperament types and treatment response to mood stabilizers will be provided. Historical risk of antidepressant-induced mania associated with temperament will also be analyzed.
Conclusions: Temperament may be an important clinical modulator in mood disorders. This study adds to the clinical literature on its relevance. Funding Source: None

REFERENCES:

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» NR4-114

LOCUS OF CONTROL, LIFE EVENTS, TREATMENT HISTORY AND LONGITUDINAL OUTCOMES OF TREATMENT FOR DEPRESSION

Stephen Woolley D.Sc., Brenda A. Woznicki, B. A., Stephen B. Woolley, D.Sc., M.P.H., John W. Goethe, M.D., Shani Bardack, B.A., Naila Azhar, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify in a population of patients treated for mood disorders 1) the association between low internal locus of control and subsequent depression and 2) the patient, family and treatment characteristics that modify this association.

SUMMARY:

Objective: To assess the role of internal locus of control (iLOC) in outcomes of psychiatric treatment, and to determine if this role is modified by life events, treatment history including adherence to and side effects of drugs, or social supports.
Methods: Adult inpatients (n=156) treated for mood disorders were interviewed at admission and 3 months after discharge, to assess personal attitudes about health, history of treatment, problems in

every day life, stressful events experienced, lifestyle behaviors, and depression at follow-up (DEP) (Beck 13-item scale). In addition, patient charts were abstracted to re-assess these factors.
Results: Overall, low iLOC was associated with a 14% decreased risk of DEP. Risk among patients with low iLOC varied by other factors. Among patients with low iLOC, DEP was twice as likely among females vs males (60% vs 28%) and those with a history of psychiatric treatment were 50% more likely to have DEP (p<.05). Overall, patients not taking medications regularly and those with extreme symptoms were more likely to have DEP (both p<.05): For these 2 characteristics, risks of DEP among low iLOC patients were increased 2- and 3-fold, respectively. Relative risks among high vs low iLOC patients also varied across other factors. Caucasians' and Latinos' risk of DEP did not vary by iLOC, but African Americans with low versus high iLOC were half as likely to have DEP. Life events and drug side effects were not associated with DEP, even when iLOC was controlled. Specific items in the LOC scale were associated with DEP: e.g., agreeing that what goes wrong is their fault (p=.04) and that even self-care won't prevent sickness (p<.01).
Conclusions: Unexpectedly, low iLOC was associated with decreased risk of subsequent DEP. The association was complex, as it was modified by factors including sex, previous treatment for mental illness, and taking medications regularly. Some elements in the LOC scale were individually associated with DEP.

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» NR4-115

LIFESTYLE, SOCIOECONOMICS, AND HEALTH HISTORY VERSUS MEDICATIONS AS PREDICTORS OF METABOLIC SYNDROME

Stephen Woolley D.Sc., Charles F. Caley, Pharm.D., John W. Goethe, M.D., David Bardack, B.A., Toni Martello, B.A., Naila Azhar, M.D., Gualberto Ruano, M.D., Ph.D., Andreas Windemuth, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify in a population of patients treated with atypical antipsychotics 1) the prevalence of metabolic syndrome symptoms and 2) personal and family characteristics associated with metabolic syndrome and its symptoms.

SUMMARY:

Objective: Examine the associations between metabolic syndrome (MetS) among mental health patients taking atypical antipsychotics (AAPs) and non-pharmacologic factors.
Methods: Participants in a study of genetic factors and the risk of AAP-associated MetS were interviewed about non-pharmaologic (demographics, socioeconomics, family and personal histories, patient body type, and life style factors [diet, physical activity, alcohol consumption, smoking]). Patients received a physical examination to screen for MetS symptoms.
Results: The sample (n=107) was 57% male, 47% Caucasian, and ages 21-57 years. Percent positive for MetS symptoms included 36% for glucose (Glu), 46% for triglycerides (Trig), 45% for HDL, 62% for waist circumference (WC), and 37% for blood pressure (HBP). Risk of MetS symptoms varied by AAP: increased risk of MetS (clozapine, olanzapine), Glu (clozapine, quetiapine), Trig (clozapine), HDL (quetiapine), WC (clozapine, olanzapine), and HBP (clozapine). Females were more often positive for HDL (52% versus 39% for males) and for WC (p<.05). African Americans (AAs) were more often positive for Trig (p<.05), and AAs and Latinos were more often positive for HBP and HDL, respectively (both p<.05). Having MetS was associated with a family history of cardiovascular disease (p<.01). Patients with MetS were more likely to have financial problems (p<.05), to drink alcohol (p<.05), and to underestimate their obesity (p<.05). Weak associations were found between smoking or alcohol use and BMI (p=.08 and .09, respectively) and alcohol and Glu (p=.09). Quality of diet and the extent of physical activity were not associated with MetS in this population.
Conclusions: Results are preliminary due to limited statistical power but are consistent with a weak role of lifestyle factors as predictors of MetS, although in this population some personal and family characteristics were associated with MetS criteria. Having MetS was associated with specific AAPs.

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2) De Hert MA, van Winkel R, Van Eyck D, et al. Prevalence of the metabolic syndrome in patients with schizophrenia treated with antipsychotic medication. Schizophr Res 2006;83:87-93.

» NR4-116

THE EFFICACY OF QUETIAPINE MONOTHERAPY IN BIPOLAR II DEPRESSION: COMBINED DATA FROM THE BOLDER AND EMBOLDEN STUDIES

Allan Young Ph.D., Ch.B., M.Phil., Ph.D., Joseph R. Calabrese, M.D., Urban Gustafsson, Ph.D., Björn Paulsson, M.D., Gin S. Malhi, M.B., Ch.B., M.D., David J. Bond, M.D., I. Nicol Ferrier, M.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should have an understanding of the efficacy of quetiapine monotherapy for depressive episodes in patients with bipolar II disorder (as defined by DSM-IV). The data presented have been pooled from 4 large, placebo-controlled studies and demonstrate a consistency of effect associated with quetiapine in this patient population that historically has been difficult-to-treat.

SUMMARY:

Introduction: Combined data are presented from 4 placebo-controlled studies (BOLDER I and II; EMBOLDEN I and II) that evaluated the efficacy of quetiapine (QTP) monotherapy for depressive episodes in patients with bipolar II disorder.
Methods: This analysis was conducted in 819 patients (safety population). All studies included an 8-week, double-blind treatment phase in which patients were randomly assigned to QTP 300 mg/d, QTP 600 mg/d, or placebo. The EMBOLDEN studies also included a 26- to 52-week continuation phase, in which patients achieving remission continued on the same dose of QTP or switched to placebo. Outcome measures included the change from baseline in Montgomery-Åsberg Depression Rating Scale (MADRS) total score at Week 8 (all studies) and time from randomization (Week 8) to recurrence of any predefined mood event (EMBOLDEN only). MADRS response and remission rates and Hamilton Rating Scale scores for Depression (HAM-D) and Anxiety (HAM-A) were also assessed.
Results: Improvements in mean MADRS total scores from baseline to Week 8 were significantly greater with QTP 300 mg/d and 600 mg/d (-15.58 and -14.88; P<0.001) compared with placebo (-11.61). The MADRS effect sizes were 0.44 and 0.47 for QTP 300 mg/d and 600 mg/d (P<0.0001 vs placebo). In the EMBOLDEN studies, continued treatment with both doses of QTP significantly reduced the risk of recurrence of a mood event versus placebo (hazard ratios of 0.47 [95%CI, 0.25-0.92] and 0.18 [95%CI, 0.07-0.51]; P=0.05 vs placebo). Common adverse events associated with QTP (both doses) included dry mouth, somnolence, sedation, dizziness, and headache. Rates of mania and hypomania were similar for QTP and placebo.
Conclusions: Quetiapine monotherapy demonstrated significant efficacy, as compared with placebo, in the treatment of bipolar

II disorder depressive episodes. Further, QTP was generally well tolerated in all four studies.
Supported by funding from AstraZeneca Pharmaceuticals LP.

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» NR4-117

THE IN VITRO PROFILE OF LU AA21004, A NOVEL MULTI-TARGET DRUG FOR THE TREATMENT OF MOOD DISORDERS

Huailing Zhong Ph.D., Tine B. Stensbøl, Ph.D., Kristen Frederiksen, Ph.D., Benny Bang-Andersen, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the unique pharmacological actions of Lu AA21004 in vitro at human 5-HT3 and 5-HT1A receptors and 5-HT transporters.

SUMMARY:

Objective: To characterize the in vitro pharmacological properties of Lu AA21004.
Methods: Affinity for human 5-HT3A receptors was measured by displacement of [3H]BRL 43694 binding. The functional response at human 5-HT3A receptors was measured as changes in serotonin (5-HT) induced currents in HEK293 cells. Affinity for human 5-HT1A receptors was evaluated by displacement of [3H]8-OH-DPAT binding at cloned receptors and native receptors in human post-mortem cortical brain tissue. The functional intrinsic activity (IA) was assessed by [35S]GTPgammaS binding using cloned human 5-HT1A receptors. Affinity for cloned human 5-HT transporters was determined by displacement of [3H]escitalopram, and functional activity was measured in a [3H]5-HT uptake assay using cloned human 5-HT transporters. IC50 values were corrected by the Cheng-Prusoff method to derive corrected IC50 (cIC50).
Results: Lu AA21004 showed high affinity binding for the cloned human 5-HT3A receptor (Ki=4.5 nM), and displayed functional antagonism using human 5-HT3A receptor expressed in HEK293 cells (IC50=10 nM). Lu AA21004 displayed moderate to high affinity binding for the cloned human (Ki=15 nM) and the native 5-HT1A receptor (Ki=40 nM). In functional [35S]GTPgammaS binding assays, Lu AA21004 demonstrated agonism (IA=96%) for the cloned 5-HT1A receptor. Lu AA21004 showed high affinity binding for the cloned human 5-HT transporter (Ki=1.6 nM), and binding to the transporter resulted in inhibition of 5-HT uptake (cIC50=5.4 nM). At 1 microM, Lu AA21004 showed no significant activity when tested against 70 other receptors, enzymes, ion channels, or transporters.
Conclusions: Lu AA21004 is a high affinity 5-HT3 receptor antagonist, a 5-HT1A receptor agonist, and a high affinity 5-HT transport inhibitor. This in vitro profile translates into enhanced levels of 5-HT as well as other neurotransmitters (ie, noradrenaline, dopamine, acetylcholine) in vivo (1,2), and may result in a unique antidepressant profile.

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» NR4-118

PSYCHIATRIC DIAGNOSES IN PATIENTS PREVIOUSLY OVERDIAGNOSED WITH BIPOLAR DISORDER

Mark Zimmerman M.D., Camilo Ruggero, Ph.D., Iwona Chelminski, Ph.D., Diane Young, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the diagnoses given to patients that have been overdiagnosed with bipolar.

SUMMARY:

Background: In a previous paper from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project, we reported that bipolar disorder is often overdiagnosed in psychiatric outpatients. An important question not examined in that paper was what diagnoses were given to the patients who had been overdiagnosed with bipolar disorder. In the present report from the MIDAS project we examined whether there was a particular diagnostic profile associated with bipolar disorder overdiagnoses.
Methods: Eighty-two psychiatric outpatients reported having been previously diagnosed with bipolar disorder which was not confirmed when interviewed with the Structured Clinical Interview for DSM-IV (SCID). Psychiatric diagnoses were compared in these 82 patients and 528 patients who were not diagnosed with bipolar disorder. Patients were interviewed by a highly trained diagnostic rater who administered the SCID for DSM-IV axis I disorders and the Structured Interview for DSM-IV Personality for DSM-IV axis II disorders.
Results: The most frequent lifetime diagnosis in the 82 patients previously diagnosed with bipolar disorder was major depressive disorder (82.9%, n=68). The patients overdiagnosed with bipolar disorder were significantly more likely to be diagnosed with borderline personality disorder compared to patients who were not diagnosed with bipolar disorder (24.4% vs. 6.1%, p<.001). A previous diagnosis of bipolar disorder also was associated with significantly higher lifetime rates of major depressive disorder, posttraumatic stress disorder, impulse control disorders, and eating disorders, though only the association with impulse control disorders remained significant after controlling for the presence of borderline personality disorder.
Conclusions: Psychiatric outpatients overdiagnosed with bipolar disorder were characterized by more axis I and axis II diagnostic comorbidity in general, and borderline personality disorder in particular.

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» NR4-119

UNDERRECOGNITION OF CLINICALLY SIGNIFICANT SIDE EFFECTS IN DEPRESSED OUTPATIENTS

Mark Zimmerman M.D., Janine Galione, B.S., Naureen Attiullah, M.D., Michael Friedman, M.D., Cristina Toba, M.D., Daniela Boerescu, M.D., Moataz Ragheb, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe problems with the assessment of side effects in depressed patients treated in outpatient practice

SUMMARY:

Background: The presence of medication side effects is one of the most frequent reasons depressed patients discontinue medication, and premature discontinuation of medication is associated with poorer outcome in the treatment of depression. Despite the clinical importance of detecting side effects, few studies have examined

the adequacy of their detection and documentation by clinicians. We are not aware of any studies comparing psychiatrists' clinical assessments to a standardized side effects checklist in depressed patients receiving ongoing treatment in clinical practice. The goal of the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project was to test the hypothesis that fewer side effects would be recorded by psychiatrists in their patients' charts compared to the number reported by patients on a side effects checklist.
Methods: Three hundred depressed outpatients in ongoing treatment completed a self-administered version of the Toronto Side Effects Scale (TSES). The patients rated the frequency of each of the 31 side effects, and the degree of trouble caused by them. A research assistant reviewed patients' charts to extract side effects information recorded by the treating psychiatrist. The study was conducted from June 2008 to July 2008.
Results: The mean number of side effects reported by the patients on the TSES was 20 times higher than the number recorded by the psychiatrists ($p<.01$). When the self-reported side effects were limited to frequently occurring or very bothersome side effects, then the rate was still 2 to 3 times higher ($p<.01$).
Conclusions: Clinicians do not document, and may not be aware of, most side effects experienced by psychiatric outpatients receiving ongoing pharmacologic treatment for depression.

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» NR4-120

AUTONOMIC, ENDOCRINE AND NEUROPHYSIOLOGIC CORRELATES OF HUMAN-ANIMAL INTERACTION

Sandra Barker Ph.D., Anand K. Pandurangi, M.D., Janet S. Knisely, Ph.D., Nancy L. McCain, D.S.N., Christine M. Schubert, Ph.D., Evren Buragkazi, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:(1) be aware of the benefits of human-animal interaction, (2) know the biological and psychological correlates of human-animal interaction, (3) appreciate the feasibility of conducting methodologically rigorous human-animal interaction studies.

SUMMARY:

Interaction with companion animals is known to moderate reaction to stress. This study explored autonomic, endocrine & neurophysiologic brain activity during a human-animal interaction in 10 adult dog owners interacting with their own or an unfamiliar therapy dog in a relaxed, controlled setting.
A pre-post within-subject design was used. Half of the subjects were therapy dog owners (TDO) interacting with their own dogs and half were dog owners interacting with an unfamiliar therapy dog (AAI). 24 leads of an XLtek Neurowork EEG were attached for monitoring during the study. Following 30-minutes of baseline, subjects completed a stress task followed by a 30 minute dog interaction and then watched a neutral video for 60 minutes. The outcome of interest was stress, measured by QEEG, diastolic and systolic BP (DBP, SBP), heart rate (HR), salivary cortisol, salivary alpha-amylase, and self report on visual analog scales (VAS). Trait anxiety, measured by the State-Trait Anxiety Inventory and attitudes toward pets, measured by the Pet Attitude Scale were assessed as moderating variables.
Results revealed consistent physiological patterns suggesting a relaxation effect in therapy dog owners interacting with their own dog that is mirrored in owners interacting with an unfamiliar dog. The QEEG measures of left & right frontal, and occipital power spectrum showed increased activity of 1 to 4 mV/Hz, suggestive of increased neuronal engagement for (possibly) cognitive and visual tasks, respectively. Other measures, especially decrease in left frontal peak frequency by 2Hz was consistent with a state of increased relaxation. Positive attitudes toward pets in the total sample of dog owners were associated with lower levels of self reported stress ($r=-0.78$, $p<0.050$), salivary cortisol ($r=-0.50$, NS) and SBP ($r=-0.36$, NS), while higher levels of trait anxiety were associated with higher levels of cortisol ($r=0.69$, $p<0.05$). In addition, higher levels of trait anxiety were associated with lower levels of autonomic system indicators of stress (SBP, DBP,$r= -0.79$ each, $p<0.05$) in this sample of dog owners. Results suggest that the buffering effect on stress response associated with owners interacting with their dogs may extend to interactions with unfamiliar therapy dogs and supports the need for replication with larger sample sizes.

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1) Allen, K., Shykoff, B. E. and Izzo, J. L., Jr. 2001. Pet ownership, but not ace inhibitor therapy, blunts home blood pressure responses to mental stress. Hypertension 38: 815-820.

2) Barker, S. B., Knisely, J. S., Mccain, N. L. and Best, A. M. 2005. Measuring stress and immune response in healthcare professionals following interaction with at therapy dog: A pilot study. Psychological Reports 96: 713-729

» NR4-121

STRESS SYMPTOMS AND LOST PRODUCTIVITY IN PHYSICIANS TREATING BATTLE INJURED SOLDIERS

Thomas Grieger M.D., Christopher A. Alfonzo, M.D.,David M. Benedek, M.D., D.F.A.P.A

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: 1. Discuss the impact of working with the injured on presence of psychiatric symptoms, 2. Address the aspects of lost productivity from psychological stress

SUMMARY:

Risk factors for stress symptoms and lost productivity were examined among military physicians involved in the care of battle wounded soldiers. Posttraumatic Stress Disorder (PTSD) symptoms, lost productivity, identification with victims, and distress and gratification from working with injured soldiers were assessed. Among the 77 respondents, PTSD symptoms were low (PCL-17 mean=20.8), but respondents endorsed 12.6% lost productive time. Weekly exposure to injured soldiers, increased risk for the presence of PTSD symptoms, but identification or distress did not increase risk of symptoms.
Lower gratification was a risk factor for PTSD symptoms and lost productivity.

REFERENCES:

1) Schlenger, W. E., Caddell, J. M., Ebert, L., Jordan, B. K., Rourke, K. M., Wilson, D., et al. (2002). Psychological reactions to terrorist attacks: Findings from the national study of americans' reactions to september 11. Jama, 288(5), 581-588.

2) Stewart, W. F., Ricci, J. A., Chee, E., Hahn, S. R., & Morganstein, D. (2003). Cost of lost productive work time among us workers with depression. Jama, 289(23), 3135-3144.

Tuesday, May 19, 2009

3:00 p.m. - 5:00 p.m.
Hall D, Exhibit Level,
Moscone Convention Center

NEW RESEARCH POSTER SESSION 5: YOUNG INVESTIGATOR POSTER 2

» NR5-001

A STUDY ON THE CAUSAL INFLUENCE PHYSIOLOGICAL RESPONSE LEVEL HAS ON DRINKING MOTIVATION AND DRINKING PROBLEMS AMONG COLLEGE STUDENTS

IL KANG, H.J. Lee, M.D.; S.W. Ki, M.D.; J. W. Kim, M.D., Ph.D.; S. E. Kim, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize various effects of physiological response from consuming alcohol.

SUMMARY:
Objective : This study was performed with the purpose of causal effect of physiological response from consuming alcohol on drinking motivation among college students.
Method : The subject pool was consisted of 115 college students, who were selected at random. The level of physiological response, drinking motivation, and drinking problems were evaluated according to Self-Report of Effect of alcohol(SRE), Drinking-Motivation Questionnaire, and Alcohol Use Disorder Identification Test(AUDIT), respectively in order.
Results : SRE total and SRE when heaviest drinking period are associated with AUDIT scores. According to the data acquired by Correlation Analysis,when comparing levels of subjects' incident of binge drinking and those of the most recent 3-month period of drinking, the SRE value showed a connection with enhancement motivation (r=0.278) and coping motivation
(r=0.259). Furthermore, Multiple-regression analysis was executed to elucidate a causal relationship, and the results pointed to SRE total's causal influence on drinking motivation total, enhancement motivation and coping motivation. Upon measuring motivation, there was a significant disparity of (p<0.05) between high-risk and low-risk groups.
Conclusions : This study was first in the field to shed a light on the effect SRE has on motivations for alcohol consumption. Upon concluding the study, the results clearly indicates that SRE has a cogent causal-influence on coping motivation, which is an incontrovertible indicator of alcohol abuse in a person.

REFERENCES:
1) Baer JS. Students factors : understanding individual variation in college drinking. J Stud Alcohol Drugs 2002; 14:40-53.

2) Carey KB, Correia CJ. Drinking motives predict alcohol-related problems in college students. J Stud Alcohol Drugs 1997; 58(1):100-105.

» NR5-002

COPING STRATEGIES IN TOGOLESE SUBSTANCE USERS

Kossi Kounou M.A., Eric Bui, M.D., Laurent Schmitt, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to look for specific coping strategies in substance users and take ethnicity into account in the assessment of coping strategies in substance users.

SUMMARY:
Background: Little data is available on the influence of ethnic background on coping strategies in Substance Users (SU).
Objective: To examine Togolese SU coping strategies compared to French SU and Togolese controls.
Methods: We enrolled 30 SU in an outpatient clinic for addictions in France as well as 30 SU in an outpatient clinic for addictions and 30 control subjects in Togo. We assessed coping strategies using the 27-item Ways of Coping Checklist (WCC) which provides scores measuring Problem-Centered Coping (PCC), Emotion-Centered Coping (ECC) and Social Support Seeking (SSS). Background variables included gender and age. ANOVA analyses were conducted between the 3 groups on the 3 coping style scores and were completed with post-hoc analyses.
Results: Mean(SD) age of French and Togolese SU, and Togolese controls was respectively 32.1(8.8), 34.8(7.9), and 29.1(5.7). Mean(SD) PCC scores of French and Togolese SU, and Togolese controls were respectively 26.1(9.8), 32.9(7.5) and 26.4(10.7). Mean(SD) ECC scores of French and Togolese SU, and Togolese controls were respectively 25.5(8.1), 31.1(5.0) and 22.5(9.7). Mean SSS scores of French and Togolese SU, and Togolese controls were respectively 20.1(7.2), 24.7(9.6) and 21.1(9.5).
An ANOVA analysis showed significant differences between the 3 groups on the PCC (F=5.725, df=3, p<.01) and ECC (F=8.351, df=3, p<.01) scores. No difference was found on the SSS scores (p=.11). Post-Hoc analyses (Tukey HSD) showed that on both the PCC and ECC scores, Togolese SU scored significantly higher than Togolese controls (p<.05 and p<.01) and French SU (p<.05 and p<.05).
Discussion and conclusion: Togolese substance users may rely more frequently on Problem-Centered and Emotion-Centered Coping than Togolese non substance users and French substance users.

REFERENCES:
1) Bowser, B.P. & Bilal, R. (2001). Drug treatment effectiveness: African-American culture in recovery. J Psychoactive Drugs; 33(4): 391-402

2) Orford, J., Natera, G., Velleman, R., Copello, A., Bowie, N., Bradbury, C. & al. (2001). Ways of coping and health of relatives facing drug and alchohol problems in Mexico and England. Addiction, 96(5): 761-74.

» NR5-003

THE ROUGH ENDOPLASMIC RETICULUM'S GLUTAMATE DEHYDROGENASE IN ALCOHOLICS' SERA

Matej Kravos M.D., Ivan Malešic, M.Pharm., Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to learn about two different intracellular origins of serum glutamate dehydrogenase.

SUMMARY:
Glutamate dehydrogenase (GLDH) is almost exclusively found in mitochondrial matrix of all tissues except erythrocytes. GLDH occurs in two catalytically active forms, determined as soluble (thermo stable) and particulate (thermo labile). In rats it also occurs in rough endoplasmic reticulum in thermo stable form. The housekeeping GLDH (thermo stable) and nerve tissue-specific (thermo labile) could be found in the human brain. The GLUD1 gene (housekeeping GLDH) is localised in human chromosome 10 and is expressed as thermo stable, but GLUD2 (nerve tissue-specific) is localised in human chromosome X and is expressed as thermo labile isoprotein. The increased sera GLDH activity is believed to be exclusively the result of liver damage caused by mitochondrial injury at cell necrosis. We wanted to examine, whether GLDH may be exclusively derived from hepatocyte mitochondria or even from rough endoplasmic reticulum in serum of alcoholics. GLDH activity was assessed in 205 patients admitted to hospital

for treatment of alcohol dependence. In serum of alcoholics we found on average 32.4% thermo-stable and 67.6% thermo-labile GLDH. 62.93 % (129) among all of them had more than 20 % thermo stable GLDH, in 59.06 % cases it was over 20th percentile. The distribution of both isoproteins was uneven. What means that almost one third of serum GLDH originates from rough endoplasmic reticulum and rest from mitochondria. It is an absolutely new finding.There was a moderate correlation between thermo stable GLDH in rough endoplasmic reticulum and GGT inducted by elevated CYP2E1 activity.

REFERENCES:

1) Shashidharan P, Clarke DD, Ahmed N, Moschonas N, Plaitakis A. Nerve tissue-specific human glutamate dehydrogenase that is thermolabile and highly regulated by ADP. J Neurochem 1997; 68: 1804-1811.

2) Lee W K, Shin S, Cho SS, Park JS. Purification and characterization of glutamate dehydrogenase as another isoprotein binding to the membrane of rough endoplasmic reticulum. J Cell Biochem 1999; 76: 244-253.

» NR5-004

THE INCIDENCE OF BIPOLAR DISORDER IN ALCOHOL-DEPENDENT PATIENTS

Damian McGovern M.D., Daniel K. Hall-Flavin, M.D. P., Mark Frye, M.D.

EDUCATIONAL OBJECTIVES:

Mood disorders are sometimes attributed to the manifestations of chemical dependency and that bipolar disorder has been missed in some patients with substance use disorders. In the Intensive Addiction Program (IAP) at the Mayo Clinic, we saw low numbers of patients with the diagnosis of bipolar disorder, compared to other epidemiologic studies. The hypothesis is that bipolar disorder is under-diagnosed. Secondary objectives include identification of endophenotypic variables and demographics.

SUMMARY:

For the past nine months, all patients entering the IAP at Mayo Clinic have been given a Mood Disorders Questionnaire (MDQ). To date, we have results for approximately 200 patients. Patients with positive MDQs are further investigated with the Mini International Neuropsychiatric Interview (MINI) for the identification of Bipolar Disorder and other Psychiatric comorbidities. We aim to gather data on at least 70 more individuals before conducting a more formal analysis of the data. Patients are monitored in a dual-diagnosis unit for four weeks and followed longitudinally with post-treatment interviews at 3, 6, 9 and 12 months. In this way, treatment outcomes, abstinence outcomes and clinical correlates are monitored and recorded.

Early results demonstrate substantially increased numbers of patients identified with underlying mood disorders, more closely approximating national studies. Though the MDQ has been administered in several different populations, we are not aware of routine use of screening instruments in chemical dependency treatment settings, despite strong epidemiologic evidence citing the association between bipolar disorder and substance use disorders. Furthermore, previous studies have noted strong connections between female gender, alcoholism severity, and Axis I comorbidity including bipolar disorder. The database collected herein represents academically fertile ground for further investigation.

REFERENCES:

1) Frye MA, Calabrese JR, Reed ML, et al: Use of health care services among persons who screen positive for bipolar disorder. Psychiatric Services 65(12): 1529-1533, 2005.

2) Hirschfeld RM, Holzer C, Calarese JR, et al: Validity of the mood disorder questionnaire: a general population study. Am J Psych 160: 178-180, 2003.

» NR5-005

MANAGEMENT OF COCAINE ABUSE (MOCA) STUDY: EVALUATION OF CARDIAC COMPLICATIONS IN COCAINE ADDICTED PATIENTS IN THE PSYCHIATRIC EMERGENCY DEPARTMENT

GULAM NOORANI M.D., Mahboob Aslam MD, Javed Iqbal MD, Valerie D'Aurora, BSc, John Charoonbara, BSc

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the current management of patients with cocaine addiction presenting to the psychiatric emergency department (ED), to identify the signs and co-morbid conditions that preclude a future coronary event, and to appreciate the necessity of quantifying cardiac risk factors and conducting simple, inexpensive diagnostic measures in order to optimize patient care.

SUMMARY:

Cocaine has been well established as the illicit drug most frequently resulting in visits to the ED and accounts for a quarter of all nonfatal myocardial infarctions (MI) in young adults. Earlier studies outlined that the risk for MI is greatest 60 minutes after cocaine use and is independent of dose, frequency or route. Accordingly, even trace levels of cocaine on urine toxicology indicate the necessity for acute coronary syndromes protocol. The data is derived from 122 charts of patients who received a DSM-IV diagnosis inclusive of cocaine dependence. It was found that out of 122 patients, 52 received an electrocardiogram (EKG) (42.6%) and 4 had measurement of cardiac bioenzymes, including troponin I and CK-MB (3.3%). Abnormal EKGs were found in 48 patients (92.3%), with the most common finding being nonspecific ST and T wave changes in 42 patients (80.8%), including peaked T waves and early afterdepolarizations each present in 20 cases (38.5%), respectively. ST elevations in 2 or more contiguous leads were found in 3 patients, with no comparison baseline EKGs available to define the acuity of the coronary changes. Additional significant EKG abnormalities included conduction defects in 16 cases (30.8%), sinus bradycardia in 11 cases (21.2%), QT prolongation in 9 patients (17.3%), and indications of cardiomegaly including left ventricular hypertrophy and atrial enlargement, each present in 6 cocaine users respectively (11.5%). Additional cardiac risk factors including concomitant alcohol dependence were identified in 40 patients (32.8%), while 81 (66.4%) admitted to long-term nicotine use, 63 (51.6%) were dependent on opioids, and 26 (21%) were addicted to benzodiazepines. A considerable proportion also had a family history of heart disease, hypertension, obesity, and diabetes mellitus. Identification of cardiac risk factors and co-morbid conditions is necessary in patients in which suspicion of cocaine abuse is high. Protocols must be established mandating the conduction of EKGs in all patients to follow the resolution or permanence of irregularities through repeat studies. Standardizing the measurement of cardiac bioenzymes and consulting a cardiologist when additional risk factors for cardiovascular disease are identified are also imperative to avoid acute coronary syndromes.

REFERENCES:

1) 1.McCord, James, Jneid, Hani, Hollander, Judd E., et al. Management of Cocaine-Associated Chest Pain and Myocardial Infarction. Circulation 2008 117: 1897-1907.

2) 2.Mittleman MA, Mintzer D, Maclure, M, et al. Triggering of myocardial infarction by cocaine. Circulation 1999 99: 2737-2741.

» NR5-006

SUBSTANCE INDUCED PSYCHOTIC DISORDER IN A PATIENT WITH 43 DAY EXPOSURE TO TOLUENE - A CASE REPORT

GULAM NOORANI M.D., Mahboob Aslam M.D, Javed Iqbal M.D, Hanif Ramay M.D., D.F.A.P.A (all Bergen Regional Medical Center) and Sam Clinch (MS IV, St.George's University School of Medicine)

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to

recognize the importance of detailed social and occupational history in patients with new onset of psychotic symptoms.

SUMMARY:

A review of the literature reveals frequent reports of abuse of various drugs leading to the onset of schizophrenia or at the very least an increased susceptibility of developing schizophrenia after prolonged drug abuse.1 Additionally, these drugs are most commonly drugs of abuse, although scattered case reports of exposure to industrial chemicals do exist, two cases of which identify toluene as a causative agent. We present the case of a 20 year old, previously healthy male with no past psychiatric history or history of substance abuse, who presented with symptoms consistent with psychosis after exposure to toluene of 43 days duration. Patient was referred to Bergen Regional Medical Center after he reported to several staff members that he wants to kill them. Additionally, the patient reported auditory hallucinations, command type telling him to cut himself. Prior to admission, the patient had been working for a company that provided industrial painting and tank lining for the petroleum industry. He had only been working at the facility for 43 days. During his employment there it was discovered that he was exposed to the organic solvent toluene. On evaluation, the patient appeared his stated age and appeared well nourished but was unkempt and unclean. He was alert, awake, and oriented in all spheres. He stated his mood to be normal, but his affect was flat and he made minimal eye contact. He acknowledged command type auditory hallucinations that instructed him to cut himself. His thought form was disorganized with looseness of associations. He maintained delusions of persecution and felt that people were after him with the intention of hurting him. The patient was grandiose and felt he was a god that could read people's minds. He also maintained ideas of things with special powers. This patient represents a unique case in his overall lack of confounding factors, lack of prodromal features, and onset of symptoms immediately after exposure to a specific chemical; in this case toluene. This case displays the rather fast progression to schizophrenia that can take place in susceptible individuals after exposure to inciting agents. We propose a prospective study using patients with a family history of schizophrenia, but no current diagnosis of schizophrenia, to better help in the understanding of the development of schizophrenia.

REFERENCES:

1) Boutros N, Bowers M: Chronic Substance-Induced Psychotic Disorders: State of the Literature. Journal of Neuropsychiatry and Clinical Neurosciences 1996; 8:262-269.

2) Tarsh MJ: Schizophreniform Psychosis caused by Sniffing Toluene. J. Soc. Occup. Med 1979; 29:131-133.

» NR5-007

THE INTERACTION BETWEEN PAIN AND DEPRESSIVE SYMPTOMS IN POLYDRUG DEPENDENT INDIVIDUALS IN EARLY METHADONE MAINTENANCE TREATMENT

David Tompkins M.D., Annie Umbricht, M.D., Erin Winstanley, Ph.D., George Bigelow, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the importance of pain assessment in a methadone program and the correlates of pain with co-morbid psychiatric symptoms.

SUMMARY:

Objective: Although self-reported pain is prevalent in methadone maintenance treatment, its relationship to psychological symptoms and drug use is not well characterized. This study examined factors associated with pain in polydrug dependent individuals during a five-week methadone run-up phase in an ongoing outpatient clinical trial.
Methods: Subjects diagnosed with active cocaine and opiate dependence were included. Pain was self-reported at baseline and once weekly; scores could range from 0-100 on a visual analogue scale. Pair-wise t-tests and chi square analyses were used to identify factors related to pain scores. Survival analysis compared treatment retention in subjects with and without significant pain (>10) at baseline.
Results: The study included 96 consecutive subjects: 43% female, 51% African American, and mean age 41.5 years. Mean lifetime heroin use was 13 years (+/- 7.6 s.d.) and cocaine use 10.4 years (+/- 7.5). 40 (42%) subjects reported clinically significant pain (>10) at baseline with a mean of 53.8(+/- 18.5). There was a non-significant increase in the odds of early study discharge with baseline pain >10 as compared to others (OR 1.55, 95% CI 0.62-3.88). Among the 67 individuals retained for 5 weeks, those with baseline pain >10 (n=24) had significantly increased baseline Beck Depression Inventory (BDI) scores (mean 16.3 vs. 11.6, p=0.038) but did not differ in terms of anxiety symptoms, PTSD symptoms, or self-reported drug use. There were no significant gender, age, or race differences in those persons with and without pain >10. Subjects with pain >10 (n=17) at week 5 continued to have significantly elevated BDI scores (9 vs. 4.7, p=.035).
Conclusions: Clinically significant pain was associated with higher depressive symptoms in patients receiving methadone maintenance treatment. And among patients who remained in treatment, clinically significant pain was not associated with continued illicit drug use.

REFERENCES:

1) Clark MR, Stoller KB, Brooner RK: Assessment and Management of Chronic Pain in Individuals Seeking Treatment for Opioid

Dependence Disorder. Can J Psychiatry 2008; 53:496-508

2) Ilgen MA, Trafton JA, Humphreys K: Response to methadone maintenance treatment of opiate dependent patients with and without significant pain. Drug Alc Depend 2006; 82:187-93

» NR5-008

PSYCHIATRIC COMORBIDITY RELATED TO DRUG ABUSE AMONG MEXICAN ADDICTIVE CLINIC

Mirna Trancoso M.D., Ricardo Nanni,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to discuss about dual diagnosis (Substance abuse disorders and psychiatric comorbidity.

SUMMARY:

Introduction: Researchers have long been aware that many drug abusers also have serious mental disorders, a status referred to as dual diagnosis or comorbidity. There is now a widespread acceptance that people with severe mental illness have an increased risk to develop substance use disorders (alcohol and drug abuse/dependence). In addition, drug abuse contributing to the development higher prevalence of psychiatry comorbidity.
Despite similar practices in psychiatry and adictology, barriers exist between both camps which represent an obstacle to treatment of individual patients.
Objective: To evaluate the performance of adults with different patterns of drug and alcohol use on screening instruments for psychiatry disorders.
Method: This is a clinical, descriptive and prospective study. Sample was 85 adults with Substance Abuse Disorders (SAD) attending at a Mexican Addictive Clinic. All patients were evaluated with clinical semi-structured interview, Mini International Neuropsychiatric Interview (M.I.N.I.) and structured questionnaire for DSM-IV-TR criteria. Statistical analysis was performed with SPSS.
Results: Sample with SAD was male 60% and female 40%. The 37.6% were unemployed, 7.1 % studied only elementary school. 41.2% had family history about alcoholism.The most frequent

psychiatric diagnosis was Mayor Depression (89.4%), Attention Deficit Hyperactivity Disorder (ADHD) (68.23%), Anxiety Disorders (40%), Panic Attack 16.5%, Eating Disorders (22.4%), Anorexia (10.6%), Bulimia (11.8 %), and Bipolar Disorder (15.3%). Antisocial Personality was 35.31%, and 29.4 report moderate suicidal risks.
The frequencies of SAD were alcohol abuse 12.9%, alcohol dependence 69.4%, Cannabis abuse (44.7%), tobacco dependence (8.2%), and cocaine dependence (48%).
Conclusions: We found dual diagnosis in all of the patients in the addiction clinic. The most frequent psychiatric comorbidity in patients with SAD were depressive disorders, anxious disorders, and ADHD. The frequency of comorbid psychiatric in a Mexican sample of people with SAD was similar to international findings. This data reinforces the importance of detailed diagnostic investigation among patients with SAD.

REFERENCES:

1) Gual A. (2007)Dual diagnosis in Spain.Drug Alcohol Rev.; 26(1):65-71

2) Drake, R., Mueser, K., Brunette, M., McHugo, G. (2004). A Review of Treatment for People with Severe Mental Illnesses and Co-occurring Substance Use Disorders. Psychiatric Rehabilitation Journal, 27(4):360-374.

» NR5-009

DOUBLE-BLIND, CROSSOVER, PLACEBO-CONTROLLED PILOT STUDY OF VARENICLINE FOR METHAMPHETAMINE DEPENDENCE

Todd Zorick M.D., Karen Miotto, M.D., Steve Shoptaw, Ph.D., Aimee-Noelle Swanson, Ph.D., Clayton Clement, B.Sci., Richard De La Garza II, Ph.D., Thomas Newton, M.D., Edythe London, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the mechanism of action of Varenicline, to identify the rationale for testing Varenicline as a potential treatment for Methamphetamine Dependence, and to understand the safety concerns for potential new pharmacological treatments for Methamphetamine Dependence.

SUMMARY:

We present here a preliminary analysis of an ongoing human behavioral pharmacology study of a double-blind, placebo-controlled, inpatient crossover pilot study of Varenicline as a potential treatment for Methamphetamine (MA) dependence. Varenicline is a full agonist at a7 nicotinic acetylcholine receptors (nAChRs) and a partial agonist at a4ß2 nAChRs that is FDA approved for smoking cessation since 2006. Given its mechanism of action and its effect on producing a sustained release of Dopamine (DA) in the Nucleus Accumbens (NA), we hypothesize that it may have efficacy in treating MA dependence. MA use is endemic in many parts of the world, including the Western US, with an increasing incidence of use in the rest of the US where it was formerly less common. Currently there are no FDA approved medications for MA dependence treatment. This study has three specific aims: 1. To test the safety and tolerability of Varenicline treatment (1 mg bid) when co-administered with 30 mg IV MA in MA-dependent research subjects; 2. To test whether Varenicline can influence MA-dependent research subjects' choice for self-administration of repeated 3 mg doses of MA versus a monetary reward; 3. To test the effect of Varenicline on the subjective effects of co-administered IV MA (30 mg) as compared to oral placebo. Preliminary analysis of data from several participants is encouraging in that oral Varenicline (1 mg bid) appears to be safe from a hemodynamic perspective when co-administered with 30 mg IV MA in MA-dependent subjects, and no adverse neuropsychiatric sequellae have been detected to date.

REFERENCES:

1) Coe JW, Brooks PR, Vetelino MG, et al. Varenicline: an alpha4beta2 nicotinic receptor partial agonist for smoking cessation. J Med Chem. 2005 May 19;48(10):3474-7.

2) Nides M, Glover ED, Reus VI, Christen AG, Make BJ, Billing CB Jr, Williams KE. Varenicline versus bupropion SR or placebo for smoking cessation: a pooled analysis. Am J Health Behav. 2008 Nov-Dec;32(6):664-75.

» NR5-010

A BRAZILIAN HIV PREVENTION INTERVENTION FOR ADULTS WITH SEVERE MENTAL ILLNESS: A RANDOMIZED CLINICAL TRIAL FEASIBILITY STUDY

Lorraine Lothringer M.D., Cristiane Borges, M.D., Katherine Elkington, Ph.D., Claudio Gruber Mann, R.N., Milton Wainberg, M.D., and the Investivators of PRISSMA: Projeto Interdisciplinar em Sexualidade, Saúde Mental e AIDS – Interdisciplinary Project in Sexuality, Mental Health and AIDS

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation the participant should be able to: 1. Recognize that Brazilian adults with SMI are at increased risk for contracting HIV. 2. Understand that, similar to other countries, the majority of Brazilian adults with SMI practice unsafe sex. 3. Demonstrate an understanding that adults with SMI are willing to participate in a clinic-based HIV prevention intervention and reduce their risk without suffering any adverse events by participating in the intervention.

SUMMARY:

Objective:Adults with severe mental illness (SMI) have elevated rates of HIV infection (1). Our NIMH community-based participatory research study with the participation of patients, providers, relatives, and community leaders developed an HIV prevention intervention (1). The aim of the study was to test the feasibility of conducting the intervention and if changes in frequency of unprotected sex from baseline to follow-up were descriptively meaningful and in the desired direction.
Methods: Sixty outpatients with SMI were assigned to the HIV prevention intervention and 38 were randomized into HIV and control interventions. All participants received assessments at baseline, one week, and three months post-intervention. The inclusion criteria included any psychiatrically stable outpatient with SMI receiving care at the clinic with capacity to participate.
Results:The total sample (n=98) was comprised of 51% women. Racial/ethnic categories were 46% white, 38% multiracial, and 16% black. The mean age was 42 years; 73% were single. Half had a diagnosis of schizophrenia; 11% had a substance use disorder; 42% engaged in vaginal/anal sex within the past three months. Only 22% of sexually active patients used condoms consistently (2). There were no significant differences in mean number of unprotected sex acts between the intervention and control groups. At the three-month follow-up, there was a non-significant reduction in the mean number of unprotected sex acts (5.6, SD=17.6) among participants in the experimental group. Most (68%) attended >5/8 intervention sessions; 93% reported being very satisfied with the intervention. No adverse events were reported.
Conclusions: The experimental group showed reduction of the number of unprotected sexual acts at follow-up from baseline. The RCT feasibility study was successfully completed. Currently, an RCT is being implemented in Rio de Janeiro, Brazil.

REFERENCES:

1) Wainberg ML, McKinnon K, Mattos PE: Is It Brazilian? How U.S. HIV prevention interventions were adapted into a new intervention for psychiatric patients in Rio de Janeiro, Brazil. AIDS and Behavior, 2007;11:872-883.

2) Wainberg ML, McKinnon K, Elkington KS, Mattos PE, Gruber Mann C, de Souza Pinto D, Otto-Salaj L, Cournos F, And The Investigators of PRISSMA: HIV risk behaviors among outpatients with severe mental illness in Rio de Janeiro, Brazil. World Psychiatry, 2008;7:166-172.

» NR5-011

ATTENTION DISORDERS IN METHADONE-TREATED

OPIATE-DEPENDENT PATIENTS

Amanda Ellenwood M.S., Adashima Muhammad M.P.H., Caroline Marvin B.A., James Prosser M.D., Igor Galynker M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, participants will be able to identify risk factors for treatment failure/non-adherence in patients receiving inpatient treatment for opiate dependence.

SUMMARY:

Attention Deficit/Hyperactivity Disorder (ADHD) is known to occur with greater frequency in patients with substance abuse/dependency disorders, and is associated with more severe abuse/dependency symptoms and prolonged course of illness. Recent studies suggest that attentional disorders may contribute to failures of addiction treatment. We measured symptoms of attention disorders, mood disorders, and treatment goals in patients receiving methadone substitution therapy in a residential treatment methadone-to-abstinence program. Using the Adult ADHD Self-Report Scale (ASRS-v 1.1) checklist, ten of 23 subjects were identified as having symptoms consistent with ADHD. The mean ADHD score was statistically greater in the subjects identified as consistent with ADHD compared to subjects without ADHD (16.1 ± 2.23 vs. 8.23 ± 3.72; $t = 5.89$; $df = 21$; $p < 0.001$). The Odds Ratio of dropping out of treatment for subjects with ADHD was 0.50 (95% CI = 0.088 – 2.84). Severity of symptoms of attention deficits did not significantly correlate with scores of the Hamilton Anxiety Rating Scale, the Hamilton Depression Rating Scale, or the Beck Depression Inventory. ADHD occurs at a higher than expected frequency among patients receiving residential treatment for opiate dependency, but does not appear to be associated with a greater likelihood of treatment failure.

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» NR5-012

PSYCHIATRIC DISORDERS AND ALCOHOLISM COMORBID IN A SAMPLE OF MEXICAN WOMEN

Armida Granados M.D., Rosa Díaz,M.D., Francisco López,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to discuss about dual diagnosis (psychiatric disorder and abuse/dependence of alcohol) in a sample of Mexican women.

SUMMARY:

Introduction: Alcohol abuse and dependence are highly comorbid with other psychiatric diagnoses, especially among women. However women frequently do not receive specialized substance abuse treatment that addresses both conditions. Some psychiatric illnesses serve as risk factors for alcohol use disorders, and others may develop as a result of chronic alcohol use/abuse.
Women appear to be more vulnerable than men to many adverse consequences of alcohol use and often are underrepresented in studies of alcohol dependence.
Objective: To describe the comorbidity of psychiatric disorders and alcohol abuse/dependence in a sample of Mexican woman.
Methods: This is a clinical, descriptive and prospective study. The sample was 100 women who were attending at a Mexican Psychiatric Hospital. All patients were evaluated with a clinical semi-structured interview, the International Diagnostic Interview Composite (CIDI) and the Index of Addiction Severity (ASI).
Results: The sample was 100 women who were divided into four groups consisting of 25 patients in each. One group consisted of patients whose principal diagnosis was depressive disorder, another with anxiety disorder, another with schizophrenia and the final group with bipolar disorder. The mean age of the women was 35.7 years (SD±11.1). Demographic variables: 56% were single or separated; 32% studied only elementary school and 37% secondary school; 56% were catholic; 66% were unemployed and 77% had children.
The frequency of alcohol abuse was 19% and alcohol dependence was 37%. The most frequent alcoholism comorbidity in patients with psychiatric disorder were bipolar disorder (16%), schizophrenia (15%), depressive disorders (13%) and anxious disorders (13%). The psychiatric disorders with alcoholism comorbid affected social, occupational, family, economic, self-care, and/or health functions.
Conclusions: We found dual diagnosis (psychiatric disorder and abuse/dependence of alcohol) in more than half women.
The severity of more frequent alcohol abuse was the average, followed by the low and high. The frequency of comorbid alcoholism in a Mexican sample of women with psychiatric disorder was similar to international findings. This data reinforces the importance of detailed diagnostic investigation among women with alcohol abuse/dependence.

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» NR5-013

COMPLETION OF INPATIENT ALCOHOL TREATMENT PROGRAM AND READMISSION : DIFFERENCES IN CLINICAL CHARACTERISTICS

ByungOok LEE M.D.,

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to learn about clinical characteristic of alcohol dependence patients who does not relapse after completion of inpatient alcohol program

SUMMARY:

Objectives: The purpose of this study was to evaluate the effect of the abstinence program on prognosis of alcoholic patients. Other factors that might also influence the prognosis of alcohol dependence were identified.
Methods: A retrospective study was done by reviewing the medical records of 416 patients diagnosed as alcohol dependence between Jan, 1, 2001, and Dec, 31, 2005, at National Health Insurance Medical Center Ilsan Hospital, and the data from records of 207 patients who has been followed up for more than 1 year were analyzed. The data included sociodemographic data.
Results: Married patients were found to have lower re-admission rate compared to single, divorced, bereaved, and separated, and those with alcoholic liver disease were more likely to relapse. Patients who have re-admitted had statistically lower abstinence program participation number and participation rate (participation number divided by admission day). Even in the re-admission group, the abstinence period was found to be longer in patients who had participated in more abstinence program during admission. Conclusion : The participation of inpatient abstinence program was found to be a major factor of the patient's prognosis. The role of spouse of alcoholic patients was also important to prevent readmission of alcoholic patients.

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» NR5-014

MAOA GENE INTERACTS WITH ALDH2 GENE IN ANXIETY-DEPRESSION ALCOHOLISM

Sheng-Yu Lee M.D., Cheng-Yi Hahn, M.D., M.S., Jia-Fu Lee, M.D., Ph.D., San-Yuan Huang, M.D., Ph.D., I-Hui Lee, M.D., Tzung-Lieh Yeh, M.D., Yen-Kuang Yang, M.D., Shih-Heng Chen, Ph.D., Huei-Chen Ko, Ph.D., Po-Hsiu Kuo,Ph.D., Ru-Band Lu, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize that the gene-to-gene interaction approach in subtyped alcoholism (to reduce heterogeneity) might be more revealing for alcoholism is a heterogeneous, highly hereditary disorder. Participant may further learn that ALDH2 and MAOA genes, the two genes involved in monoamine metabolism pathway, interact among ANX/DEP ALC subjects.

SUMMARY:

Background: Alcoholism is usually comorbid with anxiety or depressive disorder or both which might increase drinking behavior. In our previous studies, anxiety–depressive alcohol dependence (ANX/DEP ALC) has been posited as a genetically specific subtype of alcoholism. Anxiety-depressive alcoholism is related to dopamine and serotonin which are catalyzed by monoamine oxidase A (MAOA) and acetaldehyde dehydrogenase 2 (ALDH2). The objective of this study is to determine whether the interaction between the MAOA and the ALDH2 genes is associated with ANX/DEP ALC subjects.
Methods: A total of 380 Han Chinese men in Taiwan including 143 ANX/DEP ALC and 237 normal control subjects were recruited in this study. The diagnosis of alcohol dependence with past or current history of anxiety and/or depressive disorder was made according to DSM-IV criteria. Genotypes of ALDH2 and MAOA-uVNTR (variable number of tandem repeat located upstream) were determined using PCR-RFCP.
Results: Significant interaction between ALDH2 and MAOA genes were noted (p=0.036). After the stratification of the MAOA-uVNTR, significant association between controls and ALDH2*1/*2 or *2/*2 genotypes was still noted in both genotypes, but the MAOA-uVNTR 4-repeat subgroup revealed higher protection than 3-repeat subgroup.
Conclusion: We concluded that the protective effects of the ALDH2*2 allele against alcoholism might be higher in subjects with anxiety/depressive disorders carrying MAOA-uVNTR 4-repeat allele and the interaction of MAOA and ALDH2 linked to ANX/DEP ALC.
No commercial support was received in this study.

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» NR5-015

SPANISH VALIDATION OF THE ADULT ADHD RATING SCALE: RELEVANCE OF SUBTYPES

Rosa Bosch, JA Ramos-Quiroga MD., M Nogueira Ph.D., N Gómez-Barros MD, M Corrales Ph.D., G Palomar MD.,S Valero Ph.D. and M Casas Ph.D, MD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should have an understanding of the assessement and diagnosis in adults with attention deficit/hyperactivity disorder.

SUMMARY:

ADHD RS is a 18-items scale (DuPaul et al, 1998; Rosler et al, 2006) self-report version widely use for assessing symtoms in adult ADHD DSM-IV. For the validation of Spanish version of the ADHD-RS, a case control study was performed (adult ADHD vs non ADHD). The diagnosis of ADHD was carried out with SCID-I and CAADID-II. To determinate the internal validity of the two dimensions structure of ADHD-RS, an exploratory Factor Analysis was performed in the subsample of adult ADHD. The a-coefficients were taken as a measure of the internal consistency. A logistic regression study was carried out to evaluate the model in terms of sensitivity, specificity, positive and negative predictive values.
Sample consisted of 304 adult with ADHD and 94 controls. Average age was 33.29 (SD=10.50) and 66 % of subjects were men. Factor analysis was done with a Principal Component analysis followed by a normalized Varimax rotation. The Kaiser-Meyer-Olkin measure of sampling adequacy tests was 0.868 and the Bartlett's test of sphericity was c2 (153) = 1835.76, p<0.0005, indicating the appropriateness of the factor analysis. This two-factor model accounted 37,81 % of the explained variance. The a-coefficient of the two factor was 0.84 and 0.82. The original stategy proposed 24 point for cut-off: sensitivity (81.9%), specificity (74.7%), PPV (50.0%), NPV (93.0%). The new score strategy proposed by our group suggests differents cut-off for differents subtypes: the 24 points is the best cut-off for ADHD Combined subtype: sensitivity (81.9%), specificity (87.3%), PPV (78.6%), NPV (89.4%), and 21 points is the best cut-off for ADHD Inattentive Subtype: sensitivity (70.2%), specificity (76.1%), PPV (71.7%), NPV (74.8%). This study demonstrates that the Spanish version of the ADHD-RS is a valid scale to discriminate adults ADHD from controls. The new proposed score strategy suggest the relevance of subtype in the differents cut-off selected.

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» NR5-016

NOCTURNAL BINGE EATING IN ATTENTION DEFICIT HYPERACTIVITY DISORDER

Anoop Karippot M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand Binge eating in ADHD

SUMMARY:

BACKGROUND: Night eating syndrome consists of either overeating at night or waking up during the night and eating. Children with Attention Deficit Hyperactivity Disorder have difficulty with initiating and maintaing sleep. Nocturnal Binge eating is is commonly seen associated with stimulant treatment in the morning for the behavioral management of ADHD. OBJECTIVE: We describe a case series of patients with ADHD exhibiting Nocturnal Binge Eating Disorder and complaints of chronic difficulty with initiating sleep. METHOD: This is an interesting case series of 3 ADHD children with long standing maintenance treatment with stimulant medication having complaints of insomnia especially difficulty with initiating sleep and nocturnal binge eating. RESULTS: Chronic maintenace treatment of ADHD with stimulants amy result in Nocturnal Binge eating and complaints of insomnia, especially difficulty with initiating sleep at night.
DISCUSSION: Stimulants are helpful in managing ADHD symptoms in children. Long term use of stimulants amy result in

decrease eating during the day and nocturnal binge eating at night with resultant insomnia complaints. We discuss this potential side effect of utilizing stimulants in ADHD which is the main line treatment for this condition and emphasize the need for careful monitoring with this management.

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2) Links between eating disorder symptom severity and psychiatric comorbidity Anja Spindler, a, and Gabriella Milosa, Psychiatric Department, University Hospital, Culmannstrasse 8, CH-8091 Zürich, Switzerland

» NR5-017

MATERNAL DEPRESSION AND PARENTING BEHAVIOR IN MOTHERS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER CHILDREN

Hye Ji Min M.D., Jeong-Ho Seok, MD, PhD, Na Rei Hong, MD, PhD, Duk-In Jon, MD, PhD, Young Shin Kim, MD, PhD, Hyun Ju Hong, MD, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that the control of maternal depression could be important to treat their children with ADHD.

SUMMARY:

Objectives : It is widely accepted that there are problems of parent-child relationship in children with attention deficit hyperactivity disorder (ADHD) and their mothers. Therefore, we aimed to investigate the relationship among ADHD, maternal depression, and parenting attitude in a community sample.
Methods: We investigated 774 1st grade-children and their mothers. The subjects were 46 children with ADHD and 627 controls. The mothers completed parent-report questionnaires containing Korean ADHD Rating Scale-IV, Beck Depression Inventory, and Korean Maternal Behavior Inventory. Structured clinical interview was performed for diagnosing ADHD and the maternal depression.
Results : Mothers of ADHD children reported more depressive symptoms than mothers of controls. Moreover, mothers of ADHD children were more authoritative controlling and overprotective, and less reasonable guided and affectionate than mothers of controls. There was significant correlation among maternal depression, ADHD symptoms, and negative parenting behavior in all subjects. In multiple regression analysis, negative parenting behavior is explained more by maternal depression than by ADHD diagnosis.
Conclusion: Negative parenting behavior is significantly associated with maternal depression in mothers with ADHD children. These findings suggest that the control of maternal depression could be important to treat their children with ADHD. Longitudinal study is needed to confirm whether maternal depression causes negative parenting behaviors in mothers with ADHD children.

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» NR5-018

RISK FOR OVERT AGGRESSION AND PROACTIVE-REACTIVE AGGRESSIVE MOTIVATION IN REFERRED CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISOR

Ellen C. Preen, Psy.D., Karen G. Chartier, Ph.D., Richard F. Kaplan, Ph.D., Daniel F. Connor, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the relationship between comorbid psychiatric diagnoses and aggression in referred ADHD children and adolescents.

SUMMARY:

Aggression, independently of its association with the psychiatric diagnoses of Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD), is important but not well studied in clinical samples of ADHD youngsters. Objective: To investigate the contribution of psychiatric diagnostic comorbidity and ADHD symptom domain on aggression type (overt) and motivation (proactive or reactive) in a clinically referred sample of ADHD youngsters and compared to community controls. Method: Consecutively referred ADHD children and adolescents (N=268) and recruited community controls (N=100) were compared by ADHD subtype (inattentive, hyperactive-impulsive, combined, NOS) and on the presence of diagnostic comorbidity (ODD, CD, bipolar, depression, anxiety disorders) on measures assessing aggression type and motivation. We controlled for age and SES. Gender was not statistically different across groups. Results were analyzed by ANCOVA with correction for Type I statistical error. Results: The ADHD sample showed more aggression than community controls. Statistically significant ($p<0.001$) correlations were found for all measures of aggression and total number of comorbid disorders. ADHD participants diagnosed with depression ($p<.05$), CD ($p<.05$) and bipolar disorder ($p<.05$) had significantly higher scores on measures of overt aggression, and proactive and reactive aggressive motivation than ADHD children without the comorbid disorder. Overt aggression ($p<.05$) and reactive aggressive motivation ($p<.05$) (not proactive) were found to be higher for the ADHD with ODD group. No differences in aggression were found for participants diagnosed with ADHD and anxiety. The combined type of ADHD conferred most risk for aggression. Conclusions: Non-anxiety psychiatric comorbidity and the combined type of ADHD increase risk for overt aggression and proactive/reactive aggression motivation in referred ADHD youngsters. Aggression type and motivation should be assessed in ADHD patients.

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» NR5-019

CASE-CONTROL STUDY OF SIX GENES ASYMMETRICALLY EXPRESSED IN THE TWO CEREBRAL HEMISPHERES: EVIDENCE OF ASSOCIATION OF BAIAP2 WITH ADULTHOOD ATTENTION-D

J. Antoni Ramos-Quiroga M.D., M Ribasés Ph.D, R Bosch Ph.D, A Hervás MD, A Bielsa MD, X Gastaminza MD, S Guijarro-Domingo Ph.D, M Nogueira Ph.D, N Gómez-Barros MD, S Kreiker MD, Silke Groß-Lesch MD, CP Jacob MD, KP Lesch Ph.D, MD, A Reif Ph.D,MD S Johansson Ph.D,6, M Dramsdahl MD, K von Plessen MD PM Knappskog MD J Haavik Ph.D, MD X Estivill Ph.D, MD , M Casas Ph.D, MD , M Bayés Ph.D and B Cormand Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to have new information regarding genetics of adult ADHD. Different lines of evidence suggest that abnormal right-left brain asymmetries in ADHD patients may be involved in a variety of ADHD-related cognitive processes.

SUMMARY:

Attention-deficit hyperactivity disorder (ADHD) persists through-

out lifespan in at least 30% of ADHD children. Different lines of evidence suggest that abnormal right-left brain asymmetries in ADHD patients may be involved in a variety of ADHD-related cognitive processes. We selected six functional candidate genes showing at least 1.9-fold differential expression between hemispheres (BAIAP2, DAPPER1, LMO4, NEUROD6, ATP2B3, ID2) and performed a case-control analysis in an initial Spanish sample of 587 ADHD patients (270 adults and 317 children) and 587 sex-matched unrelated controls. The single- and multiple-marker analysis provided preliminary evidence for the contribution of BAIAP2 to adulthood ADHD (P=0.0026, OR = 1.69 (1.20-2.44) and P=0.0016, OR = 1.64 (1.20-2.22), respectively). We then tested BAIAP2 for replication in two independent samples from Germany and Norway (639 adult ADHD patients and 612 sex-matched unrelated controls and 417 adult ADHD cases and 469 sex-matched unrelated controls, respectively). While no significant results were observed in the Norwegian sample, we found additional evidence for association between BAIAP2 and adulthood ADHD in the German population (P=0.0062; OR=1.21 (1.03-1.42). Our results support the participation of BAIAP2 in the continuity of ADHD across lifespan, at least in some of the populations analyzed, and suggest that genetic factors potentially influencing abnormal cerebral lateralization may be involved in the predisposition to this neurodevelopmental disorder.

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» NR5-020

PREVALENCE OF ASPERGERS SYNDROME IN ADULT ADHD

Mandy Roy, Wolfgang Dillo, M.D.,Vanessa Prox-Vagedes, M.D., Marc Ziegenbein, M.D., Martin D. Ohlmeier, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to to recognize that Aspergers Syndrome is an important comorbid disorder in adult ADHD-patients, leading to extensive impairments in social life and demanding a special treatment. Additionally the participant should notice that the high rate of comorbidity indicates pathoneurophysiological commons of both disorders.

SUMMARY:

Objective: The attention-deficit/hyperactivity disorder (ADHD) often appears with comorbid diseases such as depression or addiction. Little regard is payed to the comorbidity with an Aspergers Syndrome – an autism-spectrum-disorder with impairments in social interaction, unusual and limited interests as well as stereotypic behaviour, with a prevalence of 0,02%. ADHD and Aspergers-Syndrome show overlapping symptoms, such as deficits in concentration, a sensory hypersensivity and motor clumsiness. In the present ongoing pilot-study we explored the prevalence of Aspergers Syndrome in patients with ADHD.
Method: 53 adult patients diagnosed with an ADHD (17 females, 36 males) were investigated for an Aspergers Syndrome by two special screening-instruments „Autism-spectrum-quotient“ (AQ) and „Empathie-quotient“ (EQ) by Baron-Cohen, by the computer-based „Frankfurter test and training of recognition of facial affects“ and by a clinical exploration according to the DSM-IV-criteria. In patients with both disorders the subscales of the AQ were analyzed.
Results: 8 ADHD-patients were diagnosed with a comorbid Aspergers Syndrome (15.1% of the patients; two females, six males). The score of the AQ-subscale “social skills” was significantly higher in our comorbid patients than the score of the original investigated autistic patients.
Conclusion: The prevalence of Aspergers Syndrome in adult ADHD-patients is clearly increased in contrast to the normal population (15.1% vs. 0.02%). The comorbidity causes extensive problems especially in social skills. For the clinical practice the importance of a screening for Aspergers Syndrome in adult ADHD-patients and a described adaption of the therapy are emphasized. The high rate of comorbidity indicates a pathoneurophysiological connection between both disorders, e.g. concerning executive functions.
Aspergers Syndrome seems to be a common and important comorbidity in adult ADHD with important consequences for therapy and following scientific studies.

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» NR5-021

PSYCHOLOGICAL AND PHYSIOLOGICAL MARKERS AND THE METABOLIC CONTROL OF TYPE 1 DIABETES MELLITUS

Bianca Andreica, Bogdan Lucian, MD, Simona Cainap, MD, Mariana Andreica, MD Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to point out the correlations between physiological markers, familial dynamics, personality traits, and coping mechanism for a better understanding and prediction of the chronic illness.

SUMMARY:

The aim of this study is to find some correlations between physiological markers, familial dynamics, personality traits and coping mechanism in order to define more clear the phenomenology of onset and maintenance of diabetes mellitus. A sample of 34 children (mean age – 10 years) and their parents and a second lot composed of 40 children (mean age 11 years) and their parents were recruited to assess the factors mentioned above. We assessed the children using Constructive Thinking Inventory, and their parents completed the Parental Stress Index. In our study, we have evaluated glycated hemoglobin, lipid metabolic parameters, the variation of the insuline dose, cortisol, calcium and magnesium in order to correlate these parameters with certain psychological factors.
Children and adolescents with diabetes reported more distrust of others (p .04), withdrawn (p<.01) and more conduct problems than controls. Diabetic children’s parents showed lack of emotional and active support (p .04), isolation (p<.01) and lesser competence (p .03) than controls. We have found correlations between cortisolemia, serum magnesium, insuline dose, glycated hemoglobin and acceptability and life stress, showing a direction for follow-up and interventions with diabetic patients. The results suggest that ameliorating the psychological climate of the diabetic child might improve the metabolic control of the disease and prevent the long-term complications.

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Med, 2003; 24: 39-52

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» NR5-022

SPORTS PARTICIPATION AS A PROTECTIVE FACTOR AGAINST DEPRESSION AND SUICIDAL IDEATIONS AS MEDIATED BY SELF ESTEEM AND SOCIAL SUPPORT

Lindsay Babiss B.S., James E. Gangwisch, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation the participant should be able to recognize the protective effects of participation in sports on the risk for depression and suicidal ideations in adolescents and what factors mediate these relationships.

SUMMARY:

Participation in sports has been shown to be protective against depression and suicidal ideations, but little is known about what factors mediate these relationships. No previous studies examined potential mediators between sports participation and suicidal ideations and only one study explored possible mediators between sports participation and depression. Increased sports participation could protect against depression and suicidal ideations by increasing endogenous endorphin levels, boosting self esteem, improving body image, increasing social support, and affecting substance abuse. We conducted multivariate hierarchical logistic regression analyses of ADD Health data to explore whether increased participation in sports (none, 1 to 2, 3 to 4, or 5 or more times per week) is associated with depression and suicidal ideations and whether exercise, self esteem, BMI, social support, and substance abuse mediate these relationships. Study participants included 14,746 adolescents in grades 7 through 12 drawn from a national school survey from 80 high schools plus their feeder middle schools. As the participation in sports increases by one category, the odds of suffering from depression decreases by 18% (OR = 0.82, 95% CI 0.76-0.88) and the odds of having suicidal ideations decreases by 11% (OR = 0.89, 95% CI 0.84-0.94) after controlling for covariates. Alcohol and substance abuse, BMI, and exercise did not mediate these associations. Consistent with self esteem and social support acting as mediators of these relationships, the inclusion of these variables in the multivariate models attenuated the associations for depression (OR = 0.85, 0.73-0.99) and suicidal ideations (OR = 0.92, 0.85-1.01). Depression and suicidal ideations are highly prevalent in adolescents. Adolescents should be offered ample opportunity and encouragement to participate in sports, which can protect against depression and suicidal ideations by boosting self esteem and increasing social support.

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» NR5-023

INVESTIGATING THE IMPACT OF LIGHT THERAPY ON PERFORMANCE OF ADHD CHILDREN ON NEUROPSYCHOLOGY TASKS

Johanna Cabassa M.D., Johanna A. Cabassa,MD, Gloria M. Reeves,MD, Manana Lapidus,MD, Patricia Langerberg,Ph.D.,Gina Han,BS, Mary Johnson,Ph.D., and Teodor T. Postolache,MD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to learn that SAD and ADHD share a number of clinical features, but that the data do not support immediate positive effects of bright light in children with Attention Deficit Hyperactivity Disorder (ADHD)

SUMMARY:

Introduction: Biologic interventions for Attention Deficit Hyperactivity Disorder (ADHD) have primarily focused on stimulant medication treatment. Efficacy and cost-effectiveness of stimulant treatment for ADHD is well supported. However, increasing concern over cardiovascular and growth impairment side effects has raised the need to identify alternative biologic therapies for ADHD as either primary treatment or augmentation strategies that can reduce stimulant exposure. The purpose of this pilot study was to test the effects of a single session of light therapy on pediatric ADHD symptoms. The use of light therapy is supported by overlap of cognitive symptoms between ADHD and seasonal depression; and models which propose a core impairment of "underarousal" and reduced attention to environmental cues in both disorders.
Methods: This pilot study employed a cross over randomized single blind design. We recruited children ages 5 – 18 years old with DISC IV diagnosis of ADHD. Children were tested on two sessions, scheduled approximately one week apart. One session involved administration of 30 minutes of bright light (5000 lux) and one session of placebo dim red light (<25 lux). After each light session, the child participated in tasks to assess working memory (the letter number sequencing task from the WISC IV) and inattention and impulsivity (the IVA continuous performance task).
Results: Nine children (ages 8-12) with ADHD were studied. There were no significant differences on neuropsychological task performance after bright light compared with placebo light.
Conclusion: In this small research sample, a single bright light treatment did not result in superior performance on measures of working memory and ADHD symptoms compared to placebo light. Future studies are needed to test the effects of bright light therapy with a larger population of unmedicated youth with ADHD, and over a longer course of treatment.
Acknowledgement: grant from Litebook via The Society for light treatment and biological rhythms.

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» NR5-024

THE PATTERN OF STANFORD-BINET IQ PROFILES OF LANGUAGE DEVELOPMENTAL DISORDERS IN TAIWAN

Yi-ling Chien M.D., Shang-wen Chang, M.D., Huei-ting Kuo, Hsieh Rulan, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to find the cognitive characteristics in children with language developmental disorders.

SUMMARY:

Background: This study is aimed to compare the cognitive profiles of those with and without normal language development.
Methods: There were 405 children brought to our clinic for evaluation of developmental delay from Jan, 2006 to April, 2007. Diagnosis of language developmental disorders was made by speech therapist and psychiatrist. In 405 children, 97 ones have Stanford-Binet intelligence scores, with mean age of 54.2 months in boys (n=63) and 55.3 in girls (n=34). Scores in each subscale of Stanford-Binet (including verbal, abstract, quantitative, short-term memory) were compared between normal and delayed language development.
Results: 43 cases in 97 are delayed in expressive language, and 41 cases are delay in comprehensive language. There was no gender

difference in proportion of expressive language delay, comprehensive language delay, or in total scores of SB intelligence. Ten cases with mild to moderate hearing impairment didn't have higher risk for language disorder. Lower scores in each subscale and composite score are noted either cases with mixed comprehensive and expressive speech delay compared to normal group, with total IQ 87.7±8.6 vs 104.6±10.3, verbal 76.9±14.2 vs 98.5±11.9, abstract 97.0±15.2 vs 108±14.3, quantitative 99.8±8.3 vs 112.2±13.5, short-term memory 86.5±11.7 vs 97.2±9.1; the same pattern was also found in either comprehensive or expressive disorder alone, especially in the former one.
Conclusion: Delayed language development is related to lower score in each subscale of Stanford-Binet, especially in verbal reasoning.

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2) Cognitive abilities in children with specific language impairment: consideration of visuo-spatial skills. Hick R, Botting N, Conti-Ramsden G. Int J Lang Commun Disord. 2005 Apr-Jun;40(2):137-49.

» NR5-025

PARENT RATINGS OF SOCIAL RESPONSIVENESS IN CHILDREN WITH CEREBELLAR TUMORS

Talar Hopyan Ph.D., Maureen Dennis, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to have a better understanding of the clinical consequences of childhood benign or malignant tumors of the cerebellum with respect to social behavioral outcomes.

SUMMARY:

OBJECTIVE: Recent clinical research suggests that individuals with cerebellar lesions exhibit social behavioral deficits, consistent with emerging views of the functional role of the cerebellum in cognition and emotion. Although acute clinical changes in social function following cerebellar injury in children have been reported in clinical studies, it is unclear whether deficits on social behavior are characteristics of groups of children with cerebellar lesions, or whether social behavioral deficits persist many years after lesion onset. In this study, we report parent ratings of social responsiveness in a non-clinically referred group of children treated for benign or malignant cerebellar tumors. METHOD: Participants were 34 children aged 7-16 years treated for two of the most common pediatric cerebellar tumors (18 with benign astrocytomas (AST) treated with surgery only or 16 malignant medulloblastomas (MBT) treated with surgery, radiation, with or without chemotherapy). MEASURE: Parents completed the Social Responsiveness Scale (Constantino & Gruber, 2005), which measures parent ratings of the child's problems in social interactions over the preceding six months in five domains of social function. RESULTS: The AST group performed within standardized norms (M T score = 50, SD 10) across social responsiveness measures. The MBT group showed elevated scores (M T score of > 60 = clinically significant problems) on Social Cognition (M T score = 66), Social Communication (M T score = 62), Social Motivation (M T score = 60),and Autistic Mannerisms (M T score = 65). ANOVA revealed that children in the AST group performed significantly better than children in the MBT group on Social Cognition, Social Communication and Autistic Mannerisms ($p < .05$). CONCLUSION: In the long term following treatment of cerebellar tumors, parent ratings of social responsiveness were within normal limits for children in the AST group. Children with MBT tumors requiring craniospinal radiation performed in the mild to moderate range, indicating deficiencies in reciprocal social behavior. The fact that these parent-rated social behavior deficits were found in the malignant but not in the benign tumor group suggests that parent-identified social deficits reflect the adverse effects of craniospinal radiation in children with cerebellar tumors.

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» NR5-026

PSYCHIATRIC COMORBIDITY AMONG YOUTH RECEIVING SUBSTANCE ABUSE TREATMENT: PREVALENCE AND THE EFFECTS OF INTERVENTION IN REDUCING SYMPTOMS AND INCIDEN

Viviana Horigian M.D., Carl Weems, PhD; Jessica Ucha- Vieta, M. Ed., Michael S. Robbins, Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the importance of the prevalence of comorbid psychiatric disorders in subtance abusing youth. Results will be discussed in terms of their implications for substance use interventions to reduce the incidence of mental disorders in youth.

SUMMARY:

Objective: Few studies have examined the impact of substance abuse treatments on comorbid psychopathology. The objective of this study is to explore the prevalence of anxiety and depression among substance using youth and examine the effects of substance abuse treatments in reducing these symptoms.
Method: 480 adolescents and their families were randomly assigned to Brief Strategic Family Therapy or Treatment as Usual for the treatment of drug abuse in 8 outpatient centers. 327 parents and 315 youth completed 12 month follow ups. Youth and parents were screened for anxiety and depression using the DISC predictive scales at pre treatment and again at 12 months .Youth were 12-18 years (mean age 16 years) and was 78.5% male. Forty Four percent were Hispanic (n = 213), 31% White (n = 148), 23% African-American (n = 110), and 2% (n = 9) youth were of other ethnicities
Results: Preliminary analyses suggest that anxiety and depression diagnoses were highly prevalent in the sample. Fifty-two percent of the sample had at least one anxiety disorder or depression by child report and 65% by parent report. Results of the intervention (pre- to post-treatment) were first analyzed with a series of [2 time by 2 treatment (BSFT versus TAU)] mixed factorial ANOVA's. Results on child reported depression indicated a significant effect of time [$F (1, 313) = 22.01$, $p < .001$] Results on parent reported depression indicated a significant effect of time [$F (1, 325) = 63.35$, $p < .001$] Results on child reported anxiety indicated a significant effect of time [$F (1, 313) = 70.09$, $p < .001$] .There were no significant between treatment group effects in any of these analyses. Additional analyses on diagnostic status, externalizing symptoms and the effects of ethnicity will be reported.
Conclusions: Anxiety and depressive symptoms were prevalent and results suggest that there were significant reductions in the incidence of probable anxiety and depression disorders at follow- up.

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NR5-027

ADOLESCENTS' PSYCHOPATHOLOGY RELATED TO DISCREPANCIES BETWEEN ADOLESCENTS' SELF-REPORT AND PARENTS' REPORT OF ADOLESCENTS' PROBLEM BEHAVIOR

Sojin Lee M.D., Bong Cho Kim, M.D., Ph.D.,Cheol Soon Lee, M.D., Dong Yun Lee, M.D., Ji Yun Sohn, M.D., Sun Mi Kim, M.D., Seung Nam Kim, M.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to use the adolescent-parent discrepancies as valuable information for the diagnosis of a community-based samples.

SUMMARY:

Introduction: The necessity of multiple informants in diagnostic evaluation of children and adolescents is repeatedly stressed in child psychiatric clinical work and research. When discrepancies are considerable between parents' and adolescents' reports on externalizing and internalizing symptoms of adolescents, it is important to consider how to interpret these discrepancies.
Objective: This study was conducted to facilitate understanding of disagreement between parents' and adolescents' reports on mental symptoms of adolescents. The purpose of this study was to examine how adolescents' psychopathology influence parents' account of the mental problems of their adolescents compared to what the adolescents themselves report.
Method: 876 high school students in Masan city participated in Adolescent mental health and problem behavior screening test(AMPQ). Among the students who were tested, selected eighty five adolescents(whose scores were above the cut-point) and their parents completed the questionnaire Korean-youth self report(K-YSR), Korean-child/adolescent behavior check list(K-CBCL) and symptom check list-90-revised(SCL-90-R).
Results: Depression and somatization in adolescence emerged as a significant variables predicting K-YSR-K-CBCL discrepancy on internalizing symptoms, explaining 36% of the variance. With increased levels of depression and decreased levels of somatization, adolescents tended to report more internalizing problems compared to their parents. For the discrepancy on externalizing problems, obsessive compulsive symptoms were the most significant variable. When obsessive compulsive symptoms in adolescents was increased, there were more disagreement in reports of parent' and adolescents'.
Conclusions: The psychopathologies in adolescents such as depression, somatization and obsessive compulsive symptom may be useful to consider when interpreting informant discrepancy concerning the mental problems of adolescents.

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NR5-028

AN EXAMINATION OF PTSD AND SUBSTANCE USE IN A SAMPLE OF ADOLESCENTS PRESENTING FOR TREATMENT

Ruby Lekwauwa B.S., Ernestine C. Briggs-King, Ph.D., Sarah A. Ostrowski, Ph.D., Lisa M. Amaya-Jackson, M.D., M.P.H.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to appreciate the role that the self medication hypothesis may play in understanding the relationship between trauma and substance use in adolescents.

SUMMARY:

Objective: The relationship between substance use and trauma exposure in adolescents is well documented(1). Though the directionality of the relationship is not clear there is data to support the hypothesis that substance use may be a means by which to self medicate dysphoric affect(2). It is expected that adolescents with trauma histories and problematic substance use will have higher scores on the PTSD cluster scales and overall score. Method: Participants include 2460 adolescents ages 13-18 (M=15.17, SD=1.39), enrolled in a larger quality improvement initiative, National Child Traumatic Stress Network funded by SAMHSA. All participants completed a comprehensive battery. For this study data on demographics, trauma, substance use, and PTSD symptoms were used. Substance use was derived from clinical evaluation data. PTSD symptoms were obtained via the UCLA Post Traumatic Stress Disorder-Reaction Index, a semi-structured interview that assesses trauma exposure and DSM-IV PTSD diagnostic criteria. Scores for reexperiencing, hyperarousal, avoidance and overall PTSD were computed. Multiple linear regression models that included age, gender, race, and number of traumatic events were conducted to examine the relationship between substance use and PTSD. Results: Substance use problems were reported for 17% of the sample. Preliminary regression results suggest that female gender, number of traumas, and substance use significantly predicted hyperarousal symptoms ($F(5,1137)=25.08$, $p<.000$). A similar model was tested for overall PTSD scores ($F(5, 1137)=31.21$, $p<.000$) that demonstrated a trend towards significance for substance use beyond the variance accounted for by gender and number of traumas ($p=0.059$). Additional analyses will be conducted to explore the role of gender in this complex pattern of findings. Conclusions: These findings highlight the importance of screening for substance use in patients with high levels of hyperarousal and PTSD.

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NR5-029

PSYCHIATRIC COMORBIDITIES AMONG ADOLESCENTS WITH PERSISTENT AND REMITTED ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

Hsing-Chang Ni M.D., Susan Shur-Fen Gau,M.D.,Ph.D., Wei-Tsuen Soong,M.D., Yu-Yu Wu,M.D., Liang-Ying Lin,M.D., Yen-Nan Chiu,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to know that childhood diagnosis of ADHD predicts psychiatric comorbid conditions regardless of persistence of ADHD at adolescence, and therefore, identification of severe ADHD symptoms at childhood and age-specific comorbid patterns throughout the developmental stage is important to offset the long-term adverse psychiatric outcomes of ADHD.

SUMMARY:

Objectives: To examine current psychiatric comorbidities among adolescents with persistent ADHD and remitted ADHD as compared to healthy controls, and to determine factors predicting psychiatric comorbidities.
Methods: We enrolled 296 adolescents, aged 11-17, diagnosed with DSM-IV ADHD at mean age of 6.7 and 185 school controls. We use Kiddie-Schedule for Affective Disorders and Schizophrenia-Epidemiology version to interview all the participants. We categorized the ADHD group into persistent (186, 62.8%) and remitted (110, 37.2%) subgroups based on best estimate of current ADHD symptoms.
Results: Compared to the controls, the two ADHD groups were

more likely to have oppositional defiant disorder(ODD), conduct disorder, tics, mood disorders, ever and regular uses of substances, substance use disorders and sleep disorders (odds ratios, ORs =1.8~ 25.3). Adolescents with persistent ADHD had higher risks for anxiety disorders, particularly specific phobia than the controls. Moreover, adolescents with persistent ADHD were more likely to have ODD and any psychiatric disorders than their remitted counterparts. Advanced analyses in the ADHD group revealed that more severe baseline ADHD symptoms and longer duration of methylphenidate treatment predicted ODD/conduct disorder at adolescence; longer methylphenidate treatment duration was associated with an increased risk for tics at adolescence; older age predicted higher risks for mood disorders and substance use disorders.
Conclusion: Our findings indicate that reduced ADHD symptoms at adolescence may not lead to decreased risks for psychiatric comorbidities, and suggest that identification of severe ADHD symptoms at childhood and age-specific comorbid patterns throughout the developmental stage is important to offset the long-term adverse psychiatric outcomes of children with ADHD.

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» NR5-030

METABOLIC EFFECTS OF ANTIPSYCHOTICS IN CHILDREN: PRELIMINARY RESULTS FROM THE MEAC STUDY

Ginger E. Nicol, M.D.; Dan W. Haupt, M.D.; Karen S. Flavin, R.N., C.C.R.C.; Julia A. Schweiger, C.C.R.C.; Martha J. Hessler, B.S.; Emily J. Hessler, B.S.; Susanna B. Thach, B.S.; Michael D. Yingling, B.S.; John W. Newcomer, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify indicators of cardiometabolic risk in children and adolescents taking antispcyhotic medications, and use clinically available measures to monitor metabolic changes during antipsychotic treatment in pediatric populations.

SUMMARY:

Background:Increased adiposity and reduced insulin sensitivity are major risk factors for future diabetes and cardiovascular disease (1). Antipsychotic medications, which can increase adipose tissue mass and insulin resistance in adults, are increasingly prescribed to children (2). The Metabolic Effects of Antipsychotics in Children (MEAC) study, funded by the National Institute of Mental Health, aims to quantify antipsychotic treatment-related changes in adiposity and insulin sensitivity in children and adolescents for the treatment of irritability, aggression and disruptive behavior, common presenting symptoms for many mental disorders in this patient population.
Methods:Antipsychotic-naive subjects ages 6-18 with Aberrant Behavior Checklist (ABC) irritability subscale score > 18 are randomized to 12 weeks of open-label treatment with either olanzapine, risperidone or aripiprazole. Dual energy x-ray absorptiometry (DEXA), abdominal magnetic resonance imaging (MRI), and stable isotopomer tracing during hyperinsulinemic-euglycemic clamp conditions measure treatment-related changes in adiposity and insulin sensitivity as primary endpoints.
Results:Preliminary analysis of completed subjects (n = 57), pooling results for all treatment groups, indicates that 12 weeks of initial antipsychotic treatment is associated with significant mean increases in DEXA total (2.74 kg, SD 2.21) and percent body fat (2.97%, SD 3.55), and a decrease in whole body insulin sensitivity. Clinical indicators of adiposity and insulin sensitivity also detect treatment-induced change, with significant increases in BMI percentile (14.8 %ile points, SD 14.71) and fasting plasma triglyceride (18.05 mg/dl, SD 42.95). Treatment is also associated with marked decreases in ABC irritability score (15.37 points SD 7.56).
Conclusions:Preliminary results from the MEAC study indicate adverse metabolic changes during 12 weeks of antipsychotic treatment, despite significant clinical benefit. Changes in adiposity and insulin sensitivity are readily detectable in clinical settings by monitoring BMI %tile and fasting plasma triglyceride.

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» NR5-031

CHANGES IN ADIPOSITY AND METABOLIC MEASURES DURING MEDICATION SWITCHES TO ARIPIPRAZOLE FROM OTHER ATYPICAL ANTIPSYCHOTICS

Ginger Nicol M.D., Dan W. Haupt, MD; Michael D. Yingling, BS; Peter A. Fahnestock, MD; Karen S. Flavin, RN, CCRC; Julia A. Schweiger, CCRC; Elizabeth T. Westerhaus, MA; Angela M. Stevens, BS; John W. Newcomer, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify opportunities to reduce cardiometabolic risk in persons treated with antipsychotic medications.

SUMMARY:

Background: Increased rates of premature mortality in patients with major mental illness, related primarily to cardiovascular disease and medical conditions like diabetes, have focused interest on the elevated prevalence of obesity and other cardiometabolic risk factors in this population (1). Antipsychotic medications can adversely affect risk, and recent randomized clinical trial (RCT) evidence indicates that switching treatment from a higher-risk medication to a lower-risk medication can lead to decreases in body weight and plasma triglyceride (2). Such “switch-related” changes in weight and triglyceride have been interpreted as changes in adiposity and related changes in insulin sensitivity, but no RCTs to date have explicitly tested the hypothesis that antipsychotic switch to a lower-risk medication can improve directly-measured adiposity or insulin sensitivity.
Methods: Schizophrenia patients currently treated with olanzapine, quetiapine, or risperidone are randomized to 12 weeks of continued treatment with their current medication (“stayers”) or to switch to antipsychotic treatment with aripiprazole (“switchers”). Detailed metabolic measurements, including dual energy X-ray absorptiometry (DEXA), hyperinsulinemic-euglycemic clamps, and fasting plasma lipid measurements were used to quantify whole-body adiposity, whole-body insulin sensitivity and lipid levels, at baseline and after 12 weeks of treatment.
Results:Preliminary results from this randomized study (n=35) indicate differential “stay versus switch” effects on whole-body insulin sensitivity and DEXA total fat (time x treatment condition: $F[1,32]= 5.28$, $p=0.028$ and $F[1,31]=3.36$, $p=0.076$, respectively). Baseline to endpoint change in insulin sensitivity and DEXA total fat for “stayers” indicates no improvement for either insulin sensitivity or DEXA fat, while patients who switch treatment showed improvement in insulin sensitivity ($F[1,26]=8.2$, $p=0.008$) and DEXA total fat ($F[1,26]=10.9$, $p=0.003$).
Discussion: Changes in antipsychotic treatment, to an agent associated with low risk for weight gain, is associated with improvements in whole-body adiposity and insulin sensitivity. These

results inform our understanding of opportunities to reduce cardiometabolic risk in persons treated with antipsychotic medications.

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» NR5-032

ANXIETY, DEPRESSION AND ALEXITHYMIA IN MEXICAN ADOLESCENTS WITH SOMATIC SYMPTOMS ATTENDING A GENERAL PEDIATRIC HOSPITAL

Rosalba Ochoa M.D., Diana Molina PhD, Maria Juana Piña Psy.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the importance of unexplained physical symptoms in adolescents, as indicative factors of underlying anxiety or depressive disorders.

SUMMARY:

Somatic symptoms are common among adolescents with anxious and depressive symptoms in daily pediatric practice. There are clinical reports about association of Alexithymia and emotional features in patients with negative clinical examination.
Adolescence is a transition period where many psychological processes are unstable, with a high risk for presenting anxious or depressive symptoms and difficulties for expression feelings in an assertive way, which increases trend for Alexithymia and dissociation symptoms.
Alexithymia, term introduced by Sifneos as the inability to verbalize one's feelings, as well as the inability to discriminate between feelings, physical sensations, and affective states. The Toronto Alexithymia Scale (TAS) measures the 3 domains of Alexithymia: Difficulties identifying feelings, difficulties describing feelings and externally oriented thinking, and has shown a good reliability in its Spanish version with a cutt-off score of 61 or more.
OBJECTIVE: To describe the prevalence of anxiety, depressive disorders and alexithymia in a sample of Mexican adolescents with somatic symptoms and negative medical examination referred by pediatricians to a Child and adolescents Psychiatric Service.
METHODS: Sample were 30 adolescents ages from 12 to 18 years, with unexplained physical symptoms, referred in a 6 month period to a child and adolescents psychiatric service. All with negative medical examination and laboratory search for underlying physical disease. After getting no clinical explanation for somatic symptoms patients were referred to a psychiatry service, where they were evaluated by a Psychiatric Structured Interview for Pediatric Patients, the Child Behavior Checklist (CBCL) and the Toronto Alexithymia Scale (TAS).
RESULTS: Mean age was 14.48 years + 1.72, 64.5 % girls and 35.5 % boys. Significant gender differences were found for headache and vomiting, between girls and boys 2:1 (p=.04). The more frequent symptoms were: Headache in 74 %, myalgia 58%, vertigo 42%, nauseas 41%, abdominal pain in 32 %, vomiting 19%, dyspnea 19 %, seizures 16 %, chest pain 13%, urinary symptoms 13 %. Depressive disorders were found in 51.6 % of the sample, while anxiety was present in 71 % Mean TAS score was 64.0+11.6, higher score for items of domain in difficulties describing feelings. Alexithymia was found in 67% of the patients, with main failure in the hability for describing feeling. No gender differences were found for the pre

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» NR5-033

IS SELECTIVE MUTISM AN ANXIETY DISORDER? A CASE STUDY OF A SUCESSFUL TREATMENT

Eduardo Prado, Mirian C. Revers, Rogério Marrocos, MD, Ricardo de Oliveira-Souza, Ph.D., Ana C. S. Congio, Kamylle M. Pompeu.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participants should be able to recognize the need for a new conceptualization of Selective Mutism (SM) as an anxiety disorder. Also, they will be able to use an effective treatment for children with SM.

SUMMARY:

Selective Mutism (SM) is a rare and interesting disorder that has been associated with a wide variety of childhood psychiatric conditions. More recently, controlled studies have enhanced our understanding of SM. We describe a case of 12 years old sixth grade white male who had SM in unfamiliar situations since 3 years old. The patient had no evidence of developmental or neurological disease. Between closer ones he used to engage in normal rates of conversation. However in specific social situations in which speech is typically expected he had a persistent failure to communicate with words, gestures or pantomime. After a 2 years treatment with fluoxetine the patient made significant gains with respect to frequency of verbalizations to adults and peers, number of individuals spoken to, anxiety related to speaking, and involvement in school activities. Although well documented, SM is still not clearly understood, and debate continues regarding its classification and etiology. A growing body of evidence from both descriptive and comparison studies suggest that SM and anxiety disorders are closely related. SM and Social Anxiety share many diagnostic similarities, including behavioral inhibition, poor eye-contact and reticence. Actually there is sufficient evidence in literature to support a change in the current classification from the DSM-IV of SM as an Other Disorder of Infancy, Childhood, and Adolescence. It is indispensable for correct and effective treating of those patients the SM conceptualization as an anxiety disorder.

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» NR5-034

THREE-YEAR LONGITUDINAL STUDY COMPARING BULLYING AND VICTIMIZATION: FROM MIDDLE SCHOOL TO FRESHMAN YEAR OF HIGH SCHOOL

Darren Richmond, Charlotte Richmond, Ph.D., Thomas Prihoda, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:
•Describe actions that constitute bullying in middle and high schools;•Understand the extent, and different types of, bullying within a culture of meanness;•Describe actions to resist bullying;
•Identify education resources whose common goal is to: sensitize youth to the problems of bullying, help students take responsibility in bullying incidents, and help students learn bully prevention strategies.

SUMMARY:

BACKGROUND. In 2006, Project Anti-bully set out to determine the prevalence of bullying. Although bullying is first identified in

elementary school, and is more prevalent during middle school, knowledge of bullies during high school is limited. To compare the prevalence of bullying (including cyberbullying), students were surveyed while in the 7th grade , 8th grade and during 9th grade. METHODOLOGY. 7th graders (2006), 8th graders (2007) and 9th graders (2008) attending public schools in Miami Beach, FL responded to 14 Child Abuse Prevention Services Survey items. RESULTS. Compared to the results of the 2006 surveys, in 2007 there was an increase in the bullying seen at school, bullying was more of a problem for females, more females did nothing or ignored the bully and males felt less safe at school. There were no differences in cyberbullying and the actions following it during middle school. However, at the end of their first year in high school, respondents report a decrease in the bullying seen at school and bullying was less of a problem. More students did nothing or were less likely to tell an adult if they saw someone being bullied. There was a 5% decline from middle school in the incidence of cyberbullying; however, the actions following cyberbullying were unchanged for the freshmen. Additionally, feeling safe at school during 9th grade increased by 12.1-11.7% over 7th and 8th grade respectively. CONCLUSIONS. Overall, bullying decreased from middle school to freshmen year of high school. Although there was a decrease in the incidence of bullying, how the students react when bullied or when observing bullying remains essentially unchanged. Although the prevalence of cyberbullying nationwide has increased over the past few years, cyberbullying in this study decreased. Additionally, the freshmen in high school report feeling safer at school than when they were in middle school. Students, teachers, school staff, and parents need anti-bullying education.

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» NR5-035

ASPERGER'S DISORDER AND SIBLING BIRTH ORDER

Karmen Schmidt Ed.M., Christine Ferrone, M.A., Charles A. Henry M.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session the participant will be able to recognize the need for further research on the relationship between Asperger's disorder and birth order.

SUMMARY:

Objective: Existing literature suggests a relationship between birth order and certain child psychiatric disorders including autism [1]. However, little is known about the relationship between Asperger's disorder and this variable. Existing studies present conflicting results but may suggest that first born children are at higher risk [2]. The purpose of this descriptive study is to examine birth order in a group of psychiatrically referred children with a diagnosis of Asperger's disorder.

Methods: Office charts at the Massachusetts General Hospital Learning and Developmental Disorders Evaluation and Rehabilitation Services Clinic (LADDERS) were screened. Psychiatrically referred outpatients with a DSM IV diagnosis of Asperger's Disorder were then identified. Age, sex, and birth order were determined using the documented data. Descriptive statistics were utilized in the analysis.

Results: Biological birth order was identified for 29 of 33 subjects identified as having a DSM-IV diagnosis of Asperger's (26 male, 3 female). Mean age for the sample was 11 years 2 months (SD = 3y2m, range = 16y11m). The average number of siblings for the sample (including the subject) was 2.1 (SD = 0.82, range = 3). Subjects with Asperger's disorder were oldest or only children in 86% (25/29) of families (7/29 only, 18/29 oldest). In the families with more than one child, Asperger's subjects were the oldest in 82% (18/22) of cases compared to 18% (4/22) in positions 2 or 3. Conclusion: In this small descriptive study of children with Asperger's disorder, a high percentage of the subjects are oldest or only in birth order. Given the small sample size and the descriptive nature of the study, conclusions about an association cannot be made. Larger studies with a more detailed statistical analysis would be needed to determine whether there is a relationship between birth order and Asperger's syndrome.

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2) Gillberg C: Asperger syndrome in 23 Swedish children. Developmental Medicine & Child Neurology 1989; 31(4):520-531.

» NR5-036

DIGITAL MEDIA (INTERNET, VIDEOGAMES, SOCIAL NETWORKS, CELL PHONES, MUSIC PLAYERS…): BENEFITS IN THE PSYCHOTHERAPY AND FAMILY LIVES OF YOUTH

Eitan D. Schwarz, M.D., D.L.F.A.P.A., F.A.A.C.A.P.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to utilize interactive media in therapy with children and adolescents and offer parents guidance about their beneficial use in the home.

SUMMARY:

Objective: Although digital media (DM) have penetrated deeply into children's play and family lives and are clearly here to stay, their potential benefits for mental health have received scant systematic attention. Play with children has been a potent diagnostic and therapy tool since the early days of child psychiatry. This report describes (a) DM 'play' in office practice (DMP), and (b) a development-based goal-directed structured method for parents to promote healthy DM home uses. Method: (a) During an 18 month period, 28 non-psychotic patients ages 5-20 had DMP at some point in their care. Connecting their music players to a quality stereo music system enabled comfortable shared access to the patient's personal music collection. An extra monitor and keyboard, connected to the online office computer, brought the Internet, games, e-mail, and social network sites into therapeutic interactions. (b) Parents were offered guidelines from infancy through adolescence for DM home use when indicated. Results: There have been no adverse effects. (a) DMP enabled observations of cognitive, sensorimotor, and social functioning; rich interactive therapeutic opportunities, including enhanced cooperation and self-disclosures; treatments of specific DM-related problems; and other opportunities not as easily accessible by other means. While welcoming DMP, patients sometimes preferred traditional methods. College students utilized e-mail for clinical communications. Parents accepted DMP within overall clinical plans. (b) Guidelines for DM home use were well received by parents. Conclusions: DM can benefit the mental health of youth and their families, but studies and standards are needed. (a) DMP complements traditional methods and appears effective, well accepted, and safe, but should be used cautiously and only for specific therapeutic aims and with parental approval. (b) Age-specific structured guidelines can help parents manage DM to benefit youth and family life.

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2) Axline VM: Play Therapy. New York, Ballantine Books, 1969.

» NR5-037

BEHAVIORAL MANAGEMENT OF A PATIENT WITH AICARDI'S SYNDROME -CASE REPORT

Amin Shamal M.D., Summer Jaffrey M.D, Mahboob Aslam M.D.,Edward Hall M.D., Javed Iqbal M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the challenges faced in the management of behavioral symptoms caused by a general medical condition (Aicardi's Syndrome)

SUMMARY:

Aicardi syndrome, a rare genetic disorder identified by the French Neurologist, Dr. Jean Aicardi in 1965, is characterized by three main features: 1) partial or complete absence of the corpus callosum 2) complex seizures, generally starting as infantile spasms, and 3) lesions on the retina. The number of identified cases of children with Aicardi syndrome is very difficult to calculate accurately, but has been estimated at 300 - 500 worldwide. It is a severely disabling congenital malformation and its neurological and physical manifestations have been discussed widely however there is very limited literature related to the behavioral aspects of this Syndrome. The malformation, itself, is quite uncommon; however the patient with this disability continues to struggle with the progressive physical and neurological deficits which would predispose to complicated behavioral disturbances. In this report we present a 15 year-old Caucasian female patient who was born with a congenital disorder of Agenesis of Corpus Callosum, mental retardation and congenital heart defects. RC has a history of seizure disorder, muscle hypotonia, visual impairment, urinary and bowel incontinence. This case will give us insight about the various outcomes of this chronic disabling illness including neuropsychiatric symptoms, mood lability, impulsivity, severe rage and psychosis. Further it serves as a unique teaching case, the role of corpus callosum involvement in psychiatry and finally describes some of the challenges faced in the management of behavioral symptoms caused by a general medical condition. RC's psychiatric and neurological illnesses lead to episodes of behavioral dyscontrol by verbal and physical aggression, irritability, mania and psychosis. These symptoms escalated to the point of not being manageable at home, hence, resulting in permanent residential care placement. The diagnostic impression included mood disorder, psychotic disorder or even having mixed symptoms of psychosis and mood due to a medical condition (Aicardi Syndrome). The management included mood stabilizers, anxiolytics, and antipsychotic medications. There is a need for more research of behavioral manifestations and management of psychiatric symptoms of this rare syndrome.

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1) Barkovich AJ, Simon EM, Walsh CA. Callosal agenesis with cyst: a better understanding and new classification. Neurology. 2001; 56: 220–7.

2) Aicardi syndrome. Rosser T. Department of Neurology, Center for Neuroscience and Behavioral Medicine,Children's National Medical Center, Washington, DC 20010, USA. Arch Neurol. 2003

» NR5-038

SIGNIFICANCE OF ROUTINE LABORATORY MONITORING OF LIVER FUNCTION DURING VALPROATE THERAPY

Amin Shamal M.D., Abderrahmanne Richane M.D., Mahboob Aslam M.D., Amel Badr M.D., Gulam Noorani M.D., Ajay Lall, Javed Iqbal M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the incidence of change in standard liver function parameters upon initiation of valproic acid therapy and after six and twelve months of continued treatment, and to further understand that routine liver function test monitoring as determinants of liver injury are unreliable early indicators of valproic acid induced hepatotoxicity.

SUMMARY:

Fatal hepatic failure associated with valproic acid therapy is a rare side effect occurring in patients exposed to this mood stabilizer and antiepileptic medicine. Its relevance arises from its fatal outcome and the high number of patients who are treated with it. In recent years, research studies presented controversial evidence about the importance of laboratory monitoring of liver functions in patients receiving valproic acid as a predictor of drug induced hepatotoxicity. Some studies recommended that clinical monitoring should not be neglected during the first six months of therapy. Other studies indicated that initial symptoms of valproate induced hepatotoxicity include nausea, vomiting, lethargy and patient's general well being and that isolated changes of standard laboratory liver parameters are not reliable indicators. In this study we investigate the importance of routine monitoring of liver function tests in patients on valproic acid therapy. Retrospective data collection was conducted from the charts of 150 patients aged 18-65 admitted to Bergen regional Medical Center and treated with Valproic acid. Patients with other causes of elevated liver functions including hepatitis were excluded. The dose range was 250-2200 mg daily, with VPA level ranging between 17-125. We reviewed the values of liver functions including, ALT, AST, alkaline phosphate and total bilirubin levels for each patient after one month, six months and twelve months of initiation of treatment. We also reviewed any documented changes in patient's clinical status including, nausea vomiting or lethargy as early indicators of hepatotoxicity. Out of the 150 patients, there were only two cases with changes in liver function tests. Both cases were after one month of initiation of treatment. In one patient, LFTs were mildly elevated before the treatment and came down to base line after treatment was terminated. In the other patient, liver function level returned to normal after three months without any changes to the treatment. There were no reported cases of hepatotoxicity. We conclude that routine liver function tests do not seem to have any value in predicting hepatotoxicity related to valproic acid and that clinical symptoms might be the most relevant indicators of impending complications, eventually supported by laboratory findings.

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1) Kondo T, Kaneko S, Otani K, et al. Associations between risk factors for valproate hepatotoxicity and altered valproate metabolism. Epilepsia. 1992;33(1):172-177.

2) Brusilow, SW, Maestri, NE. Urea cycle disorders: diagnosis, pathophysiology, and therapy. Adv Pediatr 1996; 43:127.

» NR5-039

LONG TERM STEROID EXPOSURE AND PSYCHOSIS IN CONGENITAL ADRENAL HYPERPLASIA: A CASE STUDY

JAHANARA ZAHID M.D., Anoop Karippot , MD, RPSGT, FAASM, D ABSM, CBSM

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the use of steroids among children and adolescents in Psychiatry.

SUMMARY:

BACKGROUND: Children with Congenital Adrenal Hyperplasia (CAH) due to 21- Hydroxylase deficiency are exposed to both prenatal and/or postnatal androgen excess. Among girls, excess fetal androgen causes varying degrees of androgenization of the external genitalia. Patients with these syndromes are administered hydrocortisone for a prolonged period of time. Several psychiatric adverse effects have been observed with short-term as well as long-term use of steroid treatment, including mood disorders, cognitive changes and psychosis.

OBJECTIVE: We describe a case of psychosis and psychiatric symptoms resulting from longterm steroid expoasure. METHOD: This is an interesting case of an 11 year-old female with CAH and history of long-term use of hydrocortisone, presents with psychosis and suicidal ideation, suggest that these symptoms may be induced by prolonged use of steroids. RESULTS: Chronic use of steroids for the treatment of Congenital Adrenal Hyperplasia resulted in psychiatric and behavioral symptoms including psychosis. DISCUSSION: Steroid induced psychosis and psychiatric symptoms secondary to long term treatment intervention for Congenital Adrenal Hyperplasia has never been reported. We discuss this potential side effect of utilizing corticosteroids which is the main line treatment for this condition and emphasize the need for careful monitoring with steroid management.

REFERENCES:

1) Francois Sirois,Steroid Psychosis: a review General Hospital Psychiatry 2003 25:27-33

2) John F Morgan, Helen Murphy, J Hubert Lacey, Gerard Conway- Long Term psychological outcome for women with congenital adrenal hyperplasia: cross sectional survey BMJ 2005 330:340-341

» NR5-040

MILITARY BEHAVIORAL HEALTH CERTIFICATION: SPECIALIZED TRAINING TO MEET THE UNIQUE MENTAL HEALTH NEEDS OF VETERANS AND THEIR FAMILIES

Elizabeth Brent M.D., Judy Kovell, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: 1) identify the cultural barriers faced by civilian mental health providers treating Service Members and their Families; 2) appreciate the specialized background, experience and training required of an effective military behavioral health specialist; and 3) recognize that a standardized training program is needed to reduce cultural barriers, improve quality of care, and promote evidenced-based treatment.

SUMMARY:

Civilian mental health providers are an essential part of the network of care for returning Service Members with psychological wounds. Most civilian providers, however, have little familiarity with military culture and terminology, or the unique aspects of combat or the military mental health system. The cultural divide between civilian and military medicine is nowhere more evident than within Behavior Health, causing significant barriers to care. According to a 2008 RAND report, an estimated 300,000 OIF/OEF Veterans currently suffer from PTSD or depression. Of these, approximately 150,000 will seek treatment, and of those seeking treatment, only about half will receive evidence-based treatment. Mental health providers with the specialized background, experience and training needed to form a therapeutic alliance and effectively treat Veterans and their Families are in short supply. The Military Behavior Health (MBH) Certification Program, focusing on military culture, terminology, unique dual agency responsibilities and treatment standards, with an emphasis on PTSD and combat stress, is needed to adequately train civilian mental health providers to treat Veterans and their Families. We propose developing a training program that leads to a nationally recognized professional certification and prepares civilian mental health providers with little or no military experience to work with Service Members, Veterans or their Families. The curriculum will include training in the most up-to-date and evidenced-based treatments for psychiatric conditions of particular concern to military populations, including PTSD and TBI, as well as lessons learned from the experiences of civilian providers in the DoD and VA. This program will formalize the unique skills required of military behavioral health specialists. It will ensure quality of care, set a standard of evidence-based treatment, and enhance the willingness of Service Members and their Families to engage care.

REFERENCES:

1) RAND Research Brief Invisible Wounds: Mental Health and Cognitive Care Needs of America's Returning Veterans RB-9336-CCF, Summer 2008.

2) Statement of Michael J. Kussman, M.D., M.S., M.A.C.P. Under Secretary for Health Department of Veterans Affairs before the United States Senate Committee on Veterans' Affairs, August 21, 2007 (http://veterans.senate.gov/public/index.cfm?pageid=16&release_id=11240&sub_release_id=11332&view=all)

» NR5-041

THE SPECTRUM OF AFRICAN-AMERICAN RACE: EXPLORING RACIAL IDENTITY ATTITUDES, DEPRESSION STIGMA, AND TREATMENT-RELATED ATTITUDES AND BEHAVIORS

Enrico Castillo, B.A., Kyaien O. Conner, Ph.D., L.S.W., M.P.H., Nancy Grote, Ph.D., Valire Carr Copeland, M.P.H., Ph.D., Charles F. Reynolds, III, M.D., Charlotte Brown, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to understand and discuss how the process of coping with one stigmatizing condition can facilitate adaptation to a second condition, specifically the concepts of stigma competence and mastery of stigma. At the end of this presentation, the participant should also be able to state how African-American identity relates to the accommodation of depression stigma and the implications on future stigma research and interventions.

SUMMARY:

Objective: African-Americans have been shown to have higher rates of depression stigma, which impacts disparities in care. Previous work reveals that strong identification with a stigmatized group in some cases may be protective from stigma by nurturing adaptive responses (1), and adaptation to one stigmatizing condition can facilitate adaptation to a second (2). We sought to examine the relationships between the degree of identification with African-American race (measured by the Racial Identity Attitudes Scale), depression stigma, and treatment-related variables.

Methods: In Allegheny County, Pennsylvania, telephone interviews were conducted with 219 African-Americans with depression without co-morbid substance abuse or bipolar disorder, selected by random digit dialing technology. We used validated measures and targeted questions to measure public (stigma perceived in one's peers) and internalized (stigma for one's own stigmatized condition) depression stigmas, attitudes and intentions toward treatment, and current treatment status.
Results: Linear regressions revealed that racial identity attitudes were significant predictors of public and internalized depression stigmas controlling for key demographics and depression severity. Strong racial identity predicted higher public stigma but also lower internalization of that stigma and positive treatment attitudes, while weaker racial identity predicted higher internalized stigma. Racial identity, however, largely did not predict treatment-related behaviors.
Conclusion: African-Americans with strong racial identities accommodate depression stigma in more positive ways. This study illustrates the potential importance of considering African-American heterogeneity in future stigma research and bolstering racial identity as part of future stigma interventions. Funding sources for this project are NIMH MH05431813 & P30MH071944, Center on Race and Social Problems Award, and Hartford Foundation Dissertation Award.

REFERENCES:

1) Corrigan PW, Watson AC: The paradox of self-stigma & mental illness. Clin Psychol Sci Pract 2002; 9:35-53.

2) David S, Knight BG: Stress & coping among gay men: Age & ethnic differences. Psychol Aging 2008; 23:62-69.

» NR5-042

GENDER DIFFERENCES IN LATINO PSYCHIATRIC AMBULATORY PATIENTS

Raquel Choua M.D., Maria I. Zapata Vega, MD, Martin Maurer, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to consider cultural and gender variables in the tailoring of treatment of patient with psychiatric illnesses.

SUMMARY:

Gender differences in Latino psychiatric ambulatory patients
Raquel Choua, Maria I. Zapata-Vega, Martin Maurer.
Objectives: This study is aimed at assessing gender differences in Latino patients receiving outpatient psychiatric services in an urban setting.
Methods: Clinical records of all adult Latino patients admitted to the psychiatry clinic of Elmhurst Hospital Center during the first semester of 2006 were reviewed. Demographic and clinical data were collected, including the use of psychiatric services following the initial evaluation.
Results: The sample (n=147) was composed mostly of females (72.8%). Males were more likely to be uninsured (60% vs. 41%) (Odds ratio: 2.2 [95%CI: 1.05-4.62]), and have histories violence (28% vs. 13%)(2.5 [1.03-6.15]), psychiatric hospitalizations (49% vs. 26%)(2.7[1.25-5.74]), psychotic disorders (28% vs. 5%) (7.7[2.49-24.07]), and substance-use disorders (15% vs.2.8%) (6.1[1.45-25.79]); whereas females reported more physical and sexual abuse in adulthood (34% vs. 3%)(19.8[2.6-149.8]) and had a higher prevalence of depressive disorders (67% vs. 43%) (2.78[1.32-5.87]).
There were no significant gender differences in age, conjugal status, immigration status, language use during intake, education, employment, abuse in childhood, suicidal behaviors, or anxiety disorders.
Women had more psychotherapy visits (3.68 vs.1.40; p=0.002) and higher overall numbers of outpatient visits (8.32 vs. 6.45, p=0.03) during the semester following the intake. No significant differences were found in medication management visits or in the use of social work, psychiatric emergency, inpatient or partial hospital services. Conclusions: Gender differences in Latino psychiatric outpatients were identified in the prevalence of certain psychiatric disorders, abuse in adulthood, insurance coverage and service use, but not in other characteristics such as suicidal behaviors and abuse in childhood. These findings suggest that treatment planning, tailored by gender, is particularly necessary for specific clinical presentations in Latino psychiatric ambulatory patients.

REFERENCES:

1) Briere J, Woo R, McRae B, Foltz J, Sitzman R. Lifetime victimization history, demographics, and clinical status in female psychiatric emergency room patients. J Nerv Ment Disease 1997; 185:95.

2) Carmen EH, Rieker PP, Mills T. Victims of violence and psychiatric illness. Am J Psychiatry 1984; 141:378. Herman JL. Histories of violence in an outpatient population: An exploratory study. Am J Orthopsychiatry 1986; 56:137.

» NR5-043

MONOAMINE OXIDASE INHIBITOR USAGE IN A PACIFIC ISLAND SETTING

John Huh M.D., Junji Takeshita, MD, Deborah Goebert, DrPH, Diane Thompson, MD, Brett Lu, MD, and Russ Muramatsu, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the characteristics of MAOI prescribing patterns in Hawaii, a state with predominantly Asian Americans and Pacific Islanders.

SUMMARY:

Objective: Previous studies involving prescriptions of monoamine oxidase inhibitors (MAOIs) have focused on predominantly Caucasian populations with little representation of Asian Americans and Pacific Islanders. The Asian American diet includes tyramine-rich fermented food items. This study describes the characteristics of MAOI prescribing patterns in Hawaii, a state with predominantly Asian Americans and Pacific Islanders.
Methods: Antidepressant usage including MAOIs were identified using a commercial insurance database from Hawaii Medical Service Association, a Blue Cross/Blue Shield subsidiary. Prescriptions from 1999-2003 were identified with basic information including ethnicity, age, diagnostic category, morbidity level, and six month adherence to MAOI medication.
Results: Of the 28,890 patients prescribed antidepressants, seventeen individuals (0.06%, 95% confidence interval 0.03%-0.09%) were prescribed MAOIs. There was no significant difference in six month adherence pattern compared with other medications. MAOI continues to be seldom used in treatment.
Conclusions: MAOIs are vastly underutilized in all ethnic groups including Asian American and Pacific Islander groups.

REFERENCES:

1) Fiedorowicz JS, Swartz KL: The role of monoamine oxidase inhibitors in current psychiatric practice. Journal of Psychiatric Practice 10: 239-248, 2004

2) Shulman KI, Walker SE: Refining the MAOI diet: Tyramine content of pizzas and soy products. Journal of Clinical Psychiatry 60: 191-193, 1999

» NR5-044

EFFECT OF A CULTURALLY-MODIFIED WEIGHT LOSS PROGRAM FOR LATINOS WITH SEVERE AND PERSISTENT MENTAL ILLNESS IN A COMMUNITY MENTAL HEALTH CLINIC

Christina Mangurian M.D., Simriti Chaudhry, B.A., Felicia Rosario, B.A., Jonathan Amiel, M.D., Michael Devlin, M.D., John Newcomer, M.D., Rohan Ganguli, M.D., Francine Cournos, M.D., Carlos Jackson, Ph.D., Diane Barrett, R.D., Lucia Capitelli, R.N., Dianna Dragatsi, M.D., Jules Ranz, M.D., Susan Essock, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize that obesity is prevalent in Hispanic people with severe and persistent mental illness (SPMI). The participant should be able to understand the components of a behavioral intervention for weight loss for this population. The participant should be able to demonstrate an understanding of the feasibility and efficacy of such a weight loss program for this patient population.

SUMMARY:

Background: Latinos and people with schizophrenia are two populations at high risk for metabolic syndrome and obesity. Urban Latino patients with severe and persistent mental illness (SPMI) seem to have an additive risk and are a highly vulnerable population. Behavioral weight control techniques have been effective in some overweight/obese SPMI patients. However, there is limited data on high risk populations, such as Latinos with SPMI.
Purpose: To determine if a culturally-modified behavioral therapy weight loss course could be feasibly delivered and effective for Latino SPMI patients.
Methods: Subjects: The Washington Heights Community Service provides outpatient services for SPMI patients, mostly Latino, living in Northern Manhattan.
Procedures: Day-treatment patients with BMI =25 were identified at two sister clinics. We obtained informed consent and baseline characteristics. A 14-week culturally-modified weight loss course was held at one clinic. After course completion, patients were re-weighed. Paired t-tests and the Sign test were used to examine effect.

Results: 89% (65/73) of patients met eligibility criteria (which included having a BMI =25) and 78% (51/65) consented. Of the first 29 patients offered the course, 90% (26/29) attended over 1/2 of the classes. Mean pre-course weight for these 29 patients was 179.7lbs (SD=36lbs) and post-weight was 178.2lbs (SD=36lbs) (p=NS). However, more lost weight than gained weight, with 69% (18/26) losing weight, 4% (1/26) maintaining weight, and 27% (7/26) gaining weight (p=0.043). [Of note, 6 mo f/u data are being collected.]
Discussion: Consent and retention rates for this course were very high. This study provides preliminary evidence that a culturally-modified behavioral weight reduction course is feasible to implement and may favorably affect body weight for Latino SPMI populations treated in community settings.

REFERENCES:

1) Brar JS, Ganguli R, Pandina G, et al.: Effects of behavioral therapy on weight loss in overweight and obese patients with schizophrenia or schizoaffective disorder. J Clin Psychiatry 66:205-212, 2005.

2) Hellerstein DJ, Almeida G, Devlin MJ, et al.: Assessing obesity and other related health problems of mentally ill Hispanic patients in an urban outpatient setting. Psychiatr Q 78:171-181, 2007.

» NR5-045

NATIONAL ORIGIN DIFFERENCES IN THE EXPRESSION OF THE SYMPTOM "HEARING VOICES" IN INMIGRANTS VICTIM OF TRAUMA

Andres Monleon, M.D., Ruth Kizza, M.D., Lawrence Hipshman M.D., Ph.D., Pablo J. Monleon M.D., Ph.D., David J. Kinzie M.D., Ph.D., Vicente J. Monleon ,Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the socio-cultural factors that influence the expression of the "hearing voices" symptom among migrants from different cultural origin that have been subject to trauma and how they may be influence by the educational level of the patient.

SUMMARY:

During clinic practice at the Torture Treatment Center of Oregon (TTCO), we observed that patients from Somalia complained from "hearing voices" more frequently than those from other countries. This observation suggested that there may be differences among different national origins in the symptom of "hearing voices", and motivated a study to identify the factors that may explain those differences. We compared the charts of 177 patients from different cultural origin treated at TTCO. Thirty two out of 177 (18%) patients reported hearing voices. The odds of reporting hearing voices differed among the five national origins (p=0.024). The odds of hearing voices for patients from Somalia were 12.4 times those of patients from Afghanistan and 3.2 times those of patients from Bosnia. There was suggestive but inconclusive evidence of a difference with the Guatemalan population (p =0.066) and no evidence of a difference with the Ethiopian population. There was no evidence of an association between national origin and the diagnosis the patient received. There was no evidence of a statistically significant association between gender, age, religion or exposure to trauma factors and the odds of hearing voices. However, the odds of hearing voices increased 1.12 times for each one-year decrease in education (p=0.0033), but this relationship dit not depend on national origin (p-value for the interaction between national origin and years of education = 0.86). After accounting for education, there was no evidence of an association between hearing voices and national origin (p=0.13). In refugee victims of trauma, the apparent relationship between national origin and hearing voices seems to actually be the result of differences in years of education. As immigration grows around the world, more studies are needed to assess if there are cultural differences in the expression of psychopathologies.

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1) Sautter Fj, Cornwell J, Johnson JJ, Wiley J, Faraone SV. Family history study of posttraumatic stress disorder with secondary psychotic symptoms. Am J Psychiatry. 2002 Oct;159(10):1775-7.

2) Frueh BC, Hamner MB, Bernat JA, Turner SM, Keane TM, Arana GW. Racial differences in psychotic symptoms among combat veterans with PTSD. Depress Anxiety. 2002;16(4):157-61.

» NR5-046

ENHANCING MEDICATION ADHERENCE TO ORLISTAT WITH ADAPTED GROUP DIALECTICAL BEHAVIORAL THERAPY AMONG OVERWEIGHT BINGE EATERS

Kim Chu M.S., Debra Safer, M.D., Sarah Adler, M.S.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to gain insight into the feasibility and efficacy of adapted Dialectical Behavioral Therapy (DBT) group therapy to enhance adherence to over-the-counter (OTC) orlistat among overweight binge eaters. The results of this study should increase understanding of the role of greater adherence to OTC orlistat with outcome (e.g., reductions in binge eating and weight) among overweight binge eating subjects.

SUMMARY:

OBJECTIVE: Adherence to anti-obesity treatment is a major challenge in the management of obesity. Although research has shown that orlistat can be effective for both significant weight loss and reduction in binge frequency among obese patients with binge eating disorder (BED), treatment gains are usually not sustained once medications are discontinued. The aim of this study was to examine whether the addition of group psychotherapy to over-the-counter (OTC) orlistat would enhance medication adherence among overweight binge eaters.
METHOD: Pilot study sample consisted of 17 overweight (mean BMI 37.6 kg/m2) binge eaters. All patients received the OTC weight loss agent, orlistat (60 mg TID). Patients were randomly assigned to receive either 12 sessions of adapted Dialectical Behavior Therapy (DBT) group therapy plus orlistat (n=8) or orlistat only (n=9).
Both groups were re-assessed at regular intervals over a 9-month f/u period.
RESULTS: There was no significant group difference in adherence to OTC orlistat at post-treatment. However, patients who continued to adhere to OTC orlistat achieved significant reduction in binge frequency (p=.023) and significant mean weight loss at post-treatment and 9-month f/u (8 lbs; p=.035 and 15 lbs; p=.007, respectively) compared to those who discontinued medication (2 lbs, p=.035 and 7 lbs, p=.007). Patients who achieved at least a 5% weight loss within the first three months had greater medication adherence (p=.045).
CONCLUSIONS: Although the addition of group therapy to orlistat to enhance adherence did not reach statistical significance in this pilot study, patients with greater adherence achieved significant weight loss and binge frequency reduction at post-treatment and at 9-month f/u. Patients who attained weight loss goals earlier were more likely to adhere to orlistat than those without early weight loss. This study highlights the need for interventions that enhance medication adherence for achieving long-term weight loss.

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2) Grilo CM, Masheb RM, Salant SL: Cognitive behavioral therapy guided self-help and orlistat for the treatment of binge eating disorder: a randomized, double-blind, placebo-controlled trial. Biological Psychiatry 2005; 57:1193-1201.

» NR5-047

USE OF PSYCHOTROPIC DRUGS IN ADULTS INPATIENTS DIAGNOSED WITH EATING DISORDER

Juan Jose De Frutos Guijarro M.D., A. A. García Rosales M.D, M. Benítez Alonso M.D., M. B. Bardón Rivera M.D., E. Román Mazuecos M.D., M. F. Bravo Ortiz.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to have a broader knowledge of naturalistic prescribing practices in a population of inpatients with ED, who more often than not suffer from a comorbid psychiatric disorder.

SUMMARY:

Objectives: The purpose of this study is to describe prescribing practices in inpatients diagnosed of eating disorders admitted in La Paz University Hospital psychiatric acute hospitalization unit.
Materials and Methods: We studied a cohort of 116 patients retrospectively between 01/01/2003 and 12/1/2008. Investigators collected clinical, diagnostic and therapeutic data from the patients' discharge summaries. A database was designed using SPSS 16 for Mac.
Results: 95% of patients were female, their mean age was 28.7 years old. 47.5% of patients were admitted for the first time. 85% of them suffered an axis II comorbid disorder. 42.5% of patients suffered from restrictive type ED, 48.8% of a purgative type ED, 6.2% of a bulimic type ED and the rest suffered from other types. The most commonly used antidepressant was venlafaxine, followed by clomipramine, mirtazapine, fluoxetine, sertraline, escitalopram, duloxetine, paroxetine and citalopram. Clorazepate was the most frequently used benzodiazepine, followed by Lorazepam. Chlorpromazine and Ziprasidone were the most commonly used neuroleptics. Gabapentine and Topiramate were the most frequently used mood stabilizers.
Conclusion: The only licensed drugs in Spain for treatment of ED are fluoxetine, topiramate and lorazepam. Nevertheless, clinicians in our inpatient unit use routinely other unlicensed drugs to treat psychopathological characteristics commonly associated with ED such as anxiety, anorexic ideation and impulsivity and the very frequent comorbid disorders.

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» NR5-048

PRESCRIBING PRACTICES FOR INPATIENTS DIAGNOSED OF EATING DISORDERS, BOTH IN CHILD AND ADOLESCENT, AND ADULT PSYCHIATRIC ACUTE WARDS

Alejandra Garcia Rosales M.D., J.J. De Frutos Guijarro M.D., M. Graell Berna M.D. PhD, M. Benítez Alonso M.D., M. B. Bardón Rivera M.D., E. Román Mazuecos M.D., G. Morandé Lavín M.D. PhD, M.F. Bravo Ortiz M.D. PhD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to have a broader knowledge of naturalistic prescribing practices in populations suffering from eating disorders. The participant should also have a greater insight into the differences between prescribing practices in pediatric and adult populations.

SUMMARY:

Objective: The purpose of this study is to describe prescribing practices for inpatients diagnosed of eating disorder as well as compare these practices between the children and adolescent patients admitted to the Niño Jesús Pediatric Hospital (HNJ) and the adult ones admitted to La Paz Hospital (HLP).
Methods: Discharge summaries of patients diagnosed with eating disorder were reviewed. Data was collected from the adult ward of patients admitted from 01/01/2003 to 12/1/2008 n=116, and the pediatric one of patients admitted from 09/01/2006 to 12/1/2008 n=149. For each drug, mean dose and differences between mean dosages in the different wards was determined, using t-student test (p= 0.05). Data processing was performed using SPSS 16.
Results: Lorazepam was the most commonly used benzodiazepine in both wards; mean dosages were statistically different (p=0.014), with 4.3mg a day used in HLP and 2.0mg a day used in HNJ. In terms of antidepressants, fluoxetine (F) and venlafaxine (V) were the most frequently used drugs. As far as F is concerned, mean dosages were not significantly different. Though, the mean dosage of V was significantly higher (p=0.049) in the adult group with a mean dosage of 165.8mg a day vs 100.0mg a day (HNJ). Considering neuroleptics, olanzapine (O) and clorpromacine (C) were the drugs most often used. There was no statistically significant difference between the mean dosages of O with an overall mean dosage of 20.0mg (s.d. 7.0). Dosages of C were significantly lower in HNJ with a mean dosage of 30.2mg versus 80.5mg in HLP. Topiramate was the most commonly prescribed antiepileptic in both wards. Dosages were significantly different (p=0.1) with a mean dosage of 254.6mg a day (HLP) vs 78.1mg a day (HNJ).
Conclusions: Overall, prescribing practices, analyzing drugs separately appears to be quite similar in both wards, though doses may increase in some cases.Hypothetically, the main difference may lie in the number of drugs that are prescribed together.

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2) Pederson KJ, Roerig JL, Mitchell JE. Towards the pharmacotherapy of eating disorders. Expert Opin Pharmacother. 2003 Oct;4(10):1659-78.

» NR5-049

USE OF PSYCHOTROPIC DRUGS IN A MONOGRAPHIC EATING DISORDER INPATIENT UNIT FOR CHILDREN AND ADOLESCENTS

Montserrat Graell Berna M.D., A. A. García Rosales M.D., J.J. De Frutos Guijarro M.D., M. Benítez Alonso M.D., G. Morandé Lavín M.D. PhD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to have a broader knowledge of naturalistic prescribing practices in a population of children and adolescents. Information may be very relevant to clinical practice since many of these drugs described are prescribed off license in Spain.

SUMMARY:

Objectives: Authors endeavor to describe prescribing practices in adolescents admitted in the acute monographic eating disorders (ED) ward.
Materials and Methods: We studied a cohort of 88 patients. Investigators collected clinical, diagnostic and therapeutic data from the patients' discharge summaries. A database was designed with SPSS 16 for Mac.
Results: 95% of patients are female, more than 50% of them are aged between 15 and 17 years old. 70% of patients were admitted for the first time. Approximately half of them, suffered from an axis I comorbid disorder and 15% of them of an axis II comorbid disorder. Nearly 50% of patients suffer from restrictive type ED, 14% of a purgative type ED, 9.1% of a bulimic type ED and the rest suffered from other types. 17.3% did not require any psychotropic medication.
The most commonly used antidepressant was fluoxetine, followed by venlafaxine, mirtazapine, clomipramine, sertraline and citalopram. Lorazepam was used in 30% of cases, being the most frequently used benzodiazepine. Olanzapine and risperidone, including the depot formulation, were the most commonly used neuroleptics. Topiramate and oxcarbamazepine were the most

frequently used mood stabilizers.
Conclusion: In this population, in which the majority of adolescents are admitted for the first time, psychotropic drugs are used on a routine basis. High comorbidity might justify the use of these drugs. Apart from that, we would like to emphasize the use of neuroleptics and mood stabilizers as anti-impulsivity agents, as in the reduction of binge-eating for example. In addition to that, they are also used with a view to diminishing anorexic ideation and dysmorphophobia, as well as to facilitate the implementation of psychotherapeutic interventions.

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» NR5-050

CHOCOLATE CRAVING, UNCONTROLLED EATING AND BODY DISSATISFACTION: EXPLORING THE AMBIVALENCE MODEL

Rachel Rodgers M.A., Eric Bui, M.D., Karine Faure, M.D., Henri Chabrol, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the ambivalence model of chocolate craving and the association between components of chocolate craving, uncotrolled eating and body dissatisfaction.

SUMMARY:

Background: Although the ambivalence model of chocolate craving is linked to disordered eating among females, the relationships between the dimensions of chocolate craving, uncontrolled eating and body dissatisfaction have not yet been investigated.
Objective: To explore the relationship between dimensions of chocolate craving, uncontrolled eating and body dissatisfaction among female students.
Method: We enrolled 255 female students from the University of Toulouse, France. Mean(SD) age was 20.7(2.2). Chocolate craving was assessed using the Orientation towards Chocolate Questionnaire (OCQ) which includes 3 subscales: guilt, approach and avoidance. Participants then completed the Uncontrolled Eating subscale of the Three Factor Eating Questionnaire (TFEQ-UE) and the Body Dissatisfaction subscale of the Eating Disorder Inventory 2 (EDI-BD), and provided their height and weight.
Results: The mean(SD) scores for the TFEQ-UE and the EDI-BD were 24.97(4.4) and 9.70 (7.4) respectively. The mean(SD) scores for the OCQ subscales were respectively: 2.98(1.9) for guilt, 4.04(1.7) for approach and 2.58(0.8) for avoidance. Controlling for BMI, TFEQ-UE and EDI-BD scores were significantly correlated with all 3 OCQ subscales: guilt ($r = .21$, $p<.001$; $r=.52$, $p<.001$), approach ($r = .26$, $p<.001$; $r=13$, $p<.05$) and avoidance ($r=.21$, $p<.01$; $r=.31$, $p<.001$). Hierarchical regression, controlling for BMI, revealed that guilt and approach were significant predictors of TFEQ-UE scores ($F(4,245)= 7.42$, $p<.001$, $R^2=.11$). Regarding EDI-BD scores, guilt was the unique significant predictor ($F(4, 245)=58.38$, $p<.001$, $R^2=.49$).
Discussion: The guilt component of Chocolate craving is associated with both uncontrolled eating and body dissatisfaction. These findings highlight the importance of negative feelings in body image and eating concerns. Understanding the role of emotions in the development of these concerns may prove useful in preventing them.

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» NR5-051

INFORMED CONSENT FOR MOOD STABILIZING AGENTS IN WOMEN OF CHILDBEARING AGE

Mitzi Albright M.D., Erick Messias, MD, PhD, Carmen Nichita, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to (1) describe the most common side effects of concern when using mood stabilizing agents (MSA), (2) understand the main teratogenic effects of common MSA, (3) become familiar with the most common MSA choice and the main side effects discussed during informed consent by psychiatrists. The effect of years in practice in this process will also be discussed.

SUMMARY:

Mood stabilizing agents (MSA) present a clinical challenge in women of childbearing age due to their potential teratogenic effects. As such, thorough informed consent regarding medication options is important in this situation. We aimed to determine which major side effects were discussed prior to prescribing MSAs. We hypothesized that (1) MSAs believed to have less adverse side effects and those that were deemed to be safer in pregnancy would be the drug of choice and (2) there would be an effect of years of experience on decision -making. METHODS: a mail-in survey was sent to all members of the Georgia Psychiatric Physicians Association (N=667), regarding their prescribing practices for MSAs in women of childbearing age.RESULTS: Response rate was 22.5% (150/667). The majority of respondents prescribed Valproic acid, Lithium, Carbamazepine, and Lamotrigine to their patients, including women of childbearing age. Those who used Carbamazepine informed about drug interactions 74% of the time, about hepatotoxicity 61%, and somnolence 55%. With Valproic acid, weight gain was the main concern for 89%, followed by hepatotoxicity (81%), hair loss (60%), and somnolence (54%). Lithium prescribers listed tremors (88%), weight gain (71%), nausea (70%), diarrhea (68%), and drug interactions (57%) as the side effects to be discussed. Stevens Johnson syndrome was the most cited side effect for Lamotrigine (95%). The first choice for MSA in women of childbearing age was Lamotrigine, irrespective of years of practice, however the second choice differed, with those with more years of practice preferring Valproic acid while those with less cited atypical antipsychotics (chi-sqr=17.4, p=.04). DISCUSSION: The informed consent process for MSA in women of childbearing age is complex and involves a number of considerations, including but not restricted to teratogenic effects. Psychiatrists agreed on the first choice of medication, while the second choice varied by years of experience.

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2) Cohen LS: Treatment of bipolar disorder during pregnancy. J Clin Psychiatry. 2007;68 Suppl 9:4-9

» NR5-052

THERAPEUTIC ALLIANCE IN FORENSIC MENTAL HEALTH

Vidis Donnelly M.D., Aideen Lynch, B.A Psychology; Conal Devlin, M.B. BSc; Damian Mohan, BSc M.D.; Prof. Harry Kennedy, BSc M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session the participant should be able to understand that therapeutic alliance can be measured as a meaningful construct that is valid and reliable; that therapeutic alliance is influenced by the mental state of the patient.

Summary:
Purpose & Content: We examined working alliance and interpersonal trust in a forensic psychiatry hospital, where all patients are detained. We hypothesised that working alliance and trust are bilateral and can be measured.
Method: We used validated tools measuring working alliance and interpersonal trust in physician. We adapted these minimally so that patients rated both their treating psychiatrist and primary nurse. We also adapted them minimally so that clinicians could rate their working alliance and trust with the patient.
Sample Size: We asked all 83 patients at the only forensic psychiatric hospital in Ireland, to complete the Working Alliance Inventory (WAI) and Interpersonal Trust in a Physician (ITP) for their treating psychiatrist, and for their primary nurse. The clinicians (seven consultant psychiatrists and 43 nurses) also completed a minimally altered version of the same questionnaires. All three (patient, nurse and psychiatrist) were blind to the ratings of the others. All patients were detained under mental health legislation for treatment of psychosis.
Results: Cronbach's alpha was greater than 0.9 for both patient and clinician versions of the WAI and greater than 0.8 for the ITP. The WAI and ITP correlated with each other (r>0.67 for all combinations). Patients ratings of WAI for their psychiatrist and nurse correlated r=0.7, and patients rating of IPT for psychiatrist and nurse correlated 0.69. Psychiatrists correlated with nurses 0.46 for WAI, 0.49 for IPT. Psychiatrists and patients mutual ratings correlated r=0.37 for WAI, 0.32 for IPT. Nurses and patients correlated r=0.4 for WAI, 0.25 for IPT. All correlations were statistically significant. Mental state (PANSS and GAF) correlated with all ratings.
Summary: Working alliance and interpersonal trust are mutual and can be measured reliably even in forensic settings.
Declaration: no commercial support, no conflicts of interest.

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» NR5-053 - CANCELLED

» NR5-054

GENDER INFLUENCE IN CLINICAL, DEMOGRAPHIC AND TREATMENT RELATED CHARACTERISTICS AMONG ADULT INPATIENTS IN AN ACUTE PSYCHIATRIC UNIT

Ainoa Muñoz San José, M.D., Jesús J. Marín Lozano, M.D., David López Gómez, M.D., Mª Eva Román Mazuecos, M.D., Rosa Villanueva Peña, M.D., Mª Fe Bravo Ortiz, M.D. Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize the differences between male and female inpatients concerning diagnosis and treatment.

SUMMARY:
Objective: Clinical differences between male and female inpatients have been classically considered and some publications have put forward this fact. The aim of this study is to demonstrate these differences regarding clinical, demographic and treatment related characteristics. Method: The sample comprises 1,301 inpatients admitted to an Acute Psychiatric Unit in a General Hospital in Madrid, Spain, between January 2006 and October 2008. A retrospective case-series study has been done, analyzing data with SPSS PC. The variables analyzed were age, nationality, length of hospital stay, type of admission (voluntary/ involuntary), marital state, history of psychiatric disorders, history of suicide attempts, alcohol consumption, substance abuse, treatment and Diagnostic Category (axes I and II, according to the APA Diagnostic Classification, DSM-IV TR). Results: the between-group difference was statistically significant (p<0,05) for admission type (women inpatients had more voluntary admission (34,9%) than men (24,8%)), history of psychiatric disorders (it was positive in 91% of female inpatients and 85% of male), history of suicide attempts (6,6% in male and 16,6% in female), alcohol consumption (19,4% of men and 10,5 of women) and substance abuse (27,3% of male and 11,4% of female). Women also received antidepressant and antipsychotic treatment in a different proportion than men. There were statistically significant more male inpatients with diagnosis of Substance Related Disorders (16,5% versus to 5,7% in women) and Schizophrenia (47,3% in men versus to 29% in women). Female inpatients had significantly more Eating Disorders and Mood Disorders. Conclusions: it is important to be aware of clinical and treatment differences between male and female inpatients in order to improve their psychiatric assistance. Future investigation in this subject will provide better management of psychiatric inpatients.

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» NR5-055

CHARLES-BONNET SYNDROME IN THE ELDERLY: DIAGNOSTIC CLUES AND MANAGEMENT

Jacqueline Dahl M.D., Maria I. Lapid, M.D., Jarrett W. Richardson, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize Charles Bonnet Syndrome in the elderly and be familiar with evaluation and management.

SUMMARY:
Charles Bonnet Syndrome (CBS) is common in the elderly with vision loss, particularly in age-related macular degeneration, with a prevalence of 10-15%. It is characterized by complex visual hallucinations that are vivid and well formed, although individuals retain insight and have preserved cognition. Although CBS can ameliorate spontaneously or with treatment, some cases report chronic visual hallucinations, but often patients are afraid to report these hallucinations for fear of being labeled as "insane". Atypical antipsychotics, anticonvulsants, SSRIs, SNRIs, cisapride, as well as behavioral modification and visual cuing have been used to treat CBS in case reports with good effect. However, despite the frequency of vision loss in the elderly, and the common occurrence of CBS in this population, little is known regarding the systematic evaluation and treatment of this syndrome in the elderly population. We report two cases of elderly women with CBS, and describe the evaluation and management of these cases. It is important to distinguish CBS from other primary psychotic disorders and other causes of visual hallucinations, as treatment is very different for alternative diagnoses. Clinicians should be aware of CBS, which may reduce the quality of life of affected individuals if undiagnosed or untreated. CBS should be considered in the differential diagnosis of any elderly individual who presents with well formed vivid visual hallucinations in the context of vision loss. We have no commercial support to disclose.

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» NR5-056

THE ELDERLY IN THE PSYCHIATRIC EMERGENCY SERVICE: IS A DIFFERENT ASSESSMENT NEEDED?

Kathleen Diller M.D., Ruth M. Lamdan, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to discuss an approach to the psychiatric emergency evaluation of the older adult.

SUMMARY:

Introduction: With the "graying" of America, the elderly using Psychiatric Emergency Services (PES) is expected to increase. Since medical illness in the elderly can manifest as psychiatric disorders, clinicians evaluating older adults in the PES must have a high index of suspicion for non-psychiatric etiologies. In this pilot study, we examined how older adult PES patients differ from younger patients. The goal is to develop a PES Geriatric Assessment Protocol.

Method: With IRB approval, we did a retrospective chart review of patients seen in our busy, urban PES over a 3-year period. We selected 105 out of 463 patients aged 65 and older seen during that period, and sex and race matched them to those aged 18-64 seen on the same day. We compared clinical presentation, diagnoses, workup and outcomes.

Results: Geriatric subjects were more likely to present on an involuntary commitment ($p<0.01$) and to present disoriented ($p = 0.03$) compared to controls. They were likely to have more medical diagnoses and to be on more non-psychiatric medications. Older adults were more likely to present psychotic ($p<0.01$) or with cognitive impairments ($p<0.01$) and to be admitted to a psychiatric facility ($p<0.01$). Despite these differences, elderly patients were not more likely to be seen in the medical Emergency Room (ER) prior to or after presenting to the PES, nor were they more likely to receive a medical workup in the ER. Urinalysis was ordered for only 9.5% of older subjects, and brain imaging was done on only 5.7%. Documentation of complete cognitive evaluation was missing in 45.7% of the older adult exams. In 27.6% orientation evaluation was not done.

Conclusion: Prospective comparisons are needed to make final recommendations for the emergency evaluation of the older adult in the PES. Our study shows that clinicians skip basic, inexpensive elements of the workup such as cognitive testing and urinalysis. Implications for geriatric training will be proposed.

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» NR5-057

OUTLOOK AT DIOGENES SYNDROME (SELF NEGLECT SYNDROME IN ELDERLY POPULATION) - A CASE REPORT

Marina Haghour-Vwich M.D., Natasha G.Baron, M.D; Amel Badr M.D, and M Javed Iqbal, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand that Diogenes Syndrome, while relatively unheard of, is not an uncommon Public Health concern. The seemingly forgotten populations who suffer from this pathology are deemed as risks to themselves, due to chronic untreated medical conditions or acute incidents such as falls; and to the public, due to the hazards hoarding and unsanitary living conditions may present.

SUMMARY:

Senile Squalor Syndrome, otherwise known as Diogenes Syndrome, is a complex spectrum of behavior found in elderly single-recluses, characterized by extreme self-neglect of environment, health, and hygiene combined with compulsive hoarding of refuse and complete denial of their surroundings or symptoms. Adult Protective Services (APS) reported in 2008 that it was the top cause of investigation and remains a prevalent but underdiagnosed health concern in many communities. The squalor is such that by the time of discovery sufferers are literally buried in excrement, refuse and disease either caused or exacerbated by gross bodily neglect and malnutrition related to their extreme isolation and refusal of assistance. Incidence of Diogenes Syndrome is 5 per 10,000 of the population in patients 60 years old and above. It was first described as a geriatric syndrome in 1966, on the basis of its multifactorial etiology, association with functional decline, shared risk factors with other geriatric syndromes, such as falling, incontinence, and most importantly, its clear and independent association with increased mortality. There has been no consensus so far as to its pathogenesis.

Conclusion : Presently, Diogenes Syndrome does not fit clearly into the current DSM-IV-TR or ICD-10 Diagnostic Criteria. Further research recommended exploring accurate classification and underlining pathology. While there appears to be a paucity of real time data regarding the complexities of the Syndrome, continued recognition and reporting of cases may be useful to its existing clinical and theoretical framework. In time, the basic developmental work will evolve into the discovery of more efficient strategies for dealing with this complex and prevalent geriatric problem.

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» NR5-058

CLINICAL USEFULNESS OF THE COMBINATION OF K-BNT & DELAYED RECALL OF SVLT IN DIAGNOSING DEMENTIA OF THE ALZHEIMER'S TYPE

Jun-Yeob Lee M.D., Bon-Hoon Koo,M.D.,Ph.D., Shin-Ho Song,M.D., Jong-Bum Lee,M.D.,Ph.D., Yoon-Jung An,M.S.W

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know that the cut-off values of K-BNT & delayed recall of SVLT is useful for clinician to diagnose dementia of the Alzheimer's type(DAT).

SUMMARY:

Objectives:Seoul neuropsychological screening battery(SNSB) is one of the most widely used neuropsychological test battery in evaluating cognitive functions of geriatric patients in Korea. But, SNSB does not have the cut-off values of each cognitive subdomain, its clinical usefulness has a limit for clinician. The purpose of this study is to estimate the cut-off values of two most useful subdomain tests[Korean Boston Naming Test(K-BNT) & delayed recall of Seoul Verbal Learning Test(SVLT)] in the diagnosis of DAT.

Methods: We compared the results of SNSB between patients with DAT who met DSM-IV criteria(N=66) and neurotic patients without any cognitive impairment(N=47) retrospectively. We made ROC curve of K-BNT and delayed recall of SVLT for the two groups. And we estimated sensitivity, specificity, positive predictability & negative predictability of K-BNT & delayed recall of SVLT based on the results, respectively.

Results: The cut-off values of K-BNT & delayed recall of SVLT determined by ROC curve in order to diagnose DAT were 11.70‰(.859, z=-1.19) & 11.31‰(.873, z=-1.22). When these two cut-off values were applied to two groups separately, sensitivity, specificity, positive predictability & negative predictability were 71% vs 85%, 92% vs 79%, 92% vs 85% & 69% vs 79%,

respectively. And these two cut-off values were applied together, sensitivity, specificity, positive predictability & negative predictability were 62%, 96%, 95% & 64%.
Conclusion: The results of this study demonstrate that reliability of K-BNT & delayed recall of SVLT in diagnosing DAT are similar to that of mini-mental state examination(MMSE) that is commonly used screening test of DAT. Moreover, positive predictability from the cut-off values of K-BNT and delayed recall of SVLT applied together may be superior to that of the MMSE. We suggest that the cut-off values of K-BNT & delayed recall of SVLT may be useful for clinician to diagnose DAT.

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» NR5-059

EFFECTS OF APOLIPOPROTEIN E E4 ALLELE ON NEUROPSYCHIATRIC SYMPTOMS IN ALZHEIMER'S DISEASE

EUNYOUNG SHIN M.D., Han Yong Jung, MD, PhD1, Shin Gyeom Kim, MD1, So Young Lee, MD, PhD1, Yu Jin Lee, MD1, Joon Ho Park, PhD1, Yeon Jung Lee MD2

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to regognize that noncognitive neuropsychiatric symptoms are common in patients with AD and have a serious impact on their quality of life and institutionalisation. Genetic determinants of BPSD in AD have been demonstrated and APOE e4 allele is the only risk factor robustly associated with AD. This study provides informations about association between BPSD of Alzheimer's disease and apolipoprotein.

SUMMARY:

Background : Noncognitive neuropsychiatric symptoms are common in patients with Alzheimer's disease(AD) and have a serious impact on their quality of life and institutionalisation. Genetic determinants of BPSD in AD have been demonstrated and apolipoprotein (APOE) e4 allele is the only risk factor robustly associated with AD. However, previous investigations on APOE have produced inconsistent findings on BPSD.
Objective : This study explored the relationship between the APOE e4 allele and a wide spectrum of neuropsychiatric symptoms of AD patients
Method : Sixty two subjects for this study were recruited from the Dementia and Age-associated Cognitive Decline clinic and already diagnosed with probable AD. All the subjects had been examined according to the protocol of the Clinical Research Center for Dementia(CRCD) supported by the Ministry of Health and Welfare, Korea and met both the DMS-IV criteria for dementia and the NINCDS-ADRDA criteria for probable AD. The subject's neuropsychiatric symptoms were assessed during an interview with the informant by using the Neuropsychiatric Inventory (NPI) consisting of 12 items of the behavioral problems and psychiatric symptoms. According to the defined criteria, the severity of each item was classified into 3 grades (from 1 to 3) and frequency of each one was classified into 4 grades (from 1 to 4). The NPI score (severity×frequency) was calculated for each item and the presence or absence of neuropsychiatric symptoms were also rated.
Results : There is no relationship between the APOE e4 allele and neuropsychiatric symptoms, even after controlling for the effects of age at onset, sex, education level, duration of illness, and severity of dementia.
Conclusions : There was no statistical significant difference in neurpsychiatric symptoms between subjects with and without APOE e4 allele in Korean elders with Alzhemer's disease.

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» NR5-060

A COMPARATIVE ANALYSIS OF THE INTERPERSONAL CONFLICT TACTICS USED BY OLDER ADULTS WITH SCHIZOPHRENIA AND THEIR AGE PEERS IN THE GENERAL COMMUNITY

Dimple Sodhi M.B.B.S, Carl I. Cohen, M.D., Paul M. Ramirez, Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the conflict tactics used by community dwelling older schizophrenia patients in comparison with their peers.

SUMMARY:

Objective: There have been numerous studies on how persons with schizophrenia handle interpersonal conflicts. However, little is known as to whether conflict tactics change with age. This study examines interpersonal conflict tactics among older adults with schizophrenia and compares them with their age peers in the community.
Methods: The sample consisted of 198 community dwelling persons aged 55 and over with schizophrenia (S) and a demographically matched group of 113 persons in the general community (C). The two groups were comparable demographically: women (49% S group; 49% C group), African Americans (35% S group; 36% C group), and mean ages (61.5 years S group; 63.0 years C group). The 25-item Straus' Conflict Tactics Scale was used to assess the ways that respondents handled interpersonal conflicts. Items were factor analyzed using a principal component analysis with equamax rotation.
Results: Seven different factors were identified and used to create corresponding subscales: Calm, Arouse, Pray, Avoidance, Tearfulness, Aggressive, and Violent. Each subscale had acceptable internal reliability. We found significant differences between the S group and the C group on the Arouse, Calm, and Crying subscales, with the C group using these tactics more commonly. However, the order of the frequency of the tactics that were used was similar in both groups. The Calm, Praying, and Avoidance were the most commonly used, and violence and aggression were very rarely utilized.
Conclusions: Although there were some absolute differences in the subscale scores between older persons with schizophrenia and their age peers, they exhibited similar patterns in the ordering of the subscales. This study supports the contention that interpersonal relationships improve and become more normalized in later life.

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» NR5-061

A COMPARISON OF TMS ADMINISTERED 3 DAYS/WEEK AND TMS ADMINISTERED 5 DAYS/WEEK IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER

Stacy Bell, Cherrie Galletly, MBChB, DPM, FRANZCP, PhD, Shane Gill, BMBS, FRANZCP, Dip Psychotherapy, Patrick Clarke, MBBS FRANZP, Jody Williams, B. Nursing

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the steps required to set up a TMS service to treat Major Depression. The participant will gain knowledge about the administration of the TMS treatment, the forms and protocols required to run the service and referral and assessment processes. The participant will learn how to formulate and test hypotheses to help define optimal treatment parameters.

SUMMARY:

Transcranial Magnetic Stimulation (TMS) is a relatively new treatment shown to be effective in treating depression. TMS relies on direct stimulation of the brain using magnets. Small electrical currents that pass through an electromagnetic coil held near the patient's scalp stimulate nerve cells in the region of the brain involved in mood regulation and depression. Advantages of TMS are that no anaesthetic is required and there is no associated cognitive impairment. In 2008 a TMS treatment service was established at The Adelaide Clinic (TAC), a private psychiatric hospital in Adelaide, South Australia. This is the only TMS service in the State. The steps required to set up this service are described. There is evidence that TMS administered five days/week and TMS administered three days/week are both effective, but little research compares the effectiveness of the two treatment regimes. As TMS becomes a more widely used clinical service it will be necessary to determine if, as with ECT, TMS administration should be spaced, or whether it should be administered daily to gain most effect. We designed a study to evaluate the optimal spacing of treatments, and treatment course length. Patients are assessed prior to treatment then randomly allocated to either (1) TMS five days/week for four weeks or (2) TMS three days/week for six weeks (in both conditions patients are assessed at four and six weeks). Pre and post-treatment scales used to compare the two treatment conditions include the HAM-D, HAM-A, MADRS and Zung depression scale. Preliminary results for the first 13 patients who have completed TMS treatment indicate that it is effective in the treatment of depression with lower average post-treatment scores than pre-treatment scores. Results also indicate very little difference in the effectiveness of the two treatment conditions. The TMS service at TAC established in June 2008 operates efficiently and to date demonstrates effectiveness in the treatment of depression.

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» NR5-062

IS NEWER BETTER? A COMPARISON OF DIRECT AND INDIRECT META-ANALYSES OF DESVENLAFAXINE AND VENLAFAXINE FOR MAJOR DEPRESSIVE DISORDER

Samuel Huber M.D., Matthew D. Engel, B.S.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe two methods for systematically comparing efficacy data about antidepressants and form a judgment about the relative effectiveness of desvenlafaxine, a recently approved medication. Social implications for further drug development will also be discussed.

SUMMARY:

Background: An increasing number of patents and new drug approvals have been granted to chemically similar agents (i.e. active metabolites). While the potential for increased benefit exists, there are often questions about the efficacy and tolerability of these agents relative to their parent compounds(1).

Objective: To systematically summarize and compare randomized controlled trials (RCT) of efficacy and safety of desvenlafaxine (DVS) and its parent compound venlafaxine (VLX) in the treatment of Major Depressive Disorder (MDD) in adults.

Design: We used meta-analysis to compare DVS and VLX directly (head-to-head trials) and indirectly (either agent vs. placebo). We systematically searched MEDLINE, Cochrane CENTRAL, PsycINFO, trial registries (ClinicalTrials.gov, FDA.gov, Wyeth.com) and the references of related studies for RCTs of adults with MDD. The authors independently assessed study quality and extracted data from included studies.

Outcomes: Efficacy was measured in 3 ways: remission, response and change in HAM-D and MADRS scores. Pooled relative risks (RR) for remission, response and adverse events were generated and compared either head to head (direct) or versus placebo (indirect).

Results: Two trials (n=715) were pooled in the direct comparison(2). In the indirect comparison, 5 trials evaluating DSV (n=2023) and 15 trials evaluating VLX (n=3702) were combined. The trials were similar in basic characteristics, quality, methods and placebo response rate.

In the direct comparison, DVS was not statistically more effective than VLX (RR remission .87 p=.30, response .90 p=.20).

In the indirect comparison, DVS was less effective than VLX in response (RR .86 p<.001) and absolute change (p<.05) and no different in remission (RR .91 p=.13). Adverse event rates were similar.

Conclusion: Based on direct and indirect comparisons of findings from RCTs of each agent, the metabolite compound DVS is neither more effective nor better tolerated than its parent compound.

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» NR5-063

EMERGENCY PSYCHIATRY: LITERATURE OVERVIEW WITH STATISTICS FROM PARIS, FRANCE

Gabriella Inczedy - Farkas M.D., Carl D. Hanson, MD, Orsolya Hadarits

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify issues characteristic of emergency psychiatry, learn the predictors of admission and release, be able to identify special features of repeat users, get an impression of the utilization of Emergency Psychiatry by the clinical and epidemiologic profile of one service.

SUMMARY:

A concise literature review about Emergency Psychiatry is given along with statistics from one hospital service in Paris, France. Special features of the emergency setting along with its special problematics are detailed.

Evaluating the patient, making a medical decision, predictors of admission and release, repeat users of these services are just a few of the mentioned topics. We deal with future challenges of Emergency Psychiatry like the spread of substance abuse or the cost – effective organization of these services.

Retrospective analysis is made of clinical data of 894 patients admitted at Hotel Dieu Hospital within 6 months of activity from

January 1st 2007 to 30th June 2007. Descriptive statistics are used to analyze these data. Patient age, mode of presentation, diagnosis and intervention as well as time taken to make the medical decision is described. Current functioning as well as future endeavors of the local service are depicted.

REFERENCES:

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» NR5-064

THE PREVALENCE OF NEUROPSYCHIATRIC DISORDERS IN VETERANS AND SERVICE MEMBERS OF OPERATIONS ENDURING FREEDOM AND IRAQI FREEDOM (OEF/OIF)

Patrick Link M.D., Alexander S. Young, M.D., M.S.H.S.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to appreciate the high rates of neuropsychiatric disorders in veterans of the conflicts in Iraq and Afghanistan, as well as the challenges in determining such rates using self-administered screening assessments. The participant will be better equipped to use appropriate neuropsychiatric screening assessments when evaluating veterans of these conflicts for neuropsychiatric disorders.

SUMMARY:

OBJECTIVE: The purpose of this review is systematically to locate data on the prevalence of neuropsychiatric disorders in OEF/OIF service members and veterans. METHOD: We entered relevant terms into PubMed to locate articles on OEF/OIF personnel. We examined article titles, locating those possibly relevant to prevalence rates for neuropsychiatric disorders. The abstracts and/or full texts of these articles were reviewed. To locate other relevant articles, we hand reviewed the bibliographies of each article found to contain appropriate prevalence estimates. For each relevant article, we determined multiple factors, including the population studied, prevalence estimation methods used, and the prevalence rates obtained. RESULTS: Twenty-nine studies provide relevant prevalence estimates, almost exclusively via self-assessments. They indicate that 10-15% of OEF/OIF personnel have acute stress disorder or posttraumatic stress disorder (PTSD) and 5-15% have major depression (MDD), rates up to four times higher than for U.S. 18-54 year olds. The data are less robust for the other conditions evaluated. Given this caveat, roughly 5-15% have generalized anxiety disorder (GAD) and 12-20% experienced a deployment-related mild traumatic brain injury (mTBI). The case definitions used to identify alcohol use disorders were too varied to produce reliable estimates of their prevalence rates. Taking into account comorbidities, roughly a third of all OEF/OIF personnel have PTSD, or have MDD, or experienced a deployment-related mTBI, while up to a half may have mental health concerns requiring further evaluation. CONCLUSIONS: Neuropsychiatric disorders are common among OEF/OIF personnel. Additional studies on the prevalence rates of GAD and mTBI should be conducted in this population. Prevalence studies on alcohol use disorders should use similar case definitions and assessment instruments. Prevalence studies using standardized clinical assessments should be conducted.

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» NR5-065

SYMPTOMATIC IMPROVEMENTS ARE ASSOCIATED WITH FUNCTIONAL IMPROVEMENTS IN VETERANS WITH DEPRESSION, ANXIETY, AND POST-TRAUMATIC STRESS

Brian Shiner M.D., Bradley V. Watts M.D., M.P.H., Yinong Young-Xu Sc.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: -Describe the symptomatic and functional levels of veterans presenting for psychiatric care at Veteran's Administration Hospital Walk-In Clinic -Understand the relationship between symptomatic and functional improvement in these veterans. -Understand which Medical Outcomes Study Short Form-36 (SF-36) summary scales and subscales are most likely to show improvement in the course of routine mental health care.

SUMMARY:

Introduction: Considerable evidence is available regarding the ability of mental health treatment to improve the symptoms of mental illness. However, less is known about the ability of these treatments to improve functional outcomes. We sought to examine the measured change in functional status associated with improvements in clinical symptoms in a heterogeneous clinical population.
Methods: Veterans presenting to a mental health clinic completed a battery of standardized assessments. Those who completed the SF-36 at least twice were selected for inclusion and divided into groups based upon their outcomes on serially-administered assessments for depression (Beck Depression Inventory, BDI), anxiety (Spielberger State-Trait Anxiety Index, STAI), and post-traumatic stress (Patient Checklist for PTSD, PCL). We grouped those that improved by 10%, got worse by 10%, or did not change by at least 10% on each symptomatic assessment. For each group, we determined the mean change in SF-36 scores. ANOVA was performed to compare SF-36 change between each group.
Results: 358 veterans completed the SF-36 at least twice. Their mean age was 51 and they were 91% male. The mean initial SF-36 mental component summary (MCS) and physical component summary (PCS) scores were 27.2 and 43.0. Those that improved by at least 10% on their BDI, STAI, or PCL had statistically-significant ($p<0.001$) improvements of 7-12 points on the MCS, but had a smaller, non-significant changes of approximately 1 point on the PCS. Of the subscales, Mental Health, Role Emotional, and Social Functioning, which contribute most significantly to the MCS, showed the most change.
Conclusion: Improvements in symptoms for depression, anxiety, and post-traumatic stress are associated with significant improvements in the SF-36 MCS and related subscales, but not the SF-36 PCS. Measurable functional improvements can be expected when patients' level of depression, anxiety, or post-traumatic stress improves.

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1) Ware JE, Kosinski M: SF-36 Physical and Mental Health Summary Scales: A Manual for Users of Version 1, 2nd ed. Lincoln, RI, QualityMetric Incorporated, 2001.

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» NR5-066

ATTRIBUTION AND RESPONSE TO CHANGES IN MOOD AND BEHAVIOR AS RELATED TO PREVIOUS

PSYCHIATRIC DIAGNOSIS

Meredith Theeman M.S.C.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize that prior psychiatric symptoms influence current perceptions of mood and behavior changes. This will allow the participant to discern the sources of illness construction and predict how it plays a continued role in attribution and treatment decisions. Overall, the participant will gain a better understanding of the relationships among psychiatric symptoms, symptom attribution, and help-seeking behavior.

SUMMARY:

This study tests if history of psychiatric diagnosis is associated with patient attribution and response to current mood and behavior changes. Participants with and without clinically diagnosed depression in the United States were sampled using an internet-based survey eliciting mood, illness perception, and illness behavior. Of 401 respondents, 324 (80.8%) completed the survey. The sample was 74% white, 81% women, and had a mean age of 33. Most had private health insurance (67%), and 55.6% had a lifetime history of mental illness. Analyses were conducted using Chi Square and logistic regression models. I report 3 main findings. (1) Attributions of current mood and behavior change significantly differed for those with and without a history of psychiatric diagnosis (X^2=39.22, p<.001). While both groups were most likely to attribute changes to stress, those with prior psychiatric diagnoses were more likely to attribute changes to chemical imbalance and genetic predisposition as well. (2) Those with a history of psychiatric diagnosis were more likely to seek treatment from physician and non-physician mental health professionals, (X^2=72.21, p<.001 and X^2=20.49, p<.001, respectively, irrespective of severity of current symptoms. (3) Those with previous diagnoses were more likely to report using medications for current mood/behavior changes, including anti-depressants (X^2=85.30, p<.001); other prescription drugs (X^2=28.41, p<.001); and homeopathic remedies (X^2=7.85, p<.05). These data strongly indicate that once a psychiatric diagnosis is incurred, people are likely to attribute future mood and behavior changes to medical conditions and seek treatment clinically. In summary, I conclude that past psychiatric diagnosis influences illness conceptualization and treatment behaviors of future mood and behavior changes.

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2) Mojtabai R, Olfson M, Mechanic D: Perceived need and help-seeking in adults with mood, anxiety, and substance use disorders. Arch Gen Psychiatr 2002; 59: 77-84

» NR5-067

FACTORS AND BARRIERS THAT LEAD TO ABSENCES AT INITIAL PSYCHIATRIC APPOINTMENTS

Adrienne Turner M.D., Anita H. Clayton. MD

EDUCATIONAL OBJECTIVES:

Participants in this presentation will be able to list at least four factors that may contribute to psychiatric patients failing to appear for their intake appointment. Furthermore, participants will be able to identify at least two actions that a clinic may take to decrease no-show rates.

SUMMARY:

This study was conducted to examine factors that contributed to patients not showing for their first scheduled intake appointment in a Psychiatric Clinic. The methodology was informed by and expanded upon studies by Korrelboom (2007) and Livianos (1999). This study was particularly timely given the economic downturn and fluctuating gasoline prices. The goal of the research was to determine if patients who show up for their appointment differ from those who do not in the following areas: transportation issues, financial concerns, the stigma of psychiatry, the extended length of time between calling for an appointment and the actual visit, and also the personal denial about having a psychiatric problem. Methods: The study was approved by the University of Virginia IRB and took place between August 28 and November 21, 2008. A survey was mailed to patients who failed to show for their intake appointment (n=143) and was hand-delivered at the time of the appointment to those who did show (n=148). The survey collected demographic information as well as solicited perceptual information regarding various barriers to showing up for the intake. Results: 26 (18%) of the no-shows returned completed surveys and 76 (51%) patients who did show completed surveys. The results were analyzed to determine if the two groups differed across any of the factors studied. Conclusion: The two groups differed significantly in age but not in gender. While distance traveled was not perceived as being a significant barrier, obtaining transportation was. Patients seeking treatment for addictions and those who were anxious and unsure about a Psychiatric interview were more likely to not show. Based on the results of the study, clinics may consider actions to reduce the number of no shows such as providing resources and information for obtaining transportation to the clinic and providing an information sheet on what to expect during an initial appointment with a Psychiatrist.

REFERENCES:

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» NR5-068

THE CO-OCCURRING STATE INCENTIVE GRANT IN DELAWARE STATE

Cynthia Zubritsky Ph.D., Gerald Gallucci, MD MHS, Aileen Rothbard, SCD, Melissa Smith, MA, Steven Dettwyler,PhD, Kimberly Beniquez,MS

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant will be able to identify two methods to create and foster practice change interventions that will address co-ocurring disorders.

SUMMARY:

Purpose The Delaware SAMHSA Co-occurring State Incentive Grant (COSIG) provides support to build a seamless system of care for persons with co-occurring disorders (COD) by providing training, technical assistance and consultation, to change practice patterns. Content The COSIG goal is to increase state capacity for integrated treatment through a practice change intervention at all system levels. The model targets medical staff, on-site change leaders, and individualized technical assistance to clinicians and administrators.

Methodology To determine the success of the practice change intervention at the system level, a set of SAMHSA standardized measures are being collected on the extent of integrated COD screening, assessment and treatment pre and post the intervention. Descriptive data on each agency's COD model (collaborative, consultative or integrated) will be collected. Descriptive data from targeted consultation and technical assistance for individual clinician attitude and knowledge change will be collected throughout the study from all participants. This poster will focus on baseline change data collected from medical staff, including medical residents, psychiatrists, nurses and nurse practitioners.

Sample Size and Characteristics Over 73 medical professionals have participated in COD training or technical assistance; 25 physicians and nurse specialists, 36 hospital staff, and 12 medi-

cal residents. Results indicate that both knowledge and attitudes changed as a result of the intervention. Importance of Proposed Presentation Current research indicates that between 40-60% of behavioral health clients are COD, yet few receive integrated treatment. This system change initiative targets medical professionals as a key element in a practice change model.
Summary This poster describes a model for the development of a state-wide COD person-centered care system through a targeted intervention with the system's medical professionals.

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1) Rothbard, A., Wald, H., & Zubritsky, C. Outcomes from Pennsylvania's COSIG Infrastructure Development Evaluation. The National Association of State Mental Health Program Directors Research Institute, Inc. Conference. Washington, DC. 2007.

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» NR5-069

NEURAL CORRELATES OF INTERNET GAME ADDICTION: AN FMRI STUDY

Hyoungyoon Chang, Shin YJ, M.D., Ph.D., Park HJ, M.D., Ph.D., Kim JH, Ph.D., Kim EJ, M.D., Park IC, M.D., Kim MK

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that internet game addiction has neurophysiological mechanism.

SUMMARY:

Internet game addiction is a fast expanding problem in South Korea, and Massively Multiplayer Online Role Playing Game (MMORPG), which includes interactive component added to preexisting internet video games, is thought to have even higher addictive potential. But the pathophysiology as well as the definition of internet game addiction is still unclear. The aim of this study was to find the underlying mechanisms of internet game addiction by assessing functional magnetic resonance imaging (fMRI) in both internet game addiction group and normal control. The present study was approved by the Committee for Medical Research Ethics at the Yonsei University, Seoul, South Korea. A total of 24 right-handed male volunteers without significant psychiatric or neurological history were recruited. 12 participants (mean age=23.33, SD=3.04; mean playing hours=8.10 hr/day) were identified as internet game addiction group by Young's Internet Addiction Scale, and the remaining 12 closely matched healthy controls (mean age=24.36, SD=2.54; mean playing hours=3.01 hr/day) were casual internet game players. fMRI was taken while the participants watched the video-screen of a popular MMORPG World of Warcraft (WoW; by Blizzard) in a fighting state and a resting state. Significant between-group differences in fMRI were found at medial, superior, and inferior frontal gyrus of left hemisphere when WoW-fighting state was compared with WoW-resting state. The fact that addiction group showed higher activation in the frontal gyrus suggests that addictive internet game behavior is constituted not only by behavioral but neurophysiologic differences. Internet game addiction group showed higher activation in frontal gyrus compared to the normal control when WoW-resting state was subtracted from WoW-fighting state in fMRI, which implicate neurophysiologic differences between these two groups.

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1) Thalemann R, Wolfling K, Grusser SM: Specific cue reactivity on computer game-related cues in excessive gamers. Behavioral neuroscience 2007; 121:614-618

2) Mathiak K, Weber R: Toward brain correlates of natural behavior: fMRI during violent video games. Human Brain Mapping 2006;27:948-956

» NR5-070

A STUDY ON THE EFFECTS OF THE PSYCHIATRIC PATIENTS´ REPEATEDLY JOINING WEIGHT CONTROL GROUP

LO Wei-Chi M.D., Yuh-Ming Hou, M.D.,Hui-Ling Chiu

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the effectiveness of repeated participations in the weight control groups in a community rehabilitation center.In this study, there is no greater efficiency for psychiatric patients to repeatedly join weight management group. The only significant improvement is hand function.

SUMMARY:

Purpose: To help psychiatric patients to reduce the problems of obesity, our health care team has held weight-loss group therapy for several times. The purpose of this study is to understand the effectiveness of repeated participations in the weight control groups. Method: The subjects included voluntary psychiatric patients who thought that they were overweight with BMI of 25 or more. The duration of a course was 10 weeks . The course includes understanding of the disease, aerobic exercise, diet education and stress management. Before each group, measuring body weight, body mass index, body fat, hand dexterity test, attention test and other laboratory data, such as blood glucose, triglycerides, cholesterol. After the end of the group, the same measurements were done again. We evaluated the effectiveness of repeated participations in weight loss group by comparing those patients who joined group several times with those who only joined once. The outcomes of the data were analyzed by SPSS 10.0 version.
Results: A total of 47 patients were enrolled in this study, with an average age of 32.06 ± 6.4 years old and an average height of 163.49 ± 8.57 cm. Among them, 23 patients repeatedly participated in group and the other 24 participated only once in a group. These patients with the diagnosis of schizophrenia accounted for the majority (54.5 percent). We used paired-t test to compare the initial record of measurements of patients who repeatedly joined groups with those who only participated once. There were no difference in body weight, BMI, cholesterol, triglycerides, AC sugar, body fat, attention and hand function. In comparing measurements of the last time of 2 groups, the only significant difference was hand function ($t = 4.304$, $p = 0.000$). Conclusions: This study shows that there is no greater efficiency for psychiatric patients to repeatedly join weight management group.

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» NR5-071

THE NATURALISTIC STUDY OF THE EFFECTS OF EEG BIOFEEDBACK IN ADULT PATIENTS WITH PSYCHIATRIC DISORDERS

Bon-Hoon Koo M.D., Jong-Bum Lee, M.D., Ph.D., Jun-Yeob Lee M.D., Shin-Ho Song M.D., Min-Ji Kim, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know that EEG Biofeedback is useful & assistant treatment in adult patients with certain psychiatric disorders.

SUMMARY:

Objectives:The purpose of this study was to evaluate the characteristics and the effects of EEG biofeedback for adult patients with psychiatric disorders in naturalistic setting.

Methods: Fifty-seven adult patients with psychiatric disorders who were applied EEG biofeedback in university hospital, Korea from July, 2005 to July, 2008 were participated in this study. The demographic data(age, sex, educational level), characteristics of psychiatric disorders(diagnosis, duration of illness, presence of medication), and states of EEG biofeedback(total frequency, protocol) were analyzed. And the effects of EEG biofeedback were also evaluated before & after training using clinical global impression(CGI) and subjective self rating scale(provided by EEG Spectrum International, Inc.).
Results: Anxiety disorders were the most common psychiatric disorder who were applied EEG biofeedback(16 patients, 28.1%), and second were the depressive disorders(13 patients, 22.8%). Fifty-one patients(89.5%) were taken medicine. The average frequency of EEG biofeedback were 55±18.56, and 32 patients(56.1%) were applied EEG biofeedback more than ten times. Thirty-six patients(63.2%) were applied both ß/SMR & a/? training. And discontinuation rate were 36.8%(21 patients). Significant change of CGI before and after training was noticed using covariance with frequency(<.001), and self rating scale also showed significant changes in depressive symptoms, anxiety, and inattention(<.001).
Conclusion: This is the naturalistic study in clinical setting, so there are several limitations such as absence of control group and validity of self rating scale, etc. But this study demonstrates the significant effects of EEG Biofeedback in objective & subjective rating scales for adult patients with certain psychiatric disorders. Prospective controlled studies are needed in the future.

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» NR5-072

PERCEPTION DIFFERENCES TOWARDS ECT AMONG PATIENTS WITH MAJOR DEPRESSIVE DISORDER AND SEVERE MENTAL ILLNESS AND THEIR RELATIVES

Angelica Ramírez-Cardenas M.D., Cesar Gonzalez-Gonzalez, M.D.,Eduardo Valle-Ochoa, M.D.

EDUCATIONAL OBJECTIVES:

The objective is to show that the perception towards ECT is positive among patients treated with this strategy and their relatives, specially patients with SMI. At the conclusion of this presentation, the participant should be able recognize ECT as a therapeutic strategy with a high rate of satisfaction to patients and their relatives.

SUMMARY:

Introduction: Electroconvulsive therapy (ECT) has been used for more than 65 years, despite the negative image it has on general population and certain professionals, it has been proven as an effective and safe therapeutic modality for a variety of psychiatric disorders.
Goal: To examine the perceptions of patients with diagnosis of Severe Mental Illnesses (SMI) and Major Depressive Disorder (MDD) and their relatives towards ECT; and analyzed the differences among the groups.
Methods: A dedicated survey was applied to 25 patients and 21 family members regarding their ECT treatment at our institution. Statistical analysis was performed using Chi square to compare answers among groups.
Resultados: 76% of patients had SMI and 24% had MDD. Mean age was 45 years, on average, ever patient had 12 sessions of ECT. Most patients believed their received adequate and sufficient information about ECT before signing the informed consent. Over 80% of patients and their relatives were satisfied with the results after ECT and they have a positive attitude toward ECT.
Regarding information and knowledge there were no differences among groups in patients and relatives. Regarding the experience, the group suffering SMI had a more positive experience than the patients suffering MDD (15.3, gl 3, p>.002), and also their relatives (9.0 gI 3, p>0.029). The positive attitude towards ECT was higher in SMI patients (10.6, gl 2, p>.016) and their relatives (18.6, gl 4 p>.001).
Conclusions: Patients treated with ECT and their relatives are satisfied and have a positive attitude towards ECT which proves that negative attitudes towards this therapeutic option are the result of false beliefs. Despite the fact that results with ECT are better in MDD, the patients and relatives more satisfied are those suffering of SMI.

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» NR5-073

A BIOPSYCHOSOCIAL APPROACH TO PAIN MANAGEMENT

Sunny Aslam M.D., Chris Faubel, MD, Adekola O. Alao, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to list basic treatment options for pain, including lifestyle, pharmacological and psychotherapy. Recognize evidence level for these treatment modalities. Be able to discuss biological, psychological and social contributions to treating pain.

SUMMARY:

Chronic pain effects up to 44% of adults in North America and involves significant financial and social costs. Pharmacologic interventions, such as non-steroidal anti-inflammatory drugs and opioids, are first line interventions. Medications are often partially effective for moderate to severe chronic pain, and have a plethora of side effects. A multidisciplinary approach is necessary for complicated pain syndromes. We reviewed the level of evidence for psychosocial techniques alone or in combination with pharmacological interventions in the treatment of pain. Exercise, biofeedback, relaxation techniques, various psychotherapies and other modalities used as pain reduction techniques were reviewed. The strongest evidence favors a comprehensive approach to pain management, particularly with Cognitive Behavioral Therapy (CBT). CBT improves mood, decreases pain, improves fatigue and sleeplessness, as well as increase physical functioning and stress management. CBT helps patients examine their maladaptive cognitions and behaviors and develop appropriate coping skills. Treatment of patients' co-morbid medical and psychiatric disorders is crucial to success in treating pain, as anxiety and depression have been shown to exacerbate pain syndromes. Combinations of education, Operant Behavioral Therapy (OBT), self hypnosis and exercise are techniques with evidence of efficacy. OBT uses conditioning of behaviors through positive and negative reinforcement. OBT and CBT focus on factors that exacerbate and maintain suffering in chronic pain. The strength of the alliance between patient and provider is associated with improvements in pain. The evidence for psychosocial interventions are similar to that of a pharmacological-only approach to pain. In conclusion, psychosocial treatments combined with pharmacotherapy are effective in treating chronic pain, and in particular, CBT. More research is needed to allow for more specific recommendations for various chronic pain syndromes.

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approaches to the management of chronic pain. Curr Opin Anaesthesiol. 2007 Oct;20(5):485-9.

» NR5-074

MAJOR DEPRESSIVE DISORDER AND THE RISK OF DEVELOPMENT OF TYPE II DIABETES

Faiz Cheema M.D., Amel Badr, M.D., Amin Shamal, M.D.,Summer Jaffrey, M.D., Nadia Khan, Mahboob Aslam, M.D., Asghar Hossain, M.D., Javed Iqbal, M.D.

EDUCATIONAL OBJECTIVES:

Recent studies have demonstrated that depression might constitute a major risk factor in the development of type II diabetes and may accelerate the onset of its complications (1). In this study we investigate the possible association between depression and impaired glucose tolerance with aim of increasing awareness of the importance of screening the fasting blood glucose in patients diagnosed with depression as a protective measure against type II diabetes and its consequences.

SUMMARY:

There has been a growing interest in depression as a novel risk factor for the development of type II diabetes. Possible proposed mechanisms include the influence of depressive symptoms on behaviors such as physical activity, diet and adherence to treatment recommendations. Another possibility is the influence of depression on the activity of hypothalamic-pituitary-adrenal axis and sympathetic nervous system. Hypercortisolism is a frequent endocrine sign in major depression and cortisole is a well known antiinsulinergic hormone (2). The goal of this study is to determine whether major depressive disorder is associated with impaired glucose tolerance and consequently predict the onset of type II diabetes.A retrospective chart review was done for patients admitted to Bergen Regional Medical Center with the diagnosis of major depressive disorder between January 2007 and December 2007. Data collected include demographic factors and axis III co morbidities. Patients with the diagnosis of Diabetes Mellitus, CAD and obesity were excluded. Fasting blood glucose levels were noted. Results showed that 21.12 % patients showed high fasting plasma glucose level of > 100 mg/dl and 13.93 % had fasting blood glucose between 90-99. We concluded that the major depressive disorder is associated with impaired glucose intolerance and signals the increased risk for the onset of type II diabetes. Physicians treating patients with depression must be vigilant to screen for and manage hyperglycemia as a protection against new onset diabetes. The possible neuroendocrine mediators of the stress–diabetes relationship require further evaluation in prospective cohort studies that uses an established tool to assess depression and incorporate neurohormonal measurements.

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» NR5-075

THE IMPORTANCE OF PSYCHOEDUCATION IN THE TREATMENT OF BIPOLAR DISORDER: AN ITALIAN EXPERIENCE.

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EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the significance of group's psychoeducation treatment.

SUMMARY:

INTRODUCTION: Psychoeducation in the treatment of Bipolar Disorder plays an important role especially in public health, where high numbers of patients and a few time available for visits makes often difficult the psycho-didactic work that psychiatrists have to carry out. The aim of our work is to show the significance of group's psychoeducation treatment, in order to support and integrate pharmacological treatment, to give patients suitable knowledge to make them fully conscious of illness.
METHODS: Our study was conducted on a sample of 62 subjects affected by Bipolar Disorder, diagnosed with DSM-IV TR. The experimental group, that had taken part in psychoeducation program, was composed of 31 subjects (25 females; 6 males). The control group was composed of 31 subjects (19 females; 12 males). The aim of our study is to compare a group of patient submitted to psychoeducation treatment with a control group and to underline final different results based on three variables: psychiatric visits number (index of compliance's degree), prescribed drugs number (pharmacological treatment type prescribed to the patient), hospitalizations average duration for psychiatric causes (pointer of relapses).
RESULTS: ANOVA has underlined significant differences (p = 0 , 05) about visits number (F = 5,431) and hospitalizations duration (F = 16,151) for patients who have taken part in the psychoeducation program. There is no significant difference about prescribed drugs number.
CONCLUSIONS: Overall results indicate that patients enrolled in the psychoeducation program had a greater and more regular frequency to follow up. This shows a greater compliance to treatment, without implement of care level, measured as adjunctive pharmacological treatment; another additional result is reduction in hospitalizations.

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» NR5-076

CLINICAL DECISION MAKING BIASES IN A GROUP OF MENTAL HEALTH PROVIDERS

Sarah A. Romeo, B.A., Kelly M. Sutton-Skinner, B.A., Timothy J. Petersen, Ph.D., Steven Sloman, Ph.D., Lee Baer, Ph.D., Jeff C. Huffman, M.D., Charissa F. Andreotti, Sc.B., John A. Fromson, M.D., Robert J. Birnbaum, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand two common clinical decision making biases and discuss the implications of these biases on clinical care.

SUMMARY:

PURPOSE: To evaluate, in a sample of mental health practitioners, the presence of clinical decision making biases.
CONTENT: Previous research suggests that medical professionals are susceptible to clinical decision making biases, which have the potential to negatively impact clinical care. In the field of psychiatry, little research has been conducted to evaluate the presence of such biases. The objective of this investigation was to evaluate, in a sample of mental health providers, the presence of two clinical decision making biases; hypothesis selection and pseudodiagnosticity.
METHOD: 265 (39% physicians; 48% female) providers, attending a psychopharmacology course, completed an instrument, created through a collaboration between Brown University and the

Massachusetts General Hospital Psychiatry Academy, designed to measure the presence of hypothesis selection and pseudodiagnosticity biases. Data analyses were conducted to evaluate two specific hypotheses: 1. Hypothesis selection: doctors will neglect alternative hypotheses during diagnosis, when reasoning from a disease to a symptom and 2. Pseudodiagnosticity: doctors preferentially select diagnostic information that is consistent with their initial hypothesis.
RESULTS: Results confirm that mental health practitioners exhibit the hypothesis selection bias, when reasoning from disease to symptom ($t=-4.914$, $df=129$, $p<0.001$). However, respondents to this instrument did not demonstrate the pseudodiagnosticity bias ($z= 3.82$, $p<0.001$); rather, they chose to obtain information that challenged their hypothesis.
CONCLUSIONS: In this sample of mental health practitioners, we found the presence of the hypothesis selection bias, which could result in sub-optimal clinical care. However, clinicians did choose information that would expand their diagnostic capabilities. Further research is needed to identify what decision making biases are most common in this population, and to formulate methods to address these biases.

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» NR5-077

PERFORMANCE DISPARITIES BY HEALTHCARE PROVIDER DISCIPLINE UTILIZING A PSYCHIATRIC CLINICAL CASE VIGNETTE

Kelly Sutton-Skinner B.A., Sarah A. Romeo, B.A., Robert J. Birnbaum, M.D., Ph.D., Timothy J. Petersen, Ph.D., Lee Baer, Ph.D., Jeff C. Huffman, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: 1. Understand differences among healthcare provider disciplines in baseline knowledge regarding a patient presenting with irritability. 2. Discuss the implications of these differences in the creation of psychiatry CME curricula.

SUMMARY:

PURPOSE: To compare, across different mental healthcare provider disciplines, diagnostic and treatment approaches endorsed in response to a clinical vignette of a patient presenting with irritability.
BACKGROUND: Live CME is the most common source of postgraduate education for healthcare providers. Within the field of psychiatry, educational events are often attended by a broad array of providers which may include psychiatrists, primary care physicians, psychologists, etc. Given this diversity, it is critical to ascertain knowledge gaps that may differ by specialty and inform curriculum design. The objective of this investigation was to compare, across mental health provider disciplines, responses to a series of key clinical decision points embedded in a case vignette of a patient presenting with irritability.
METHOD: Participants attended live CME symposia hosted by the Massachusetts General Hospital Psychiatry Academy in one of four cities. Prior to lectures, participants completed a vignette of a patient presenting with irritability; the case was accompanied by four open-ended questions on key decision-making points in the case. Responses were scored using a numerical system based on consensus practice guidelines. Analyses compared individual question and total scores across disciplines.
RESULTS: 192 attendees completed the vignette. Physicians, prescribers and psychiatrists significantly outperformed non-physicians, non-prescribers and non-psychiatrists, respectively, on three of the four questions and achieved higher overall scores ($p<0.01$). Only one question, regarding diagnostic workup, revealed no significant differences.
DISCUSSION: This study found significant discrepancies in baseline clinical performance among different healthcare disciplines. Given that curricula should be matched to learners' baseline level of knowledge, our results suggest the need to design discipline-specific CME curricula.

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» NR5-078

EFFECTIVENESS, SAFETY AND TOLERABILITY OF CLOMIPRAMINE AUGMENTATION OF SSRI IN TREATMENT-RESISTANT OBSESSIVE-COMPULSIVE DISORDER

Pino Alonso M.D., Jose M. Menchon, M.D., Ph.D., Cinto Segalàs, M.D., Javier Labad, M.D., Eva Real, M.D., Alberto Pertusa, M.D., Susana Jiménez-Murcia, Psy.D., Blanca Bueno, Psy.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to consider the different augmentation and switching pharmacological strategies for resistant obsessive-compulsive patients and specially to discern the benefits and risks of one of these strategies: the clomipramine augmentation of selective serotonin reuptake inhibitors (SSRI).

SUMMARY:

Combination of clomipramine and selective serotonin reuptake inhibitors (SSRI) constitutes a therapeutic strategy for resistant obsessive-compulsive patients although published data is scarce. We evaluated the effectiveness and tolerability of clomipramine augmentation of SSRI in a sample of resistant OCD patients.
Methods: Eighty-eight OCD out-patients (51 males/37 females), attending the OCD Clinic of Bellvitge Hospital (Barcelona, Spain) from 2000 to 2008 were included in the study. They were resistant to at least two SSRI and clomipramine in monotherapy; to one trial of SRI augmentation with antipsychotics and showed no response, reject or drop out from behavioral cognitive therapy. The Clinical Global Impression Scale (GCIi) was used to assess changes on OCD severity after twelve weeks of treatment. Side effects were assessed by the UKU scale.
Results: During the study, 165 combinations of clomipramine and SSRI were implemented and maintained for 18.3 months ± 19.3 (range: 3-96) (clomipramine + fluoxetine (n=46), clomipramine + fluvoxamine (n=50), clomipramine + paroxetine (n=13), clomipramine + citalopram (n=7), clomipramine + escitalopram (n=12) and clomipramine + sertraline (n=16). Thirty patients (34.0%) were considered much improved, twenty-three patients mildly improved (26.1%) and twelve (13.6%) lightly improved. Adverse effects included sexual dysfunction 25%, anticholinergic effects 44.3%, somnolence 42%, weight increase 23.9%, cognitive difficulties 9.1%, and tremor 5.68%, but only in 21 cases (12.7%) obliged to interrupt treatment. No cardiac significant adverse effect was detected. Five patients presented an epileptic complication (tonicoclonic seizures or myoclonic epilepsy) that responded to antiepileptic drugs.
Conclusion: The combination of clomipramine and SSRI appears to be an effective and well-tolerated strategy for highly resistant OCD patients. Neurological complications appeared in 3.0% of cases but could be pharmacological controlled.

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» NR5-079

TREATMENT OF MUTISM WITH ORAL OLANZAPINE, A CASE STUDY

Gregory Boyarsky M.D., Janay Fake, M.D., Robin Tassinari, M.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to diagnose mutism and be able to provide treatment of mutism with antipsychotics.

SUMMARY:

Patient is a 51-year old Caucasian female, seen at Albany Medical Center Hospital by Consultation-Liaison Psychiatry for mutism. Patient had numerous prior episodes of mutism, which had spontaneously resolved within a few days, per patient's family. This episode was prolonged (lasting 4 days), compared to her prior episodes (lasting 1-2 days). Patient was admitted to neurology service to rule out status epilepticus, and complex partial seizures (based on an abnormal EEG from another hospital). We were consulted to rule out conversion disorder, and to help manage patient's mutism. Patient presented with no spontaneous speech, (only uttering 'ouch' when pinched); she did make eye contact with people in room but gave no response, either verbal or with gestures to any question. Per family, patient presented this way numerous times in the past, but they worried about the length of nonresponse, which was uncharacteristic for her. Patient was started on a trial of low-dose antipsychotic, olanzapine 2.5 mg, by mouth at bedtime. Patient was seen daily. She became spontaneously verbal on day 2 after treatment, with some word finding difficulty and complete amnesia for the episode. Patient was discharged the next day, with continuation of the antipsychotic, and follow up with a psychiatrist. Differential diagnosis and treatment of mutism is presented. On literature review of akinetic mutism, there are case reports using intramuscular olanzapine (with rapid resolution of symptoms), but no prior studies using oral olanzapine. The authors have no disclosures of commercial support.

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» NR5-080

DO PERSONALITY TRAITS AFFECT SUBJECTIVE OUTCOMES FOLLOWING TOTAL KNEE ARTHROPLASTY?

Heather Church M.D., Raymond J. Walls, M.D., Kieran Hirpara, M.D., John M O'Byrne, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant will have learnt that patients with a greater BMI tend to be more content with their surgery, despite the presence of complications suggesting obese subjects have lower expectations from TKA. In addition, patients who were satisfied with their surgery are more open to experiences than those not satisfied.

SUMMARY:

Introduction: Pain and stiffness are uncommon complications of total knee arthroplasty (TKA) however disparity exists in terms of patient satisfaction should either occur after surgery. Several personality dimensions have been described which may affect subjective outcomes seen following TKA.
Aims: The purpose of this study is to determine if personality traits can influence patient outcomes following TKA.
Methods: Patients who underwent TKA between January and June 2007 were identified from the joint registry with documentation of body mass index (BMI) and pre and post-operative subjective outcome scores (WOMAC, SF36). A telephone-administered personality questionnaire (TIPI) determined the strength of specific character traits (extraversion, agreeableness, conscientiousness, emotional stability, and openness to experiences).
Results: There were 121 eligible patients (124 primary TKA's) of which 110 were recruited. Patients were classified into three groups: satisfied with no complications (SN; n=74), satisfied with complications (SC; n=21), and unsatisfied (U; n=15). The SC group had a significantly greater BMI than the U group ($p<0.05$). All groups had significant improvement in WOMAC scores ($p<0.005$) however only the SN and SC groups had improvement in SF-36. There was a significant difference between the SC and U groups in terms of "openness to experiences" ($p<0.05$) with the SC group scoring higher. Between the satisfied groups, there was a trend in the SC group towards greater "extroversion" ($p=0.058$) and "openness to experiences" ($p=0.055$).
Conclusions: This study suggests that patients with greater BMI's are more likely to be satisfied with their TKA despite the development of postoperative knee pain/stiffness. Satisfied patients are more open to experiences than unsatisfied patients and more extrovert than patients with no complications.

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» NR5-081

DEPRESSION, ANXIETY AND QUALITY OF LIFE IN HEMODIALYSIS PATIENTS

Seyeon Lee M.D., Jong-Hyun Jeong, M.D., Seung-Chul Hong, M.D., Jin-Hee Han, M.D., Sung-Pil Lee, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant could realize the significance of psychiatric problems in hemodialysis patients and should be able to demonstrate the factors have impacts on quality of life of hemodialysis patients.

SUMMARY:

Objective: Depression and anxiety are the most common psychiatric illness in hemodialysis(HD) patients, and can have negative impact on quality of life(QoL). We aimed to assess QoL status among chronic HD patients compared with normal controls and to research various influencing factors on QoL, taking into account psychological and social aspects.
Method: Data were collected from 92 HD patients(52 male, 40 female) in a university hospital in Korea. We enrolled 71 healthy controls matched by age and sex(30 male, 41 female). WHO-QoL, Beck Depression Inventory(BDI), State and Trait Anxiety Inventory(STAI), Toronto Alexithymic Scale(TAS) and Stress Response Inventory(SRI) were performed.
Results: 1) The study was performed with 92 HD patients, whose mean age was 52.7±13.3 years(range 21~81). They had been receiving HD for an average of 62.6±94.5 months before the study. The average body mass index was measured as 21.7±2.8 and 35 patients(38%) had diabetes mellitus.
2) In WHOQoL, we found HD patients had significantly lower scores in all the assessed domain compared with controls($p<0.001$) as well as in overall QoL(69.4±14.5 vs. 82.1±10.0, $p<0.001$).
3) State anxiety scores of HD patients were higher(39.7±6.2 vs.

30.1±7.1, p=0.026) than controls, whereas Trait anxiety scores have shown no differences between the two groups(40.6±7.1 vs. 39.4±6.9, p=0.26).
4) All other scores regarding psychological problems were significantly higher in HD patients compared with controls.
5) In correlation analysis, overall QoL score have shown positive correlation with educational year(r=0.225, p=0.032) and negative correlation with BDI(r=-0.668, p<0.001), Trait anxiety scores(r=-0.382, p<0.001), STAI(r=-0.255, p=0.017), TAS(r=-0.263, p=0.015) and SRI(r=-0.615, p<0.001).
Conclusions: QoL in HD patients was lower than in age-matched controls. Among assessed factors, we found depression, anxiety as traits not as states, and high educational level to be associated lower QoL scores.

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» NR5-082

PARTIALLY REVERSIBLE DEMENTIA ASSOCIATED WITH NAPHTHALINE ABUSE IN A CASE OF A THIRTY TWO YEAR OLD FEMALE PATIENT.

Victoria Passov M.D., James R. Rundell, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation the participant should be able to recognize the main neuropsychiatric outcomes of chronic naphthalene use as well as the potential for reversibility of some of them in the context of complete abstinence. Naphthalene's toxicity has been previously described in relation to acute exposure (1, 2) but this case represents consequences of long term use.

SUMMARY:

A 32 year-old African-American female was seen by the Psychiatry and Psychology Assessment Service at Mayo Clinic, Rochester Minnesota. At the age of twenty seven, she began sniffing naphthalene balls and soon started ingesting them and would usually swallow one moth ball per day. The patient reported no euphoria from the substance, but it had a calming effect on her. The choice of this particular substance was related to significant exposure to mothballs in her house during her childhood. In February 2008 the patient was brought to the clinic by her husband with symptoms of loss of memory, slurred speech, dry skin, and catatonia. She was wheelchair-bound, and was unable to talk. The patient required inpatient treatment on the medical floor and was diagnosed with encephalopathy. Following this event, she decided to discontinue the use of naphthalene and became sober by May 2008. At that point she admitted naphthalene use to her providers and was ultimately diagnosed with leukoencephalopathy due to chronic naphthalene use. Three months after the discontinuation of substance use the patient's symptoms improved. In August 2008, she still had significant lethargy, slurred speech, cognitive impairment, and diffuse weakness. She was seen at that time in psychiatric consultation; her Montreal Cognitive Assessment (MOCA) score was 17. Aside from significant impairment of her short term memory, she demonstrated decline in visuospatial and executive functions, which resolved by October 2008. Re-evaluation at that time revealed her MOCA score was 21. The patient was also able to walk again and her speech improved quite dramatically over Fall 2008. The short term memory deficits seem to be more permanent, although further assessments will be conducted. This case report illustrates a number of specific neuropsychiatric consequences of chronic naphthalene ingestion and highlights the potential for reversibility of many of the effects with discontinuation.

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» NR5-083

A COMPARISON OF LOW VS. HIGH UTILIZERS OF SERVICES IN AN URBAN PSYCHIATRIC EMERGENCY SERVICE

Guillermo Portillo M.D., Barbara Sparacino, M.D., William R. Dubin, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify characteristics of patients with frequent visits to the psychiatric emergency service. The participant should be able to appreciate the impact of symptomatic chronic mental illness on PES high utilizers.

SUMMARY:

OBJECTIVE: This study examined the differences in clinical characteristics and socioeconomic demographics between patients who are low utilizers (2 visits in a year) versus high utilizers (7 or more visits) of a Psychiatric Emergency Service (PES). Our goal was to gain a better understanding of the factors that lead to high utilization.
METHODS: One hundred thirty-four patients were equally divided into two groups composed of patients who visited the PES over a 12 month period. The patients were matched for age, sex and race. Based on the current literature, high utilizers were defined as those who visited seven or more times.
RESULTS: In contrast to low utilizers who visited the PES only twice, high utilizers averaged 10 visits to our PES and 3.8 additional visits to other PESs in the city. High utilizers were more likely to have auditory hallucinations, delusions and express homicidal ideation when compared to patients who only visited twice. A significantly higher number of high utilizers were medicated with antipsychotic medication in the PES. High utilizers were more likely to report being physically abused and were less likely to have intensive case managers. High utilizers were more likely to be unemployed and using government financial assistance. There was no significant difference in suicidal ideation or illicit drug use as measured by a urine drug screen.
CONCLUSION: Clinical characteristics and socioeconomic demographics are important in identifying patients who may be at an increased risk for high frequency utilization of a PES. High utilizers generally exhibited more severe mental illness and received less intensive case management. These findings illustrate the need to avoid dismissing or providing these patients cursory treatment given their severe level of psychopathology. Our findings suggest that high utilizers use the PES as a sanctuary for shelter and for primary psychiatric services.

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» NR5-084

METABOLIC SYNDROME AWARENESS IN BIPOLAR AND SCHIZOPHRENIC PATIENTS AND PHARMACOTHERAPY IMPACT QUESTIONNAIRE: A VENEZUELAN PSYCHIATRISTS REALITY

Gustavo Resler M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize the Venezuelan psychiatrists awereness on metabolic syndrome in bipolar and schizophrenic patients

SUMMARY:
Objective: This study was conducted to assess psychiatrists knowledge on metabolic syndrome (MS) and its components and also to evaluate their perceived antipsychotic adverse effects on metabolism of bipolar and schizophrenic patients.
Method: A cross-sectional study was performed among a random sample of Venezuelan psychiatrists active in clinical practice. They were encouraged to fill-out a questionnaire with closed options about clinical components of MS, opinions about the relation between antipsychotics and MS and interventions to modify this illness. Results were tabulated using Microsoft Office Excel 2003.
Results: A total of 182 Venezuelan psychiatrists completed the questionnaire. Most of the interviewed (98.35%), known what MS is, but only 11.54% have ever made a diagnosis. These results are corroborated with a poor performance of the physicians recognizing part or mostly all of clinical criteria for this diagnosis (media of 56.25%). At the same time, only 10.44% always made MS research on their bipolar or schizophrenic patients, 2.75% measures blood pressure routinely, 21.43% and 17.58% respectively advise to their patients with MS to changes their nutritional habits and increase overall activity. The questionnaire also shown the psychiatrists metabolic concerns about some antipsychotics, were olanzapine is the most frequently associated with adverse effects, followed by quetiapine and risperidone. The antipsychotic mostly associated with MS is olanzapine and the rarely associated are aripiprazole and haloperidol.
Conclusions: In our Country mostly all psychiatrists are aware on MS, but only a few made clinical efforts to research and diagnose this clinical condition. This study confirm that mentally ill patients often do not receive adequate recognition, monitoring or caring of their medical illnesses and we need to increase our professional skills to detect and to manage metabolic diseases among bipolar and schizophrenic patients.

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» NR5-085

HOMOCYSTEINE AND CHOLESTEROL LEVELS AND TYPES A/B AND D PERSONALITY IN PATIENTS WITH RECURRENT DEPRESSIVE DISORDER, BIPOLAR DISORDER, SCHIZOPHRENIA

Radmila Topic M.D., Ivona Markelic, Bjanka Vuksan-Cusa M.D., Darko Marcinko Ph.D., Miro Jakovljevic Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to have better insight into use of homocysteine and cholesterol levels in psychiatric patients with regards to evaluation of cardiovascular risks and rational choices of drug treatment.

SUMMARY:
Background: Recurrent major depression (RMD), bipolar disorder (BD), schizophrenia (SCH) and post-traumatic stress disorder (PTSD) are very often associated with coronary heart disease and other cardiovascular disorders. Hyperhomocysteinemia and hypercholesterolemia are risk factors for CHD. Relatively high plasma homocysteine and cholesterol levels have been reported in patients with SCH, BD and RMD. Personality types A and D are associated with CHD. Subjects and methods. One hundred sixty patients with RMD, BD, SCH or PTSD and 40 healthy controls were assessed for serum levels of homocysteine and cholesterol as well as for features of A/B and D personality.
Results: We found that patients with RMD, BD, SCH and PTSD had higher homocysteine and cholesterol levels than a comparison healthy group. Among psychiatric patients type A was found to be more frequent in patients with BD. Type D was more frequent in patients with SCH and RMD. Social inhibition score was significantly higher in patients with SCH in comparison with patients with RMD, while negative affectivity score was similar in both groups. Higher plasma homocysteine and cholesterol levels were found in males with SCH, RMD and BD. Some interesting correlations between serum homocysteine and cholesterol levels, personality types and clinical features of SCH, RMD, and BD were observed, particularly with regards to cardiovascular comorbidity.
Conclusion: Serum homocysteine and cholesterol levels may be useful parameters in psychiatric patients from clinical point of view, although hyperhomocysteinemia and hypercholesterolemia were not specific for any psychiatric diagnosis in our sample.

REFERENCES:
1) Jakovljevic M, Reiner Z, Milicic D. Psychiatr Danub. 2007 Dec;19(4):270-81. Review. Mental disorders, treatment response, mortality and serum cholesterol: a new holistic look at old data.

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» NR5-086

HOMOCYSTEINE AND CHOLESTEROL LEVELS AND TYPES A/B AND D PERSONALITY IN PSYCHIATRIC PATIENTS WITH AND WITHOUT CARDIOVASCULAR DISORDERS

Radmila Topic M.D., Ivona Markelic, Bjanka Vuksan-Cusa M.D., Darko Marcinko Ph.D., Miro Jakovljevic Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to have better insight into use of homocysteine and cholesterol levels in psychiatric patients with regards to evaluation of cardiovascular risks and rational choices of drug treatment.

SUMMARY:
Background: Recurrent major depression (RMD), bipolar disorder (BD), schizophrenia (SCH) and post-traumatic stress disorder (PTSD) are very often associated with coronary heart disease and other cardiovascular disorders. Hyperhomocysteinemia and hypercholesterolemia are risk factors for CHD. Relatively high plasma homocysteine and cholesterol levels have been reported in patients with SCH, BD and RMD. Personality types A and D are associated with CHD.
Subjects and methods. One hundred sixty patients with RMD, BD, SCH or PTSD and 40 healthy controls were assessed for serum levels of homocysteine and cholesterol as well as for features of A/B and D personality.
Results: We found that patients with RMD, BD, SCH and PTSD had higher homocysteine and cholesterol levels than a comparison healthy group. Among psychiatric patients type A was found to be more frequent in patients with BD. Type D was more frequent in patients with SCH and RMD. Social inhibition score was significantly higher in patients with SCH in comparison with patients with RMD, while negative affectivity score was similar in both groups. Higher plasma homocysteine and cholesterol levels were found in males with SCH, RMD and BD. Some interesting correlations between serum homocysteine and cholesterol levels, personality types and clinical features of SCH, RMD, and BD were observed, particularly with regards to cardiovascular comorbidity.
Conclusion: Serum homocysteine and cholesterol levels may be useful parameters in psychiatric patients from clinical point of view, although hyperhomocysteinemia and hypercholesterolemia

were not specific for any psychiatric diagnosis in our sample.

REFERENCES:

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» NR5-087

PERCEPTIONS OF MENTAL HEALTH DISORDERS IN AMERICAN MUSLIM WOMEN

Rania Awaad M.D., Natalie Rasgon, M.D., Ph.D, Heather Kenna, M.S.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to better understand the barriers faced by American Muslim women in seeking mental health care. The participants will also learn the effect certain beliefs inherent to the Islamic faith may have on perceptions of mental health disorders held by American Muslim women.

SUMMARY:

Objective: This study investigated perceptions towards mental health care and barriers from seeking adequate care in American Muslim women.

Method: The study group consisted of 1,279 women who self-identified themselves as American Muslim women via a web-based survey. This survey was comprised of a 41 question psychometric scale created by the authors and was adapted from the following instruments: Orientations to seeking Professional Help (Fisher and Turner, 1990), Cultural Beliefs about Mental Health Problems, their Causes and Treatments (Aloud, 2003), Knowledge and Familiarity with Formal Mental Health Services Instrument (Aloud, 2003). These instruments were then tailored to address the religious beliefs of this population.

Results: Preliminary analysis showed a significant relationship between age and levels of religiosity as well as between belief in certain Islamic concepts such as the "evil eye", "spirits", fate and the reluctance to seek mental health care.

Conclusions: These findings suggest that a large proportion of American Muslim women view mental health illnesses as a spiritual deficit as opposed to a medical condition; an outlook which may contribute to the lack of adequate mental health care sought by this population. We recommend that mental health professionals spend more time finding out about clients' religious beliefs, carefully explaining diagnoses and treatments, listening to, and when possible, facilitating religious views on mental health issues in order to form a therapeutic alliance with this population.

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» NR5-088

SPIRITUALITY AND SUICIDE: RESULTS FROM THE NATIONAL COMORBIDITY SURVEY REPLICATION

Erica Smith M.D., Erick Messias, MD, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to (1) understand the associations between spirituality and suicidal ideation and (2) learn about the negative association between spirituality and history of suicide attempts.

SUMMARY:

Objectives: In recent years there has been increasing interest in examining how spirituality may affect mental health. We studied how spirituality affects history of suicidal ideation and attempts. Large population-based samples are useful as they tend to eliminate sources of biases and test hypotheses. Methods: The National Comorbidity Survey Replication (NCS-R) is a probability sample of the US population designed to constitute a nationally representative sample (N = 9,882). In the suicidality section subjects were asked "Have you ever seriously thought of committing suicide?"; those who responded yes were asked a follow-up question "Ever attempted suicide?". Spirituality was measured as a sum of four Likert items, such as "how important are religious or spiritual beliefs in your daily life?" The higher the sum, the more spiritual the person was classified. Results: Spirituality score varied from 4 to 16 (mean=8.4, S.D. 3.2, skewness .48). Chi square tests comparing prevalence of suicide ideation across the spirituality score were not significant (17.6, d.f.=12, p=.126), while there was a significant difference across the spirituality score in the prevalence of history of suicide attempts (30.5, d.f.=12, p=.002). Logistic regression models confirmed this pattern, with the spirituality score holding a strong negative association with attempts (p=.01), and a weak association with suicidal ideation (p=.04). Conclusions: In a population based study, no difference was found with respect to suicidal ideation between those with a high level of spirituality and those with a low level. However, those with a higher spirituality score showed a statistically significant decrease in history of suicide attempts. This suggests that possessing a high level of spirituality may be protective against attempting suicide. However, it does not appear to convey protection against suicidal ideation.

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1) Rasic DT, Belik SL, Elias B, Katz LY, Enns M, Sareen J; Swampy Cree Suicide Prevention Team. Spirituality, religion and suicidal behavior in a nationally representative sample. J Affect Disord. 2008 Sep 15.

2) Colucci E, Martin G. Religion and spirituality along the suicidal path. Suicide Life Threat Behav. 2008 Apr;38(2):229-44. Review.

» NR5-089

CORRELATES OF FATIGUE IN MEDICAL RESIDENTS: LOOKING BEYOND SLEEP DEPRIVATION

Kanwar Ajit Sidhu M.D., Cristian Sirbu, Ph.D., Veena Bhanot, M.D.,John Linton, Ph.D., Mary Emmett, Ph.D., T.O. Dickey, M.D., Martin Kommor, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand that fatigue in residents is a complex phenomenon influenced by multiple factors in addition to sleep deprivation. The presentation will emphasize the relevance of resident's working conditions, workload, emotional well-being and family responsibilities as additional correlates of fatigue. The complex interaction of these factors needs to be understood and addressed for optimal learning and functioning of the reside

SUMMARY:

Introduction:Studies conducted after the implementation of ACGME work hour requirements aimed at reducing sleep deprivation indicate that fatigue continues to be an important challenge for residents.

Aims/Objectives:To determine the relationships among fatigue and residency work environment (i.e. conflict, workload, supervision), family factors (i.e. caring for own children), burnout, anxiety, and depression after controlling for chronic sleep deprivation.

Method/Design:Cross-sectional, anonymous survey of 139 residents in nine specialties at a community teaching hospital in Southern West Virginia using validated measures of fatigue, anxiety, depression (Profile of Mood States), burnout (Maslach Burnout Inventory-Human Services Survey), resident work and family environment, and sleep quantity. Chronic sleep deprivation was defined as < 42 hrs of sleep in the prior week (< 6 hrs/night). Burnout was defined as a score >27 on the Emotional Exhaustion

or a score >10 on the Depersonalization subscales of Maslach Inventory.
Results:A total of 110 residents completed all the measures (79% response rate). The average age was 30.7 years (SD=5.28), 60 residents (54%) were male and 44 (40%) had children. Chronic sleep deprivation was reported by 51% (n=56) and burnout by 39% (n=43) of the residents. Two hierarchical linear regression analyses were conducted to investigate after controlling for sleep deprivation: (1) individual factors (burnout, tension, and depression) and (2) environmental factors (work and family) associated with fatigue. (1) In the first analysis, sleep deprivation alone explained 7% of the variance, while individual factors explained 39% of the variance in fatigue [tension (18%), burnout (16%) and depression (5%)]. (2) In the second analysis, sleep deprivation alone explained 10% of the variance while work and family factors explained 28% of the variance in fatigue [hostility/conflict in the work environment (11%), caring for own children (9%), workload (5%), lack of supervision (3%)].
Conclusions:This study identified factors with additive value for predicting fatigue beyond sleep deprivation alone. The development of programs targeting these factors at both individual and organizational levels might provide important avenues for reducing residents' fatigue.

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» NR5-090

DEPRESSION IN INTERNS: USE OF MENTAL HEALTH SERVICES AND BARRIERS TO USE

Heather Speller, Constance Guille, M.D., C. Neill Epperson, M.D., Srijan Sen, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the current treatment rates for depression in interns, and demonstrate an understanding of the major barriers to mental health service utilization facing interns today.

SUMMARY:

BACKGROUND: Internship is a time of high stress, and elevated levels of depression among interns have been reported for decades. However, little is known about the use of mental health services among depressed interns and the barriers to use.
OBJECTIVES: To determine the rate of mental health service utilization among interns with depression, and to describe the perceived barriers to mental health treatment among interns.
METHODS: Interns from residency programs at six U.S. academic medical centers completed an anonymous online questionnaire prior to the start of internship, with follow-up at 3-month intervals throughout the year. At each time point, depressive symptoms were measured using the Patient Health Questionnaire, and mental health service utilization was assessed based on self-reported use of counseling, psychotherapy, and/or psychotropic medications.
RESULTS: 241 of 398 invited interns (61%) agreed to participate in the study. Of the 32% of interns who screened positive for depression at least once during intern year, only 13% of them reported using mental health services. The greatest perceived barriers to treatment among interns were time (80.2%) and a preference to manage problems on one's own (78.4%). Compared to interns without a positive depression screen, interns who were depressed at least once during the year were more likely to be concerned about what others would think (43.7% vs 20.5%, p=.006), and more likely to believe that their colleagues would have less confidence in them (39.1% vs 15.5%, p=.001).
CONCLUSIONS: The vast majority of interns with depression are not receiving treatment. Major barriers include time, a preference to manage problems on one's own, and a fear of stigmatization. Further efforts are needed to provide depressed interns with more effective mental health services.

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» NR5-091

PROJECT ANTI-BULLY: BULLYING IN MIDDLE SCHOOLS YEAR TWO SURVEY

Fabianna Pergolizzi

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to •Describe actions that constitute bullying, including cyberbullying in middle schools;•Understand the extent, and different types of, bullying within a culture of meanness; •Describe actions to resist bullying; and •Recognize the gender differences that exist related to bullying.

SUMMARY:

Background. In 2006, Project Anti-bully started a project to determine the prevalence of bullying in middle schools. Although bullying and victimization in the United States are first identified in elementary school, the problem becomes particularly acute, in terms of frequency and severity, in early adolescence. Yet our knowledge of bullies and victims and their peer affiliations during this period is limited. This poster presents the results of the 2007 surveys and their comparison to the first year's surveys. Anti-bullying legislation mandates anti-bullying education, the content for which will be based on surveys such as the one presented in this paper.
Methodology. 7th-8th graders at 5 schools (Naples, FL; Miami Beach, FL, Palo Alto, CA (2 schools); Durham, NC) responded to 14 Child Abuse Prevention Services Survey items.
Results. 631 surveys were analyzed. In 2006, about half of respondents reported that they, personally, had never been bullied in school. That number dropped in 2007 for both boys and girls. However, the majority of respondents in both 2006 and 2007 found bullying was a problem at their school, and females found bullying more of a problem in 2007 than 2006 ($p<0.001$). When asked how safe children felt in school, most respondents found it was "safe" or "very safe," with boys finding rating school significantly more in the category "very unsafe" in 2007 than 2006 ($p=0.042$). Boys and girls differed in how they dealt with bullies. The main tactic used by girls in both 2006 and 2007 was to ignore the bully, closely followed by doing nothing. Boys were more likely to hit or push a bully in 2006 and 2007 (nearly unchanged) followed by ignoring the bully. Relatively few children of both genders asked for help from a friend or adult, but girls were more likely than boys to request help from their friends. However, when a child observed someone else being bullied, boys and girls had similar reactions with the vast majority reporting that they did nothing, followed by telling the bully to stop or talking to the victim. Far fewer observers of bullying behavior reported that they summoned help from a friend or adult. The majority of respondents did not report ever having been cyberbullied and there was no significant difference in cyberbullying scores year over year. Compared to the result of the 2006 surveys, there was an increase in bullying observed at school ($p<0.05$), bullying was more of a problem for females ($p<0.001$).

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» NR5-092

IS CHILDHOOD PSYCHOPATHOLOGY PREDICT TO INTERNALIZING PROBLEM IN ADOLESCENCE : A 8-YEAR POPULATION-BASED FOLLOW-UP STUDY IN KOREA

Yunmi Shin M.D., Sun-Mi Cho, Ph.D., Hey Young Kang, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the importance of the early screening and intervention about the emotional, behavioral disturbance in childhood.

SUMMARY:

Objectives: In a recent review of the relevant evidence from epidemiological, community-based studies, that internalizing disorders in early life consistently predict internalizing problems in later life. Studies concerning the links between child and adult psychopathology are of importance both from the theoretical and clinical point of view. Many studies have shown that rates of depressive symptoms increase in early adolescence. It examined which childhood psychopathology predicted the development of a depressive symptoms in adolescent most accurately.
Methods: The present study is part of an ongoing longitudinal study that started in 1998-2000 in the Osan city of Korea. After the first measurement (1998-2000, time 1), the sample was approached again in 2006 (time 2) Instruments: Child Behavior Checklist, YSR, Child Depression Inventory, Internet Addiction Scale.
Results: The follow-up sample included 1899 adolescent. Childhood immaturity, thought problem predicted internalizing problem in adolescence (14-16 years)
Conclusions: This study shows that childhood thought problem, immaturity present a high risk for development internalizing problem in adolescence. Efforts to prevent psychiatric disturbance in early life are emphasized. The use of screening methods in school health settings to detect children in need of child mental health services is justified.

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1) Caspi, A., Moffitt, T. E., Newman, D. L., & Silva, P. A. (1996). Behavioral observations at age 3 years predict adult psychiatric disorders. Longitudinal evidence from a birth cohort. Arch Gen Psychiatry, 53(11), 1033-1039.

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» NR5-093

WHY PATIENTS MISS APPOINTMENTS: BARRIERS TO MENTAL HEALTH TREATMENT ENGAGEMENT AMONG A VETERAN POPULATION

Lauren Gerlach B.S., Shahrzad Mavandadi, Ph.D., David Oslin, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify potential barriers to mental health treatment engagement. This session should help the participant recognize common causes of treatment disengagement and promote ideas on how to reengage patients in care.

SUMMARY:

Engagement in mental health care is low with studies suggesting that one-third of patients miss their initial scheduled appointments. The goal of this study is to evaluate potential predictors of mental health treatment engagement and determine health care utilization of patients who miss initial appointments. We performed a prospective cohort study at an urban Veteran Affairs out-patient mental health clinic. A consecutive sample of adults who were scheduled for an initial mental health intake appointment 5 days/wk, over a 4-month period in 2006 were identified for the study. Medical chart reviews provided information regarding demographics, clinical data, and hospital utilization for 2 years before and after the initial appointment date. A subset of subjects who missed their initial appointment were interviewed and asked to report on their perceived barriers to engaging in mental health treatment. Logistic regression analysis was performed to determine potential predictors of treatment engagement and the association of missed appointments on health care utilization. A total of 422 patients were identified (91% male, 66% African American, mean age 54 yrs). Of these patients 35% missed their initial intake evaluation. Five predictors of treatment engagement were found to be significant: mania diagnosis, drug use, at risk drinking status, smoking, and social support. No association between engagement and subsequent ER use or hospitalization was found. Among those patients that missed their initial intake appointment the most commonly reported barriers included forgetting about the appointment (56%), desire for autonomy in solving problems (22%), and denial of problems (14%). Clinical factors surrounding health behaviors and social support appear to be associated with mental health treatment engagement while no association between engagement and subsequent health care utilization was demonstrated.

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» NR5-094

WHAT DO PATIENTS WANT TO KNOW? AN UPDATED ANALYSIS OF THE QUESTIONS POSTED BY USERS OF AN INTERNET-BASED INFORMATION SERVICE ON MENTAL DISORDERS

Antonio Nascimento M.D., Joao A. Carvalho MD, PhD;Marco A. Brasil MD, PhD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify patient's and their relative's specific needs for information based on diagnosis, age and/or sex of the patient. The participant should also be able to list a series of resources available on the internet to help patients gather information on their disorders, the treatments and their rights.

SUMMARY:

Introduction: Over the last decade, several databases on health topics (both focused on professional and patient information) have become available over the internet. Mental disorders are the health topics which generate most of internet searches for information. In spite of the widespread use of the internet to obtain information on health topics, few studies have addressed the patients need for information and their satisfaction with the information services available.
Objective: to analyse the demands of the users of an internet based psychiatric information service on the disorders which generate most questions and on the demands about each diagnosis.
Methods: Questions sent to the ABP Comunidade service over a one year period have been classified according to the user's data (sex, place of living among others), the mental disorder it was related to and on the demand of the user.
Results: 66,6% of the questions were asked by women and 33,3%,

by men. 20% of the questions were sent by patients and 23,3%, by relatives. The mental disorders which generated most questions were: Bipolar Mood Disorder (13,3%), Depression (10%), Addiction (8,3%), Panic Disorder (5%) and Schizophrenia (5%). The demands on each subject (requests for indication of an institution for treatment; information on incidence, evolution and treatment or indication of literature on the subject) were then separated accordingly to diagnosis, in order to provide the clinician information on which topics should be mentioned to each group of patients.
Results: The internet might be an efficient mean to provide information on health topics. More studies are needed to evaluate if the information is adequate for the patients' needs.

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2) Powell J, Clarke A. The WWW of the World Wide Web: Who, What, and Why? J Med Internet Res. 2002 Jan-Mar;4(1):e5

» NR5-095

CORRELATES OF SELF-STIGMA AMONG CONSUMER FAMILY MEMBERS

Deborah Perlick, Ph.D., Ann Nelson, BSN, Silvia Corbera, Ph.D., Jennifer Edidin, M.A., Lisa Costello, B.A., Masai McIntosh, B.A., Victoria Adzhiashvili, B.A., Jim Seltzer, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: understand the concepts of public & self stigma & how they relate to consumer family members, recognize how both types of stigma negatively affect the efficacy & well being of caregivers to those with schizophrenia, list the negative effects as well as state proposed methods of coping, & recognize aspects of the "self-stigma" scale development, which measures the degree to which caregivers stigmatize themselves.

SUMMARY:

Purpose: Mental illness stigma is associated with adverse outcomes for consumers; less is known about its impact on consumer families. We evaluated associations between perceived stigma, coping, and distress reported by caregivers of persons diagnosed with schizophrenia. Methods: This study reports baseline data from a collaboration with NAMI to develop a stigma reduction program for families. Participants were 82 primary caregivers of consumers admitted to Hartford Hospitals' psychiatric programs from 5-11/08 carrying a chart diagnosis of schizophrenia. Stigma measures reflected Corrigan's (2004) model: Public stigma towards families was assessed by Struening et al.'s (2001) "most people" items a= .78; the self-stigma scale modified these items to indicate self-concurrence, e.g., "I sometimes feel I am to blame for my relative's mental illness" a= .78. Results: Public and self-stigma scales were not significantly correlated (r=.10). Self-stigma was positively associated with depression and anxiety on the C-ESD and BSI and with ruminative response style (RSS), and negatively associated with social support (SS) on the Abbreviated Duke scale: p's < .007. None of these variables was significantly associated with public stigma. Hierarchical MR found that anxiety and depression were uniquely associated with self-stigma (DV), controlling for caregiver age and gender; after introduction of SS and RSS, both significant, the associations between anxiety and depression and self-stigma were no longer significant, suggesting SS and RSS may mediate the relationship between distress symptoms and self-stigma among caregivers (adjusted R^2 for model=.347). Significance: Internalization of negative views of society towards family members of people with schizophrenia is associated with symptoms of anxiety and depression that are exacerbated by rumination and reduced by social support; clinicians should offer or direct family members to support groups such as NAMI.

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» NR5-096

BEHAVIORAL PATTERN, PHYSICAL APPEARANCE AND PSYCHIATRIC ILLNESS ASSOCIATED WITH CHILDREN WHO ARE A PART OF A NEW EMOTIONAL GROUP CALLED "EMO-CULT"

Lorerky Ramirez Moya M.D., Gulam A.Noorani M.D.,M.P.H

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation the participant should be able to recognize the behavioral pattern and appearance of children who are a part of a new group called "Emo-cult".

SUMMARY:

The origin of the word "emo" is unclear. In the 1980's, members of a famous band noted that some of their fans in DC were starting to call them "emo", arguably because of the state of emotion that the band displayed during their shows. In later years, the word emo was viewed as a contraction of "emotional hardcore" or "emocore", which was the popular designation of the music genre. With the increase in number of children being diagnosed with psychiatric illness, a new culture of children and teenagers is arising. "EMO" is the password of emotional disturbed youngster in middle schools and high school in USA and other parts of the world. They are becoming a part of a cult where self mutilation, bisexuality, black cloths and specific hair cut are part the main characteristics. According to Freud, during the latency stage identification is one the most important factors and there is a speculation that it is this stage when children tend to be more vulnerable to identity crisis. In the past, children with mental illness were isolated and having a mental illness or taking psychotropic medications was considered a shame. Today the same is a part of being popular group at school. Children who do not have a psychiatric illness are trying to mimic role of a psychiatric patient to be a part of this cult. There is an urgent need for the Child Psychiatrists and therapists to recognize this new cult and intervene with treatment strategies and utilize the resources at school and home. This intervention will prevent the spread of this behavior in the vulnerable patient population. Special education and preventive strategies need to be implemented with help of School authorities to prevent the spread of this dangerous behavior.

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» NR5-097

SUICIDE ATTEMPTS ARE ASSOCIATED WITH WORSE QUALITY OF LIFE IN PATIENTS WITH BIPOLAR DISORDER

Lena Abreu M.D., Fabiano G. Nery, M.D., Karla Mathias Almeida, M.D. Bernardo Carramao Gomes, Maria A. Oquendo, M.D., Beny Lafer, M.D, PhD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the relationship between suicide attempts and quality of life in bipolar disorder. Also, participants will be able to use quality of life as an outcome measure in bipolar disorder.

SUMMARY:

Objective:To investigate the relationship between QoL and suicide attempts in patients with bipolar disorder (BD). We hypothesized that BD patients with history of suicide attempts would present worse QoL compared to BD patients without suicide attempts. Materials and Methods: This study is a cross-sectional survey of 108 DSM-IV BD patients consecutively recruited between 2006 and 2008 at the Bipolar Disorder Research Program, a tertiary care center at University of São Paulo Medical School, São Paulo, Brazil. Patients were divided in two groups: attempters (n=44; mean age 38.53 ± 10.25; males: 25% and females 75%) and nonattempters (n=64; mean age: 43.31 ± 12.63; males: 39.1% and females 60.9%), according to the presence of previous suicide attempts. We administered SCID I (Structured Clinical Interview for DSM-IV) for clinical diagnosis. The Hamilton Depression Rating Scale- 17 items and the Young Mania Rating Scale were used to rate depressive and manic symptoms. Columbia Suicide History Form was used to assess suicide behavior. QoL was considered our primary outcome measure and was assessed with the World Health Organization's Quality of Life Instrument-Short Version (WHOQOL-Bref). Results: Attempters had worse QoL in all domains of the WHOQOL-Bref in comparison with nonattempters (physical domain, p=0.001; psychological domain, p<0.001, social domain, p=0.002 and environmental domain, p=0.029). Even after controlling for depressed state, euthymic patients with suicide attempts had lower scores on the physical(p= 0.038), psychological (p=0.018) and social domains (p=0.007).Conclusion: We found that BD patients with history of suicide attempts have worse QoL in all domains of the WHOQOL-brief scale, and this association is present even in euthymic BD patients. Poorer QoL and suicide behavior might be different expression of a more severe Bipolar illness. Further longitudinal studies are warranted to clarify the causal relationship of this association.

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» NR5-098

A NOVEL WORKSHOP FOR HEALTHCARE WORKERS DEALING WITH TBI PATIENTS

Dimitri Bollegala B.S.C., Lori Wasserman, M.D., Michael Vu, Najma A. Ahmed, M.D., Ph.D., Tammy Shaw, B.Sc., M.D., Clara Ko, B.Sc., Mary Preisman, B.Sc., M.D., Shree Bhalerao, B.A., B.Sc., M.D.

EDUCATIONAL OBJECTIVES:

1. To highlight the relationship between traumatic brain injury (TBI) and suicide.
2. To demonstrate that a workshop can increase knowledge and confidence related to the assessment and management of at-risk TBI patients.

SUMMARY:

Traumatic Brain Injury (TBI) is a leading cause of death and disability. Research has demonstrated an increased likelihood of suicide following TBI. Individuals with TBI are more likely to attempt, and four times more likely to die of suicide. This research study evaluated the effectiveness of a newly created suicide awareness workshop aimed at medical and allied staff involved in the care of TBI patients. Four identical workshops were held for separate shifts of the Neurotrauma Nursing Unit (NNU) at St. Michael's Hospital in Toronto, Canada. The format was a one-hour "Lunch and Learn" session. Participants included the nursing and allied staff from the NNU (n=39). The following components were featured: a case study, an overview of suicide and its relationship to TBI, and suicide risk factors and assessment scales (SAD PERSONS Scale and Powell Suicide Risk Factor Scale). The workshop was interactive; participants applied risk factor scales during the case study and contributed to the list of suicide risk factors and possible interventions.

Outcomes of the study were assessed using three quantitative sets of measures, including: a participant demographic assessment, a knowledge assessment of suicide following TBI, and a self-rating component regarding the participants' skills and confidence in dealing with at-risk patients. Evaluations occurred prior to the workshop, immediately after it, and one month later.

The results demonstrate that the workshop was successful in improving staff knowledge about the relationship between TBI and suicide, and in increasing confidence related to the assessment and management of at-risk patients. Feedback from participants was positive. The comprehensiveness and conciseness of the workshop were viewed as its greatest assets. In addition, the format of the workshop makes it suitable for presentation in other healthcare settings where TBI patients are treated.

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» NR5-099

ANTIDEPRESSANTS AND YOUTH SUICIDE IN MIAMI-DADE COUNTY, 1990-2007

Edmi Cortes M.D., Antonio Cubano, M. D., John E. Lewis, Ph.D., Daniel Castellanos, M. D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to
1.Recognize the frequency of antidepressant medications at autopsy in Hispanic and non Hispanic youth who committed suicide in Miami-Dade County from 1990 to 2007
2.Recognize the relationship of antidepressants with sociodemographic and clinical characteristics of the victims.

SUMMARY:

Context: Controversies regarding the relationship between suicide and antidepressant use in youth have dominated the literature and lay press. The prevalence of antidepressants in postmortem studies in youth has ranged from 4 to 13%, but the rate of use is unknown in Hispanics. Objective: To determine the use of antidepressants at autopsy in Hispanic and nonHispanic youth who committed suicide in Miami-Dade County, Florida, from 1990 to 2007. Methods: The total sample (N=253) consisted of persons 24 years or younger. Victims' records from the Medical Examiner's office were abstracted to collect demographic information, suicidal characteristics, psychiatric and psychosocial factors, and toxicology results. Data were analyzed using SPSS 15.0 employing a 0.05 level of significance. Results: Eighty-five percent of the sample was male, and 53.4% of the subjects were Hispanic, 26.9% were Caucasian and 15.4% were African-American. Almost 76% had some type of life stressor. The primary method of suicide was firearm (53%), followed by hanging (24%). Over 77% of the cases had left a note. Almost 45% of the cases had a history of psychiatric illness, about 8% of the cases had a history of psychiatric treatment, and 14% had previously attempted suicide. Toxicology reports revealed the presence of antidepressants in 6% (n=15) of the victims; comprised of SSRIs (n=6), SNRIs (n=4), or TCAs or other type (n=5). The use of antidepressants was not significantly different between Hispanics (n=7) and nonHispanics (n=8). The use of antidepressants was weakly correlated with a tendency to be male and no history of psychiatric illness. No other significant associations were found. Conclusion: The use of antidepressants

in Hispanic youth suicide victims was similar to non-Hispanics. Consistent with previous literature, the presence of antidepressants at autopsy was rare in youth suicides in Miami-Dade County from 1990-2007.

No commercial support was received for this study.

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» NR5-100

PANIC ATTACK AND SUICIDE RISK: A MULTIVARIATE LOGISTIC REGRESSION ANALYSIS OF THE NATIONAL EPIDEMIOLOGICAL SURVEY OF ALCOHOLISM AND RELATED CONDITIONS

Curren Katz Ed.M., Ramin Mojtabai,M.D. Ph.D. M.P.H.,Janine Samuel,BA,Kathleen Cammacho,BA,Igor Galynker,M.D. Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, participants should gain an understanding of the association between panic attacks and suicidal behavior.

SUMMARY:

Objective: To asses panic attacks as risk indicators for suicide attempts and to examine the utility of panic attack comorbidity in differentiating individuals with major depression who have attempted suicide from those with a history of suicidal ideations only. Introduction: Past attempts at predicting suicidal behavior have had limited success. Discovering risk indicators with greater predictive validity for suicide attempts remains a major challenge for prevention of suicide. One candidate risk indicator is panic attack. An association between panic attacks and suicide has been noted in previous work, although findings have been inconclusive. Furthermore, past studies have rarely examined different types of panic attacks or specific panic symptoms. Method: In data from 3,485 adult respondents with past year major depression drawn from the US National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), we examined the association of panic attacks and specific panic symptoms on the one hand with suicide attempts, on the other hand. Results: Respondents with past year panic attacks had increased odds of suicide attempts versus suicidal ideations only (AOR=2.3, 95% CI=1.6-2.5). Furthermore, within the group of respondents with comorbid depression and panic attacks, those with symptoms of dissociation from reality and distorted or confused thinking had an increased odds of suicide attempts versus suicidal ideations only (AOR=2.2, 95% CI=1.7-2.8). Conclusion: In subjects with major depression, panic attacks are associated with increased risk of suicide attempts. The risk is especially pronounced among respondents with panic attacks characterized by dissociative symptoms and confused thinking. These symptoms may represent specific risk indicators for suicidal behavior. The utility of dissociative symptoms and distorted or confused thinking in predicting future suicide attempts needs further assessment.

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» NR5-101

PSYCHOPATHOLOGY IN PATIENTS WITH SUICIDAL ATTEMPT IN A MEXICAN PSYCHIATRIC HOSPITAL

Tizbé Sauer M.D., Mirna Trancoso, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know the comorbid psychopathology in Mexican patients with suicide behavior at psychiatric hospital's emergency service.

SUMMARY:

Suicide is an act or behavior that harms or destroys the agent themselves. Autolysis and related behaviors have become one of the main causes of the demand for emergency services. It is a complex phenomenon involving psychological, biological, social and familial factors. More than 90% of all suicides are related to a mood disorder or other psychiatric illness and has become a public health problem in recent years.
Objective. To explore the comorbid psychopathology of suicidal ideation and suicide attempts of female patients at the psychiatric hospital's emergency service.
Methods. This is a clinical, prospective study, in a sample of 30 adults recruited from emergency service of a Psychiatric Hospital in Mexico City; who suffered suicidal behavior (both attempt and ideation) with co-morbid psychiatric diagnosis. The patients had signed an informed consent. The following instruments were used: Suicide Intent Scale, SIS, Scale for Suicidal ideation, SSI, MINI International Neuro-psychiatric Interview and Montgomery-Asberg Depression Rating Scale.
Results. The women with suicidal ideation were 36.7% (N=11) and with suicide attempts were 63.3% (N=19) from total sample. The women's age mean with suicidal ideation was 30.7 (SD±9.1) and 33.3 had attempted suicide. Demographic variables: 43% were single, 36% were married, 13% were living with their partners and 7% were separated. Educational attainment averaged 7.6 years' schooling (SD±3.4). The most frequent psychiatric diagnosis were affective disorders (40%), emotionally unstable personality disorder (23.3%) and anxiety disorder (10%). A total of 53.4% of cases were housewives, 23.4% were unemployed, 6.6% were students, 6.6% looked after people that were ill, 6.6% had another job (one being a lawyer, another an archivist) and 3.4% were shopkeepers.
Conclusion: This study described principal suicide risk factors as affective disorders, unemployment and single marital status. All of the people who attempted suicide reported a psychiatric disorder therefore there should be a focus for preventive interventions. Many of the suicidal behaviors of the Mexican sample demographic correlate to international reports.There need to be studies focusing on the short-term course of suicidal ideation in special subgroups, such as cluster B personality and affective disorders.

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» NR5-102

ONE HOUR OF BRIGHT LIGHT VERSUS PLACEBO LIGHT TREATMENT FOR WINTER SEASONAL DEPRESSION

Manana Lapidus,MD, Gloria Reeves,MD, Gagan Virk,MD, Johanna Cabassa,MD, Soren Snitker,MD, Debra Scrandis,Ph.D, Mary Johnson,Ph.D, Alvaro Guzman,MD, Patricia Langenberg,PhD, Leonardo Tonelli,Ph.D, and Teodor Postolache,MD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able

to understand that bright light has immediate mood improvement effects.

SUMMARY:

Introduction: Seasonal affective disorder (SAD) winter type is a debilitating illness that is characterized by episodes of major depressive disorder during winter months and spontaneous remission of depression in spring and summer. There are several effective treatments for seasonal depression, including antidepressant treatment, light therapy, and/or psychotherapy. Empirically, light appears to improve mood faster than antidepressants, but the time frame of response is not well established. In this study, we investigated if mood improvement can be detected after one hour of bright light treatment and if that response is superior to one hour of placebo light.
Methods: Participants were adults (18 - 64 years old) with SCID diagnosis of major depressive disorder with seasonal specifier, and a score of 21 or greater on the Hamilton Rating Scale for Depression - Seasonal Affective Disorder Version (SIGH-SAD). The initial light session consisted of one hour of bright light (10,000 lux) and one hour of placebo light(<50 lux). Participants were randomized to the order that the two lights were administered. A treatment expectation survey was administered at 5 minutes of exposure after each light condition. Mood ratings were assessed at baseline and after each light treatment (3 observations total) by a blinded rater using the SIGH-SAD, Beck Depression Inventory (BDI), and the Profile of Mood States (POMS) self-report forms (depression-dejection subscale). We compared the depression-dejection subscale of POMS on bright light with dim controlled light using Friedman ANOVAs and Wilcoxon signed ranks tests.
Results: Eight participants completed the full six weeks of treatment during year one of this three year study. The Friedman analysis for total scores on the POMS scale at baseline, after red light and after bright light treatment showed a significant effect for the different conditions (Friedman test statistic=9.176, df=2, p<0.01). POMS scores were significantly lower after bright light treatment than after red light treatment ($p < 0.05$). Analysis of SIGH-SAD and BDI scores did not yield significant differences. A majority of participants reported an expectation that the placebo light would have either an equal or superior benefit compared to bright light.
Discussion: After only one hour of treatment, a significant mood improvement on a self-report scale designed to detect rapid change occurs on bright light as compared to a placebo light.

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» NR5-103

THE COURSE OF POSTTRAUMATIC STRESS SYMPTOMS OVER 66 MONTHS AFTER AN INDUSTRIAL DISASTER: A STRUCTURAL EQUATION MODELLING STUDY

Eric Bui M.D., Laurent Tremblay, M.A., Rachel Rodgers, M.A., Alain Brunet, Ph.D., Stephane Vautier, Ph.D., Philippe Birmes, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the predictors of chronic PTSD and understand structural equation modelling statistics applied to PTSD research.

SUMMARY:

Introduction: Few studies have explored the course of PTSD for durations longer than 5 years.
Objective: to examine individual latent change in PTSD symptoms after an industrial disaster over a 66-month period.
Method: Participants were recruited among 892 survivors of a factory explosion. Five to 10 weeks after the event, they were retrospectively assessed with the Peritraumatic Distress Inventory (PDI), the Peritraumatic Dissociative Experiences Questionnaire (PDEQ) and the Stanford Acute Stress Reaction Questionnaire (SASRQ). Posttraumatic stress symptoms were then assessed at 6, 15 and 66 months using the self-report PTSD Check List (PCL). In total 78 participants gave informed consent and returned the questionnaires at the 4 time points. Three competing models were tested via structural equation modelling. In model 1: 6, 15 and 66-month PCL were entered as measurements of a single latent variable. In model 2: 6 and 15-month PCL were entered as measurements of a latent variable F; F predicting 66-month PCL. In model 3: 15 and 66-month PCL were entered as measurements of a latent variable predicted by 6-month PCL. In each model, the manifest or latent PCL variables were regressed on the PDI, PDEQ and SASRQ variables.
Results: Mean age was 40.4 (SD 16.1) and 53.8% (n=42) were male. Mean PDI, PDEQ and SARQ scores were respectively 22.5 (SD 11.3), 27.5 (SD 10.1) and 74.2 (SD 32.5). Six, 15 and 66-month PCL scores were respectively 47.3 (SD 16.9), 46.2 (SD 16.9) and 45.1 (SD 18.8).
Model 1 has a poor fit (RMSEA= 0.169), rejecting the hypothesis of the absence of change between the 3 PCL time points. Model 2 showed poorer fit indices (RMSEA= 0.215) proving change in PTSD symptoms between 6 and 15 months. Only model 3 provided a good fit (Chi2(n=78,df=5)=2.40 ; p=.79 ; RMSEA=0.000), suggesting that change might occur between 6 and 15-month follow-up in PTSD symptoms.
Conclusion: PTSD symptoms evolve between 6 and 15 months but seem stable thereafter.

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» NR5-104

SEXUAL ASSAULT AND LIFETIME DIAGNOSIS OF PSYCHIATRIC DISORDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Laura Chen B.S., M. Hassan Murad, M.D., Molly L. Paras, B.S., Erin N. Goranson, B.S., Amelia L. Sattler, B.S., Kristina M. Colbenson, B.S., Mohamed B. Elamin, M.B.B.S., Richard Seime, Ph.D, L.P., Larry J. Prokop, M.L.S., Ali Zirakzadeh, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the association between a history of sexual abuse and multiple psychiatric diagnoses, thus improving screening and treatment. These psychiatric diagnoses include depression, suicide attempts, anxiety disorder, bipolar disorder, alcohol abuse, drug abuse, alcohol and drug abuse, eating disorders, posttraumatic stress disorder, and somatization disorders.

SUMMARY:

Several studies have reported an association between a history of sexual abuse and psychiatric diagnoses, yet no comprehensive systematic review has been conducted. Our research sought to assess the association between sexual abuse and lifetime psychiatric diagnoses.
A systematic literature search of MEDLINE, EMBASE, CINAHL, Current Contents, PsycINFO, ACP Journal Club, CCTR, CDSR, and DARE databases from January 1980 to August 2007 was performed. Original comparative studies that reported selected psychiatric outcomes in persons with a history of sexual abuse and control group were included. Study selection and data extraction were performed by pairs of blinded reviewers. Odds ratios (OR)

and 95% confidence intervals (CI) were pooled across studies using the random-effects model. The I2 statistic was used to assess heterogeneity.We found 187 observational studies that fulfilled eligibility criteria. A history of sexual abuse was associated with lifetime diagnosis of depression (OR 2.63; 95% CI, 2.38-2.90, I2=69%), suicide attempts (OR 4.07; CI, 3.46-4.78, I2=93%), anxiety (OR 2.25; CI, 1.99-2.56, I2=66%), posttraumatic stress disorder (OR 5.28; CI, 4.31-6.47, I2=75%), somatization disorders (OR 3.45; CI, 1.14-10.47, I2=56%), alcohol abuse (OR 1.95; CI, 1.69-2.24, I2=32%), drug abuse (OR 3.18; CI, 2.48-4.08, I2=43%), alcohol and drug abuse (OR 1.81; CI, 1.29-2.56, I2=43%), and eating disorders (OR 2.27; CI, 1.97-2.61, I2=13%). A trend for significant association was noted with lifetime diagnosis of bipolar disorder (OR 1.90; CI, 0.93-3.87, I2=46%). History of sexual abuse did not increase risk of lifetime diagnosis of obsessive compulsive disorder, schizophrenia, or sleep disorders. The sex and age of the abused did not significantly alter these associations. Awareness of the association between a history of sexual abuse and lifetime diagnosis of several psychiatric disorders may lead to improved psychiatric screening and more prompt treatment.

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» NR5-105

VIOLENT BEHAVIOR AND ITS PREDICTORS IN SCHIZOPHRENIA PATIENTS IN HONG KONG

Kavin Chow

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify associated risk factors for violence in schizophrenia patients in Hong Kong and preventive measures should be implemented accordingly.

SUMMARY:

Introduction: Violence in patients with psychiatric disorder has always been an important area of concern. In the last two decades, most of the studies supported the view that there was a moderate and reliable association between mental illness and violence (1). Schizophrenic patients were suggested to be more likely to act violently comparing to other patients (2). Certain socio-demographic characteristics and symptomatology were considered to be predictors of violent behavior in schizophrenia patients.
Objective: The objectives of this study are to investigate the prevalence of violence among schizophrenic patients in Hong Kong and to investigate the risk factors related to violent behavior. In addition, this study also explored the nature and targets of violence committed by schizophrenic patients.
Study design: This was a retrospective case notes study of schizophrenic patients who admitted to the psychiatric units of the New Territories East Cluster (NTE) hospital in Hong Kong during the period from 1 January 2005 to 31 March 2005. In total, 515 patients, aged between 18 to 64, were reviewed personally by the author. Among these patients, 193 patients were diagnosed to have Schizophrenia.
Case definition: Patients with schizophrenia were divided into two groups: “with violent behavior” and “without violent behavior”. Violent behavior was defined as those having verbal threat towards person, physical aggression against persons or physical aggression against objects within 4 weeks prior to the admission. This study was approved by the local Clinical Research Ethics Committee.
Results: The prevalence of violent behavior within 4 weeks before the index admission was 24.4% among schizophrenic patients. Patients of older age and living in the hostel were found to be associated with violence. Specific clinical variables, including having substance used prior to admission, having grandious delusion and agitated mood were associated with violence. Among the victims, parents and acquaintance were the main targets of violence.
Conclusion: The prevalence of violent behavior was comparable to what has been reported in western countries. Associated risk factors were identified for which preventive measures should be implemented accordingly.

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» NR5-107

THE EFFECTS OF DAILY EXPERIENCES DURING CAPTIVITY ON MENTAL HEALTH OF KOREAN-TALIBAN HOSTAGES

Youngjoon Lee M.A., Jeon WT, Ph.D, Eom SY, M.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that various daily experiences in captivity could be either risk or resilience factors for psychopathologies and posttraumatic responses of hostage survivors. Therefore, comprehensive interview about their life events in captivity should be the primary process for their psychological intervention.

SUMMARY:

Background: 21 Korean hostages (5 males and 16 females) who had been captured by the Taliban in 2007, experienced various daily events in captivity. Some of their experiences were reported as painful, but others were reported as helpful.
Objective: The aim of this study was to find out which daily experiences during captivity affected positively or negatively on the mental health of hostage survivors.
Method:Through the interviews with hostages, 81 stressful and 28 helpful daily events were collected and measured as stressful or helpful with 5-point Likert scale by them. And then, 18 stressful events and 10 helpful events were picked out. All of 21 hostage survivors were also completed Symptom Checklist 90-Revised (SCL-90-R) and Impact of Event Scale-Revised(IES-R) five times at their returning home, 1, 2, 4, and 12 weeks later. Stepwise regression analyses, adjusted for time, were performed to find out the effect of daily experiences in captivity on general psychopathology and posttraumatic response of hostage survivors.
Result:Difficulties with drinking water, loss of hope, difficulties with dwelling and keeping up personal hygiene, detention in limited and dark space, forced interview, and bad smell were risk factors for trauma-related psychopathology and posttraumatic stress responses. And adequate drinking water, experience of kindness of natives, adequate food, and faith were found out as resilience factors against psychological sequelae.
Conclusion:Many of Daily events in captivity affected on psychopathologies and posttraumatic stress responses. Especially, difficulties with drinking water, loss of hope, difficulties with dwelling and keeping up one’s hygiene were common risk factors, and adequate drinking water and kindness of natives were common resilience factors.

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displaced persons in northern Uganda. BMC Psychiatry 2008;8:38

» NR5-108

SUDANESE REFUGEES IN CAIRO, EGYPT: A RANDOMIZED CONTROLLED TRIAL OF INTERPERSONAL PSYCHOTHERAPY FOR TRAUMA, DEPRESSION AND INTERPERSONAL VIOLENCE

Susan M. Meffert M.D., M.P.H., Magda Ali, M.B. B.Ch., MSc., Yassir Mostafa, Sahar Yousif, Afrah Abdel Rahim, Omayma Fargouny, Akram Osman Abdo, Charles R. Marmar, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to (1) Understand the effect of Sudanese intrastate conflict on individual and interpersonal emotional functioning; (2) Identify Interpersonal Therapy delivered by community therapists as an effective, sustainable and empowering mental health treatment for broadly traumatized populations.

SUMMARY:

Although approximately one quarter to one third of a population exposed to extreme stressors such as ethnic conflict develops chronic symptoms of PTSD causing significant disability, the research and application of psychological trauma and other mood treatment modalities in this context is currently in its infancy. One of the most neglected aspects of mental health care in post-conflict settings is the impact of psychological trauma on interpersonal relationships. We conducted a randomized controlled trial, with a wait list control group, of Interpersonal Therapy (IPT) for Sudanese refugees living in Cairo, Egypt. Two hypotheses were tested in twenty two subjects: (1) After IPT intervention, Sudanese refugees will have lower levels of depression and trauma symptoms compared to wait list controls; (2) After IPT intervention, Sudanese refugees will have lower levels of interpersonal violence compared to wait list controls. Community members were trained in IPT for one week and supervised during delivery of six sessions of twice weekly IPT. Data was analyzed using bootstrapping hierarchical linear regression. Controlling for baseline symptoms, IPT treatment, compared to wait list controls, predicted a significant decrease in symptoms of Posttraumatic Stress Disorder (PTSD), Depression and State Anger. The first hypothesis was confirmed. IPT treatment, compared to wait list controls, was also associated with a decrease in state anger. To our knowledge, this study represents the first attempt to use IPT to address PTSD symptoms and interpersonal violence in a refugee population and the first attempt to use community therapists, without prior mental health mental health care training, to deliver individual IPT. The study's success has positive implications for the future development of effective, sustainable and empowering global mental health interventions to support the recovery of traumatized populations.

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» NR5-109

SYMPTOMS OF TRAUMA SCALE: DEVELOPING A PSYCHOMETRIC TOOL FOR PTSD

Michael Pratts M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the challenges of developing a user-friendly reliable PTSD rating scale that is sensitive to change-over-time.

SUMMARY:

The huge rise in traumatic events worldwide has increased the need for proven PTSD treatments. The development of this scale will allow us to reliably measure both symptoms of PTSD and Complex PTSD and thus improve measures for PTSD treatment trials. This expertise made clear to us that a reliable, easy to use PTSD scale is desperately needed. The goals of this study were to test and validate the Symptoms of Trauma Scale (SOTS), a newly developed nine-item seven-point symptom severity rating scale, and to develop a comprehensive training program for investigators intended to be co-marketed with the scale. Development of the SOTS was guided by the insights of clinicians, researchers, and opinion leaders working with patients with posttraumatic stress disorder (PTSD); informed by lessons learned in developing and refining the Positive and Negative Syndrome Scale (PANSS); and motivated by the need for a reliable, comprehensive, time-efficient symptom severity rating scale sensitive to change in persons with simple, complex, subsyndromal, and prodromal PTSD.

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2) Trauma and Recovery: The Aftermath of Violence--from Domestic Abuse to Political Terror by Judith Herman (Paperback - May 29, 1997)

» NR5-110

THE SIGNIFICANT IMPACT OF CHILD ABUSE ON THE WIDE RANGE OF CHARACTERISTICS OF DEPRESSED INPATIENTS

Magdalena Romanowicz M.D., Gen Shinozaki,M.D.,Victoria Passov, M.D. ,Simon Kung,M.D.,Renato D. Alarcon,M.D.,M.P.H,David A. Mrazek, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize that the child abuse history impacts significantly upon the wide range of characteristics of depressed inpatients. The influence includes the increased risk of suicide attempt, substance use disorder, and cluster B personality disorder, as well as earlier onset of mental illness and more psychiatric hospitalizations.

SUMMARY:

Introduction: The impact of child abuse is known to increase the risk of suicidality (1, 2). However, the literature about the extent of the impact on the other characteristics of depressed inpatients is scarce. We examined if this impact would extend to the wide range of comorbidities as well as their use of mental health services.
Methods: Retrospective chart review of 283 patients hospitalized for depression on a Mood Disorders Unit from 2005-2007. Patient characteristics were recorded including comorbidity with bipolar disorder, alcoholism, anxiety disorder, personality disorder and suicide attempt, as well as age of onset and number of psychiatric hospitalization. The subjects were divided into 2 groups (with/without child abuse history), and for each characteristics, chi square comparisons or 2 sample t-test was performed.
Results: Of the 283 patients, 155 had no history of child abuse, whereas 128 had abuse history (sexual, physical, or emotional). We found significant increases among those with abuse history for suicide attempt (24.5% to 51.6%, $p<0.01$), alcohol addiction (21.3% to 40.6%, $p<0.01$), cluster B personality trait (20.0% to 50.0%, $p<0.01$), younger age of onset (25.9 y.o. to 21.1 y.o., $p<0.01$), and more psychiatric hospitalizations (3.0 to 4.7. $P<0.01$). (Factor for multiple comparisons was adjusted.) Prevalence of bipolar disorder and anxiety disorder did not show significant differences ($p>0.05$).
Conclusions: Our findings showed that a history of child abuse significantly impacts the wide range of characteristics of depressed inpatients including the increased risk of suicide attempt, co-morbidity of substance use disorder and cluster B personality disorder, as well as earlier onset of mental illness and more psychiatric

hospitalizations. While these associations do not confirm causality, these findings remind us of the importance of more aggressive approaches to prevent child abuse from the public health perspective.

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» NR5-111

COMPARISON OF THE PES MANAGEMENT BETWEEN THE FIRST AND SECOND YEAR GENERAL PSYCHIATRY RESIDENTS: A PILOT STUDY

Xiangyang Zhao M.D., Toni Love Johnson M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to 1) be aware of the issues in psychiatric emergency services (PES) provided by general psychiatry residents 2) participate the discussion of the improvement of PES in current community psychiatry model 3) raise the attention in the residents' education in Emergey Psychiatry.

SUMMARY:

Hypothesis: we hypothesized that, despite the difference in knowledge, skill and attitude in psychiatry, PGYI and II GPRs were able to formulate similar disposition plans in PES.
Methods: •National data of PGYI and II GPRs' PRITE performance from 2003 to 2007 were reviewed. Standard Scores of Global Psychiatry, Emergency Psychiatry and Evalution&Treatment were analyzed.
•A group of residents who have successfully finished both PGYI and II general psychiatry training were chosen. PES from 2004 to 2008 provided by these residents were identified. Their PES disposition in PGYI was compared with in PGYII. The primary measurement was the discharge rate. The secondary measurement includes the referral to Mobile Crisis and the interrater agreement in the discharge between the referring residents and the mobile crisis staff.
Results:1)GPRs improved significantly in the Standard Score of Global Psychiatry, Emergency Psychiatry and Evalution& Treatment in PRITEs between PGYI and II (414±4 vs. 488±5, p=0.0025; 446±19 vs. 498±1, p=0.02; 444±7 vs. 493±2 p=0.004) 2)From 2004 to 2008, 3730 psychiatric emergency services were provided by 17 residents. No difference in discharge rate was seen between PGYI and II (37±6 % vs. 37±10% p=0.89). The PGYII residents had significant more referral to Mobile Crisis. The agreement of the discharge was higher among the PGYII and Mobile Crisis staff (9±6% vs. 24±5% p=0.02; 71±25% vs. 86±12% p=0.03). Statistical analysis: data were expressed as means ± STDEV. Means between two groups were compared using t-test. $p < 0.05$ was considered to be significant.
Discussion: in this study, the formulation of disposition in PES was quantitatively studied among the same group of GPRs during their PGYI and II. The data indicate no difference in the primary measurement (discharge rate), but the significant difference is seen in the secondary measurement (mobile crisis referral and the interrater agreement). These findings provide the evidence that, despite their difference in skill, knowledge and attitude, which is evidenced by the cross-section improvement in PRITE during the training, PGY I and II residents are able to reach the consensus in discharge and admission, which is essential for PES, but PGYII residents are more adept in utilizing the system and reach higher interrater agreement.

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» NR5-112

PEDIATRIC PSYCHIATRIC EMERGENCIES AFTER TWO SCHOOL SHOOTING INCIDENTS

Xiangyang Zhao M.D., Toni Love-Johnson, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to : 1) be aware that pediatric psychiatric emergency is associated with numerous varibles and school shooting maybe is one of them 2) be aware that the " jury is out" and more research is needed in this area.

SUMMARY:

Background: pediatric Psychiatric Emergencies (PPE) was associated with confounding factors. To illustrate the relationship between school shooting and PPE, we studied two recent school shooting incidents: 1) Cleveland school shooting happened on Oct. 10, 2007. A 14-year-old student wounded four people before he killed himself. 2) Northern Illinois University campus shooting happened on Feb. 14 2008. One former student killed six persons before killing himself.
Method: Site of the study: ER of MetroHealth Medical Center (Metro), Cleveland, OH.
Design: a retrospective chart review. Based on patient's chief complaint at the ER triage, Psychiatric Emergency (PE) was identified. Average daily PE, adult PE and PPE during the acute phase (from day 1 to 7 of the individual event) of shooting were calculated and compared with that of the rest of the month when the individual event took place.
Results: in Oct. 2007- the month of Cleveland school shooting, total month PEs in Metro were 271, of which 32 was PPE. Average daily PE, adult PE and PPE in the acute phase has no difference compared with the rest of the month (8.7±3.2 vs. 9.0±3.2 p= 0.49; 7.2±3.2 vs. 7.8±3.1 p=0.68; 0.7±0.8 vs. 1.1±1.1 p= 0.36)
In Feb. 2008- the month of Northern Illinois University campus shooting, total month PEs were 264, in which 32 was pediatric PE.. Average daily PE, adult PE and PPE in the acute phase have no difference compared with the rest of the month (8.4±3.4 vs. 9.8 ±3.3 p=0.36; 7.7±3.0 vs. 8.5±3.3 p=0.8; 0.7±0.8 vs. 1.3±1.0 p=0.2). Statistical analysis: Data were expressed as means ± STDEV. Means between two groups were compared using t-test. $p < 0.05$ was prospectively considered to be significant.
Discussion: neither school shooting incident had any impact on total PE or adult PE. This is consistent with some previous reports. However, even though we found that more PPEs were seen during the acute phase of Virginia Tech Massacre, this phenomenon was not seen in post-Cleveland School shooting and Northern Illinois University Campus Shooting. The inconsistence of PPE after 3 school shootings indicates that the relationship between school shootings and PPE is still elusive. The proximity of the event to the ED does not appear to be a predictive factor according to these 3 incidents. More study is needed.

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» NR5-113

DEFICIT IN EYE CONTACT IN NEGATIVE EMOTIONAL SITUATION DURING INTERACTION WITH VIRTUAL AVATAR IN PATIENTS WITH SCHIZOPHRENIA

Soo-hee Choi M.D., Soo-hee Choi, M.D., Jeonghun Ku, Ph.D., Kiwan Han, M.S., Sun I. Kim, Ph.D., Eosu Kim, M.D., Jae-Jin Kim, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that patients with schizophrenia had negative symptom-related deficit in eye contact, which was more marked in the negative emotional situation. Defective social behaviors, particularly in negative situations, should be considered in clinical practices for treatment of schizophrenia.

SUMMARY:

Objective: Social cognitive impairment has been implicated in patients with schizophrenia. Although it is difficult to analyze social behaviors objectively in a real-world situation, the virtual reality (VR) would be a promising alternative tool for social behavioral study. We aimed to examine the characteristics of interpersonal behaviors in the virtual environment and their relations with symptomatology in patients with schizophrenia. Method: Twenty six patients with schizophrenia and 26 normal controls conducted a set of VR conversation tasks that consisted of 4 positive and 4 negative emotional situations. We measured behavioral parameters such as the frequency of looking around, the duration of eye contact, the time taken to start a reply, and the length of the reply during the listening and answering phase of the conversations with virtual avatar. We analyzed repeated measures ANOVA with the main effects of group and emotions and correlations between behavioral parameters and the PANSS scores. Results: In both listening and answering phases, there were significant group effects ($p = 0.004$, $p = 0.031$, respectively), and also group x emotion interactions ($p < 0.001$, $p = 0.004$, respectively) in the duration of eye contact. The patient group did not show increase in eye contact in negative emotional situations compared to positive situations, and their durations of eye contact were significantly correlated with negative symptom scores ($r = 0.418$, $p = 0.037$). There were neither group effects nor group x emotion interactions for other behavioral parameters. Conclusions: The results indicated that patients with schizophrenia had negative symptom-related deficit in eye contact, which was more marked in the negative emotional situation. Defective social behaviors, particularly in negative situations, should be considered in clinical practices for treatment of schizophrenia.

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» NR5-114

FACTORS ASSOCIATED WITH MEDICATION TREATMENT DECISIONS AMONG PREGNANT WOMEN WITH BIPOLAR DISORDER

Rachel Vanderkruik, Adele C. Viguera, M.D., Theodore Hatch Whitfield, Sc.D., Ross J. Baldessarini, M.D., Lee S. Cohen, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the most important factors for women with bipolar disorder when making decisions regarding their psychiatric medications during pregnancy. These factors will be compared between women who continued medication to women who discontinued medication during pregnancy. The participant will learn which categories of psychiatric medication were most likely to be discontinued.

SUMMARY:

OBJECTIVE: This pilot study ascertained treatment-decisions by pregnant women with bipolar disorder (BPD).
METHOD: We administered a treatment-preference questionnaire to consecutive pregnant women diagnosed with DSM-IV BPD (48.0% type-I) as part of a longitudinal study of BPD patients during pregnancy.
RESULTS: We included 43/48 subjects (89.5%) who completed all required follow-up assessments through week six-postpartum. Of women choosing to continue treatment with at least 1 psychotropic drug during pregnancy (69.8%), stated reasons ranked: [a] concern for relapse if medication were discontinued (73.3%) > [b] physician-recommendation (70.0%), > [c] new illness after previous discontinuations (53.3%) > [d] partner's-wishes (40.0%) = [e] risk of ability to care for other children (40.0%). For subjects discontinuing treatment within 6 months before conception (25.6%), drugs discontinued ranked: [a] mood stabilizer (63.6%) = [b] benzodiazepines (63.6%) > [c] antipsychotics (54.5%) > [d] antidepressants (27.3%). Reported reasons for discontinuing (53.0% of subjects) ranked: [a] fear of potential fetal teratogenic risks (90.9%) > [b] physician-recommendation (45.5%) > [c] medication no longer seemed needed (36.4%) > [d] advice of family-members (36.4%).
CONCUSION: These findings indicate that treatment-discontinuation with fear of teratogenic effects despite fear of illness-recurrence was common among pregnant women with BPD, although some failed to appreciate the need for maintenance medication, especially when well.
[Supported in part by: NIH Collaborative Grant: R01 MH 071762 [Viguera]; R01 MH 07153 [Newport]).

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Wednesday, May 20, 2009

12:00 p.m. - 2:00 p.m.
Hall D, Exhibit Level,
Moscone Convention Center

NEW RESEARCH POSTER SESSION 6: TREATMENTS AND TREATMENT SETTINGS

» NR6-001

THE TRIAL-BASED THOUGHT RECORD, A NEW COGNITIVE THERAPY STRATEGY TO CHANGE CORE BELIEFS IN SOCIAL PHOBIA

Irismar Reis De Oliveira M.D., Vania Powell, Camila Pereira, Claudia de Almeida, Maria Conceição Grangeon, Milke Caldas, Thais Bonfim, Martha Castro, Amanda Galvão, Roberta Moraes, Amy Wenzel, Donna Sudak

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to 1) recognize the value of belief change in CBT for social anxiety disorder 2) identify differences between conventional methods of belief change and the Trial-Based Thought Record

SUMMARY:
Objective: To assess the efficacy of a new cognitive therapy technique, the Trial-Based Thought Record (TBTR), in generalized social anxiety disorder patients.
Methods: A randomized study comparing TBTR with a conventional 7-column thought record plus positive data log (i.e., comparison treatment) was conducted. Patients in both groups were seen in 12 weekly one-hour sessions for 10 weeks and then biweekly for four weeks (4-month duration). Statistical analyses included paired-samples (baseline vs. last observations in both groups) and independent-samples (TBTR vs. conventional treatment) t-tests to examine differences in clinician-rated, interview, and self-report measures.
Results: There were significant reductions ($p<0.001$) in both the TBTR (n= 17) and the comparison treatment (n= 15) on the Liebowitz Social Anxiety Scale, Social Avoidance and Distress Scale, Clinical Global Impression, and Beck Anxiety Inventory. TBTR was significantly more effective than the comparison treatment on the Fear of Negative Evaluation scale ($p<0.001$) and on the following dimensions of SF-36: bodily pain ($p=0.04$), social functioning ($p=0.02$), and mental health ($p=0.05$).
Conclusions: The preliminary results of this study suggest that TBTR is more effective than the conventional treatment in changing the fear of negative evaluation, bodily pain, social functioning and mental health. These results support additional studies of TBTR in social phobia and other psychiatric diagnoses.

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» NR6-002

DEVELOPING CULTURALLY SENSITIVE COGNITIVE BEHAVIOUR THERAPY FOR PSYCHOSIS FOR ETHNIC MINORITY PATIENTS

Shanaya Rathod M.D., Prof David Kingdon, MD; Peter Phiri

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to: 1.Understand the need for culturally sensitive and adapted Cognitive behaviour therapy in engagement and improving outcomes in patients from ethnic minority communities. 2. Recognise themes and adaptations of therapy that are specific to certain cultures and impact on treatment when interacting with patients from these communities

SUMMARY:
Cognitive behavioural therapy (CBT) is beneficial in the treatment of psychosis. However, difficulties in engagement and poor outcomes have been reported for Black and minority ethnic populations (Rathod et al).
Aim: The main aim of the study is to produce a culturally sensitive adaption of an existing CBT manual that is (a) well suited to the needs of clients with psychosis from three specified ethinic minority communities- Black Caribbean, Bangladeshi and Pakistani and (b) is accompanied by guidance for health professionals to enable them to deliver CBT that is culturally sensitive and responsive for clients with psychosis from these communties.The main aim of the study is to 1.To gain meaningful understanding concerning the way members of the Black Caribbean, Bangladeshi and Pakistani communities typically view psychosis, its origin, and management. 2.To elicit those cultural influences, values and attitudes that shape a patients degree of participation and response to CBT. 3.To elicit from CBT therapists/mental health practitioners (MHPs) from these communities, their experiences and interpretations of the way a client's culture influences their attitude and response to CBT. 4.To identify those stratgies that CBT therapists and other MHPs identify as being supportive or non supportive with clients from the above ethnic communities.
Methodology: The study has been conducted in 2 centres in the UK: Hampshire and London. It adopts an overarching qualitative methodology including face-to-face in-depth semi-structured interviews and focus groups
Results: Interviews have been conducted until themes have been saturated. 20 Face to face interviews and 16 focus groups have been conducted. NVivo 8 (computer-assisted qualitative data analysis software) was used to manage and explore qualitative data in-depth. The emergent themes have been grouped in different phases of the therapy pathway i.e. Pre-engagement, Engagement, theoretical modifications and Philosophical reorientation. These will be presented in detail at the session along with recommendations for modification of CBT
Conclusion: This study has important implications in the development of culturally sensitive and responsive therapies for psychiatric disorders.

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» NR6-003

IS COMBINED TREATMENT BETTER THAN USUAL CARE IN IMPROVING QUALITY OF LIFE IN A ONCOLOGIC DEPRESSED SAMPLE?

Beatriz Rodríguez Vega M.D., Angela Palao, Guillermo Benito, Guadalupe Torres, Ana Hospital, Carmen Bayón.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize different effects on quality of life of oncology patients, depending on psychiatric intervention.

SUMMARY:
Introduction: Measurement of quality of life in cancer patients has acquired an increasing interest in current psycho oncology.

Quality of life is directly related to psychological well-being, and psychiatric treatment for depression can improve some aspects related to it.The goal of our study is to evaluate the improvement of quality of life in a sample of depressed oncologic patients randomised to two different strategies of intervention, combined treatment and usual care. Methodology: 67 depressed cancer patients were randomized to combined treatment (pharmacological and psychotherapeutic) or drug treatment plus usual care. Psychotherapy intervention was Narrative Brief Therapy. The main outcome measure was the QLQ C-30, a specific measure of Quality of Life in cancer patients, measured at 12 and 24 weeks. It has 15 sub-scales concerning: 5 functional scales (Physical, social, emotional, cognitive and role), 9 symptoms scales (Fatigue, pain, nausea, economics, sleep, appetite, choking, constipation and diarrhea), and global health scale.
Results: Patients treated with combined treatment had higher scores on functional variables at 12 weeks compared to patients treated with usual care (p=0.05). However, in symptomatic variables there were no significant differences on symptomatic variables, except in "fatigue" (p=0,014). The differences at 24 weeks remained statistically significant in all functional variables. Pain was the only symptomatic variable (p=0,034).
Conclusion: Oncologic patients who received combined treatment for depression showed a better response on all the functional scales of quality of life of QLQ C-30 at 12 and 24 weeks. Treatment groups differed on fatigue and pain scores of symptom subscales, although differences were not consistent in time. Self reported quality of life also showed a bigger improvement on combined treatment group. This study is part of the research projects FIS 05/0737 and 05/2062.

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» NR6-004

FACTORS AFFECTING MENTAL FITNESS FOR WORK IN A SAMPLE OF MENTALLY ILL PATIENTS

Yasser Elsayed M.D., Mohamed Al-Zahrani, Ph.D. Mahmoud Rashad,Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to
-Recognize the importance and the main principles of assessment of mental fitness for work.
-Identify the demographic and clinical characteristics of mentally unfit patients.
- Know the main obstacles facing psychiatrists during assessment of mental fitness for work.

SUMMARY:

Background: Mental fitness for work is the ability of workers to perform their work without risks for themselves or others . Mental fitness to work is an important issue the same as physical fitness, however it was a neglected area of practice and research. Mental ill health at work seems to be rising as a cause of disablement. Psychiatrists who may have had no experience in relating mental health to working conditions are increasingly being asked to undertake these examinations. Aim of the work: This reserach was done to :- a) Study the relatioship of mental ill health and fitness to work. B) Recognize the differences between fit and unfit mentally ill patients. A lot of other study questions were also addressed. Subjects and methods: This study was a prospective one.. All cases referred to Alamal complex for assesment of mental fitness during a 12 month period were included. Data collected included demographic and clinical characteristics diagnosis, characteristics of the work environment, data about performance at work.. All data were subjected to statistical analysis Results: Total number of cases was 116 case, the mean age was 34.5±1.4 . Females were 35.3% of cases. The highly educated patient constitute 50.8% of cases. The decision of the committee was fit for regular work for 52.5% , unfit for 19.8% and modified work for 27.7%. The decision was appreciated only by 29.3% of cases. There were significant differences between fit, unfit and modified work groups. The fit group had higher level of education, less duration of illness, younger age, and better performance at work. Patients of The modified work group had more physical hazards in work environment and had more work shift and more frequent diagnosis of substance abuse and dependence. The unfit group had more duration of illness, more frequent hospitalizations, and more communication skills needed at work, more disturbed relationship with their colleagues, less productivity and more diagnosis of schizophrenia. conclusion: There are many factors affecting the mental fitness the most important are the charcteristics of work environment and diagnosis and the most serious is the overall job safety of patient to self and others. A lot of ethcial and legal issues should be kept in mind during such assessmet as patient's rights , society's rights, and the laws applied to non fit people.

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» NR6-005

CHARACTERISTICS OF MENTALLY ILL OFFENDERS FROM 100 PSYCHIATRIC COURT REPORT

Yasser Elsayed M.D., Mohamed A. Al-Zahrani, Ph.D., Mahmoud Rashad, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to :
-Recognize the importance and the main principles of psychiatric court report.
-Identify the demographic and clinical characteristics of mentally ill offenders.
- Know the main obstacles facing psychiatrists during assessment of criminal responsibility of offenders.

SUMMARY:

There is an increasing probability that the psychiatrist will, willingly or not, come into contact with mentally ill offenders in the course of practice. Hypothesis and Aim of the work: The growth of economy of the Arab Gulf Countries at the last decades was associated with growth of all systems needed to support this economy including mental health and Justice systems. So, what about the process of legal accountability in this region? The aims of this work were to investigate the rates of different mental disorders in 100 court report and to know the characteristics of mentally ill offenders and a lot of other study questions were also addressed. Subjects and Methods: All cases referred from different departments of the legal system to the forensic committee for assessment of criminal responsibility during 13 month duration were included. A specially designed form was done for data collection and included demographic characteristics, clinical variables and details of the crimes and investigations. Results: Men constitute 93% of cases. Offenders who were younger than 40 years were 73%. Schizophrenic cases were 13%, substance related cases constitute 56% and amphetamine alone were 21% of cases, 8% were bipolar manic, 4% were major depressive disorders, 10% were antisocial personality disorder, 51% of cases were classified as having low education. Unemployment was found in 34% of cases. The final decision of the forensic committee was full responsibility in 46% of cases and partial responsibility in 11% of cases and 33% were

irresponsible. 58% of cases had a contact with psychiatric health care prior to the offence and in 9% of cases contact was in the previous 12 weeks. History of similar offence was found in 32% of cases. 14% of offences were murder, 8% were sexual crimes, and 31% were violence and Simple crimes. Discussion and Conclusion: the ability of the legal system to detect cases was good as only 10% were free from mental illness. The ability of the health care system to predict crimes and offences was weak as 58% of cases had previous contact with health care system before the crime. Substance abuse especailly amphetamine played an important role. More research is needed to further our understanding of the association between mental disorders and antisocial behavior.

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» NR6-006

IS THE CRIMINAL JUSTICE SYSTEM GETTING IT RIGHT? A SIX MONTH RETROSPECTIVE STUDY OF COURT REQUESTED FORENSIC REPORTS IN THE REPUBLIC OF IRELAND

Grainne Flynn M.D., Conor O Neill, MD, MRCPsych

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that a certain proportion of defendants are actively psychotic,and a proportion of these defendants are incompetent to stand trial. Substance misuse is common in this group, as are prior convictions.

SUMMARY:

The aim of this study was to assess the forensic psychiatric profile of remand prisoners upon which Irish District Court Judges requested reports for the presence of mental illness and competence to stand trial.
Methods: All district court requests and completed reports for forensic psychiatric evaluation of defendants, by the National Forensic Psychiatric Service, were reviewed over a six month period from July to December 2007, after the introduction of the Criminal Law Insanity Act (2006). The type and number of charges were assessed for each defendant report, as were previous charges, current active mental illness,co morbid substance misuse and previous psychiatric history. Opinions on competence to stand trial were also studied.
Results: Seventy eight forensic psychiatric assessments were requested and completed by the National Forensic Psychiatric Service between July and December 2007. In this group 70 (89.7%) were men. The mean number of current charges per case report was 5.5+/-1.4, one defendant was on remand for homicide and the most common offence was Public Order (71 cases – 91%). Seventy-two(92.3%) of the 78 defendants had previous convictions. Of the 78 defendants, 19 (24.3%) had an acute psychotic illness(15 paranoid schizophrenia, 3 manic phase of bipolar affective illness, 1 schizo-affective). Seven(9.85%) of these defendants were incompetent to stand trial. Thirty five defendants (45.2%) had a history of poly substance misuse without any active mental illess.
Conclusion: Forensic psychiatric assessments are requested on a group of defendants with mainly substance abuse problems by the Irish District Courts. A smaller number of requests deal with defendants who are actively psychotic and are incompetent to stand trial.

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» NR6-007

EEG ABNORMALITIES IN DIFFERENT TYPES OF CRIMINAL BEHAVIOR

Ilja Zukov M.D., Radek Ptacek,Ph.D., Slavomil Fischer, Ph.D., Jiri Raboch,Ph.D.,Daniela Domluvilova, M.D., Petr Kozelek, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to , discuss EEG problematic in context of -forensic psychiatry, neurobiology of violence

SUMMARY:

Electroencephalographic abnormalities in psychopathic personalities and in forensic population were reported in many EEG studies but at this time the problem presents still unresolved question. Within this context aim of this study is to present findings of several EEG abnormalities in different types of criminal behavior in comparison to healthy controls. Studied sample included four groups. The first group (n=20) included offenders of violent criminal activity evaluated as impulsive, non-deliberate, affectively motivated and affectively aggressive. The second, control group (n=20) included individuals who committed no criminal activity and has no mental disorder. The third group (n=20) included violently deliberately behaving delinquents and the fourth group (n=20) included delinquents performing property criminal activities, non-violent and non-impulsive.
An EEG abnormality was found in 70 % of subjects. Multiple abnormalities were found in 35% of the subjects. In non-impulsive delinquents higher rate of EEG abnormalities were found (30 % and multiple abnormalities in 5 %). Other groups i.e. thefts and the control group show no significant EEG changes. In summary, the results show the highest occurrence of EEG abnormalities in the group of impulsive criminals. The results are in agreement with previous findings that did not find specific EEG signs in different types of criminal behavior exception of impulsive aggressive criminals.

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» NR6-008

REDUCING AGGRESSIVE BEHAVIOR ON A CHILD DAY TREATMENT UNIT: THE DEVELOPMENT AND USE OF A COMMUNITY MEETING FOR CHILDREN

Melissa Greene Ph.D., Lisa Defelice, M.Ed., Kathleen Clarkson, M.S.W

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize the challenges associated with managing aggressive behavior on a child day treatment unit, understand how to begin to implement a psychotherapeutically-oriented community group meeting on a child unit, and appreciate how the use of this meeting can foster improved relationships on the unit, and encourage a decrease in aggressive behavior.

SUMMARY:

Despite the long-standing belief that regular community meetings improve the therapeutic climate of a psychiatric milieu, little research has systematically investigated what, if any, changes are associated with the use of community meetings. Furthermore, there is limited literature on the development and use of these types of groups on child psychiatric units. The current presentation

will examine the development and use of a psychotherapeutically-oriented community meeting protocol in decreasing aggressive behavior among children. The setting for the study is a day treatment program that serves the educational and psychiatric needs of children ages 6 though 12. The unit census is anywhere from 20-29 children, with the majority of children being male, and of either African American or Hispanic ethnicity. The average length of stay on the unit is approximately 2 years. In order to understand the needs of the unit, data was collected for a six month period on the frequency and types of incidents of aggressive behavior occurring on the unit. We also examined the use of PRN medications on the unit. During the baseline period, we developed a protocol and agenda for a psychotherapeutically-oriented community meeting to specifically address interpersonal relations and aggressive behavior. Results indicate frequent incidents of aggressive behavior and use of PRN medication in the six month baseline period. The highest number of incidents per week fell into the category of verbal aggression, usually taking the form of verbal threats or provocations made to patients or staff. However, there were also frequent incidents of physical aggression directed towards patients and staff. The number and types of incidents of aggression highlighted the need for an intervention to address relationships among patients on the unit, as well as between patients and staff. The current presentation will outline and discuss the challenges involved in the various steps of creating and implementing a community meeting protocol on a child psychiatric unit, and results will summarize how the implementation of this intervention was related to the behavioral functioning of the children on the unit.

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» NR6-009

DEEP BRAIN STIMULATION OF THE VENTRAL CAPSULE/VENTRAL STRIATUM FOR TREATMENT-RESISTANT DEPRESSION

Donald Malone M.D., Darin Dougherty,M.D., Ali Rezai,M.D., Linda Carpenter,M.D., Gerhard Friehs,M.D., Emad Eskandar,M.D., Scott Rauch,M.D., Steven Rasmussen,M.D., Andre Machado,M.D., Cynthia Kubu,Ph.D., Audrey Tyrka,M.D.Ph.D.,Lawrence Price,M.D.,Paul Stypulkowski,Ph.D., Jonathon Giftakis,Ph.D., Mark Rise,Ph.D.,Paul Malloy,Ph.D., Stephen Salloway,M.D.Ph.D., Benjamin Greenberg,M.D.Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the effects of long-term continuous deep brain stimulation of the ventral capsule/ventral striatum in patients with highly refractory major depression.

SUMMARY:

Purpose: This report extends previously published findings investigating the use of deep brain stimulation (DBS) of the ventral capsule/ventral striatum (VC/VS) for treatment refractory depression.
Methods: 17 patients with severe, chronic, highly refractory major depression were treated with DBS of the VC/VS at three collaborating centers. Stimulation was titrated to therapeutic effect and the absence of adverse effects. All patients received continuous stimulation in an open-label design. Outcome measures included the Hamilton Depression Rating Scale (HDRS-24), the Montgomery-Asberg Depression Rating Scale (MADRS), and the Global Assessment of Function Scale (GAF).
Results: The mean age at implant was 46.3 years with a 21.0 year mean duration of illness. In their current depressive episode, patients had an average of 6.1 antidepressant trials and 6.1 augmentation/combination trials. The mean number of lifetime ECT treatments was 30.5 with 15 of 17 patients having an adequate trial of bilateral ECT in their current episode. At the time of this report, patients have been followed for an average of 37.4 months (range 14-67). The average reduction in the MADRS was 52.7% at 3 months, 48.8% at 6 months, 54.8% at 1 year, and 59.2% at last follow-up ($p < .0001$ all time-points). Responder rates at these time points were 53%, 47%, 53%, and 71% respectively. Corresponding remission rates were 35%, 29%, 41%, and 35%. At 1 year, the average MADRS reduction in responders (n=9) was 78% versus an average of 28.7% in the non-responders (n=8), and GAF scores in these two groups showed a similar large difference. Stimulation was well tolerated overall. Suicidality improved significantly by 1 month. There was one completed suicide in a patient who received over 5 years of continuous DBS.
Conclusions: DBS of the VC/VS shows significant promise for the long-term treatment of patients with severe, refractory major depression. Research funding was provided by Medtronic.

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» NR6-010

COMBINED USE OF ELECTROCONVULSIVE THERAPY AND PSYCHIATRIC MEDICATION IN PSYCHIATRIC DISORDERS

Omer Saatcioglu M.D., Murat Kalkan M.D., Esra Ugurlu M.D., Ertugrul Cekic M.D., Nesrin Tomruk M.D., Dogan Yesilbursa M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize and treat in the combination of electroconvulsive therapy and psychiatric medication

SUMMARY:

Introduction: Combined use of electroconvulsive therapy (ECT) and psychotropic medication in acute phases of psychiatric disorders controversial and inadequately was investigated. This study tried to examine whether the ECT - psychotropic combination was effectiveness and side effects in the acute phase treatment of schizophrenia and mood disorder. Method: An open acute study of the combination of ECT and antipsychotics or antidepressants in the treatment of 65 (33 male and 32 female) psychiatric inpatients who were nonresponsive to psychotropic medication. In acute phase, patients were given the Brief Psychiatric Rating Scale (BPRS) for psychosis, the Young Mania Rating Scale (YMRS) for mania, Hamilton Depression Rating Scale (Ham-D) for depression, Clinical Global Index (CGI), and Mini-Mental State Exam (MMSE). Results: Before ECT, among patients with major depression with psychotic features, 20% (13/65) did not use adequate dose of an antidepressant. The majority of patients (65%) were treated with combination of atypical antipsychotics and other psychotropic agents (mood stabilizers, benzodiazepine or antidepressants) after ECT. Among all patients, 49.2% (32/65) used at least one benzodiazepine before ECT and only 0.03% (2/65) benzodiazepine after ECT. The majority of diagnoses was bipolar patients (43.1%) which were depressive and manic episode were 17.9% (5/28) and 82.1% (23/28) respectively. In acute phase, there were marked reductions in BPRS, YMRS, Ham-D, CGI scores into the combination of treatment. Conclusion: ECT combined with psychotropic drugs was effective in improving psychopathology in patients. The data provided by research is still insufficient to allow definitive conclusions on the combination of psychotropic medica-

tions and ECT. The combination is a safe and efficacious treatment strategy for patients with schizophrenia and affective disorder.

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2) Painuly N, Chakrabarti S: Combined Use of Electroconvulsive Therapy and Antipsychotics in Schizophrenia: The Indian Evidence. A Review and a Meta-analysis. J ECT 2006; 22:59-66.

» NR6-011

0.5 MS PULSEWIDTH PREVENTS BASIC ECT SIDE EFFECTS, AND PROPOFOL INTERRUPTION DIMINISHES EVEN SUBTLE SIDE EFFECTS

Ronald Warnell M.D., Conrad M. Swartz, Ph.D., M.D, Alice Thomson, M.A., Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should know about previously reported cognitive side-effects of ECT and how pulsewidth affects ECT stimulus efficiency. They will learn how ECT stimuli of 0.5 ms pulsewidth produced no decrease in basic cognitive functioning with bitemporal ECT and about how a new propofol interruption technique decreased even subtle cognitive dysfunction from ECT and diminished undesirably long ECT seizures.

SUMMARY:

OBJECTIVE: We aimed to decrease ECT cognitive side-effects by preventing long seizures with propofol infusion 15 sec post-stimulus.

METHODS: 15 patients completed six bitemporal ECTs after randomization to standard technique (N=7) or propofol interruption (N=8), double-blinded. We used brief-pulse 900 mA stimuli of 0.5 ms pulsewidth and etomidate anesthesia. WMS-III and MMSE were given before and after ECT and post-anesthesia reorientation times were recorded.

RESULTS: MMSE remained high for all (standard pre-ECT 29.4 post-ECT 28.6, propofol interruption pre-ECT 28.5, post-ECT 28.5), compared to highest previously reported post-ECT MMSEs of 26 for bitemporal, 28 for bifrontal, and 28.4 for LART. Standard treatment produced significantly more ECT-induced cognitive changes on Auditory Delayed Memory, Verbal Paired Associates Recall, Letter-Number Sequencing, Auditory Immediate Memory, Visual Immediate Memory, Faces I, and Immediate Memory WMS-III subtests. Other tests were not statistically significant but all favored propofol interruption. Standard technique produced the longest seizures (p=0.027).

CONCLUSIONS: This is the first cognitive data about 0.5 ms pulsewidth. Six bitemporal ECTs with 0.5 ms pulsewidth stimuli produced no decrease in basic cognitive functioning. Our post-ECT MMSE of 28.5 leaves no room for further improvement. The results suggest that 0.5 ms is the optimum pulsewidth, with both superior efficiency and minimal side-effects. Propofol interruption decreases even subtle ECT cognitive effects. It may be clinically useful for patients with past ECT cognitive dysfunction, for those who receive more than six ECTs, or for ECTs with a pulsewidth wider than 0.5.

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1) Swartz CM, Manly DT. The efficiency of ECT stimulus characteristics. Am J Psychiatry 2000; 157:1504-6

2) Swartz CM, Nelson AI. Rational electroconvulsive therapy electrode placement. Psychiatry 2005, 2005; 2(7):37-43

» NR6-012

ROLE OF ACUTE AND MAINTENANCE ECT IN CHRONIC PAIN: NEW CASE REPORTS AND CLINICAL LITERATURE REVIEW

Muhammad A. Abbas, M.D., Mitchell J.M. Cohen, M.D., John M. Balacius, M.D.

EDUCATIONAL OBJECTIVES:

1.Recognize that electroconvulsive therapy (ECT) has been used for over 60 years to treat chronic pain unresponsive to other modalities, with and without presence of co-morbid depression

2.Learn the differential responses to ECT reported for specific pain conditions

3.Recognize the successful use of maintenance ECT through 2 case reports unique in the literature, demonstrating ongoing effectiveness of outpatient ECT over 6-12 year periods.

SUMMARY:

Reports dating back 60 years describe ECT, proven effective in severe depression, as also effective for chronic pain, and if present, comorbid depression.1,2,3 Some pain disorders reported as ECT-responsive include trigeminal neuralgia, complex regional pain, and phantom limb pain.4,5,6 Others show less clear ECT response, e.g. thalamic pain, postherpetic neuralgia, and fibromyalgia. Longer ECT courses and bilateral lead placement may increase efficacy.7, 8,9 We present 2 neuropathic pain cases with comorbid depression controlled by ECT over longest as-yet reported periods. Case #1: 75-yo woman with peripheral neuropathy causing burning and numbness in feet and paresthesias of hand, complicated by severe depressed mood, ruminative anxiety, and isolation. Multiple consultations and trials of over 20 drugs were unhelpful. ECT: Admitted for ECT 11 months after presentation. Five weeks after hospital discharge, gains noted in pain and mood eroded despite outpatient care. Maintenance ECT started for recurrent symptoms at 2-week, 3-week, now 4-week intervals (> 6 years of steady ECT). Results: Pain and mood improved, sustained with maintenance ECT at widening intervals. Pre-ECT to post-ECT changes were clinically apparent and seen on measures including: 44-point drop on VAPS (visual analogue 0-100 point pain scale), Beck Depression Inventory (BDI) drop 35 to 21, 50% less self-reported functional impairment. Case #2: 52-yo male with burning right anterior chest pain, right upper extremity (RUE) "frostbite" pain shooting to fingers, and light-touch allodynia after cervical spine injury and multiple related surgeries. He was severely depressed and kept RUE close to body, flexed at elbow, with diffuse RUE muscle atrophy. ECT: Admitted for ECT 18 months after presentation; ECT provides pain reduction, RUE mobility, and resolution of depression. Maintenance ECT continued after discharge with relapse of symptoms upon attempts to taper ECT, so bilateral ECT ongoing at 2- to 3-week intervals for 12 years. Results: Pain, mood, RUE mobility improve consistently with ECT. Pre-ECT to post-ECT changes: 35-point VAPS drop, BDI drop 28 to 19, 18% less self-reported functional impairment. Conclusion: Our experience supports analgesic ECT effect and authors' case reports show longest documented ongoing ECT benefit.

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in patients with depression and fibromyalgia. European J Pain 2004; 8(4):371-6.

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» NR6-013

THE EFFECT OF MILNACIPRAN ON PAIN MODULATION IN FIBROMYALGIA: AN FMRI ANALYSIS

Ernest Choy M.D., Frank Petzke, M.D., Hanke Marcus, M.D., Karen Jensen, M.D., Eva Kosek, M.D., Martin Ingvar, M.D., Olivier Vitton, M.D., Yves Mainguy, M.D., Richard H. Gracely, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of the presentation, the participant should be able to identify brain regions associated with pain in normal vs fibromyalgia patients and understand the effect of milnacipran on pain modulation in patients with fibromyalgia.

SUMMARY:

Introduction: Fibromyalgia (FM) is characterized by chronic widespread pain and tenderness. The relationship of tenderness to the pathophysiology of FM is poorly understood, but has been proposed to be a correlate of dysfunctional endogenous pain modulatory mechanisms in FM patients. Whether experimental tenderness measured at baseline improves with effective symptomatic treatment is unknown. This study examined the effect of milnacipran on tenderness in FM patients. Methods: Ninety-two female FM patients received milnacipran 200 mg/d or placebo in a 13-week, double-blind, placebo-controlled trial. Patients received individually calibrated painful (50 mm rating on a 100 mm VAS scale) or non-painful (VAS rating of 0) blunt pressure stimuli randomly applied for 2.5 s to the left thumbnail. Experimental tenderness and fMRI assessments were performed at baseline and post-treatment. Results: Baseline fMRI analysis of all patients showed pressure-evoked brain activity in the pain matrix, including the insular and cingulate cortices, cerebellum, thalamus, and primary and secondary somatosensory cortices. Milnacipran-treated patients reported a reduction in VAS ratings of experimental tenderness compared to placebo (P=.055). fMRI analysis of milnacipran-treated patients revealed significantly increased brain activity in the caudate nucleus, anterior insula, anterior cingulum, and amygdala. In contrast, placebo-treated patients showed activity in the parietal region and mid-insula. Conclusions: Milnacipran reduced tenderness and increased pressure-evoked brain activity in regions known to be involved in pain modulation, resulting in activity similar to that found previously in normal subjects. Placebo treated patients demonstrated a different fMRI pattern. This effect of milnacipran on experimental tenderness suggests an association between the clinical symptoms of FM and increased tenderness noted in FM. Supported Statement: Study supported by Pierre-Fabre Medicament

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» NR6-014

A DAY-TO-DAY ANALYSIS OF THE ANALGESIC EFFICACY OF MILNACIPRAN IN THE TREATMENT OF FIBROMYALGIA

R. Michael Gendreau M.D., Philip Mease, M.D., Robert H. Palmer, M.D., Ph.D., Yong Wang, Ph.D., Michael R. Hufford, Ph.D., Srinivas Rao, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to explain that fibromyalgia patients experience day-to-day variability in pain intensity, and should be able to recognize the role of milnacipran in the treatment of pain associated with fibromyalgia.

SUMMARY:

Introduction: The chronic pain associated with fibromyalgia (FM) is characterized by marked day-to-day fluctuations in intensity. Thus, an important therapeutic goal is to substantially increase the number of days that FM patients experience pain relief over an extended time. Two double-blind trials previously demonstrated safety and efficacy of milnacipran in FM patients. Using pain data recorded daily from patients using electronic diaries (e-diaries), milnacipran's day-to-day effects on pain during these 2 studies were examined. Methods: FM patients were randomized to receive placebo, milnacipran 100, or 200 mg/d for 27 weeks (Study 1) or 15 weeks (Study 2). Pain was assessed by a 24-hour recall VAS pain scale (0-100) collected daily using e-diaries. Days with meaningful pain relief were defined as days that a patient reported >/=30% or >/=50% improvements from their mean baseline pain score. The effect of milnacipran treatment vs placebo on the proportion of days with meaningful pain relief was analyzed over the entire 3-month treatment period, based on Week 15 observed cases. Results: Patients treated with milnacipran 200 mg/d (n=264) and 100 mg/d (n=140) achieved >/=30% pain reduction in 47% and 46% of days, respectively, during the 3-month period compared to 31% for placebo (n=161; P<.001, both doses) in Study 1, and 45% (200 mg/d, n=256) and 44% (100 mg/d, n=262) of days compared to 34% for placebo (n=288; P<.001, both doses) in Study 2. Similarly, milnacipran-treated patients achieved >/=50% pain reduction in a significantly greater proportion of days over the 3-month period than patients on placebo (Study 1: both doses, 30% vs 17%, respectively; Study 2: 28% and 25% vs 18%, respectively; P<.01, both doses, both studies). Conclusions: Milnacipran treated FM patients experienced more days of meaningful pain relief over a 3-month treatment period than patients on placebo. Supported Statement: Supported by Forest Laboratories, Inc. and Cypress Bioscience, Inc.

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» NR6-015

EFFECT OF MILNACIPRAN ON FATIGUE AND COGNITIVE DYSFUNCTION IN FIBROMYALGIA PATIENTS

Alan Manevitz M.D., Kim Thacker, M.D., Joel Trugman, Ph.D., Srinivas G. Rao, M.D., Ph.D., Yong Wang, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of the presentation, the participant should be able to identify multiple symptoms of fibromyalgia, explain the term "fibrofog," and convey the effects of milnacipran on fatigue, cognitive dysfunction, and energy in fibromyalgia patients.

SUMMARY:

Introduction: Fibromyalgia (FM) is a chronic pain disorder associated with multiple other symptoms including fatigue and cognitive dysfunction (sometimes termed "fibrofog"). Cognitive dysfunction in FM patients commonly involves problems with memory, concentration, and verbal fluency. Fatigue may exacerbate cognitive difficulties in FM patients. Methods: A pooled analysis from 2 FM studies was conducted. Patients were randomized to placebo (n=624), milnacipran 100 mg/day (n=623), or milnacipran 200 mg/day (n=837). Analyses assessed self-reported measures of cogni-

tion (Multiple Ability Self-report Questionnaire [MASQ]), fatigue (Multidimensional Fatigue Inventory [MFI]), and energy/vitality (SF-36 vitality subscale). Pooled data on mean changes from baseline at Week 15 were analyzed using mixed model repeated measures. Results: Patients treated with milnacipran 200 mg/day demonstrated significantly greater improvement over placebo in MASQ total scores (P=.007) and MASQ attention scores (P<.001). Both milnacipran groups had significant improvements compared to placebo on MASQ verbal memory scores (P<.05). MFI total scores were significantly improved with both doses of milnacipran (P<.05, vs placebo). Significant improvements compared to placebo were observed with milnacipran 200 mg/day on all MFI domains, including MFI mental fatigue (P=.006). Milnacipran 100 mg/day significantly improved the MFI physical fatigue and MFI reduced motivation domains (P<.05). SF-36 vitality scores were significantly improved over placebo in both milnacipran dose groups (P<.05).
Conclusions: Milnacipran produced significant reductions in fatigue and improvements in energy levels and cognitive function in FM patients. Furthermore, significant improvements were observed in cognitive symptoms common among FM patients, such as attention and memory deficits. Supported Statement: Study supported by Forest Laboratories, Inc. and Cypress Bioscience, Inc.

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» NR6-016

EFFICACY OF MILNACIPRAN IN FIBROMYALGIA IS INDEPENDENT OF ANTIDEPRESSANT PROPERTIES: A EUROPEAN MULTICENTER, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Michael Spaeth M.D., Jaime Branco, M.D., Bjorn Bragee, M.D., Olaf Zachrisson, M.D., Ph.D., Knut Mikkelsen, M.D., Luis De Teresa, M.D., Yves Mainguy, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of the presentation, the participant should be able to explain the clinical relevance of a composite responder analysis, recognize the role of milnacipran in the treatment of fibromyalgia in both US and European patient populations, and understand that milnacipran's efficacy in fibromyalgia is likely independent of antidepressant properties.

SUMMARY:

Introduction: Milnacipran, a dual norepinephrine-serotonin reuptake inhibitor, has demonstrated efficacy in the treatment of fibromyalgia (FM) in US patients. This study investigated the efficacy and safety of milnacipran for the treatment of FM in a European population. Methods: A total of 884 FM patients received placebo (n=449) or milnacipran 200 mg/d (n=435) for 12 weeks of fixed dose exposure following a 4-week dose escalation phase. The primary efficacy analysis was a 2-step sequential testing procedure performed at Week 16. Step 1 utilized a composite response criterion (individuals concurrently having >/=30% improvement from baseline in 24-hour recall pain and a rating of "very much improved" or "much improved" on the Patient Global Impression of Change scale). Step 2 subsequently compared the mean change from baseline in Fibromyalgia Impact Questionnaire (FIQ) total score. Subset analyses based on baseline Beck Depression Inventory (BDI) scores were also performed. Results: Milnacipran-treated patients showed a significantly greater improvement over placebo in the proportion of composite responders (P=.0003; odds ratio=1.9; 95% CI, 1.34-2.68) and in the FIQ total score (P=.015). Overall improvements in condition and functioning was confirmed by significant improvements in PED weekly-recall pain (P=.001), Brief Pain Inventory (P=.0008), SF-36 MCS (P=.007), SF-36 PCS (P=.025), Multidimensional Fatigue Inventory (P=.006), FIQ Physical Function (P=.021), and the Multiple Ability Self-Report Questionnaire (P=.041). Between group differences in the number of composite responders were largest in patients with lower baseline BDI scores (BDI</=10). The most common adverse events with milnacipran were nausea and headache. Conclusions: These findings confirm that milnacipran is an effective treatment for the multiple symptoms of FM and suggest that efficacy is independent of the antidepressant effect. Supported Statement: Study supported by Pierre-Fabre Medicament

REFERENCES:

1) Mease PJ, Clauw DJ, Gendreau RM, et al. The Efficacy and Safety of Milnacipran for Treatment of Fibromyalgia. A Randomized, Double-Blind, Placebo-controlled Trial. J Rheumatol. 2008:In press.

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» NR6-017

MILNACIPRAN IMPROVES FUNCTIONING IN PATIENTS WITH FIBROMYALGIA (FM): RESULTS FROM A 15-WEEK, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Vibeke Strand M.D., David A. Williams, Ph.D., Daniel J. Clauw, M.D., Robert H. Palmer, M.D., Ph.D., R. Michael Gendreau, M.D., Ph.D., Rong Zablocki, Ph.D., Wei Chen, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to identify common symptoms of fibromyalgia and recognize the potential role of milnacipran in improving physical and mental functioning and overall health related quality of life in patients with fibromyalgia.

SUMMARY:

Introduction: In addition to chronic pain, FM patients suffer from deficits in physical and mental functioning, fatigue, and decreased well being. Milnacipran, a dual reuptake inhibitor of NE and 5-HT with a preference for NE reuptake inhibition, has demonstrated efficacy in treatment of FM. Methods: FM patients (N=1196) were randomized to placebo, milnacipran 100 mg/d, or 200 mg/d. Global improvement was assessed by the Patient Global Impression of Change (PGIC) scale. Health related quality of life (HRQOL) was assessed by Short Form-36 (SF-36) Physical and Mental Component Summaries (PCS and MCS, respectively) and individual domain scores. Changes from baseline were analyzed using observed cases; responder rates were determined using a mixed-effects model. Results: Significantly more milnacipran-treated patients reported clinically meaningful improvements (rating of very much improved or much improved) on the PGIC at each visit (Week 15: 100 mg/d, 44.9%; 200 mg/d, 51.3%; placebo, 26.4%; P</=.001, both doses vs placebo). SF-36 PCS scores were significantly improved vs placebo at all visits with milnacipran 100 mg/d (P<.05), with significantly more milnacipran- vs placebo-treated patients reporting a >/=6 point improvement, exceeding MCID values of 2.5 to 5.0. Significant improvements vs placebo were also observed in physical functioning and bodily pain domains with both doses of milnacipran at endpoint and most visits (P<.05). Improvements in physical domains with milnacipran 200 mg/d, were accompanied by strong improvements in mental domains; SF-36 MCS, mental health, and role-emotional domain scores were significantly improved with milnacipran 200 mg/d vs placebo at all visits (P<.05). Conclusions: In patients with FM, treatment with milnacipran resulted in improvements in patient's perceptions of their global status as well HRQOL, both physical and mental domains. Supported Statement:

Study supported by Forest Laboratories, Inc. and Cypress Bioscience, Inc.

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» NR6-018

POSTTRAUMATIC STRESS SYMPTOMS AFTER ADMISSION TO THE EMERGENCY ROOM FOR DELIBERATE SELF POISONING

BENJAMIN BOUSQUET, Bui Eric, M.D., Ladois Agnes, Cailhol Lionel, M.D., Schmitt Laurent, M.D., Arbus Christophe, M.D., Birmes Philippe, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize and question how he can prevent the traumatic impact of an admission in an emergency unit after a suicide attempt by self poisoning. He also should be able to question the impact of the suicide attempt.

SUMMARY:

We wanted to question the impact that may generate some of our interventions in psychiatry and psychiatric emergency.
OBJECTIVES: This study aimed to assess the impact of psychological trauma after a suicide attempt by self poisoning followed by an admission to an emergency unit.
METHOD: This is a cohort study, 198 participants were recruited from three general emergency wards after psychiatric assessment, then they have received a letter at 6 months with a PTSD Checklist self-administered in order to assess the PTSD symptoms related to the suicide attempt and admission in an emergency unit.
RESULTS: Thirty seven percents (n = 74) of patients have completed and returned the questionnaire. Thirty percents of them (N = 22) had symptoms of PTSD clinically significant for the population suffering from serious mental illness.
CONCLUSION: These results indicate that there is a traumatic impact after an admission to an emergency unit following a suicide attempt. There are iatrogenic psychological traumas of care in emergency and we question the impact of suicide attempt itself.

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» NR6-019

THE EFFECTIVENESS OF "HOME TREATMENT" FOR THE ACUTELY MENTALLY ILL IN A RURAL CATCHMENT AREA IN SOUTHERN GERMANY

Karel Frasch M.D., Miriam Ott, Henriette Jahn, M.D., Annett Rauscher, Markus Jaeger, M.D., Thomas Becker, M.D., Reinhold Kilian, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize Home Treatment as a clinically effective alternative to hospitalization in some acutely mentally ill patients and that in contrast to the US and the UK, this kind of mental health service is still in its infancy in many European countries. Furthermore, attendees should be able to name the most frequent diagnoses in a suchlike program and be in a position to specify rating scales measuring its clinical effectiveness.

SUMMARY:

Introduction: In contrast to a broad empirical data base in the US and the UK (Burns et al. 2002), non-British European "Home Treatment" (HT) services have rarely been scientifically evaluated. HT means psychiatric intervention in the acutely mentally ill by a multiprofessional team mainly in the patients' usual environment and is hypothesized to be an equally effective alternative to inpatient treatment (TAU) in a subgroup of patients with mainly schizophrenia and affective disorders (Berhe et al. 2005). The first suchlike service in southern Germany was established in Guenzburg / Bavaria in 2005 - is our adaptation of HT clinically effective ?
Method: We prospectively studied 60 of our HT patients over a period of about two years by comparison of PANSS, HAMD-21 and HoNOS ratings at admission and discharge.
Results: According to ICD-10, our patients suffered mostly from schizophrenia / schizoaffective (n=25) and affective disorders (n=26, among them 5 bipolar depressive patients), 6 had adjustment disorders, one was mainly diagnosed with a personality disorder and two with organic mental disorders.
Patients with affective disorders showed a significant improvement of the PANSS total, general psychopathology and negative subscale, HAMD and HoNOS scores ($p<0,05$). Significant decreases in schizophrenia / schizoaffective patients occurred with respect to PANSS general psychopathology, HAMD and HoNOS scores. In the non-affective-non-schizophrenic group (n=9), significant improvements were found with respect to PANSS general psychopathology and HAMD scores.
In all other investigated dimensions, we found nonsignificant trends towards clinical improvement.
Conclusion: HT as we practice it seems to be clinically effective in all studied subgroups, especially with regard to depressive symptomatology, which turned out to be the most frequent reason for allocation to this kind of service.

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» NR6-020

PATIENT RELOCATION TO A NEW HOSPITAL: SOME CLINICAL PARAMETERS

David Mayerhoff M.D., Steven J. Schleifer, MD, Jeffry R. Nurenberg, MD, Roland Limosnero, MD, Paresh Kasabwala, Psy.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, participants will have a better understanding of clinical aspects of a wholesale move of largely long-term psychiatric inpatients to a new facility, and the ability of clinicians to predict patient adaptation to such events. Better understanding by participants of the clinical dimensions of this major patient event will facilitate their development and implementation of administrative and clinical strategies for similar future transitions.

SUMMARY:

Moving a state hospital population (57% hospitalized >2 years) to a new facility on a single day is likely to pose considerable stress for patients. Preparation for our July,2008 transition of 414 patients from several older buildings to a newly built hospital proceeded over 18 months. In a performance improvement project to determine the clinical impact of this event, the Brief Psychiatric Rating Scale (BPRS), as well as a 4-point "transition" scale assessing anticipated and then post-move perceived patient difficulty ("none" to "a lot"), and the single-item Likert-type Greystone Intrusiveness Measure (GIM) of perceived patient intrusiveness were completed by staff. On one discharge-focus unit, measures

obtained 2 months before were compared with measures three months after the move (with a further measure 1 month later). Of 38 patients resident on that unit or its successor during the transition, 28 had both pre- and post-measures. BPRS appeared to increase during the interval (paired t=1.91,df 27, p<0.07), with no significant increase in GIM (t=1.43,df 27, p ns). GIM at baseline was correlated with concurrent (r=0.37,p<0.06) and post-move (r=.38,p<0.05) BPRS. Predicted move difficulty at baseline (46% "some"/11% "a lot") was not associated with concurrent BPRS (r=.23), but was with GIM (r=.43, p<0.025). Predicted difficulty was not associated with post-move BPRS (r=.11), GIM (r=.13), or clinical difficulty (r=.25)(46% some/7% a lot; 1 of 3 patients predicted to have much difficulty, reportedly did so). Difficulty post-move was not predicted by any pre-move measure. (Similar patterns were found for 6 patients resident on the unit throughout). These data suggest that the transition to a new facility was associated with a modest increase in clinical symptomatology, while clinicians have only a modest ability to predict which patients will have difficulty with the transition. The brief GIM measure appears to have clinical and administrative utility.

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» NR6-021

A TWO-STATE ANALYSIS OF EMERGENCY DEPARTMENT UTILIZATION BY PERSONS WITH MENTAL HEALTH AND/OR SUBSTANCE ABUSE DISORDERS

Meera Narasimhan, Elsie Freeman, Benjamin Druss, Joe Morrisey, Jeanne Rivard and John Magill

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to 1.To understand the workings of state collaborations used pooled analysis of data from data warehouses.
2.Review the utilization of emergency departments by those with behavioral health and physical health conditions.

SUMMARY:

Objective: To study the use of emergency departments in four study groups: mental disorders substance abuse disorders co-occurring mental and substance abuse disorders and persons with no mental health or substance abuse disorders.
Background: National data estimates that as many as 70% of all Emergency Room (ER) visits are either non urgent or could have been treated in a primary care setting. These avoidable ER visits contribute to rising health care costs. Most state mental health authorities are also concerned with high rates of ER use by persons with behavioral health problems.
Methods: The sample was composed of all Medicaid eligible individuals in South Carolina (SC) and Maine (ME) who met the following criteria: 1) were continuously eligible 11 out of the 12 months during that 2006-2007 fiscal year 2) at least one service claim based on service rendered date, not including pharmaceutical claims; between the ages of 19 to 64 years. The project was approved by the Medicaid review board.
Results: The overall rate of ER usage differed in the two states, with an overall rate of 1425 visits/1000 members /year for ME and 827 visits/ 1000 members/ year for SC, compared to a national average of 566 visits/1000 for Medicaid HMO's. The highest percentage of users in both states was in the co-occurring group (ME 80% and SC 70%). The percent of high users (>4 visits/year) in the co-occurring group was 24.9-34.5% . Persons with behavioral health conditions used the ER for medical reasons 3.5 -4.0 times more than did the non-behavioral health group in both states.
Conclusions: The analyses presented was conducted as part of a project, funded by the NIMH, to develop infrastructure for conducting multi-state mental health policy analyses. The expectation is that greater utilization of such databases can strengthen our understanding of mental health system problems to stimulate cross-fertilization of innovative state strategies to solve long standing mental health problems.

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» NR6-022

OPEN ACCESS TO ANTIPSYCHOTIC AND PRESCRIBING TRENDS AND QUALITY OF LIFE

Meera Narasimhan,Robert Bank and John Magill

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to 1. Understand the implications of open access on quality of care of patients with mental illness 2. Evaluate the prescribing trends of antipsychotics in real world clinical practice

SUMMARY:

Objective: To identify opportunities for quality improvement and cost reduction with an analysis of antipsychotic prescribing trends within an open access fee for service Medicaid organization.
Background: There have cost containment strategies employed by agencies such as Medicaid involving restricted access to certain antipsychotics that can have a bearing on the overall quality of life of a patients and implications in terms of increased healthcare utilization.
Methods: South Carolina Medicaid is a fee for service Medicaid serving approximately 782,000 lives. Prescription pharmacy claims identified from January2007 through December 2007 were analyzed. The study was approved by the Medicaid Review Board.
Results: There were 148,823 claims evaluated for 20,625 Medicaid beneficiaries. Among those on antipsychotic medications, 78% (16,068) were dispensed atypical antipsychotics (AA) and 27% (5,532) conventional antipsychotics (CA) The mean age of patients was 31 years for AA and 44 years for CA agents. The percentage claims for oral AA was81% (120,713) as compared to 16% for oral CA and 3% for risperidone long-acting therapy (RLAT). Risperidone was the most frequently prescribe oral atypical antipsychotic agent (33%) followed by quetiapine (26%), aripiprazole (15%), olanzapine (13%), ziprasidone (9%) and paliperidone (2%). The average daily dose for oral atypical antipsychotics was aripiprazole 15.2mg, clozapine 408.6mg, olanzapine 15.1mg, quetiapine 354.3mg, paliperidone 6.3mg, risperidone 2.5mg, ziprasidone 128.5mg. Concomitant antipsychotic therapy was 4% for oral antipsychotics. The medication possession ratio (MPR) was highest 0.87 for RLAT; 0.83 for oral AA; and 0.79 for oral CA.
Conclusions: In clinical practice certain atypical oral antipsychotics commonly above FDA approved ceiling doses are utilized. Educational initiatives and targeted communication aimed at prescribers of high dose therapy, concomitant antipsychotics and patient adherence are required.

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2)Importance of open access to atypical antipsychotics for the treatment of schizophrenia and bipolar disorder: a European perspective.Altamura AC, Armadoros D, Jaeger M, Kernish R, Locklear J, Volz HP. Curr Med Res Opin. 2008 Aug;24(8):2271-82. Epub 2008 Jun 26.

» NR6-023

THE USE OF FILM PRODUCTION ABOUT MENTAL HEALTH ON REHABILITATION OF PATIENTS WITH CHRONIC PSYCHOSIS: WELL BEING AND QUALITY OF LIFE OF PARTICIPANTS

Mauro Giovanni Carta M.D., Enrico Pau, Giovanni Piras, Laura Pilutzu, Carlo Zuddas, Psy.D., Maria Carolina Hardoy, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to coordinate a project on the production of didactic short films about mental health in the work of rehabilitating chronic psychotic patients and to evaluate the wellbeing and the quality of life of participants.

SUMMARY:

Objective: This work presents the results of a project that utilized the production of a didactic short film on mental health in the work of rehabilitating persons suffering from chronic psychosis. Data regarding the subjective wellbeing of patients, measured by structured tools is presented, together with a sample of the cinematographic material produced.
Methods: Setting: 2 outpatient psychiatric care units in Sardinia (Italy). Subjects: 10 patients (2 Schizophrenia, 8 Bipolar Disorder) participated in an educational film about mental health.
Conductors: 15 students of a Psychiatric Rehabilitation Technician career program as stagehands, 2 directors, a screenwriter, 4 collaborative writers (together with patients), and 2 psychiatrists. Themes for the film: personal stories and explication of the symptoms from a "patient centered" point of view. Interventions: group discussion, creative text writing, problem solving. Measures: CGI for general clinical conditions, WHOQOL-BREF for life satisfaction.
Controls: 20 patients not participants in the study. Evaluation time: 4 months after the start of the project.
Results: At the start point 10 subjects had a mean score on the CGI of 3.5±0.3, at the end 3.2±0.4 (F=5.0 P<0.05 19 DF), against controls: initial score of 3.5±0.4 and end score of 3.5±0.4 (F=0.1, P=0.9 29 DF). One subject had a 32-day interruption of work for a depressive episode, but following improvement re-joined the study. Concerning WHOQOL-BREF only the social relationship domain showed an improvement in the "short film" group against the control group (P<0,05).
Conclusions: A working activity, with a mental health professional support, seems to represent an effective tool to increase the social competence of patients with chronic psychosis. The study seems to suggest that the specific tool of film, focusing on the personal stories of the patients may constitute an optimal rehabilitative instrument. A study on a larger sample of patients is needed.

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» NR6-024

THE PRACTICE OF RECOVERY: A DESCRIPTIVE ANALYSIS OF A COMMUNITY MENTAL HEALTH PROGRAM

CHIH-TAO CHENG M.D., Leonard S. Miller, Ph.D., Sheng-Chang Wang M.D.,M.Sc., Yi-Ling Chien M.D.

EDUCATIONAL OBJECTIVES:

The concept of 'recovery' is often not well understood and operationalized. The audience of this poster should be able to identify the key components of a recovery-oriented mental health service through this qualitative analysis.

SUMMARY:

Objectives: To provide empirical evidence about recovery practice and illustrate the problems encountered by the clients and services provided to them at different stages of recovery.
Method: We analyzed the progress notes of 23 clients from different stages of recovery in a model community mental health program. A ground theory based approach was used to identify prominent themes in the progress notes. Secondly, a content analysis was done to evaluate the frequency of the 3 types of services (treatment, rehabilitation and case-management) provided at different recovery stages.
Results: The analysis identified the problems encountered by the clients, the service provider roles, the interventions, and the techniques used in the progress notes. Secondly, we found that there's a relatively higher frequency of rehabilitation services provided at the middle stages of recovery.

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1) Davidson, L., Tondora, J., O'Connell, M. J., Kirk, T., Jr., Rockholz, P., & Evans, A. C. (2007). Creating a recovery-oriented system of behavioral health care: moving from concept to reality. Psychiatr Rehabil J, 31(1), 23-31.

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» NR6-025

MENTAL HEALTH DISPARITIES AMONG ASIAN AMERICAN AND PACIFIC ISLANDERS IN CALIFORNIA: AN APPLICATION OF THE INSTITUTE OF MEDICINE HEALTH DISPARITY MODEL

CHIH-TAO CHENG M.D., Diana D. McDonnell, Ph.D., Hyun-Ju Lee, B.A., Joel M. Moskowitz, Ph.D.,Sheng-Chang Wang M.D.,M.Sc., Yi-Ling Chien M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the key components (medical conditions, preferences of the clients and the treatment differences) in the health disparity model proposed by the Institute of Medicine. The participant should also be able to recognize the mental health disparities encountered by the Asian American and Pacific Islanders in California using this model.

SUMMARY:

Background: Asian Americans and Pacific Islanders have been reported to use fewer mental health services than non-Asian Americans. Some researchers claimed that it's because they have less need for the mental health services.
Objectives: This study updated the information on the mental health need and access to mental health services by analyzing the California Health Interview Survey (CHIS) data collected in 2005.
Method: We examined the mental health disparities among Asian Americans and Pacific Islanders by looking at their psychological stress, self-reported need, and use of mental health services.
Results: We found significant disparities in the access to mental health services among Asian Americans and Pacific Islanders even after taking into account of their mental health conditions and perceived need. We also discussed the potential factors that might lead to the mental health disparities among them, such as linguistic and cultural barriers.

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1) Institute of Medicine, Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care. 2002, Washington, DC: National Academy Press.

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NR6-026

PSYCHOSOCIAL REHABILITATION'S IMPACT ON THE NUMBER AND TOTAL LENGTH OF INPATIENTS' ADMISSIONS

Tiago Rodrigues M.D., Rosa Quelhas, M.D., Joaquim Ramos, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to to acknowledge the importance of Psychosocial Rehabilitation (PR) intervention in reducing the patients' needs for psychiatric hospitalization, and recognize its benefit in other than severe mental disorders. Therefore, after this presentation the participant must consider PR intervention for a larger group of patients, including those with "minor" mental disorders, offering them the possibility of a better clinical course.

SUMMARY:

Objective: Psychosocial rehabilitation's (PR) major goals include patients' social integration and improvement of their general outcome. Most of the previous studies assessing the impact of PR interventions focused on patients with severe mental disorders, and pointed out several outcome improvements. To our knowledge, there is no previous study evaluating the impact of PR in the number and total length of inpatients' admissions among different diagnoses. The authors' main goal was to study the impact of PR intervention in patients' needs for acute hospitalization among different diagnostic groups (DG).

Method: This longitudinal retrospective study reviewed social and diagnostic features of all patients admitted in the PR Service (PRS) of Hospital Magalhães Lemos (Portugal) for 17 years. The outcome measures were "number of inpatient admissions" (NIA) and "total length of stay" (LS) per unit of time, before and after patients' admission in PRS.

Results: Our sample included 590 subjects, with 53% men and a mean age of 39 years old. The most prevalent DG was Schizophrenia/Delusional Disorder (46%), followed by Neurotic, stress-related and somatoform Disorders/Depressive Disorder Unspecified (21%); other important diagnoses were Major Affective Disorder (13%) and Personality Disorder (8%). The results showed significant reduction in NIA/year and/or LS/100days after PRS admission regardless of sex, marital status and diagnosis. Multivariate analysis showed that previous LS/100days predicted LS/100days reduction after PRS admission; female gender, older age and higher previous LS/100days predicted a higher reduction in LS/100days after PRS.

Conclusion: PRS intervention significantly impacts on patients' clinical course and its benefit is not restricted to severe mental disorder diagnosis. Psychiatrists must regard PR as a cost-effective intervention in major and minor psychiatric diagnoses, and base their referral criteria in individualized clinical and socio-demographic factors.

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NR6-027

PALIPERIDONE PALMITATE: CLINICAL RESPONSE IN SUBJECTS WITH SCHIZOPHRENIA WITH RECENT VS. LONGER-TERM DURATION OF ILLNESS

Larry Alphs M.D., Cynthia Bossie, Ph.D., Jennifer Kern-Sliwa, Pharm.D., B.C.P.P., Yi-Wen Ma, Ph.D., J. Thomas Haskins, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participants should be able to describe the differences in recurrence rates, time to recurrence, study completion rates, and reasons for early study withdrawal among subjects with a more recent diagnosis of schizophrenia compared to those with a longer duration of illness receiving paliperidone palmitate or placebo. This information may help guide the treatment of patients with schizophrenia, particularly for those with a more recent diagnosis.

SUMMARY:

Background: The early identification and effective treatment of psychosis may contribute to a better therapeutic response and less deterioration in patients with schizophrenia. A recent trial (CRO004198) of schizophrenia subjects stabilized on paliperidone palmitate showed a lower recurrence rate in those randomized to continue paliperidone palmitate in the double-blind phase compared to those given placebo (15% [31/205] vs 47% [95/203], p<0.0001).

Objective: To characterize clinical responses in those with a more recent diagnosis of schizophrenia (≤5 years [yrs]) compared to those with a diagnosis >5 yrs.

Methods: Post-hoc analyses of the CRO004198 database were performed.

Results:Among the subjects who entered the double-blind study, 145 (70 paliperidone palmitate, 75 placebo) were diagnosed ≤5 yrs and 263 (135 paliperidone palmitate, 128 placebo) >5 years. The recurrence rate was lower with paliperidone palmitate compared to placebo in those with a time since diagnosis ≤5 yrs (20% vs. 44%, p=0.0025) and those with a time since diagnosis >5 yrs (13% vs. 48%, p<0.0001). Paliperidone palmitate was associated with a longer time to recurrence compared to placebo in those with a diagnosis ≤5 yrs (p=0.0011) and >5 yrs (p<0.0001). Among paliperidone palmitate subjects with a diagnosis ≤5 yrs, 71% (50/70) completed the double-blind study without recurrence compared to 45% of placebo-treated subjects (34/75, p=0.0023); findings were similar in those with a diagnosis >5 yrs ago (69% [93/135] vs. 36% [46/128]; p<0.0001). Early withdrawals (other than recurrence) in the population diagnosed ≤5 yrs vs. >5 yrs were reported as: subject choice (3% vs. 9%), adverse events (0% vs. 2%) and other (6% vs. 6%).

Conclusions: This post-hoc analysis suggests that paliperidone palmitate has a lower recurrence rate and increases the time to recurrence as compared to placebo in subjects with schizophrenia, regardless of time since diagnosis. Supported by Ortho-McNeil Janssen Scientific Affairs, LLC, Titusville, New Jersey, USA.

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NR6-028

EVALUATING THE EFFECT OF DESVENLAFAXINE AND PAROXETINE ON THE CYP2D6-MEDIATED BIOTRANSFORMATION OF CODEINE TO MORPHINE

Susan Baird-Bellaire Ph.D., Stéphan Chalon, M.D., Ph.D, Jeffrey Paul, Ph.D, Alice Nichols, Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to 1. Recognize the potential negative effect of coadministering a CYP2D6 inhibitor with an agent that requires biotransformation via CYP2D6 to a pharmacologically active metabolite
2. Understand that desvenlafaxine does not impact the pharmacokinetics of agents metabolized by CYP2D6

SUMMARY:

Objective: This study assessed multiple doses of desvenlafaxine (administered as desvenlafaxine succinate) and paroxetine on the CYP2D6-mediated biotransformation of codeine to morphine.

Method: This randomized, open-label, 3-period, crossover study was conducted in healthy subjects. During period 1, subjects were administered a single dose of codeine 60 mg, followed by a wash-out period. In period 2, subjects received either desvenlafaxine 100 mg or paroxetine 20 mg for 8 days, on the 7th day they received codeine 60 mg concomitantly. Subjects received the alternate treatment combination during period 3. The mean area under the concentration-time curve to the last measurable concentration (AUCT) of codeine and morphine were the primary outcomes.
Results: In this population (n=37), which was primarily comprised of Caucasian males aged 21-45 years, no differences in the AUCT of codeine were observed between those receiving codeine (349 ng*hr/mL) and desvenlafaxine/codeine (348 ng*hr/mL). However, an increase in the AUCT of codeine was observed for paroxetine/codeine (382 ng*h/mL) compared with codeine (349 ng*hr/mL). In contrast, decreases were observed in exposure to morphine: codeine alone: 6.6 ng*hr/mL; desvenlafaxine/codeine: 6.1 ng*hr/mL; paroxetine/codeine: 0.2 ng*hr/mL. The mean difference in morphine AUCT following treatment with codeine alone and paroxetine/codeine treatment was 7.2 ng*h/mL (90% CI: 5.8-8.6 ng*h/mL; P<0.01). The mean difference in morphine AUCT for codeine alone and desvenlafaxine/codeine was 0.6 ng*h/mL (90% CI: -0.6-1.7 ng*h/mL; P=NS). No significant differences in safety and tolerability were observed.
Conclusions: The biotransformation of codeine to morphine was not significantly impacted by desvenlafaxine 100 mg; however, paroxetine significantly reduced exposure to morphine. Treatment with codeine and desvenlafaxine does not require dose adjustments that are necessary for drugs that inhibit CYP2D6 activity.
Supported by Wyeth Research

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» NR6-029

METFORMIN FOR BODY WEIGHT AND METABOLIC CONTROL IN PATIENTS WITH SCHIZOPHRENIA DURING LONG-TERM CLOZAPINE ADMINISTRATION

Trino Baptista M.D., Edgardo Carrizo, MD., Virginia Fernandez MD, Ignacio Sandia, MD, Lisette Connell, MSci., Dexy Prieto, MD., Dunnys Valbuena, MSci., Iliana Fernández, MSci.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to consider the use of the antidiabetic agent metformin to control excessive body weight and hyperglycemia in schizophrenia patients undergoing chronic treatment with clozapine, and to manage the expected side effects of this adjunctive pharmacological treatment.

SUMMARY:

The use of the atypical antipsychotic clozapine is associated with a high frequency of excessive body weight gain and the metabolic syndrome. To develop pharmacological strategies to counteract these side effects we administered Metformin XR (500 mg BID, n = 30) or placebo BID (n = 30) to long-term clozapine-treated subjects with schizophrenia in a randomized, double-blind, parallel group protocol for 14 weeks. The study was completed by 22 Metformin- and 28 placebo subjects. Analysis was conducted with and without the Last Observation Carried Forward method. Metformin was well tolerated and induced a significant body weight loss compared to placebo (-1.85 ± 3.1 vs. + 0.2 ± 2.9 kg; t (48) = 2.9, p = 0.02). The serum insulin levels were also significantly decreased by Metformin (p = 0.04) but the change in the Insulin Resistance Index (HOMA-IR) did not differ between the groups (p = 0.3). The HDL-cholesterol levels were significantly decreased by metformin (p = 0.02) but the change in triglycerides did not differ between the groups (p = 0.4) The positive effects ob body weight, insulin and HDL levels support the use of Metformin in psychiatric patients during treatment with atypical antipsychotics with high propensity to induce obesity and metabolic dysfunction.

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» NR6-030

QUETIAPINE INDUCED PROLONGED QTC INTERVAL IN PREGNANCY

Smitha Battula, M.B.B.S., M.D., Mary L. Miller, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the potential cardiovascular complication of quetiapine induced QTc interval prolongation in pregnancy.

SUMMARY:

Introduction:Data on quetiapine use in pregnancy is limited. Here we describe quetiapine induced QTc prolongation in a pregnant patient.
Case:A 25-week pregnant woman in her mid thirties with history of CAD, hyperlipidemia, obesity, and psychotic disorder was admitted with symptoms of chest pain on rest. Her previous cardiac cath showed 60% stenosis in obtuse marginal and mild disease in the rest of the coronary arteries. Initial ECG revealed a prolonged QTc interval of 505 milliseconds. Psychiatry consult liaison was notified.
The patient reported a diagnosis of schizoaffective disorder since the past 10 years and was being treated with 1000 mg of quetiapine and 20 mg of fluoxetine. Due to worsening sense of agitation quetiapine was increased to 1200 mg a week before the presentation. Serum electrolytes and cardiac enzymes were negative with no other precipitating cause of prolonged QTc. Quetiapine was decreased to 200 mg a day and olanzapine was added to the drug regimen. Repeat ECG showed normalization of QTc interval.
Discussion:Antipsychotic drugs are effective and frequently prescribed (1). However, serious cardiovascular side-effects including prolonged QTc interval, torsades de pointes and sudden cardiac death (SCD) have been infrequently reported (1, 2). Endogenously increased catecholamine levels influence cardiac repolarization leading to prolonged QTc in acute psychotic episodes (1). It is interesting to note that antipsychotic drug use is more frequent in females and females seem to be more prone to drug-induced QTc prolongation than males (1).
The lack of perinatal extrapyramidal side effects and experiences of safe use of atypical antipsychotics during pregnancy can support using antipsychotic treatment (2). However, data on long-term complications following in-utero exposure to the antipsychotics is not well studied (2). Tenyi et al reported quetiapine use in a schizophrenic pregnant female without complications (2).

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» NR6-031

LEVETIRACETAM DECREASES CORTISOL REACTIVITY IN HEALTHY WOMEN

Linda Carpenter M.D., Aaron P. Tracy, B.A., Audrey R. Tyrka, M.D., Ph.D., Charles W. Wilkinson, Ph.D, Lawrence H. Price M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize a possible mechanism of action of levetiracetam, particularly in relation to the biology of mood disorders and stress system funcion.

SUMMARY:
Background: The novel anticonvulsant Levetiracetam has been shown to lower corticosterone stress response in rodent models. The Dexamethasone/Corticotropin Releasing Hormone (Dex/CRH) test is a neuroendocrine probe of HPA axis function in humans. The Dex/CRH test was used before and after treatment with Levetiracetam to evaluate its effects on cortisol responsivity in healthy adults without psychiatric or neurological disorders. Methods: Healthy, medication-free adults (n=11) meeting a priori criteria for elevated cortisol response to baseline Dex/CRH test were given 6 weeks of open-label treatment with Keppra (500 mg bid), followed by a repeat Dex/CRH test. Post-treatment cortisol response (concentrations over six serial time points) was compared with pre-treatment response. Data from male and female subjects were then evaluated separately. Results of a prior study in our lab showed no change in Dex/CRH cortisol response following 6 weeks of double-blind treatment with placebo. Results: One subject did not complete the post-treatment Dex/CRH test. The evaluable group as a whole (n=10) showed no significant pre- to post-treatment change in cortisol response. However, among women(n=6), open-label levetiracetam produced a significant lowering of cortisol reactivity. Post-hoc tests revealed that high baseline cortisol reactivity, rather than sex, was the significant predictor of dampened cortisol response to Dex/CRH after Levetiracetam. While excessive cortisol response to the Dex/CRH test has been associated with depression and some medical illnesses, the full implications of our finding await larger, controlled trials with longitudinal follow-up to evaluate the durability and health consequences of this effect.

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1) Lamberty Y, Falter U, Gower AJ, and Klitgaard H. Anxiolytic profile of the antiepileptic drug levetiracetam in the Vogel conflict test in the rat. Eur J Pharmacol, 2003. 469(1-3): p. 97-102.

2) Lamberty Y, Gower AJ, and Klitgaard H. The new antiepileptic drug levetiracetam normalises chlordiazepoxide withdrawal-induced anxiety in mice. Eur J Pharmacol, 2002. 439(1-3): p. 101-6.

» NR6-032

RELATIONSHIP BETWEEN NEUROCOGNITION AND SYMPTOMS IMPROVEMENT WITH RISPERIDONE LONG-ACTING INJECTABLE

ROSA CATALÁN M.D., Penadés, R., Masana, G., Navarro, V., Guarch, J., Gastó, C.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to realize what are the neurocognitive effects of long-acting risperidone on patients with chronic schizophrenia. Also what is the relationship between symptom improvement and its repercussion in cognition after the switch to long-acting risperidone.

SUMMARY:
Improving cognitive dysfunction is an important treatment outcome for clinicians. When treated with atypical antipsychotics, including risperidone, patients with schizophrenia show improvements in cognition, both when switched from typical agents and treated de novo. However, little is know about the effects of long-acting injectable drugs on neurocognition and its putative with symptoms improvement. The study was a 48-week, open label, non comparative trial on risperidone long-acting injectable. 40 patients with DSM-IV schizophrenia were switched to risperidone long-acting injectable from their previous antipsychotic without a washout phase. A comprehensive neurocognitive assessment battery was performed at baseline, and weeks 6, 12, 24, Positive and Negative Syndrome Scale (PANSS) and UKU side effect scale were also used. 24-week endpoint data on these cognitive measures were analysed with a repeated measures analysis of variance. A total of 70 patients completed the cognitive assessment battery. Change from baseline to endpoint was assessed for all cognitive measures. Significant improvements were noted in 4 of the 6 domains evaluated, with improvements of many domains occurring at time of first re-assessment (week 12). These improved domains (baseline to endpoint) included attention [($P < 0.05$)], processing speed [($P < 0.001$)], working memory [$P < 0.05$] executive function [($P < 0.05$)]. Differences in symptomatology were also found. Finally, the improvement in attitudes toward medication showed a signitficant correlation with improvements in psychomotor speed ($P< 0.001$) and working memory ($P< 0.05$). Improvements in cognitive functioning were observed in stable patients switched to maintenance treatment with long acting risperidone over the course of one year. More positive attitude toward medication was related to neurocognitive improvement after switching. Further analyses will look to explore the relationship between cognitive functioning and social functioning and putative relationship with a more favorable subjective experience of long-acting injectable in schizophrenics.

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1) P.D. Harvey, T.L. Patterson, L.S. Patterson, L.S. Potter, K. Zhong, M. Brecher Improvement in social competence with short-term atypical antipsychotic treatment: a randomized, double-blind comparison of quetiapine versus risperidone for social competence, social cognition, and neuropsychological functioning. American Journal of Psychiatry, 2006; 136(11): 1918-25.

2) W.W. Fleischnacker, J. Rabinowitz, G. Kemmler, M. Eerdekens, A. Mehnert. Perceived functioning, well-being and psychiatric symptomps in patients with satble schizophrenia treated with long-acting risperidone for 1 year. British Journal Psychiatry, 2005; 187: 131-136

» NR6-033

A PILOT STUDY OF DIFFERENTIAL EFFECTS OF DYSLIPIDEMIA ON NEURO-COGNITION WITH ATYPICAL ANTIPSYCHOTIC TREATMENT IN SCHIZOPHRENIA

*Simon Chiu M.D., *Zack Cernovsky PhD,**Mariwan Husni MD , #John Copen MD M.Sc. *Jason Carr PhD*

EDUCATIONAL OBJECTIVES:
Towards the end of the session, the audience will be able to
1.to recognize importance of lipid monitoring in atypical treatment in schizophrenia ;
2.to relate lipid profiles to cardio-metabolic risk assessment
3.to evaluate evidence linking dyslipidemia to neurocognition in schizophrenia.

SUMMARY:
Introduction: Dyslipidemia has recently been found with atypical antipsychotics treatments in schizophrenia.
Objective: to examine whether neuro-cognition measures are differentially correlated with parameters of lipid metabolism in clozapine- or olanzapine-treated schizophrenia.
Method: The study was cross- sectional. Subjects diagnosed with DSM IV-TR Schizophrenia completed computerized Neuro-Cognitive Screening Test (NCS) and body composition. Fasting blood samples were obtained for measuring total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL), high density lipoprotein (HDL) ,glucose and insulin.
Results: We recruited 41 patients with schizophrenia (male: 27, female:14; mean age 37.5 yrs) maintained on clozapine (37/41)or olanzapine (4/41) with mean BMI = 32.0 and mean serum HDL 1.2 mmol/L, LDL 3.0 mmol/L, mean total cholesterol/HDL ratio

4.8, mean TC 5.2 mmol/L. and mean TG 2.21 mmol/L. Insulin resistance was calculated from HOMA-IR with log IR: 3.0.
We have calculated Pearson product moment correlation coefficients of lipid measures and logIR to neurocognitive correlates (at p<.05, 2-tailed significance level). Elevated TC values were associated with significantly shorter reaction time with increased error responses on attention and working memory tasks (r= -.35). Similar correlation was found for TC/HDL ratio (r= -.34). Higher TG values were associated with significantly poor performance on tasks of verbal memory (r= -.35, p=.025), attention and working memory (r= -.35), and abstraction/inhibition (r=.35, p=.034). Higher log IR was associated with lower performance on attention task (r= -.35, p=.026). HDL levels were non-correlated with log IR at (r=. -19, p=.232).
Conclusion: Our findings implicate lipid signaling dysregulation mediates selective neurocognitive deficits in atypical antipsychotic-treated schizophrenia.
Supported by Stanley Medical Research Institute, Bethesda, MD, USA

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» NR6-034

SUICIDE IN A PROSPECTIVE COHORT OF PATIENTS WITH SCHIZOPHRENIA TREATED WITH SERTINDOLE OR RISPERIDONE

Marc-Antoine Crocq M.D., Malcolm H. Lader, M.D., Aurélia Mittoux, Ph.D., Per Tanghøj, Ph.D., Florence Thibaut, M.D., Jozef Peuskens, M.D., Brian Everitt, Ph.D., Ronald Mann, M.D., Nicholas D. Moore, M.D., Dieter Naber, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know more on the frequency of death by suicide and on the assessment of various forms of suicidal behavior in patients with schizophrenia, and obtain information on the differential impact of first- and second-generation antipsychotic drugs on suicidal behavior in schizophrenia.

SUMMARY:

The occurrence of death by suicide and suicide attempts was analyzed in a prospective cohort of patients with schizophrenia who were randomly assigned to treatment with sertindole (4,905 pts.) or risperidone (4,904 pts.) in a parallel-group open-label study with blinded classification of outcomes (SCoP study). The total exposure was 6,978 and 7,975 patient-years (mean number of days: 489.6 and 564.0) in the sertindole and risperidone groups, respectively. Suicide mortality in the study was fairly low (0.21 and 0.28 per 100 patients per year with sertindole and risperidone, respectively). There was a tendency for sertindole-treated patients to have a lower risk of death by suicide than risperidone-treated patients, but this was not statistically significant (hazard ratio [95% CI]: 0.72 [0.36—1.41], p = 0.34). Suicide attempts, defined by the association of suicidal act and intent to die, were reported by the treating psychiatrists. Cox's proportional hazards model analysis of the time to the first suicide attempt showed a significantly lower risk of suicide attempt for sertindole-treated patients than for risperidone-treated patients (HR [95% CI]: 0.67 [0.45—0.99], p = 0.04). When suicide attempts were classified by an independent safety committee using a broader definition including suicidal behavior, suicidal ideation, suicidal tendency, and self-injuries and overdoses for which there was no clear suicidal intent, the results were still in favor of sertindole, although not statistically significant (HR [95% CI]: 0.93 [0.66—1.29], p = 0.65). A history of previous suicide attempts was significantly associated with completed and attempted suicides in both treatment groups. Patients who had attempted suicide within the 5 years prior to study entry had a significantly higher risk of death by suicide than patients who had never attempted suicide (p <0.0001). Sertindole with its specific pharmacological profile might confer protection from suicide.

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1) Peuskens J, Tanghøj P, Mittoux A; Sertindole Cohort: The Sertindole Cohort Prospective (SCoP) study: rationale, design and methodology. Pharmacoepidemiol Drug Saf. 2008; 17:425-433

2) Aguilar EJ, Siris SG. Do Antipsychotic Drugs Influence Suicidal Behavior in Schizophrenia? Psychopharmacology Bulletin. 2007; 40(3):128-1 42

» NR6-035

EFFICACY AND SAFETY OF LURASIDONE IN PHASE 2/3 ACUTE SCHIZOPHRENIA TRIALS

Josephine Cucchiaro Ph.D., Antony Loebel, M.D., Robert Silva, Ph.D., Debra Philips, M.S., Masaaki Ogasa, M.S., Jane Xu, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to have a better understanding of the efficacy and safety profile of lurasidone based on placebo-controlled trials in patients with schizophrenia, including the potential for dose-response.

SUMMARY:

Objective: Lurasidone is a novel psychotropic agent with high affinity for D2 and 5-HT2A receptors, as well as for receptors implicated in the enhancement of cognition, mood and negative symptoms (5-HT7, 5-HT1A and a2c). The objective of the studies discussed here was to assess the efficacy and safety of lurasidone in the treatment of patients hospitalized for an acute exacerbation of schizophrenia.
Method: Data were obtained from 3 randomized, double-blind, placebo-controlled trials: 2 Phase II studies (total N=329) and 1 Phase III study (total N=500) in which patients meeting DSM-IV criteria for an acute exacerbation of schizophrenia were randomized to 6 weeks of double-blind treatment with a fixed daily dose of lurasidone 40 mg, 80 mg, or 120 mg. Cohen's d effect sizes were calculated for baseline to Week 6 change in PANSS and BPRSd total scores. The potential dose-response of lurasidone was also evaluated using a linear dose-response model.
Results: In the Phase II trials, effect sizes of BPRSd at endpoint were higher on the 120 mg dose of lurasidone (0.78) compared to the 40 mg (0.43) and 80 mg (0.42) doses. Results from the Phase III study support the potential for a greater treatment effect at higher doses. Lurasidone was generally well-tolerated with few discontinuations due to adverse effects and minimal effects on weight, lipids and glucose.
Conclusion: The results of these placebo-controlled studies in patients with acute schizophrenic illness, suggest that lurasidone is efficacious and well-tolerated in a dose range of 40 -120 mg/day.
Study funded by Dainippon Sumitomo Pharmaceuticals America, Ltd.

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1) Ishiyama T, Tokuda K, Ishibashi T, et al. Lurasidone (SM-13496), a novel atypical antipsychotic drug, reverses MK-801-induced impairment of learning and memory in the rat passive-avoidance test Eur J Pharmacol 2007;572:160-170.

2) Enomoto T, Ishibashi T, Tokuda K, et al. Lurasidone reverses MK-801-induced impairment of learning and memory in the Morris water maze and radial-arm maze tests in rats. Behav Brain Res 2008;186:197-207.

» NR6-036

LATE-DAY SUSTAINED PLASMA CONCENTRATIONS FOLLOWING ARMODAFINIL ADMINISTRATION

Mona Darwish, Ph.D., Mary Kirby, M.S., Edward T. Hellriegel, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, participants should be familiar with the relative steady-state pharmacokinetic profiles of armodafinil and modafinil after once-daily administration; they should be able to discuss the implications of the unique pharmacokinetic characteristics of armodafinil relative to modafinil.

SUMMARY:
Objective: Armodafinil is the R- and longer-lasting isomer of modafinil. Armodafinil, a non-amphetamine, wakefulness-promoting medication, improves wakefulness in patients with excessive sleepiness associated with obstructive sleep apnea, shift work disorder, or narcolepsy. Some patients receiving modafinil require higher and/or split doses to maintain wakefulness throughout the day. Armodafinil produces higher plasma levels late in the day compared with modafinil. A post-hoc analysis of two randomized, placebo-controlled, double-blind studies compared plasma concentrations of armodafinil and modafinil on a milligram-to-milligram basis.
Methods: Adult subjects (20-39 years) received once-daily armodafinil or modafinil for 14 or 7 days, respectively. Day 7 data from armodafinil doses (50 to 400 mg) and modafinil doses (200 to 600 mg) were normalized to 200 mg and pooled for each medication. The ratios of [maximal (Cmax)-minimal (Cmin) plasma drug concentration]/Cmin and (Cmax-Cmin)/average concentration (Cavg) over the 24 hour dosing interval as measures of concentration swing and fluctuation, respectively, were calculated, as was the late-day Cavg (3 to 7 PM).
Results: Both Cmax and Cmin were higher with armodafinil (n=34) compared with modafinil (n=18). Concentration swing and fluctuation following armodafinil administration were lower by 42% and 28%, respectively, compared with modafinil. Average plasma drug concentration late in the day was ~43% higher for armodafinil than for modafinil.
Conclusions: At steady state, there was less concentration swing and fluctuation over the dosing interval following armodafinil administration compared with modafinil. Plasma concentrations of armodafinil were higher, with the greatest difference late in the day, when compared to modafinil on a milligram-to-milligram basis. The distinct pharmacokinetics of armodafinil may maintain the therapeutic benefit by improving wakefulness throughout the day with once-daily dosing.

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1) 1. Dinges DF, Arora S, Darwish M, Niebler GE. Pharmacodynamic effects on alertness of single doses of armodafinil in healthy subjects during a nocturnal period of acute sleep loss. Curr Med Res Opin 2006;22:159-167.

2) 2. Darwish M, Kirby M, Hellriegel ET, Yang R, Robertson P, Jr. Pharmacokinetic profile of armodafinil in healthy subjects. Clinical Drug Investigation. (In Press, 2009.)

» NR6-037

ARMODAFINIL AND MODAFINIL HAVE SUBSTANTIALLY DIFFERENT PHARMACOKINETIC PROFILES DESPITE SIMILAR TERMINAL HALF-LIVES

Mona Darwish, Ph.D, Mary Kirby, M.S., Edward T. Hellriegel, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, participants should be able to recognize important pharmacokinetic differences between armodafinil and modafinil, and how these differences may influence wakefulness throughout the day; and understand how differences in elimination characteristics of armodafinil and modafinil, independent of absorption and terminal half-life, influence plasma concentrations over a dosing interval.

SUMMARY:
Objective: Armodafinil, a non-amphetamine, wakefulness-promoting medication, significantly improves wakefulness in patients with excessive sleepiness associated with obstructive sleep apnea, shift work disorder, or narcolepsy. Armodafinil, the R- and longer-lasting isomer of modafinil, provides higher late-day plasma concentrations than modafinil despite similar terminal half-lives (t1/2s). This analysis will identify the specific pharmacokinetic feature(s) underlying the higher late-day plasma concentrations following armodafinil versus modafinil administration.
Methods: Individual subject data from multiple studies in healthy subjects administered single doses of either armodafinil or modafinil were dose-normalized to 200 mg and then pooled for each medication. Pharmacokinetic parameters assessed included t1/2, maximum plasma drug concentration (Cmax), time to Cmax (tmax), and area under the plasma drug concentration-versus-time curve (AUC).
Results: The terminal t1/2s for armodafinil and modafinil were both ~13 hours. The two medications also had comparable mean Cmax and median tmax values. However, after reaching Cmax, armodafinil concentrations declined monophasically while racemic modafinil levels showed a biphasic decline due to the more rapid elimination of the S-isomer, compared to the R-isomer. The mean AUC was 40% higher for armodafinil compared with modafinil when compared on a milligram-to-milligram basis.
Conclusions: Armodafinil and modafinil have similar absorption and t1/2 values. Monophasic elimination differentiates armodafinil from the racemate, resulting in higher total systemic exposure and higher concentrations later in the day relative to those with modafinil compared on a milligram-to-milligram basis. The unique pharmacokinetics of armodafinil may allow for improved wakefulness later in the day compared with modafinil.
Funding Source: Sponsored by Cephalon, Inc.

REFERENCES:
1) 1. Dinges DF, Arora S, Darwish M, Niebler GE. Pharmacodynamic effects on alertness of single doses of armodafinil in healthy subjects during a nocturnal period of acute sleep loss. Curr Med Res Opin. 2006;22:159-167.

2) 2. Darwish M, Kirby M, Hellriegel ET, Yang R, Robertson P, Jr. Pharmacokinetic profile of armodafinil in healthy subjects. Clinical Drug Investigation. (In Press, 2009.)

» NR6-038

ARIPIPRAZOLE AUGMENTATION OF STANDARD TREATMENTS IN PATIENTS WITH RESISTANT OBSESSIVE COMPULSIVE DISORDER: A PILOT STUDY

Roberto Delle Chiaie M.D., Pierluigi Scarciglia, MD; Maria Caredda, MD; Massimo Pasquini MD and Massimo Biondi MD

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize and treat properly SSRI resistant OCD patients with specific add-on treatments

SUMMARY:
Objective: This study was conducted to evaluate the effectiveness and tolerability of Aripiprazole, an atypical antipsychotic with dopamine- and serotonin-modulating properties, for the augmentation of standard treatments in patients with resistant Obsesive Compulsive Disorder (OCD).
Method: Twenty patients diagnosed with OCD according to DSM IV TR criteria and having a history of resistance to standard pharmacological treatment were included in the study. Aripiprazole was added to ongoing SSRI or clomipramine treatment with a starting dose of 5 mg/day and titrated up to a maximum of 20 mg/day (mean dose 12.62 mg ± 4.25).
Efficacy was assessed with Y-BOCS and the Clinical Global Impression-Improvement scale at baseline and at week 12 of Aripiprazole augmentation. Side effects were monitored by the UKU side effect rating scale.
Results: All 20 subjects enrolled in our study completed the full

12-week course of treatment.
Our observation demonstrated a reduction in Y-BOCS score between the baseline (29.8 ± 3.6) and the end of treatment (9.85 ± 8.27), statistically significant (p=0.0001). On the basis of the Y-BOCS total score reduction response criterion (=60% or more: significant improvement; 30-60%: partial improvement; =30%: no improvement), after the aripiprazole add-on 15 patients (75%) showed significant improvement, 4 patients (20%) showed partial improvement, and 1 patient (5%) showed no improvement. Aripiprazole was well tolerated. The most commonly observed side effects after its introduction included: akathysia, nausea/vomiting, hyperkinesia, tension/inner unrest, tremors, asthenia/lassitude/increased fatiguability. These symptoms never reached a score of 3 on the UKU scale and progressively weakened.
Conclusions: Although results of this pilot study are preliminary and require confirmation in randomized controlled trials, our experience suggested that Aripiprazole is effective and well-tolerated as an augmenting agent in patients with treatment resistant OCD.

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2) Stein DJ: Obsessive-compulsive Disorder. The Lancet 2002, 360: 397-405.

» NR6-039

AN OPEN-LABEL STUDY OF COMBINATION THERAPY WITH NALTREXONE SR + BUPROPION SR FOR NICOTINE DEPENDENCE IN OVERWEIGHT AND OBESE SUBJECTS

Eduardo Dunayevich M.D., Janelle Erickson, Ph.D., Nader Oskooilar, M.D., Ph.D., Sonja K Billes, Ph.D., Charles Wilcox, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that open-label combination therapy with naltrexone + bupropion plus behavioral modification may be associated with abstinence rates that are similar to current smoking cessation aids without the usual weight gain that occurs with smoking cessation.

SUMMARY:

Nicotine withdrawal syndrome and weight gain are common deterrents to smoking cessation(1). Combination therapy with naltrexone and bupropion (NB) for smoking cessation has been associated with decreased weight gain compared with bupropion alone in a short-term open-label study(2). The present study was designed to further evaluate the therapeutic potential of NB in overweight or obese smokers. This was a 24-week open-label study of sustained release (SR) naltrexone (32 mg/day) plus bupropion SR (360 mg/day) for smoking cessation and minimization of weight gain in subjects with BMI =27 and =45 kg/m2. Subjects also received behavioral counseling. The primary outcome was subject-reported continuous abstinence at week 12. Other efficacy measures were: change in serum continine levels, expired CO, body weight, and nicotine craving and dependence. Of the 30 subjects enrolled, the average age was 43, 16 were male, and 28 were Caucasian. 27 subjects provided at least one post-baseline evaluation, and 85% and 63% of these subjects completed 12 and 24 weeks. In the full analysis set, 48% and 41% of subjects were continuously abstinent from week 4 through weeks 12 and 24. 78% and 74% of subjects had CO =10 ppm at these respective timepoints. Serum cotinine decreased from 185 ng/mL to 43 and 53 ng/mL at weeks 12 and 24. Tobacco use decreased from 129 cigarettes/week to 15 and 18 at weeks 12 and 24. Body weight remained essentially unchanged (-0.3% and +0.2% at week 12 and 24). Nicotine withdrawal scale scores generally remained unchanged with the exception of a significant increase at week 5. The most common adverse events were nausea, insomnia and constipation; these tended to be transient and mild or moderate in severity. In overweight or obese subjects, NB plus behavioral counseling for smoking cessation decreased nicotine use and limited nicotine withdrawal symptoms while preventing weight gain. Funded by Orexigen Therapeutics, Inc.

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2) Toll BA, Leary V, Wu R, Salovey P, Meandzija B, O'Malley SS: A preliminary investigation of naltrexone augmentation of bupropion to stop smoking with less weight gain. Addict Behav 2008; 33(1):173-9

» NR6-040

TOLERABILITY AND ADHERENCE OF RISPERIDONE LONG ACTING INJECTABLE (RLAI) IN SEVERE SCHIZOPHRENIC PATIENTS

JUAN FERNANDEZ-MIRANDA M.D., Victoria Caramés-García, M.D., Arantxa Sánchez-García,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to treat severe schizophrenic patients, in in a comprehensive psychiatric rehabilitation program, with high doses of long acting risperidone in order to improve treatment adherence; and to recognize levels of effectiveness and tolerability of this pharmacological approach.

SUMMARY:

Objectives: Tolerability of antipsychotic treatments is important to increase adherence, and consequently to reach rehabilitation goals in people with severe schizophrenia. The purpose of this study was to evaluate tolerability and adherence to antipsychotic treatment with high doses of RLAI in these patients.
Methods: the present study is a 52 weeks prospective, observational, open label and not randomized study of patients with schizophrenia according to CIE-10 criteria (F-20). The study was conducted from September 2007 to August 2008 in a Severe Mental Illness Programme in Gijón (Spain). Patients undergoing treatment with RLAI (doses over 75 mg every 14 day) for one year (N=40; 18 men and 22 women; average age: 43,5+/-7,8 years old). The study was performed in accordance with the Declaration of Helsinki and was described comprehensively to all patients prior to their enrolment.
Assessment included the GCI severity scale and the Camberwell Assessment of Need (CAN) at the beginning and after one year of treatment. Drug tolerance was monitored with laboratory test (including haematology, biochemistry and prolactin levels), weight gain and reasons for treatment discharge. Hospital admissions the year before and during the year of follow-up were measured.
Results: average dose of RLAI was 104,5+/-18 mg/14 day. Tolerability was good and there were almost no discharges due to side effects or to relevant biological parameters alterations (one due to metabolic syndrome). Retention rates in treatment after one year was 95% (another discharge due to lack of effectiveness). GCI and CAN showed significant changes (GCI 5,5+/-0,7 vs 4,35+/-0,9; CAN 16,75+/-2,1 vs 11,8+/-2,8) and also there were significant less hospital admissions than during the previous year (1,7+/-1,3 vs 0,45+/-0,2).
Conclusions: Tolerability of high doses (over 75 mg every 14 day) of RLAI was good, being useful in improving treatment adherence in severe schizophrenic patients.

REFERENCES:

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disorder. Brit J Psych 2007; 7.

» NR6-041

EFFECT OF ARIPIPRAZOLE ADDITION TO ANTIPSYCHOTIC TREATMENT IN SCHIZOPHRENIC PATIENTS

Felix GONZALEZ M.D., Fabrice Duval, M.D., Marie-Claude Mokrani, Ph.D., Thanh Son Diep, M.D., Hassen Rabia, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand that aripiprazole addition to antipsychotic treatment in schizophrenic patients induces a clinical improvement correlated to partial displacement by aripiprazole of ongoing antipsychotic treatment.

SUMMARY:

Background: The aim of this study was to evaluate the relationship between clinical changes and dopamine (DA) activity after aripiprazole addition (a high-affinity DA-D2 receptor partial agonist) to ongoing antipsychotic treatment in schizophrenic patients.
Methods: Cortisol response to the DA agonist apomorphine (APO, 0.75 mg SC) was measured at baseline in 10 DSM-IV schizophrenic inpatients treated with antipsychotics (haloperidol [n=3], loxapine [n=3] and risperidone [n=4]), and after 2 weeks of adjunctive aripiprazole treatment (fixed dose 10 mg/d); and in 22 healthy hospitalized controls. The intensity of clinical symptoms were evaluated using the Brief Psychiatric Rating Scale (BPRS) at baseline and at endpoint.
Results: Adjunctive aripiprazole treatment decreased significantly BPRS scores ($p<0.008$) and BPRS clinical factor 1 (anxiety-depression; $p<0.005$), and factor 2 (anergia; $p<0.005$).
Compared to controls, patients showed significant lower APO-induced cortisol stimulation at baseline ($p<0.0007$), while at endpoint cortisol response was not significantly different from controls ($p=0.09$). Cortisol response to APO at endpoint was positively correlated to improvement of clinical factor 1 (rho= 0.74, $p=0.02$), factor 3 (thought disturbance; rho= 0.78, $p<0.02$), factor 4 (activation; rho= 0.83, $p=0.01$), and factor 5 (hostility-suspiciousness; rho= 0.69, $p<0.04$). Patients who did not improve factors 3, 4, and 5 still showed lower cortisol response at endpoint compared to controls ($p<0.01$).
Conclusions: The increase in cortisol response to APO suggests a partial displacement of antipsychotics by aripiprazole at the level of DA receptors connected to the HPA axis; the degree of this displacement appears to be correlated to clinical improvement.

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1) Kuo J, Hwu HG. Aripiprazole and haloperidol: beneficial combination antipsychotic therapy for a schizophrenic patient. Clin Neuropharmacol. 2008;31:173-175.

2) Hirose T, Uwahodo Y, Yamada S, Miwa T, Kikuchi T, Kitagawa H, Burris KD, Altar CA, Nabeshima T. Mechanism of action of aripiprazole predicts clinical efficacy and a favourable side-effect profile. J Psychopharmacol. 2004;18:375-383.

» NR6-042

DESVENLAFAXINE 50 MG/D IMPROVES FUNCTIONING AND QUALITY-OF-LIFE MEASURES IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

Christine Guico-Pabia M.D., Qin Jiang, M.S, Bruno Pitrosky, Ph.D, Karen A. Tourian, M.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to
1.Recognize patterns of improvement in well-being and functional outcome measures in major depressive disorder patients treated with desvenlafaxine 50 mg/d
2.Describe well-being and functional outcomes using common rating scales in major depressive disorder patients treated with desvenlafaxine 50 mg/d

SUMMARY:

Objective: To evaluate outcomes related to functioning and well-being with desvenlafaxine (administered as desvenlafaxine succinate) 50 mg/d in patients with major depressive disorder (MDD).
Methods: Data from the Sheehan Disability Scale (SDS) and 5-item World Health Organization Well-Being Index (WHO-5) were pooled from 3 double-blind, placebo-controlled, 8-week desvenlafaxine clinical trials (ie, all trials that included a fixed 50-mg/d dose arm) in outpatients meeting the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria for MDD. Final observation (LOCF) data were compared between groups using analysis of covariance; adjusted mean differences (desvenlafaxine 50 mg/d vs placebo) are presented here.
Results: The intent-to-treat population included 462 patients in the desvenlafaxine 50 mg/d group and 470 patients in the placebo group. Desvenlafaxine 50 mg/d was associated with significantly greater improvement vs placebo in the SDS total score (-1.81; $P<0.001$), as well as in each of the 3 SDS domains: work (-0.58; $P<0.001$), social life/leisure activities (-0.70; $P<0.001$), and family life/home responsibilities (-0.61; $P<0.001$).Desvenlafaxine was also associated with significantly greater improvement vs placebo in the WHO-5 total score (1.51; $P<0.001$), as well as in each of the WHO-5 domains: good spirits (0.30; $P<0.001$), calm/relaxed (0.36; $P<0.001$), active/vigorous (0.21; $P=0.015$), fresh/rested (0.40; $P<0.001$), and interested in activities (0.29; $P<0.001$).
Conclusions: Desvenlafaxine 50 mg/d effectively improved functioning and well-being in patients with MDD, with significant improvements seen in SDS and WHO-5 total scores, as well as in each domain of these clinical measures.
Research supported by Wyeth Research

REFERENCES:

1) Boyer P, Montgomery S, Lepola U, Germain JM, Brisard C, Ganguly R, Padmanabhan SK, Tourian KA: Evaluation of the efficacy and safety of fixed doses of desvenlafaxine succinate at 50 mg and 100 mg in outpatients with major depressive disorder in a placebo-controlled trial. Int Clin Psychopharmacol 2008; 23:243-253

2) Liebowitz M, Manley AL, Padmanabhan SK, Ganguly R, Tummala R, Tourian KA: Efficacy, safety, and tolerability of desvenlafaxine 50 mg/d and 100 mg/d in outpatients with major depressive disorder. Curr Med Res Opin 2008; 24:1877-1890

» NR6-043

ONDANSETRON AUGMENTATION IN TREATMENT RESISTANT OCD: A PRELIMINARY SINGLE-BLIND PROSPECTIVE STUDY

Eric Hollander M.D., Silvia Bernardi, M.D.., Sarah Antonini, M.D., Nikhilesh Singh, Ph.D.., Stefano Pallanti, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to diagnose and manage treatment- resistant obsessive compulsive disorder . The participant should be able to list and select the several treatment alternatives available and to understand in which cases ondansetron augmentation may represent a useful option and in which cases its use in not indicated. The participant will learn the possible mechanism of ondansetron augmentation in OCD.

SUMMARY:

BACKGROUND: Serotonin (5-HT) and dopamine (DA) neuronal systems have been implicated in the modulation of obsessive-compulsive disorder (OCD) symptoms. About 40% of OCD patients do not respond to first line serotonin reuptake inhibitor (SRI) treatment, and of those, dopamine blocker augmentation has been reported to improve the rate of response by an additional one third. Given that 5-HT3 receptors are indirect inhibitors of cortico-mesolimbic DA release, augmentation with the 5-HT3 receptor antagonist ondansetron in combination with SRIs and

antipsychotics might potentially have efficacy in the treatment of resistant OCD patients. METHOD: Fourteen patients with a DSM-IV diagnosis of treatment resistant OCD, under stable treatment with SSRI's and neuroleptic augmentation, entered an 12-week single blind trial of ondansetron initiated at a dose of 0.25 mg twice daily for 6 weeks, and titrated to 0.5 mg twice daily for 6 weeks. RESULTS: Nine of 14 subjects (65%) experienced a treatment response at 12 weeks (> or = 25% reduction in Yale Brown Obsessive Compulsive Scale (YBOCS) score). The average reduction in YBOCS-rated symptoms of the whole group was 23.2 %. None of the treated patients experienced symptom exacerbation or significant side effects. CONCLUSION: These results suggest that low-dose ondansetron may have promise as an augmentation strategy for some patients suffering from OCD resistant to SRIs and antipsychotic augmentation, but further controlled trials are required. Drs. Hollander and Pallanti have served as consultants to Transcept. Dr. Singh is an employee of Transcept. Drs. Bernardi and Antonini have no interests to discuss.

REFERENCES:

1) Bloch MH, Landeros-Weisenberger A, Kelmendi B, Coric V, Bracken MB, Leckman JF.A systematic review: antipsychotic augmentation with treatment refractory obsessive-compulsive disorder. Mol Psychiatry. 2006 Jul;11(7):622-32.

2) Hewlett WA, Schmid SP, Salomon RM. Pilot trial of ondansetron in the treatment of 8 patients with obsessive-compulsive disorder. J Clin Psychiatry. 2003 Sep;64(9):1025-30

» NR6-044

RECEPTOR BINDING PROFILE OF LURASIDONE: A NOVEL PSYCHOTROPIC AGENT UNDER DEVELOPMENT FOR SCHIZOPHRENIA AND BIPOLAR DISORDER

Tomoko Horisawa B.S., Kumiko Tokuda, B.S., Tadashi Ishibashi, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to have a better understanding of the receptor binding profile of lurasidone, a drug currently in development for the treatment of schizophrenia and bipolar disorder. The participant should also have a better understanding of the relationship between receptor binding and the potential risk of clinically relevant adverse events.

SUMMARY:

Objective: Lurasidone is a novel psychotropic agent under development for the treatment of schizophrenia and bipolar disorder. Lurasidone has been reported to reverse MK-801-induced impairment in learning and memory in various animal models.1, 2 We summarize here in vitro studies designed to characterize the receptor binding profile of lurasidone.
Method: We evaluated the receptor binding affinities of lurasidone and several antipsychotic drugs. Compounds were tested under comparable assay conditions using cloned human receptors or membrane fractions prepared from animal tissue.
Results: Lurasidone had high affinity for dopamine D2 and serotonin 5-HT2A receptors. Compared with other atypical antipsychotics, lurasidone had notably greater affinity for serotonin 5-HT7, 5-HT1A, and noradrenaline a2c receptors. Lurasidone had minimal affinity for a1 adrenoceptors, dopamine D1 and D3 receptors, serotonin 5-HT2C receptors, and a2A adrenoceptors; and no affinity for histamine H1 and muscarinic M1 receptors.
Conclusion: The binding profile of lurasidone suggests potent antipsychotic effects, as well as the potential for favorable effects on depressive symptoms. Due to its lack of affinity for histamine H1 or muscarinic M1 receptors, as well as high affinity for receptors implicated in enhancement of cognitive function (e.g., 5-HT7, 5-HT1A, a2c), lurasidone might be expected to have favorable effects on learning and memory. Furthermore, lurasidone may have a reduced potential for weight gain and related metabolic consequences (due to low histamine H1 and serotonin 5-HT2C affinity), a reduced risk of extrapyramidal symptoms (due to its serotonin 5-HT2 antagonist and 5-HT1A partial agonist activity), and a reduced risk of orthostatic side effects (due to low a1 adrenergic affinity). Confirmation of the clinical implications of the receptor binding profile of lurasidone awaits the results of ongoing clinical trials.
Study funded by Dainippon Sumitomo Pharma Co., Ltd

REFERENCES:

1) Ishiyama T, Tokuda K, Ishibashi T, et al. Lurasidone (SM-13496), a novel atypical antipsychotic drug, reverses MK-801-induced impairment of learning and memory in the rat passive-avoidance test Eur J Pharmacol 2007;572:160-170.

2) Enomoto T, Ishibashi T, Tokuda K, et al. Lurasidone reverses MK-801-induced impairment of learning and memory in the Morris water maze and radial-arm maze tests in rats Behav Brain Res 2008;186:197-207.

» NR6-045

ANTIPSYCHOTIC-RELATED DIABETES MAY BE REVERSIBLE IF TREATED EARLY: TWO-YEAR CASE SERIES WITH ONE-YEAR FOLLOW-UP

Shang-Chien Huang M.D., Hsiang-Hsiung Huang, M.D., Hsiang-Ping Huang, M.S.N., Bing-Wen Soong, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the high likelihood that antipsychotic-related diabetes may be reversible if detected as early as possible such as within half an year and the previous antipsychotic can be replaced by the safer one on the moment. In addition, a close monitoring on fasting plasma glucose should be taken into consideration.

SUMMARY:

Introduction: Although antipsychotic is efficacious and prerequisite for schizophrenic patients both in acute stage and on maintenance treatment, comorbid diabetes is often related to antipsychotic treatment in schizophrenic patients and has brought crisis of clinical application of antipsychotics. We attempted to use low risk antipsychotic to replace previous antipsychotic for patients suffered from diabetes due to antipsychotic to evaluate whether the diabetes is reversible. Method: The study recruited the patients diagnosed with schizophrenia from April 2005 to March 2007. Two receipt standards from patients were adopted: 1. patients with previous diabetes related to take high or moderate high risk antipsychotic (clozapine, olanzapine, zotepine); 2. patients took high or moderate high risk antipsychotic and detected new onset diabetes in regular metabolic profile follow-up per half an year. Diagnostic criterion for diabetes was at least twice fasting blood glucose more than 126 mg/dl. Without delay, the previous antipsychotic was replaced with low risk antipsychotic (amisulpride, aripiprazole, or haloperidal). Fasting plasma glucose was closely monitoring at least once a week in first three months after changed, then once every three months in the following year. Results: Two schizophrenic patients suffered with diabetes for more than one year. Although one patient's diabetes situation was improved and her oral hypoglycemic agents dosage could be reduced, neither of their diabetes could be cured as one-year follow-up monitoring showed. As for three schizophrenic patients whose diabetes occurred in less than half an year all could recover and didn't relapse in one-year follow-up monitoring after changed no matter whether they had family history of diabetes or not. Conclusion: Medicine safety consideration for antipsychotic-related diabetes deeply affect compliance of treatment and long-term treatment effect. The result suggests if new onset diabetes can be detected in half an year and the antipsychotic can be changed on the moment, the diabetes is possible to reverse; on the contrary, if the diabetes has lasted for more than one year prior to change antipsychotics, it is likely to be irreversible. Close fasting plasma glucose monitoring such as once every half an year or even shorter period should be taken into consideration.

REFERENCES:

1) American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists: Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. J Clin Psychiatry 2004;65:267-272

2) Newcomer JW, Haupt DW, Fucetola R, Melson AK, Schweiger JA, Cooper BP, Selke G: Abnormalities in glucose regulation during antipsychotic treatment of schizophrenia. Arch Gen Psychiatry 2002;59:337-345

» NR6-046

THE EFFICACY OF QUETIAPINE IN PATIENTS WITH BIPOLAR DEPRESSION: A MULTI-CENTER, PROSPECTIVE, OPEN-LABEL, OBSERVATIONAL STUDY(QUEEN STUDY)

Jong-Hyun Jeong,M.D.,Won-Myong Bahk,M.D., Chan Hyung Kim, M.D.,Young Sup Woo,M.D.,Ho-Jun Seo,M.D.,Duk-In Jon,M.D., Hyun-Sang Cho,M.D., So Young Yoo,M.D., Kyung Joon Min,M.D.,Bo-Hyun Yoon,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that quetiapine could be a effective and safe modality in treating bipolar depression.

SUMMARY:

Bipolar depression has a disabling course and its treatment represents a major challenge to clinician. Recently, a randomized controlled trial (RCT) with quetiapine monotherapy in patients with bipolar depression reported significant reduction in depressive symptomatology. The purpose of this study was, at the real clinical setting, to evaluate the clinical efficacy of quetiapine in bipolar depression. This study was multi-center, prospective, open-label, observational, 8-week evaluation of the efficacy of quetiapine in patients with bipolar depression. In this study, patients with DSM-IV-TR diagnosis of bipolar depression (bipolar I disorder, most recent episode depressed and bipolar II disorder, most recent episode depressed) were included and treated with quetiapine. The dosage of quetiapine was flexible and concomitant mediations were permitted by clinical judgements. Clinical improvements were rated by Clinical Global Impression-Bipolar version (CGI-BP), Montgomery-Asberg Depression Rating Scale (MADRS) at baseline, week 4 and week 8. Total 1,193 patients were recruited and 46 (3.9%) patients were dropped out from this study. The mean initial dose of quetiapine was 192.3±181.9mg/day and mean dose at week 4 and week 8 were 315.2±229.7mg/day and 337.1±229.9mg/day, respectively. CGI-BP and MADRS were significantly improved at week 4 and 8 as compared to baseline. And improvements at week 8 were greater than at week 4. Subjectively, 75% of patients were reported therapeutic compliance above 75% at week 4 and 8. Seven (0.6%) and four (0.3%) patients showed manic/hypomanic episode at week 4 and 8, respectively.This study suggest that quetiapine has approving effects on depressive symptoms with minimal incidence of manic switching in bipolar depression. We propose that quetiapine could be a effective and safe modality in treating bipolar depression.

REFERENCES:

1) Weisler RH, Calabrese JR, Thase ME, Arvekvist R, Stening G, Paulsson B, Suppes T: Efficacy of quetiapine monotherapy for the treatment of depressive episodes in bipolar I disorder: a post hoc analysis of combined results from 2 double-blind, randomized, placebo-controlled studies. J Clin Psychiatry. 2008;69:769-782.

2) Thase ME, Macfadden W, Weisler RH, Chang W, Paulsson B, Khan A, Calabrese JR; BOLDER II Study Group : Efficacy of quetiapine monotherapy in bipolar I and II depression: a double-blind, placebo-controlled study (the BOLDER II study). J Clin Psychopharmacol. 2006;26:600-609.

» NR6-047

ASSESSMENT OF SUBJECTIVE QUALITY OF LIFE IN STABLE SCHIZOPHRENIC PATIENTS AFTER SWITCHING ATYPICAL ANTIPSYCHOTICS

Song Jin Ok M.D., Lee JH, Psy.D., Lee SJ, Psy.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that how switching atypical antipsychotics in stable schizophrenic patients have an effect on the subjective quality of life.

SUMMARY:

Objectiveas: The purpose of this study is to assess the subjective quality of life in schizophrenic patients switched from risperidone or olanzapine to ziprasidone and to identify how the subejctive quality of life is related with depression, drug attitude, drug satisfaction, and psychopathology.

Methods: Twenty-three schizophrenic patients in 3 hospitals were switched to an 8-week, open label, flexible dose(80-160mg/day) of ziprasidone. Pyschiatric status was evaluated by Schizophrenia Quality of Life Scale, Calgary Depression Scale for Schizophrenia, Drug Attitude Inventory, Drug Satisfaction, Positive and Negative Syndrome Scale, and Clinical Global Impression scale at baseline, day 1, week 4, and week 8.

Results: Subjective quality of life and depressive symptom was not improved significantly after switching to ziprasidone. Subjective quality of life was related significantly with depressive symptoms and drug attitude, but not drug satisfaction. Subjective quality of life correlated significantly with total scores and positive symptom scores in PANSS, and GCI-S.

Conclusion: This study suggests that if schizophrenic patients had treated by atypical antipsychotics, the subjective quality of life is not signicantly influenced by switching atypical antipsychotics. Active treatment for depressive and positive symptoms, and drug side effect is recommended to improve patients' quality of life.

REFERENCES:

1) Simpson G, Glick ID, Weiden PJ, Romano SJ, Siu CO: Randomized controlled, double-blind multicenter comparison of the efficacy and tolerability of ziprasidone and olanzapine in acutely ill inpatients with schizophrenia or schizoaffective disorder. Am J Psychiatry 2004;161:1837-1847

2) Norman RM, Malla AK, McLean T, Voruganti LN, Cortese L, McIntosh E: The relationship of symptoms and level of functioning in schizophrenia to general wellbeing and the Quality of Life Scale. Acta Psychiatr Scand 2000;102:303-309

» NR6-048

A PRACTICAL, RANDOMIZED COMPARISON OF THE EFFECTIVENESS OF RISPERIDONE, OLANZAPINE, QUETIAPINE, AND ZIPRASIDONE.

Erik Johnsen M.D., Rune A. Kroken, M.D., Tore Wentzel-Larsen, Hugo A. Jørgensen, M.D, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize differences among second generation antipsychotics regarding antipsychotic effectiveness.

SUMMARY:

Objectives: The evidence base has no clear recommendation regarding which antipsychotic drug should be prescribed first for a patient suffering from psychosis. The main aims of the study were to determine whether differences exist among first-line second-generation antipsychotics regarding symptom relief, tolerability, and global outcomes, when the drugs are investigated in a novel naturalistic design.

Method: Patients (>18 years) admitted to the catchment University mental hospital with psychosis were eligible for the study. The patients were randomized to risperidone, olanzapine, quetiapine, and ziprasidone. The raters were blind to treatment allocation. The patients were followed at intervals for up to 2 years. The main outcome measures were change of the scores of the Positive and Negative Syndrome Scale (PANSS), Calgary Depression Scale for

Schizophrenia (CDSS), Global Assessment of Functioning (GAF-F), the Clinical Global Impressions scale (CGI-S), tolerability and side effects, time until drug discontinuation, discharge from index admission, and rehospitalization.
Results: A total of 213 men and women were included. Quetiapine was superior to risperidone and olanzapine in reducing PANSS total score, P=.049 and P=.005, respectively; in reducing PANSS positive subscore, P=.005 and P=.005, respectively; in reducing PANSS general psychopathology subscore, P=.033 and P=.006, respectively; and in decreasing CGI-S, P<.001 and P<.001, respectively. Quetiapine was superior to risperidone (P<.001), olanzapine (P<.001), and ziprasidone (P=.010) in increasing the GAF-F. There were only minor differences among the drugs in tolerability and side effect outcomes. Patients treated with olanzapine took a longer time until drug discontinuation compared with those treated with ziprasidone (P=.007), but not those treated with quetiapine or risperidone.
Discussion: Quetiapine appears to be the starting drug of choice for patients admitted to hospital for symptoms of psychosis.

REFERENCES:

1) American Psychiatric Association. Practice Guidelines for the Treatment of Patients with Schizophrenia. Arlington, VA: American Psychiatric Association; 2004.

2) Johnsen E, Jørgensen HA. Effectiveness of second generation antipsychotics: a systematic review of randomized trials. BMC Psychiatry. 2008;8:31.

» NR6-049

A RANDOMIZED CONTROLLED, PILOT STUDY OF ZIPRASIDONE IN THE TREATMENT OF DELIRIUM

Sung Won Jung M.D., Kyung Sik Kim,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize and understand the potential clinical use of ziprasidone in the treatment of delirium.

SUMMARY:

Objective:Ziprasidone also has less extrapyramidal and anticholinergic side effects, but there has been little information published on ziprasidone for the treatment of patients with delirium. Therefore, this study investigated whether ziprasidone had effectiveness for treatment of delirium and whether there was a differential effect between risperidone and ziprasidone.
Methods:16 patients with delirium were enrolled in this study. All subjects(16 patients) were randomized to receive either risperidone(7 patients) or ziprasidone(9 patients) with fixed dose at the first day of treatment. Risperidone group was given 1 mg and ziprasidone group was given 20 mg at the first day of treatment in the night. Then, all subjects received either medications with flexible doses according to the clinicians' assessment and clinical status of patients. The effectiveness was evaluated using Clinical Global Impression-Severity(CGI-S),Korean version of Delirium Rating Scale(K-DRS), Korean Mini Mental Status Examination(K-MMSE), and Korean version of Delirium Rating Scale-Revised-98(K-DRS98).The side effects was evaluated using Extrapyramidal Symptom Rating Scale(ESRS). Analysis were performed by paired t-test(CGI-S,K-DRS,K-MMSE,K-DRS98).
Results: There was no significant difference between both groups in the baseline K-DRS, K-DRS-R-98, K-MMSE and CGI scores. At the 7th day of the treatment, K-DRS, K-DRS-R-98 and CGI scores were significantly decreased from the baseline in the ziprasidone group.(CGI-S; p=0.007,K-DRS;p=0.005,K-DRS98; p=0.018),but Risperidone group did not show any stastically difference. ESRS scores were not different between two groups
Conclusion:The result suggests that ziprasidone appears to be more effective and has lesser side effects than risperidone for treatment of delirium.

REFERENCES:

1) Leso L, Schwartz TL: Ziprasidone treatment of delirium. Psychosomatics 2002; 43: 61-2.

2) Young CC, Lujan E: Intravenous ziprasidone for treatment of delirium in the intensive care unit. Anesthesiology 2004; 101: 794-5.

» NR6-050

ASSESSING THE PHARMACOKINETICS OF VENLAFAXINE ER 75 MG AND DESVENLAFAXINE 50 MG IN CYP2D6 EXTENSIVE AND POOR METABOLIZERS

Cecelia Kane M.D., Alice Nichols, Ph.D, Kristin Focht, M.B.A, Qin Jiang, Sheldon Preskorn, M.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to
1.Understand the role of the CYP2D6 enzyme in the metabolism and pharmacological activity of venlafaxine extended release
2.Be aware that genetic polymorphisms of the CYP2D6 metabolic enzyme significantly impact desvenlafaxine plasma concentrations when treated with venlafaxine extended release but not desvenlafaxine

SUMMARY:

Objective: The primary goal of this study was to evaluate the impact of CYP2D6 extensive metabolizer (EM) or poor metabolizer (PM) genotypes on the pharmacokinetics of single doses of venlafaxine extended release (ER) and desvenlafaxine (administered as desvenlafaxine succinate) in healthy adults.
Method: This was an open-label, crossover study, in randomized sequence, of single doses of venlafaxine ER 75 mg and desvenlafaxine 50 mg. CYP2D6 genotyping was performed using internally developed and commercially available assays. The geometric means (LSGM) for area under the plasma concentration-versus-time curve (AUC) and peak plasma concentration (Cmax) were calculated. Comparisons between EMs and PMs were made using a 2-tailed Wilcoxon exact test.
Results: No carry-over effect was observed. The AUC and Cmax of desvenlafaxine in subjects receiving desvenlafaxine 50 mg were comparable between EMs (n=7; 2455 ng*h/mL and 83 ng/mL) and PMs (n=7; 2702 ng*h/mL [P=0.38; EMs vs PMs] and 101 ng/mL [P=0.26; EMs vs PMs]). However, significant differences (P<0.05) were observed between subjects receiving venlafaxine ER 75 mg in the AUC and Cmax of desvenlafaxine for EMs (2534 ng*h/mL and 90 ng/mL) and PMs (465 ng*h/mL and 17 ng/mL). In addition, the ratio of desvenlafaxine:venlafaxine on AUC and Cmax for subjects receiving venlafaxine ER 75 mg were significantly higher (P=0.001 for both comparisons) for EMs (7.5 and 4.0) than PMs (0.5 and 0.4).
Conclusions: These results indicate that the pharmacokinetics of desvenlafaxine 50 mg is not significantly impacted by CYP2D6 metabolic polymorphisms, whereas PMs receiving venlafaxine 75 mg had significantly lower desvenlafaxine plasma concentrations.
Research supported by Wyeth Research

REFERENCES:

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2) Patroneva A, Connolly AM, Fatato P, Pedersen R, Jiang Q, Paul J, Guico-Pabia C, Isler JA, Burczynski ME, Nichols AI: An assessment of drug-drug interactions: the effect of desvenlafaxine and duloxetine on the pharmacokinetics of the CYP2D6 probe desipramine in healthy subjects. Drug Metab Dispos 2008; 36(12):2484-2491

» NR6-051

NEW COST-EFFECTIVE HPLC/UV-SYSTEM FOR THERAPEUTIC DRUG MONITORING OF ANTIDEMENTIA DRUGS IN MEDICAL ROUTINE

ANALYSIS SHOWN BY THE EXAMPLE OF MEMANTINE

Ralf Koeber, Ralf Koeber, Hans-Hermann Kluenemann Reinhold Waimer, Sandra Beck, Tatjana Jahner, Doris Melchner, Ekkehard Haen

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know that Therapeutic Drug Monitoring (TDM) is a valid tool to adjust dosages of antidementia drugs according to characteristics of individual patients. This method is suitable for controlling compliance, lack of clinical response, adverse effects at recommended doses, drug interactions and genetic variations of metabolism. Therefore it is an important contribution to complement pharmacovigilance programs.

SUMMARY:

A novel High Performance Liquid Chromatography assay for detection and estimation of all antidementia drugs (donepezil, galantamine, rivastigmine and memantine) in serum samples has been developed and validated in our lab. This concept based on four standardized isocratic HPLC/UV-runs with one identical column and two mobile-phase components. We present a solid phase extraction using Oasis MCX (Waters) to isolate memantine from serum followed by a derivatisation with dansyl chloride. The chromatographic analyses were performed on a Dionex system with a Phenomenex Luna Phenyl-Hexyl analytical column. The mobile phase consists of 0,02mol/l K2HPO4/acetonitrile (70/30). The flow rate was 0,4ml/min and the detection wavelengths were kept at 218nm and 254nm. Interference tests between memantine and the most commonly used concomitant medications supported the valuation of suitability in routine analysis. The retention time was 12,1min for memantine. Our method recovered >90% of memantine from the serum samples. The method was validated according to the guidelines of GTFCh in consideration of ISO 5725: The calibration curve was linear (r=0,9998/n=9) over memantine concentrations ranging from 5 to 160ng/ml. No endogenous compounds were found to interfere with the analyte. The method had an accuracy of >90%. Intra- and interday precision were <5% and <7%, respectively, at three different concentrations of 5, 40, and 160ng/ml. The limit of quantification (LOQ) was found to be 3ng/ml and the limit of detection (LOD) 2ng/ml. Conclusion: The method reported here is simple, reliable, precise, and accurate and has the capacity to be used for detection of memantine in human serum samples. It currently runs in our gerontopsychiatric routine. Case histories of the AGATE pharmacovigilance program already demonstrate the benefit of this individualized approach to drug therapies with antidementia drugs.

REFERENCES:

1) Baumann P, Hiemke C, Ulrich S, et al. The AGNP-TDM Expert Group Consensus Guidelines: Therapeutic Drug Monitoring in Psychiatry. Pharmacopsychiatry 2004; 37: 243-265

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» NR6-052

ONCE-DAILY TRAZODONE: OVERVIEW OF PHARMACOKINETIC PROPERTIES

William Kramer Ph.D., Caroline Fradette, Ph.D., Claire Brullé, M.D., Arnelle Mostert, MBChB, Tanja Cronjé, MBChB, David Karhu, B.Sc.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should have an understanding of the key pharmacokinetic results from Phase I studies of a once-daily extended-release formulation of trazodone HCl.

SUMMARY:

BACKGROUND: An extended-release formulation of trazodone HCl was developed as scored 150 mg and 300 mg caplets for once-daily administration. OBJECTIVE: To characterize the PK of this formulation. METHOD: A comprehensive Phase I program included the following studies: relative bioavailability studies comparing the extended-release formulation (trazodone ER) and an immediate-release reference product (trazodone IR) following single- and multiple-dose administration; assessment of dose proportionality; and evaluation of the effect of food on absorption. All 4 studies were conducted in healthy adult subjects. RESULTS: After single-dose administration of 300 mg trazodone ER in 26 subjects, AUC and Cmax for trazodone ER were 20% and 60% lower, respectively, than for trazodone IR 100 mg tablets administered 3 times, 8 h apart. After multiple-dose administration of 300 mg daily in 30 subjects for 7 days, trazodone ER given QD and trazodone IR given TID were equivalent with respect to AUC, while Cmax was 43% lower for trazodone ER. Trazodone AUC following single-dose administration of trazodone ER was similar to AUC at steady state, suggesting that steady-state exposure can be predicted from single-dose data. Trazodone ER caplets are dose proportional with respect to Cmax and AUC after single-dose administration of 75 mg, 150 mg, 300 mg and 375 mg doses in 45 subjects. When trazodone ER was taken shortly after ingestion of a high-fat meal in 36 subjects, Cmax increased 86% compared with fasting conditions. However, AUC and Tmax were not affected by food. A t½ of 8 to 12 h was reported for trazodone ER across studies, compared with 8 h for trazodone IR. CONCLUSION: Trazodone ER exhibits linear pharmacokinetics over doses ranging from 75 mg to 375 mg. Administration of 300 mg QD provides equivalent steady-state exposure to, with a lower Cmax than, trazodone IR 300 mg TID. A high-fat meal results in an increase in Cmax but no increase in AUC.

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2) Nilsen OG, Dale O: Single dose pharmacokinetics of trazodone in healthy subjects. Pharmacol Toxicol. 1992;71:150-3.

» NR6-053

ANTIPSYCHOTIC TREATMENT OF SCHIZOPHRENIA IN NORWEGIAN EMERGENCY WARDS

Rune Kroken M.D., Erik Johnsen,M.D.,Torleif Ruud,M.D., Tore Wentzel-Larsen, Hugo A. Jørgensen,M.D.,Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand how patients with schizophrenia is treated in the emergency wards with respect to antipsychotic medication.

SUMMARY:

Objective: Evaluation of Norwegian practice of antipsychotic treatment of patients with schizophrenia at discharge from acute in-patient settings in order to compare practice with international guidelines. The dimensions in focus were monotherapy versus polytherapy, the choice of antipsychotics and dosing.
Method: 486 discharges from emergency in-patient treatment of patients with schizophrenia were drawn from a large national study which covered 75% of hospitals receiving acute in-patients. Antipsychotic treatment, demographic variables, symptom scores (GAF and HoNOS), and information about comorbid conditions and prior treatment were analysed in order to look for predictors for non-adherence to guideline.
Results: In 7.6 % of the discharges no antipsychotic treatment was given, of the remaining discharges 35.6% were prescribed antipsychotic polytherapy, and 41.9 % first-generation antipsychotics (FGAs). The mean chlorpromazine equivalent dose was 450 (SD 347, range 25-2800). In the multivariate regression analyses younger age, inpatient treatment the last 12 months or a comorbid diagnosis of personality disorder or mental retardation predicted

antipsychotic polytherapy, while inpatient treatment the last 12 months also predicted prescription of FGAs.
Conclusion: Our national survey of antipsychotic treatment at discharge from emergency in-patient treatment reveals drug regimes that to some degree are at odd with current guidelines, with increased risk of side effects. Patients with high degree of recidivism, comorbid conditions and previous in-patient treatment are especially prone to receive deviating antipsychotic drug regimes.

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» NR6-054

A POSITIVE ASSOCIATION BETWEEN SERUM PROLACTIN LEVEL AND PSYCHOPATHOLOGY AMONG PEOPLE WITH SCHIZOPHRENIA IN 3-MONTH ARIPIPRAZOLE TREATMENT

Tsuo-Hung Lan M.D., Chin Cheng, MD, Hsien-Jane Chiu1,MD, Ph.D., Yu-Chuan Wu, Bo-Jian Wu, MD, M.S., Chin-Hong Chan, MD, eMBA

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand a significant association between the change of psychopathological score and the change of prolactin level after aripiprazole administration, which might be a good biomarker to follow up the efficacy of medication intervention.

SUMMARY:

Background: Aripiprazole as a partial dopaminergic agonist seems to reduce prolactin level in people treated with other antipsychotics previously on the basis of its pharmacological characteristics. Whether this trend correlates with other clinical observations such as psychopathological change or other side effects is not well defined.
Methods: This is a randomized open-label trial on serum prolactin monitoring in schizophrenic subjects within 12 weeks aripiprazole treatment. We enrolled 48 inpatients (29 Males, 19 Females) meeting DSM-IV criteria for schizophrenia in Taiwan. With consent form completed, participants were then randomly assigned to three different treatment groups: (1) A - 10~15 mg aripiprazole per day ; (2) B - 20~30mg aripiprazole per day; (3) C - 10 mg aripiprazole augmented with 1 mg risperidone per day. All subjects were evaluated by using PANSS scale, CGI scale, UKU scale, AIMS scale, and serum prolactin level at baseline, 4th week, 8th week, and 12th week.
Results: The mean serum prolactin level reduced from 54.1± 40.9 ng/ml (baseline) to 12.0± 24.8 ng/ml (12th week) with a significant p-value < 0.00001. The comparison of prolactin level between three groups of aripiprazole intervention shows no significant difference in the same direction, although the reduction trend of Group C was more than the other two Arms. The maximal prolactin level reduction was observed in the third week of aripiprazole intervention, and remains a normal level till the end of this study. The association between CGI scale and serum prolactin level shows statistically significant even after adjusted for sex and age.
Conclusions: It is suggested that prolactin level returns to the normal range after 3 weeks of aripiprazole intervention progressively and remains until the 12th week. The reduction of prolactin level seems to predict the improvement of CGI in our schizophrenic patients.

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1) Hummer M and Huber J (2004) Hyperprolactinaemia and antipsychotic therapy in schizophrenia. Curr.Med.Res.Opin. 20 (2):189-197

2) Byerly MJ et al. (2008)Effects of aripiprazole on prolactin levels in subjects with schizophrenia during cross-titration with risperidone or olanzapine: Analysis of a randomized, open-label study.Schizophr Res. 2008 Nov 25. [Epub ahead of print].

» NR6-055

ZIPRASIDONE AUGMENTATION OF CLOZAPINE IN REFRACTORY SCHIZOPHRENIA

Hwang Bin Lee M.D., Joon-Noh Lee, MD; Minyoung Sim, MD; Seon-jin Yim, MD; Keum-Hee Ok, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the effectiveness of augmentation of clozapine with ziprasidone in refractory schizophrenia.

SUMMARY:

Objectives: While clozapine represents the treatment of choice in refractory schizophrenia, some patients are still nonresponsive or only partially responsive to clozapine treatment. In such patients, augmentation of clozapine with other atypical antipsychotics is an often-used strategy. Since the information of atypical antipsychotics augmentation of clozapine therapy is still not enough to be an evidence to support combining therapy, we tested the hypothesis that ziprasidone augmentation of clozapine would lead to an improvement in the psychotic symptoms of patient with refractory schizophrenia. Also we evaluate the other benefits of combining of clozapine and ziprasidone, such as the improvement in lipid profile and obesity caused by clozapine treatment.Methods: Patients with refractory schizophrenia, who were partial responders or nonresponders to clozapine monotherapy, as evidenced by at least 25 points on the BPRS scores and at least 4 points on CGI- S score, were enrolled and received a ziprasidone augmentation. All patients had to have remained on a stable dose of clozapine for at least 6 months to ensure a reasonable opportunity to respond to clozapine monotherapy. The BPRS scores and metabolic syndrome parameters were measured at baseline and 3 months' follow up visit.Results: 38 patients completed this combination treatment (mean aged 42.5±7.5yrs; mean duration of illness 20.7±7.4yrs; 100% Asian; 31.3% women; mean clozapine dose 434.2±101.8mg/day; mean duration of clozapine monotherapy 36.0±24.1 months). Mean clozapine dose was decreased to 397.8±123.5 mg/day and mean ziprasidone dose was 104.5±44.6mg/day at 3 months follow up. The BPRS scores was reduced from 34.9±11.4 to 31.1±13.4 over the 3 months treatment, especially in anergia subscale scores (from 8.0 ±3.4 to 7.1 ±2.8) and anxiety-depression subscale scores (from 5.2 ±3.0 to 4.4 ±3.2). The ziprasidone augmentation did not result in an adverse event rather UKU side effect rating scale was reduced (3.3 ±2.9 to 2.3 ±2.5). There was no significant change in abdominal obesity, blood pressure, fasting triglycerides HDL-cholesterol and glucose levels.Conclusion: The Augmentation of clozapine with ziprasidone is an effective treatment in refractory schizophrenia.
This combination appears to be safe and well tolerated.

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1) Lewis SW et al. Randomized controlled trial of effect of prescription of clozapine versus other second-generation antipsychotic drugs in resistant schizophrenia. Schizophr Bull. 2006 Oct;32(4):715-23.

2) Meyer JM et al. Change in metabolic syndrome parameters with antipsychotic treatment in the CATIE Schizophrenia Trial: prospective data from phase 1. Schizophr Res. 2008 Apr;101(1-3):273-86.

» NR6-056

AN EXPLORATORY STUDY ON THE CLINICAL USAGE OF AMISULPRIDE IN A PSYCHIATRIC HOSPITAL IN TAIWAN

Shih-Ku Lin M.D., Yen-Feng Lin, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to

know the clinical usage of amisulpride in a psychiatric hospital in Taiwan.

SUMMARY:
Objective: Atypical antipsychotics are at least as effective as conventional drugs, and some may be superior in treating negative and cognitive symptoms of schizophrenia. Amisulpride, a substituted benzamide derivative that preferentially binds to dopamine D2/D3 receptors in limbic rather than striatal structures, is one of the second-generation antipsychotics. In Taiwan, the usage of this drug usually follows the recommendations of expert consensus or treatment guidelines from the Western Countries. In this study, we try to collect and analyze the data about the demographics and clinical profile of patients who are prescribed amisulpride in a psychiatric hospital in Taiwan. Method: Subjects included in this study were sampled from the inpatients and outpatients of Taipei City Psychiatric Center.We enrolled all individuals received the prescription of amisulpride in TCPC from January 1, 2007 to December 31, 2007. We reviewed the records of all the subjects about the followings: (i) Demographic characteristics; (ii) Mental illness diagnosis according to ICD-9-CM code; (iii) Inpatient/outpatient status; (iv) The prescribed dosage of amisulpride. Results: A total of 795 subjects consisting of 381 male patients (47.9%) and 414 female patients (52.1%) had received amisulpride therapy during the study period. The mean age of subjects was 38.3± 12.7 years. These patients included 484 (60.88%) with the diagnosis of schizophrenic disorders (ICD-9-CM code 295.XX), 155 (19.50%) with mood disorders (ICD-9-CM code 296.XX), and 156 with other mental illnesses. The mean dosage for schizophrenia, bipolar mania and dysthymia was 362.6, 336.8 and 294.1 mg/day, respectively. Conclusion: Amisulpride is widely used in Europe and Australia to treat psychoses and schizophrenia. In Italy, the recommended dosage for dysthymia is 50 mg/day. Our data showed this drug was widely prescribed by clinicians to treat schizophrenic disorders and other mental illnesses including mood disorders, neurotic disorders and organic mental disorders. The dosage prescribed for neurotic patients (ICD-9-CM code 300.XX) in this hospital is higher than the dosage used in the European. More studies are needed to find the optimal amisulpride dose for patients with dysthymic disorders and anxiety disorders.

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» NR6-057 - WITHDRAWN

» NR6-058

HYPERGLYCEMIA IN ASIAN PATIENTS TREATED WITH SECOND GENERATION ANTIPSYCHOTICS

Rathi Mahendran M.B.B.S, Margaret Hendricks, BSc.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to 1)reinforce the need to educate patients on the risk associated with SGA use, 2)reinforce the need for screening and regular metabolic monitoring for hyperglycemia and diabetes.

SUMMARY:
Introduction: There are increasing concerns about risks of hyperglycemia and diabetes associated with second generation antipsychotic (SGA) use. There is increased mortality and significant morbidity from microvascular complications such as retinopathy, neuropathy and macrovascular complications which can lead to stroke, myocardial infarction and coronary artery disease. The extent of the association with hyperglycemia is largely unknown. The literature indicates clozapine and olanzapine had the greatest potential to induce glucose abnormalities, risperidone and quetiapine were less associated and ziprasidone and aripiprazole are probably not associated with increased risk of diabetes.
Methodology: Outpatients with a diagnosis of schizophrenia and schizoaffective disorder newly started on SGAs in a 2 year period had their fasting plasma glucose regularly monitored.
Results: 266 patients were started on SGAs during this period; 14 had diabetes and were excluded from this study. 65.5% were women and 34.5% men. Racial distribution was 202(80.2%) Chinese, 27(10.7%)Malays, 16(6.3%)Indians and 7(2.8%)other ethnic groups.
SGA use was as follows: risperidone 152(60.3%), olanzapine 45(17.9%), clozapine 29(11.5%), quetiapine 22(8.7%), aripiprazole 3(1.2%) and ziprasidone 1(0.4%).
Hyperglcyemia was found in 85 patients (33.7%). The majority of patients experieneced increased in glucose levels at 12 weeks (64 patients 25.4%). At 4 weeks, only 3 patients (1.1%) had hyperglycemia and at 12 months, 17 pateints (6.4%). Howveer the level of glucose increase was highest at 4 weeks (1.37mg% above baseline +/-1.25).
Discussion: The study indicates that Asian patients are also at high risk of developing hyperglycemia with SGAs and reinforces the need for screening and metabolic monitoring for all patients on SGAs.

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2) Adverse Drug Reaction news 2003: 5(3): 1. Increased risk of hyperglycemia and diabetes with atpical antipsychotics. Published by: Centre for Pharmaceutical Administration HSA and the Pharmacovigiliance Advisory Committee, Singapore.

» NR6-059

LURASIDONE IS ASSOCIATED WITH ANXIOLYTIC AND ANTIDEPRESSANT EFFECTS IN RODENT MODELS

Yuji Matsumoto M.S., Kenji Matsumoto, B.S., Tomoko Horisawa, B.S., Kazuki Yabuuchi, Ph.D., Tadashi Ishibashi, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand the effects of lurasidone on animal models predictive of anxiolytic and antidepressant effects in humans.

SUMMARY:
Objective: Lurasidone is a novel psychotropic agent currently in phase 3 trials for schizophrenia and bipolar disorder. In addition to potent D2 and 5-HT2A affinity, lurasidone has significant affinity at 5-HT7, 5-HT1A, and a2c receptors and no affinity for histamine H1 and muscarinic M1 receptors. In the present studies, we investigated the anxiolytic- and antidepressant-like actions of lurasidone in various rodent models.
Method: Conditioned fear stress-induced freezing behavior was evaluated in rats previously conditioned with an electrical stimulus. Anxiolytic action was also evaluated with Vogel's anticonflict model as well as a social interaction model in rats. Antidepressant action was evaluated by the olfactory bulbectomy model.
Results: Unlike conventional antipsychotics, lurasidone attenuated conditioned fear stress-induced freezing behavior. Furthermore, lurasidone showed anxiolytic-like actions in the Vogel's test or social interaction model at antipsychotic equivalent doses. In the olfactory bulbectomy model, chronic administration (14 days) of lurasidone produced a dose-dependent attenuation of the bulbectomy-induced hyperactivity in rats. These results indicate that lurasidone possess anxiolytic- and antidepressant-like actions in animal models.

Conclusion: The results of these preclinical studies suggest that lurasidone may produce a range of anxiolytic, antidepressant and related prosocial effects in humans. Clinical studies in schizophrenia and bipolar disorder are underway to explore these potential effects. Study funded by Dainippon Sumitomo Pharma Co., Ltd

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1) Ishida-Tokuda K, et al. Evaluation of perospirone (SM-9018), a novel serotonin-2 and dopamine-2 receptor antagonist, and other antipsychotics in the conditioned fear stress-induced freezing behavior model in rats. Jpn J Pharmacol 1996;72:119-126.

2) Kelly JP, et al. The olfactory bulbectomized rat as a model of depression: An update. Pharmacol Ther 1997;74:299-316.

» NR6-060

VALPROIC ACID AND THE INCIDENCE OF FALLS IN AN INPATIENT SETTING

Harlan Mellk M.D., Jeffry R. Nurenberg, M.D., David I. Mayerhoff, M.D., Milton Luria, M.D., Steven J. Schleifer, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should understand and be better able to anticipate potential side effects associated with valproic acid, including side effects that may not have been recognized previously. Participants will be better able to assess potential risks for falls in the context of pharmacotherapeutic decision making for valproic acid and related agents.

SUMMARY:

Valproic acid has become the most widely prescribed antiepileptic drug and its use in the treatment of psychiatric disorders has expanded dramatically. The perception that valproic acid has mostly modest side effects contributes to its high utilization, however, increasing attention is being paid to side effects and toxicities. Commonly reported side effects include somnolence, abnormal gait, dizziness, tremor, confusional states, hepatotoxicity, and cases of neurotoxicity, which may be difficult to detect in some clinical settings. As part of a patient safety initiative at our 450 bed non-geriatric adult state hospital, we have begun to explore the incidence of patient falls in relation to valproate use, an association that has not been reported extensively but was suggested by our clinical experience. Incident reports for patient falls during a three month interval (July-September, 2008) were examined in relation to hospital records of valproate use during that interval; when available, mean valproate dose and blood level, and blood ammonia were examined secondarily. Of 488 patients hospitalized during that interval, 17% experienced one or more falls, and 36% of patients were prescribed a valproic acid compound. Rates of falls were higher among valproate users than among non-users, with 22.8% of valproate users experiencing falls, vs 16.8% of non-users (ChiSquare=4.93, p<0.03). There was no evidence that falls among valproate users were related to dose or blood level of valproic acid or to ammonia levels, which have been associated with valproate toxicity in some cases. Factors such as age, gender, associated medical conditions and other medications may have contributed to the association. While valproic acid in the treatment of mood and other psychiatric disorders may provide substantial clinical benefits, there may be a relatively large group of patients who are at increased risk for falls and other toxicities.

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» NR6-061 - WITHDRAWN

» NR6-062

LURASIDONE IN THE TREATMENT OF ACUTE SCHIZOPHRENIA: A DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Mitsutaka Nakamura Ph.D., Masaaki Ogasa, M.S. John Guarino, Ph.D., Debra Philips, A.S., Joseph Severs, M.S., Josephine Cucchiaro, Ph.D., Antony Loebel, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should have a better understanding of the potential efficacy and safety of lurasidone for the treatment of an acute exacerbation of schizophrenia patients, including how to initiate treatment, the time-course of response, and what adverse event profile to expect.

SUMMARY:

Objective: Lurasidone is a novel psychotropic agent with high affinity for D2 and 5-HT2A receptors, and for receptors implicated in enhancement of cognition, mood and negative symptoms (5-HT7, 5-HT1A and a2c). The objective of the study was to evaluate the safety and efficacy of lurasidone in patients with an acute exacerbation of schizophrenia.

Method: Patients were randomized to 6 weeks of double-blind treatment with a fixed dose of lurasidone 80 mg (N=90; 75.6% male; mean age, 39.7 years; baseline BPRSd, 55.1) or placebo (N=90; 77.8% male; mean age, 41.9 years; BPRSd, 56.1). Patients remained in the hospital until Day 28, after which they could be discharged at the discretion of the investigator. The primary efficacy measure was the Brief Psychiatric Rating Scale derived (BPRSd) from the Positive and Negative Symptoms of Schizophrenia Scale (PANSS).

Results: At day 42 LOCF endpoint, treatment with lurasidone was associated with significant improvement compared to placebo on the BPRSd (-8.9 ± 1.3 vs. -4.2 ± 1.4; P=0.012), as well as on all secondary efficacy measures, including the PANSS total score (-14.1 ± 2.1 vs. -5.5 ± 2.2; P=0.004), PANSS positive (-4.3 ± 0.7 vs. -1.7 ± 0.7; P=0.006), PANSS negative (-2.9 ± 0.5 vs. -1.3 ± 0.5; P=0.025), and PANSS general psychopathology (-7.0 ± 1.1 vs. -2.7 ± 1.2; P=0.0061) subscales. Significant improvement was seen by day 3 on the BPRSd (P<0.01), PANSS total (P<0.05) and CGI-S (P<0.05) scores. Treatment with lurasidone was generally well-tolerated, with a similar proportion of adverse events rated as severe on lurasidone and placebo (7.8% vs. 5.6%). There were no treatment-emergent differences in metabolic or ECG parameters, or objective measures of extrapyramidal symptoms.

Conclusion: The results of this study indicate that the novel psychotropic agent lurasidone is a safe and effective treatment for patients with an acute exacerbation of schizophrenia.

Study funded by Dainippon Sumitomo Pharma America, Inc.

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1) Ishiyama T, Tokuda K, Ishibashi T, et al. Lurasidone (SM-13496), a novel atypical antipsychotic drug, reverses MK-801-induced impairment of learning and memory in the rat passive-avoidance test Eur J Pharmacol 2007;572:160-170.

2) Enomoto T, Ishibashi T, Tokuda K, et al. Lurasidone reverses MK-801-induced impairment of learning and memory in the Morris water maze and radial-arm maze tests in rats. Behav Brain Res 2008;186:197-207.

» NR6-063

REDUCED EPS RISK WITH LURASIDONE, A NOVEL PSYCHOTROPIC AGENT UNDER DEVELOPMENT FOR SCHIZOPHRENIA AND BIPOLAR DISORDER

Hiroyuki Nishikawa Ph.D., Kumiko Tokuda, B.S., Kenji Matsumoto, B.S., Yoko Ueda, B.S., Tadashi Ishibashi, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to better understand the effects of lurasidone upon animal models of EPS, in comparison with other agents, and the potential clinical

relevance of these findings.

SUMMARY:

Objective: Lurasidone is a novel psychotropic agent currently in phase 3 trials for schizophrenia. In addition to potent D2 and 5-HT2A affinity, lurasidone has significant affinity at 5-HT7, 5-HT1A, and a2c receptors and no affinity for histamine H1 and muscarinic M1 receptors. The goal of the current studies was to evaluate the EPS liability of lurasidone compared to other antipsychotics in standard animal behavioral models.
Method: The EPS potential of lurasidone was evaluated in animal models, in comparison to other conventional and atypical antipsychotic agents, using clinically equivalent doses. Rat and mouse catalepsy was measured by duration of immobile posture (ie keeping both forelimbs on the horizontal bar). The mouse pole test was used to measure bradykinesia. The rat paw test was used to measure forelimb retraction time.
Results: Lurasidone was associated with a lower propensity to induce catalepsy compared with other antipsychotic drugs in both rats and mice (ED50 >1000 mg/kg (p.o.) versus ED50 values ranging from 0.85 for risperidone to 63 for ziprasidone). In the mouse pole test, lurasidone was less likely than other antipsychotics to induce bradykinesia or delay in a pole-descending behavior (MED>1000 mg/kg versus MED values ranging from 1 for haloperidol to >/=30 for ziprasidone, thioridazine, and clozapine). In the rat paw test (an index of EPS), lurasidone was less likely than other antipsychotics to increase the forelimb retraction time (MED >1000 mg/kg for lurasidone, sertindole and thioridazine, versus ED50 values ranging from 1 for haloperidol to 300 for clozapine).
Conclusion: The results of these preclinical studies suggest that lurasidone has a low potential for causing clinically significant EPS.
Study funded by Dainippon Sumitomo Pharma Co., Ltd

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1) Pierre JM. Extrapyramidal symptoms with atypical antipsychotics: incidence, prevention and management. Drug Safety 2005;28:191-208.

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» NR6-064

EFFECT OF LURASIDONE ON DEPRESSIVE SYMPTOMS IN PATIENTS WITH SCHIZOPHRENIA

Masaaki Ogasa M.S., Antony Loebel, M.D., Josephine Cucchiaro, Ph.D., Joseph Severs, M.S., Mitsutaka Nakamura, Ph.D., John Guarino, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should have a better understanding of the potential efficacy and tolerability of lurasidone for the treatment of the subgroup of schizophrenia patients who present with clinically significant depressive symptoms.

SUMMARY:

Objective: Clinically significant depression occurs in approximately 25% of individuals with schizophrenia and is associated with greater functional impairment and worse outcomes. Lurasidone is a novel psychotropic agent with high affinity for D2 and 5-HT2A receptors, as well as for receptors implicated in the enhancement of cognition, mood and negative symptoms (5-HT7, 5-HT1A and a2c). The goal of this secondary analysis was to evaluate the efficacy of lurasidone in patients diagnosed with schizophrenia who were experiencing clinically significant depressive symptoms.
Method: Data for this analysis came from a 6-week, placebo-controlled study in which patients meeting DSM-IV criteria for schizophrenia were randomized to 6 weeks of double-blind treatment with a fixed dose of lurasidone 80 mg (N=90; baseline MADRS score = 14.2; subgroup with MADRS >/=12, N=55) or placebo (N=90; baseline MADRS score = 14.5; subgroup with MADRS >/=12, N=58).
Results: On an ANCOVA analysis, treatment with lurasidone was associated with significantly greater LOCF-endpoint improvement than placebo on the MADRS in the total sample (-2.72 and -0.11; P=0.026), and in the subgroup with MADRS >/=12 (-6.02 vs. -2.77; P=0.04). The Cohen's d effect size for endpoint change in the MADRS was 0.44 for the depressed subgroup. Treatment with lurasidone was also associated with significantly greater improvement than placebo on the PANSS depression item (G6; -1.03 vs. -0.30; P<0.01).
Conclusion: These exploratory findings from a double-blind, phase 2 study suggest that lurasidone is effective for the treatment of depressive symptoms associated with schizophrenic illness. Phase 3 double-blind studies are underway to fully characterize lurasidone's clinical profile and confirm its potential antidepressant benefit in patients diagnosed with schizophrenia who present with clinically significant symptoms of depression.
Study funded by Dainippon Sumitomo Pharmaceuticals America, Ltd.

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» NR6-065

PREGABALIN AUGMENTATION OF ANTIDEPRESSANTS IN PATIENTS WITH ACCIDENT-RELATED POSTTRAUMATIC STRESS DISORDER: AN OPEN LABEL PILOT STUDY

Chi-Un Pae M.D., David M. Marks, M.D., Ashwin A. Patkar, M.D., Prakash S. Masand, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to potential utility of pregabalin augmentation to antidepressants in patients with posttraumatic stress disorder

SUMMARY:

Objective: This study evaluated the efficacy of pregabalin augmentation of antidepressant treatment in patients with posttraumatic stress disorder (PTSD).
Methods: Nine patients meeting Diagnostic and Statistical Manual, fourth edition criteria for PTSD who were on stable doses of antidepressants were treated open label with flexibly dosed pregabalin for 6 weeks. All patients were assessed with the Short PTSD Rating Interview (SPRINT), Montgomery–Asberg Depression Rating Scale (MADRS), Patient Global Impression-severity (PGI-S), Visual Analog Scale-pain (VAS-pain), and Sheehan Disability Scale (SDS)at baseline and weeks 2, 4, and 6.
Results: The scores of the SPRINT, PGI-S, VAS-pain, MADRS and SDS at week 4 (-18.2%, -34.8%, -40.0%, -18.9%, -11.9% respectively, all p values < 0.001) and week 6 (-29.8%, -47.8%, -53.4%, -24.7%, -16.1% respectively, all p values < 0.001) showed statistically significant reduction from baseline, while these parameters were not significantly reduced at week 2. Furthermore, 5 (55.6%) and 6 (66.7%) patients showed a = 50% reduction in PGI-S and VAS-pain scores at week 6, although this trend was not observed in the scores of the SPRINT, MADRS and SDS during the study. Conclusion: Pregabalin augmentation was effective and well tolerated during the study. Our findings warrant adequately powered, placebo-controlled clinical trials to confirm the usefulness of pregabalin augmentation of antidepressants in patients with PTSD.

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» NR6-066

TESTING ANXIOUS DEPRESSION AS A PREDICTOR AND MODERATOR OF SYMPTOM IMPROVEMENT IN MAJOR DEPRESSIVE DISORDER

George I. Papakostas, M.D., Klaus Larsen, Ph.D, M.Sc.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize the role of anxious depression as a predictor and treatment moderator in major depressive disorder.

SUMMARY:

Background: Reports suggest the presence of anxious major depressive disorder (MDD) to predict poorer response to antidepressants (1), as well as to serve as a moderator of antidepressant treatment response. It has also been hypothesized that serotonin-norepinephrine reuptake inhibitors (SNRIs) may be more effective than selective serotonin reuptake inhibitors (SSRIs) in anxious depression (2). The purpose of this analysis was to explore the potential role of anxious depression as a treatment predictor and moderator in MDD using a large escitalopram clinical trial dataset.
Methods: Individual patient-level data from 13 double-blind, randomized controlled trials in patients with MDD were pooled. Both univariate, last observation carried forward (LOCF) analyses and repeated measurements analyses without imputation are carried out for change in symptom scores, response and remission rates.
Results: Of the 3951 patients pooled, 47.0% were classified as having anxious depression (HAMD anxiety-somatization subscale score>6 (sum of items 10-13, 15, 17). Patients with anxious depression were less likely to improve during treatment than patients without anxious depression on some outcome measures (remission, change in MADRS scores), but not others (response, change in HAMD scores). Escitalopram was more effective than placebo, and as effective as the SSRIs, and SNRIs in the treatment of anxious depression. The presence of anxious depression was not a moderator of symptom improvement for escitalopram versus placebo, the SSRIs, or SNRIs.
Conclusions: The present analysis provides some evidence that anxious depression is difficult to treat. Escitalopram was more effective than placebo, and as effective as other antidepressants (SSRIs, SNRIs) in anxious depression. The present analysis did not support the notion that SNRIs are more effective than SSRIs in the treatment of anxious depression, nor was there evidence to support treatment moderating effects for anxious depression.

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» NR6-067

A DOUBLE-BLIND COMPARISON OF THE SAFETY AND EFFICACY OF LURASIDONE AND ZIPRASIDONE IN STABLE OUTPATIENTS WITH SCHIZOPHRENIA OR SCHIZOAFFECTIVE DISORDE

Steven Potkin M.D., Josephine Cucchiaro, Ph.D., Masaaki Ogasa, M.S., Antony Loebel, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should have a better understanding of the comparative safety and tolerability of lurasidone and ziprasidone across key metabolic, cardiac, extrapyramidal, and tolerability parameters.

SUMMARY:

Objective: Lurasidone is a novel psychotropic agent with high affinity for D2 and 5-HT2A receptors, and for receptors implicated in enhancement of cognition, mood and negative symptoms (5-HT7, 5-HT1A and a2c). The current study is the first to evaluate the comparative safety and efficacy of lurasidone vs. ziprasidone in stable outpatients with schizophrenia or schizoaffective disorder.
Method: Outpatients were recruited who met DSM-IV criteria for chronic, stable schizophrenia or schizoaffective disorder. After a 1-3 day single-blind, placebo run-in period, patients were randomized to 21 days of treatment with a fixed daily dose of lurasidone 120 mg (N=150; PANSS total = 68.7; starting dose, 80 mg for 3 days) or ziprasidone 160 mg (N=151; PANSS total = 68.9; starting dose, 80 mg/day for 3 days).
Results: The proportion of patients reporting at least one adverse event was lower for lurasidone compared to ziprasidone (57% vs. 66%; P=0.05). Median endpoint change in weight was similar for both lurasidone and ziprasidone (-0.65 vs. -0.35 lbs). Treatment with lurasidone versus ziprasidone was associated with greater median reduction in triglycerides (-2.6 vs. +22.4 mg/dL), similar endpoint reduction in total cholesterol (-6.4 vs. -4.4 mg/dL), and similar change in glucose (+4.7 vs. +4.8 mg/dL). Treatment with lurasidone was associated with lower endpoint change in the QTcF: +0.3 vs. +3.3 msec). Treatment with lurasidone versus ziprasidone, respectively, resulted in significantly greater early improvement on the PANSS total score at Week 1 (-4.1 vs. -1.6; P<0.05), but not Week 2, (-6.0 vs. -3.7) or Week 3 (-6.2 vs. -4.5; MMRM analysis).
Conclusion: Treatment with lurasidone was safe and well-tolerated, and was not associated with clinically significant changes in weight, lipids or QTc. The efficacy of lurasidone was comparable to ziprasidone, but with earlier improvement in the PANSS total score. Study funded by Dainippon Sumitomo Pharmaceuticals America, Ltd.

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» NR6-068

CHANGE OF METABOLIC PARAMETERS DURING PSYCHIATRIC INPATIENT TREATMENT: A PROSPECTIVE NATURALISTIC STUDY

Hans Rittmannsberger M.D., Christian Foff, M.D., Robert Frühwirth,M.D., Hildegard Lindner, M.D., Rosa Mayr, M.D., Vera Pihurik,M.D. Thomas Zaunmüller M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that inpatient treatment of psychiatric patients can lead to an increase in weight and a deterioration of lipid values.

SUMMARY:

Objective: Metabolic disturbances are more common in some psychiatric disorders (1) and they might develop as a side effect of psychotropic drug treatment(2). Inpatient treatment offers a key opportunity to control these data. Consequently, it is important to learn in which way these parameters change during inpatient treatment.
Methods: A prospective monitoring of metabolic parameters was

conducted in a psychiatric hospital department in Linz, Austria. Weight/BMI, fasting glucose, total cholesterol, HDL, LDL and triglycerides could be assessed in 407 consecutive patients at admission and prior to discharge. Results were stratified according to diagnosis, drug classes and second generation antipsychotics. Results: Mean age of the patients was 45.9 years, mean duration of inpatient treatment was 24.05 days. Diagnostically most prominent was F3 (35%), followed by F2 (27%), F1 (19%) and F4-6 (16%). Comparing changes between admission and discharge we found a decrease of patients with fasting glucose >100mg/dl (25.9% to 19.6%) and an increase of patients with pathological lipid values: total cholesterol >200mg/dl from 50.5%, to 53.6%), LDL >130mg/dl from 43.3% to 52%), HDL <40mg/dl from 17.3% to 24%) and triglycerides >150mg/dl from 32.8% to 38.2%. The rate of patients with an BMI >25 increased from 48.8% to 52.7%.Worsening of serum lipids and weight gain were most prominent in patients with a diagnosis of F2 and in patients receiving second generation antipsychotics. Among the latter ziprasidone was the only drug which was not associated with weight gain.
Conclusion: While fasting glucose improved, serum lipid values and weight deteriorated during inpatient treatment, despite efforts to improve patients' lifestyle. This is an alarming finding, since this process might continue even more pronounced after discharge.
This study was supported by E. Lilly.

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» NR6-069

ATYPICAL ANTIPSYCHOTIC METABOLISM/ BIOTRANSFORMATION AND EXCRETION

John Sheehan R.Ph., Jennifer Kern-Sliwa, Pharm.D., B.C.P.P., Augusto Grinspan, M.D., Joan C. Amatniek, M.D., Carla M. Canuso, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participants should be able to describe the pharmacokinetic parameter differences including metabolism/biotransformation and excretion that exist among currently available atypical antipsychotics. Participants should then be able to make more informed choices among these agents in the treatment of patients with psychiatric disorders, especially those with comorbid conditions, genetic variations or comedications that may impact pharmacokinetic parameters.

SUMMARY:

Background: Atypical antipsychotics (aripiprazole, clozapine, olanzapine, paliperidone, quetiapine, risperidone, and ziprasidone) share the common characteristic of dopamine-and serotonin-receptor modulation; however, each has unique pharmacodynamic and pharmacokinetic characteristics.
Objective:To compare the pharmacokinetic profiles of atypical antipsychotics with particular emphasis on pathways and extent of metabolism, biotransformation, and excretion.
Methods:Manufacturer's radiolabeled drug absorption, distribution, metabolism and excretion (ADME) study data, available in the primary literature or United States Food and Drug Administration (FDA) submission document, and prescribing information of each atypical antipsychotic were reviewed.
Results: Atypical antipsychotics, with the exception of paliperidone, undergo extensive metabolism (i.e., ≤50% of dose recovered unchanged). The greatest overall metabolism is seen with quetiapine (<1% of the dose recovered unchanged) and the least with paliperidone (59% recovered unchanged in the urine). The metabolism of atypical antipsychotics is primarily due to hepatic cytochrome (CY) P450 enzymes. Between-agent differences exist in the extent of CYP450 metabolism and specific CYP450 enzyme involvement. After administration of a radioactive dose, fecal elimination of radioactive compounds (i.e., unchanged drug plus metabolites) ranged from 11% (paliperidone) to 71% (ziprasidone). By comparison, renal elimination ranged from 21% (ziprasidone) to 80% (paliperidone).
Conclusions:Understanding the differences in metabolism between atypical antipsychotics may permit better-informed drug and dose selection in special populations such as those with comorbid conditions (e.g. hepatitis, diabetes, end-stage renal disease); those with pharmacogenetic variability; or those at risk for drug-drug interactions. The use of patient-tailored drug and dose-selection may result in greater treatment efficacy as well as a reduction in adverse events that may occur as a result of drug-drug interactions.
Supported by Ortho-McNeil Janssen Scientific Affairs, LLC, Titusville, New Jersey, USA.

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» NR6-070

A MULTI-SITE,OPEN-LABEL,RANDOMISED,HALOPERIDOL-CONTROLLED STUDY TO EVALUATE QUETIAPINE AS MONOTHERAPY IN THE TREATMENT OF AGITATED ACUTE SCHIZOPHRENIA

Tianmei Si, Huang Ji Zhong, MD, Su Yun'Ai, MD, PhD, Tang Mao Qin, MD, Li Ke Qing, MD, Yang Pu De, MD, Shu Liang, MD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to learn some information which will helpful to choose better strategy to control the acute emergency psychosis.

SUMMARY:

Purpose Acutely psychotic patients with aggression or agitation are often administered conventional antipsychotics or benzodiapine intramuscularly or orally in China, which are viewed as coercive and are often associated with adverse events (AEs).The primary objective of this study was to compare the onset of action of quetiapine (Que) 600-750 mg/day (n = 40), an atypical antipsychotic that has been shown to be clinically effective and well tolerated in patients with schizophrenia,with haloperidol (Hal) 10-12 mg/day (n = 40) orally,on agitation and hostility symptoms in Chinese patients with acute psychosis.Methods: Patients presenting with an acute exacerbation of schizophrenia with mean PANSS total score at least 60 and PANSS-EC(PANSS exciting factor, sum of item scores on excitement, poor impulse control,hostility and uncooperativeness) score at least 15 were included.Onset of action was defined as a reduction in PANSS total score?20%.Response was defined as a reduction of PANSS total score?50%.Results 71 patients (Que: 36 vs Hal: 35) completed the 4 week study. The mean changes of PANSS total score was -30.6 for Hal, from 90.2 at baseline to 56.5 at the endpoint of 4 wks, and was -32.0 for Que, from 97.0 to 61.5 (p=0.697, que vs. hal). The mean change of EC was -12.1 for both group(p= 0.654) ; the time to 50% response was 3 days for Hal and 5 days for Que. The mean decrease at study end-point in the PANSS total score and PANSS-EC was comparable in the Que and Hal group (36.8% for Hal vs 36.4% for Que, p=0.889. Overall, 87.5% of Hal-treated and 40.0% of Que-treated patients reported AEs(p<0.001 vs Hal). 21.0% of Hal patients showed EPS, whilst only 5.5% of Que- patients had mild EPS(p

< 0.001). Prolactin levels in Hal patients increased significantly at the endpoint comparing to baseline; whilst prolactin levels decreased in Que (P<0.001, Que vs Hal). Conclusion quetiapine was effective and well tolerated in the treatment of Chinese patients with acute psychosis.

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» NR6-071

EFFICACY, SAFETY, AND TOLERABILITY OF DESVENLAFAXINE 50 MG/D IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

Karen Tourian M.D., James Groark, M.D, Claudine Brisard, M.D, Qin Jiang, M.S., Bruno Pitrosky, Ph.D., Michael R. Liebowitz, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to 1.Understand the efficacy of desvenlafaxine 50 mg/d in the treatment of major depressive disorder in short-term, placebo-controlled studies
2.Recognize the most common treatment-emergent adverse events occurring with desvenlafaxine 50 mg/d in the treatment of major depressive disorder in short-term, placebo-controlled studies.

SUMMARY:

Objective: Evaluate the efficacy, safety, and tolerability of desvenlafaxine (administered as desvenlafaxine succinate) 50 mg/d compared with placebo in patients with major depressive disorder (MDD).
Methods: Data were pooled from 3 double-blind, placebo-controlled, 8-week trials in outpatients with DSM-IV MDD. The primary efficacy measure was the 17-item Hamilton Rating Scale for Depression (HAM-D17). Other efficacy measures were the HAM-D6, Montgomery Åsberg Depression Rating Scale (MADRS), and Clinical Global Impression–Improvement (CGI-I). Response rate (CGI-I score of =2 or decrease =50% in HAM-D17 or MADRS scores) and remission rate (HAM-D17 score =7) were assessed. Final observation (LOCF) data are reported. Data for the rating scales were evaluated using ANCOVA; Fisher exact test was used for response/remission rates.
Results: Desvenlafaxine 50 mg/d (n=462) resulted in a statistically significant improvement vs placebo (n=471) on the HAM-D17 total score (–11.5 vs –9.6; P<0.001). Statistically significant improvements were also observed for HAM-D6, MADRS, and CGI-I (P<0.001 for each). The rates of response (HAM-D17: 52.8% vs 43.9%; MADRS: 52.7% vs 41.8%; CGI-I: 57.8% vs 46.5%; P<0.01 for each) and remission (HAM-D17: 30.7% vs 24.4%; P=0.034) were also statistically significantly higher with desvenlafaxine 50 mg/d vs placebo. Discontinuation rates due to AEs were 4.5% for desvenlafaxine 50 mg/d and 4.0% with placebo. The most frequently reported TEAEs included nausea, headache, dry mouth, dizziness, diarrhea, insomnia, hyperhidrosis, and constipation.
Conclusions: In short-term clinical trials of MDD, desvenlafaxine 50 mg/d was statistically superior to placebo on depression rating scales and measures of global severity and in response/remission rates. Desvenlafaxine 50 mg/d was well tolerated with discontinuation due to AEs similar to placebo and an overall tolerability profile that compares favorably with the SNRI class.
Research supported by Wyeth Research

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» NR6-072

MEDICATION ACCESS/CONTINUITY PROBLEMS AND SUICIDAL IDEATION AND BEHAVIOR AMONG DUAL ELIGIBLE PSYCHIATRIC PATIENTS UNDER MEDICARE PART D

Joyce West Ph.D., Joshua E. Wilk, Ph.D., Eve Moscicki, Ph.D., Donald S. Rae, M.S., Maritza Rubio Stipic, Sc.D., Darrel A. Regier, M.D., M.P.H.

EDUCATIONAL OBJECTIVES:

At this session's conclusion, participants should be able to: 1) Identify medication access problems associated with increased suicidal ideation among psychiatric patients; and 2) Understand this warrants additional study as clinically vulnerable patients with elevated rates of suicidal ideation may be at greater risk for medication access problems under Medicare Part D – or medication access problems under Part D may put patients at greater risk for suicidal ideation.

SUMMARY:

Objective: Assess the relationship between medication access problems and suicidal ideation or behavior among psychiatric patients with Medicare and Medicaid during the first year of Medicare Part D.
Methods: Psychiatrists were randomly selected from the AMA Masterfile, with 1,556 (62%) responding; 63% met eligibility criteria of treating dual eligible patients and reported clinically detailed information on one systematically selected patient (N=986). Results: Overall, 16% of patients had an increase in suicidal ideation/behavior reported during the past year. Patients with medication access problems had four times the rates of suicidal ideation or behavior compared to patients with no access problems (22% vs. 5%, P<.0001). Adjusting for patient sociodemographics, diagnoses, and psychiatric symptom severity, the predicted probabilities of increases in suicidal ideation and behavior were significantly greater for patients who: were previously stable, but required to switch medications (29%, P<.001); couldn't access "off-label" medications (29%, P<.001); had problems accessing benzodiazepines (26%, P<.01); couldn't access refills or new prescriptions because they were not covered (24%, P<.001); or stopped/discontinued medications because they were not covered (23%, P<.05). Conclusions: Patients with medication access problems had significantly higher rates of suicidal ideation or behavior. These observational findings warrant investigation as they may indicate more clinically vulnerable patients with elevated rates of suicidal ideation and behavior may be at greater risk for medication access problems under Medicare Part D – or medication access problems occurring under Medicare Part D may put these patients at greater risk for suicidal ideation or behavior.
Funded by a grant from the American Psychiatric Foundation through support from Astra Zeneca, Bristol Myers Squibb, Eli Lilly, Forest, Janssen, Pfizer and Wyeth.

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» NR6-073

DO TRAMADOL AND DOPAMINE-BLOCKING AGENTS ENHANCE THE RISK OF MIRTAZAPINE-ASSOCIATED RESTLESS LEGS SYNDROME?

Jin-Sang Yoon M.D., Sung-Wan Kim, M.D., Yo-Han Lee, M.D., Il-Seon Shin, M.D., Jae-Min Kim, M.D., Tak Youn, M.D., Jun-Young Cho, M.D., Yong-Hwan Kim, M.D., Jeong-Hoon Lee, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand the factors potentiating the risk of mirtazapine-associated restless legs syndrome.

SUMMARY:
Objective: Mirtazapine is known to often provoke restless legs syndrome (RLS). In this retrospective chart review study, we evaluated the socio-demographic and clinical factors related to mirtazapine-associated RLS.
Methods: Computerized medical records of 181 patients treated with mirtazapine from May 2004 to October 2007 were reviewed. RLS was identified using the diagnostic criteria of the International RLS Study Group. Socio-demographic and clinical characteristics were gathered, including comorbid physical illness and concomitant medications
Results: Mirtazapine-associated RLS was observed in 14 patients (8%), and most cases had developed within a few days after starting mirtazapine. Concomitant medication with tramadol, non-opioid analgesics, antihistamine, and dopamine-blocking agents was more frequently prescribed in subjects developing mirtazapine-associated RLS. In logistic regression analysis, concomitant medication with tramadol (odds ratio: 8.61, 95% confidence interval: 1.71–43.49) and dopamine-blocking agents (odds ratio: 4.67, 95% confidence interval: 1.31–16.70) enhanced the risk of mirtazapine-associated RLS.
Conclusion: The combined use of mirtazapine with tramadol or dopamine-blocking agents could potentiate the risk of RLS. Clinician should watch carefully for the development of RLS when mirtazapine is administered to patients who are taking tramadol or dopamine-blocking agents.

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1) Markkula J, Lauerma H. 1997. Mirtazapine-induced restless legs. Human Psychopharmacol 12:497-499.

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» NR6-074

MILD COGNITIVE DISORDER AND DEPRESSION: TREATMENT WITH ASSOCIATION BETWEEN GALANTAMINE AND ESCITALOPRAM

Julio Zarra, Schmidt Luisa, MD

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to demonstrate, identify,So there is a possible relation between the deficit of cerebral oxygenation and depression or relation between the serotonin system and cholinergic system in relation with disease comorbidity cognitive-depression. The discuss describe and analyze, is a possible relation between the deficit in cholinergic systems and depression.

SUMMARY:
INTRODUCTION: To evaluate the efficacy of galantamine-escitalopram association in patients with Mild Cognitive Disorder and Depression. So there is a possible relation between the deficit of cerebral oxygenation and depression or relation between the serotonin system and cholinergic system in relation with disease comorbidity cognitive-depression
OBJECTIVE: To evaluate the therapeutic response in patients with comorbility between Mild Cognitive Disorder and Depression in treatment with Galantamine , Escitalopram and the two drugs associated. METHOD: A group of 300 patients with symptoms of Mild Cognitive Disorder and Depression (DSM IV-R criteria) were separated in 3 groups of 100 patients. Each group received different treatment in an 8 months period:
Group 1: Galantamine 16 mg/day.
Group 2: Escitalopram 20 mg/day.
Group 3: both drugs , same dose.
RESULTS: The therapeutic response evaluated in Hamilton Scale for Depression(HAM-D), Montgomery and Äsberg Depression Rating Scale (M.A.D.R.S.), Mini Mental State Examination (M.M.S.E.) and Global Clinical Impression (G.C.I.) scores during 8 months. In the third group who received the two drugs associated, had much better response than the others and "brain enhancer".
CONCLUSION: The group who received the association of the nootropic agent Galantamine with antidepressant (SSRIs) Escitalopram had a relevant satisfactory therapeutic response (the best result), so there is a possible relation between the deficit in cholinergic systems and depression. Could be cerebral cholinergic systems deficit a generator of Depressive Disorder?

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» NR6-075

PREVALENCE OF DEPRESSION AND ANXIETY IN PERITONEAL DIALYSIS PATIENTS AND POSSIBLE CORRELATIONS WITH MORTALITY AND MORBIDITY

Sinem Gonenli M.D., Oguz K. Karamustafalioglu, M.D., Abdulkadir Unsal M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize the frequency of depression and anxiety in patients treated with continuous ambulatory peritoneal dialysis (CAPD) and to reveal possible relationships between these disorders mortality and morbidity.

SUMMARY:
Objective: The aim of this study is to determine the frequency of depression and high anxiety level in patients treated with CAPD and to reveal possible correlations between these disorders and mortality and morbidity rates.
Methods: 81 outpatients treated with CAPD included into the study. SCID-I research version, Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were used.
Results: Mean age of patients was 37.4±14.3. 41 patients had SCID-I diagnosis, major depression was found to be most frequent diagnosis (39,5%). We evaluated patients as "high anxiety level" and "low anxiety level" according to cut-off point of 17 in BAI. Depression and high anxiety level is not associated with sociodemografic and metabolic variables. After the 3 years follow-up period; 54 patients are still under treatment of peritoneal dialysis, 16 patients move to hemodialysis, 6 patients are having renal transplantation and 5 patients was died. In four group of patients, we didn't find any correlation between having both depression and mortality; anxiety and mortality. Complications were classified as; "peritonitis", "complications other than peritonitis" and "total complications". There was no statistically significant relationship between the complications and both depression or anxiety.
Conclusion: Psychopathology is commonly encountered in patients with end-stage renal disease. Some researchs reported that psychiatric comorbidity worsen prognosis of disease but contrary findings are also known. We didn't find any statistically significant relationship between depression and anxiety in mortality and morbidity.

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D. Depression, perception of illness and mortality in patients with end-stage renal disease. Int J Psychiatry Med. 1991;21(4):343-54

» NR6-076

PARENTAL QUALITY OF LIFE AND DISTRESS IN X-LINKED MUSCULAR DYSTROPHY

Hwang Jun Won M.D., Seung Ug Yoon, M.D., Sung Jong Park, M.D., Hong Sup Yoo, M.D., Soo Churl Cho, M.D., Ph.D., Jong Hee Chae, M.D., Ph.D., Bong Jin Hahm, M.D., Ph.D., Hong Jin Jeon, M.D., Ph.D.,

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the relationship between psychological distress and health-related quality of life in parents of children with X-linked muscular dystrophy

SUMMARY:

The purpose of the current study was to evaluate health-related quality of life in parents of boys with X-linked muscular dystrophy, namely, Duchenne/ Becker muscular dystrophy. In addition, a relationship between psychological distress and health-related quality of life in parents was investigated. The participants were 50 parents (43 mothers and 7 fathers) whose child had Duchenne/ Becker muscular dystrophy. Among them, 19 parents had significant psychological distress. All participants completed Symptom Checklist-90-Revised and World Health Organization Quality Of Life Scale, Brief Version. Other instruments included Family Relationship Scale and Child Behavior Checklist.
Parents with psychological distress had significantly lower scores on all 4 domains of WHOQOL-BREF including physical health, psychological health, social relationships, and environment, relative to parents without psychological distress (df= 48, t= 6.55, p< .001; df= 48, t= 5.21, p< .001; df= 48, t= 5.92, p< .001; df= 48, t= 4.84, p< .001, respectively). Hierarchical multiple regression analyses were performed to examine the influence of predictors on 4 domains of WHOQOL-BREF in parents of boys with DMD/ BMD. Model predictors included psychological distress and perceived family relationship of parents as well as types of muscular dystrophy, mobility, duration of illness, and problematic behavior of their children. Parental age, sex, and economic difficulty were controlled in the analyses. Among 6 model predictors, only higher T score of Global Severity Index significantly predicted lower scores on all 4 domains of WHOQOL-BREF (multiple regression analysis, ß= -0.588, t= -4.38, p <.001; ß= -0.586, t= -4.07, p< .001; ß=-0.812, t= -6.22, p< .001; ß= -0.330, t= -2.08, p= .046, respectively). Thus, findings of the current study suggest that all domains of health-related quality of life may be strongly influenced by psychological distress in parents of boys with DMD/ BMD.

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» NR6-077

THE PREVALENCE OF ANXIETY AND IMPACT OF UNRECOGNIZED ANXIETY ON HEALTH-RELATED QUALITY OF LIFE IN KOREAN PATIENTS WITH FUNCTIONAL DYSPEPSIA

Sang-Yeol Lee Psy.D., Duk-In Jon, MD, Ph.D., Bo-Hyun Yoon, MD, Ph.D., Young Chul Schi, MD, Ph.D., Kyung Joon Min, MD, Ph.D., Won-Myong Bahk, MD. Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understanding the relationship between unrecognized anxiety and health related quality of life in patients with functional dyspepsia
Summary:

Objective: Gastroenterologists have been criticized for underrecognizing and undertreating mental health disorders. This criticism assumes patients with recognized disorders and those with unrecognized disorders suffer the same burden of illness. The current investigation examined the impact of unrecognized anxiety disorders on health-related quality of life(HRQOL) in patients with functional dyspepsia
Methods : 347 functional dyspepsia subjects were recruited from Wonkwang and Catholic university's gastroenterologic clinic. The patient were selected from a population of outpatients who were diagnosed with functional dyspepsia by gastroenteroglogists. The patient completed Spielberger state-trait anxiety inventory(STAI), Nepean dyspepsia index scale-Korean version(NDI-K) and SF-36-Korean version(SF-36-K).
Results : The prevalence of state anxiety was 20%. The patient with state anxiety showed significantly lower score in interference, knowledge and sleep disturbance dimensions of NDI-K than the patient without state anxiety as well as showed significantly lower score in each dimension of SF-36-K. There was no significant difference between the patient with trait anxiety and the patient without trait anxiety in NDI-K. In addition, higher state anxiety and/ or trait anxiety on the STAI were associated with poorer disease specific HRQOL(NDI-K) and general HRQOL.
Conclusion : Patients with functional dyspepsia that have been had unrecognized anxiety appear to suffer from poorer HRQOL than patients without anxiety. This study suggest that we must realize that anxiety likely to be prevalent sources of excess poor general health among patients with functional dyspepsia and that when anxiety strike the patient with functional dyspepsia, these often go unrecognized and untreated.

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» NR6-078

EFFECT OF MINDFULNESS BASED GROUP PSYCHOTHERAPY ON DEPRESSION, QUALITY OF LIFE AND HEART RATE VARIABILITY IN PATIENTS WITH BREAST CANCER

Sang-Yeol Lee Psy.D., Min-Cheol Park, MD, Ph.D., In-Sook Kim, Ph.D., Young-Hoon Cheon, MD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the effect of mindfullness based group therapy on the depression, quality of life and heart rate variability in paients with breast cancer

SUMMARY:

Objective : The purpose of this study was to examine the effect mindfulness based group therapy(MBGT) on the depression, quality of life, and heart rate variability(HRV)
Methods : Seventeen patients of subjects were selected according to the patients' informed consent among the 52 patients with breast cancer who completed surgery and adjuvant therapy at the Department of Surgery from Wonkwang University Hospital. Before and after of 12 weeks MBGT, Beck depression inventory(BDI) and Short-form health survey 36-Korean version(SF-36-K)) were measured. Heart rate variability were also measured by S-2000(Medicore) before and after MBGT
Results : 1)The prevalence of depression in patients with breast cancer was 41%. 2)There were significant difference in results of HRV between patients with breast cancer and healthy control.

3)The MBGT for 12 weeks significantly decreased BDI, and improve role physical and general health perception of SF-36-K.
4)The MBGT significantly increased Standard Deviation NN interval(SDNN) and total power(TP) in HRV.
Conclusion : These result suggest that MBGT is a program that is feasible for breast cancer, and the result provide preliminary evidnece for beneficial effects of MBGT on depression, quaility of life and HRV in patients with breast cancer.

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» NR6-079

PSYCHOLOGICAL CHARACTERISTICS AND COPING STYLE IN HOSPITALIZED PNEUMOCONIOSIS PATIENTS

Sae-Han Park M.D., Joung-Sook Ahn, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the association between psychological characteristics and coping style in hospitalized pneumoconiosis patients.

SUMMARY:

Objectives : We examined the presumptive association between psychological characteristics and coping style in hospitalized pneumoconiosis patients.
Method : Eighty-five hospitalized pneumoconiosis patients were divided into two groups according to their Hamilton Depression Rating Scale(HAM-D) scores ; Group A consisted of 22 patients with HAM-D score higher than 18, Group B had 63 patients with HAM-D score lower than 18. All of them were interviewed with the Hamilton Depression Rating Scale(HAM-D) and completed the Symptom Checklist-90 items-Revised(SCL-90-R), the State-Trait Anxiety Inventory(STAI) and Ways of Coping Checklist. Days of hospital care, socio-demographic data and three evaluation scores were compared between two groups.
Results : HAM-D scores of 22 patients were higher than 18. Group A patients were older. Problem focused coping scores and educational levels of Group A patients were lower. Hospitalized pneumoconiosis patients showed somatization, depression, phobic anxiety and anxiety, in order.
Conclusion : In our study, pneumoconiosis patients showed more depressive symptoms and less problem focused, less active coping strategies. Therefore, in the management of patients with pneumoconiosis, it is important to evaluate their depressive symptoms as well and start therapeutic intervention from the outset of treatment.

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» NR6-080

COMMUNITY INTEGRATION AND ASSOCIATED FACTORS AMONG OLDER ADULTS WITH SCHIZOPHRENIA

Chadi Abdallah M.D., Carl I. Cohen, M.D., Miguel Sanchez-Almira, M.D., Pia Reyes, M.D., Paul M. Ramirez, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to define Community Integration and its four components: social integration, psychological integration, physical integration, and independence. He will be able to compare the level of community integration among older schizophrenic persons to that of their age peers in the community. Participant should also be able to name some factors impacting community integration.

SUMMARY:

Objective: Community Integration has been increasingly recognized as an important element in recovery. There are a paucity of data on Community Integration among older adults with schizophrenia. We compare Community Integration among older schizophrenic persons with their age peers in the community, and examine factors associated with Community Integration among the schizophrenia group.
Methods: The Schizophrenia Group consisted of 198 community-dwelling persons aged 55 years and older who developed schizophrenia before age 45. A Community Comparison Group (N=113) was recruited using randomly selected block-groups.
Wong and Solomon's (2002) conceptual framework was used to develop a 12-item Community Integration Scale with 4 components: independence, psychological integration, physical integration, and social integration. Moos' Ecosystem Model was used to examine the personal and environmental factors associated with Community Integration.
Results: The Schizophrenia Group had a significantly lower Community Integration Scale mean score than the Community Comparison Group. The two groups differed on 7 of the 12 items of the Community Integration Scale and on each of its 4 dimensions. Within the Schizophrenia Group, in regression analysis, 7 variables were significantly associated with Community Integration: being female, higher personal income, lower depressive symptoms, lower negative symptoms, lower AIMS score, higher CAGE lifetime scores, and greater control of one's life. The model was significant and explained 54.7% of the variance.
Conclusion: Our data confirmed that older persons with schizophrenia have lower level of Community Integration than their community age peers. Our findings suggest that the factors impacting on Community Integration are potentially ameliorable, and therefore provide an opportunity to enhance the well-being of this population.

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» NR6-081

A FACTOR ANALYSIS OF DIFFERENT TEMPERAMENT DOMAINS IN A BORDER REGION IN RURAL SOUTHERN CALIFORNIA

Alvaro Camacho M.D., Alan N. Simmons, Ph.D., Bernardo Ng, M.D., Scott C. Matthews, M.D., Hagop S. Akiskal, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the different temperament domains that are present in different clinic settings in rural southern California. This will help the clinician consider the TEMPs as a valuable tool to elucidate temperaments domains that might help clarify difficult overlapping mood or anxiety diathesis.

SUMMARY:

Temperament has been described as an oligogenic model that confer attributes to individuals in their daily functioning. The dif-

ferent types of temperaments described are depressive, cyclothymic, hyperthymic, anxious and irritable. To describe the different temperament domains in a community vs a private practice clinic, a retrospective record review was conducted in 117 patients with mood disorders who received the Temperament Scale (TEMPS). Forty nine were from a Community clinic (CM) and 68 from a private practice (PP). Frequencies of temperament, demographic variables and a factor analysis of TEMPS are presented. The majority were Spanish speaking (76%) at the CM compared to 25% in PP. Ninety percent were Hispanic in the CM vs 35% in the PP. Regarding years of education, 8 years (SD 3.5) was the mean for CM patients, compared to 13 years (SD 3.6) in PP patients. The following temperament domains were found. In PP: Depressed 17/69 (25%); Cyclothymic 18/69 (26%); Hyperthymic 16/69 (23%); anxious 14/68 (20%); Irritable 4/69 (5%). Among CM. Depressed 10/49 (20%); Cyclothymic 14/49 (28%); Hyperthymic 8/49 (16%); anxious 15/49 (30%); Irritable 2/49 (5%). Using Factor Analysis to determine the significant domains among clinics, Cyclothima (0.82) and Irritability (0.81) were the most relevant, regardless of psychosocial background and language differences. This study elucidates how temperament domains could be considered a valuable tool in evaluating patients in mood disorders clinic. The tool elucidates valuable characteristics that could be applied for guidance in diagnosis and treatment without being biased by different socio-cultural background or language differences. The factor analysis helps elucidate the pertinence of TEMPS scores that may not be the focus of clinical intervention although they contribute significantly to the structure of an individual's temperament, specifically emotional labiality (i.e., cyclothima and Irritability).

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» NR6-082

THE EFFECTIVENESS OF SUICIDE PREVENTION PROGRAM IN A TAIWAN METROPOLITAN CITY

Frank Huang-Chih Chou, Frank Huang-Chih Chou,Psy.D., Ph.D., Wei-Jen Chen, Psy.D., Cheng-Chung Chen, Psy.D,Ph.D., Chi-Kung Ho,M.D., Ming-Hui Kuo,M.S., Chao-Yueh Su, M.S., Ming-Bing Lee, Psy.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to how to organized and develop suicide prevent strategy, and outcome evaluation.

SUMMARY:

Background: According to the 1995-2005 annual report of Department of Health, Taiwan, the overall suicide rate was gradually increasing. Suicide became an important social issue in Taiwan. However, the suicide rate in Kaohsiung, a Taiwan metropolitan city, was higher than average suicide rate in Taiwan.
Aims: The purpose of this study is to evaluate the effectiveness of suicide prevention program from 2005 to 2008, June in Kaohsiung.
METHODS: We used context-input-procedure-product (CIPP) to evaluate suicide prevention program in Kaohsiung which was modified from that in Australia. The strategies of suicide prevention in Kaohsiung are universal, selected, and indicated strategy. At the beginning of suicide prevention program, we organized and trained the suicide prevention team and designed the suicide prevention program including standard operation of procedure, and mult- disciplinary involvement. The index uses of measures are 'reported person-times, telephone counseling intervention response and one-session call-in telephone counseling person-times, and suicide rate'.
RESULTS: From 2005 to 2007, the reported person-times of suicidal attempt were 1217, 2625, and 2795 person-times. The telephone counseling intervention response person-times of suicidal attempters were 1432, 2010, and 7051 person-times. The one- session call-in telephone counseling person-times were 0, 4320 and 10456 person-times. The suicide rates (number of committed suicide) were 21.6 per 100,000 (324) in 2005, 20.3 per 100,000 (304) in 2006, 19.4 per 100,000 (276) in 2007 and estimated 16.9 per 100,000 (130) until 2008, June.
CONCLUSION: According to the above results, the suicide prevention program in Kaohsiung is effective. However, the longer followed up of this program for evaluating effectiveness is necessary. Key words: suicide prevention, suicide rate, context-input-procedure-product (CIPP).

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» NR6-083

THE RELATIONSHIP AMONG SCHIZOPHRENIA CAREGIVERS' BURDEN, QUALITY OF LIFE AND SCHIZOPHRENIA SYMPTOM SEVERITY IN TAIWAN

Frank Huang-Chih Chou, Chao-Yueh Su,M.S., Ming-Hui Kuo,M.S., Frank Huang-Chih,Psy.D., Ph.D. Shih-Pei Shen, Li-Hsing Chang, M.S., Shih-Shih Chao, M.S.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to realize what various factors influence schizophrenic caregivers' burden.

SUMMARY:

Background: Most schizophrenics in Taiwan live with their families. The family themselves may suffer due to the disability of schizophrenia. Aims: To evaluate the relationship among schizophrenia caregivers' burden, quality of life, mental health and schizophrenia symptom severity and their associated factors .
Method: We used the Taiwan caregivers' burden scale, Short Form-12 (SF-12), and Brief Symptoms Rating Scale (BSRS -5) to evaluate 359 schizophrenia caregivers in Kaohsiung, Taiwan.
Results: When schizophrenic patients' symptoms are severe, their Physical Component Summary scores are lower than schizophrenic patients with mild or moderate symptoms. When the schizophrenic patients' symptoms are mild or more, their caregivers' Mental Component Summary scores are lower than schizophrenic patients with none or almost no symptoms. The greater the scores of caregivers' burden, the lower the scores of caregivers' Physical Component Summary and Mental Component Summary scores. In addition, there is a positive relationship between the scores of caregivers' burden and BSRS –5.
Conclusion: There is a negative relationship between schizophrenic patients' symptoms and the caregivers' quality of life. There is a positive relationship between schizophrenic caregivers' burden and psychiatric impairment. Key words: caregivers, burden, quality of life, and schizophrenia

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» NR6-084

THE EFFECTIVENESS OF THE CRISIS INTERVENTION TRAINING (CIT) PROGRAM ON OFFICER EFFECTIVENESS AND BURNOUT

Shah Jalees M.D., Mark R. Munetz, MD., Jennifer L.S. Teller, PhD., Karen M. Gil, PhD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, participants will have an understanding of the skills taught during Crisis Intervention Team(CIT) training, changes in the perceptions of the responsiveness of the mental health system, how the perceptions of CIT trained and non-CIT trained police officers differ on the effectiveness of CIT, and differences between the two groups of officers on a burnout scale.

SUMMARY:

Background. Crisis Intervention Training (CIT) is a cooperative effort between law enforcement and the mental health community to help police officers handle incidents involving mentally ill people in crisis. This research study examines perceptions of the training by CIT and non-CIT officers. We additionally examine burnout rate among these two groups of officers.
Methods. Ten CIT and ten non-CIT officers volunteered for the study. The first author conducted a 45-minute ride-along session on patrol with each of the volunteers. Officers were asked open-ended, semi-structured questions to assess their view of the CIT program. At the end of the session, the officers completed a burnout questionnaire, composed of 5 questions. Quantitative data were analyzed using SPSS version 12.0.
Results. CIT officers believed their attitudes toward people with mental illness in crisis were changed because of the training. They tended to use force less often and used alternate techniques such as verbal de-escalation more often. They believed they were more empathic and understanding and thought communication was improved between law enforcement and the mental health system. A majority (60%) of non-CIT officers wanted to volunteer for the program after working with CIT officers and observing their skills in handling mentally ill people in crisis.
CIT officers' mean burnout score was 14.8 + 7.4 (SD), range 6 - 30, non-CIT officers' mean burnout score was 10.1 + 4.7, range 5 - 19 (t=1.692; p=.108).
Conclusion. The officers felt CIT provided skills to identify people in crisis and changed their attitude toward mental illness. They believed their competence in handling those in a mental illness crisis increased and they were better trained in techniques that did not utilize force. Although not significant, perhaps because of the small sample size, CIT officers' burnout score was higher than those of non CIT officers. Future research should explore this possible result of CIT training.

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» NR6-085

THE VARIABLES AFFECTING THE JUDGMENT FOR CONTINUING HOSPITALIZATION IN PATIENTS WITH MENTALLY ILL IN KOREA

Min-Cheol Park M.D., San-Su Lee, M.D., Chong-Ill Park, Hyo-Sun Ko, M.D., Yong-Hoon Shon, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the variables affecting the judgment of continuing hospitalization in the patients with mentally ill in Korea.

SUMMARY:

The present study surveyed the current state of continuing hospitalization disapproval by the Mental Health Judgment Board of an area and the factors affecting the disapproval based on items recorded in the application for the judgment of continuing hospitalization in Korea.
During the 5 years' period from January 2002 to December 2006, there were a total of 14,782 applications for judgment of continuing hospitalization. Among them, 1,832 were disapproved, showing a disapproval rate of around 12.4%.
As to disapproval rate related to each factor, according to facility, the disapproval rate was 10.6% for patients at mental hospitals and 14.6% for those at nursing homes.
According to diagnosis, the disapproval rate was 27.9% for alcoholism, 17.1% others, 16.4% mental retardation, 12.5% mood disorder, 11.5% schizophrenia, and 8.6% organic mental disorder, and the differences were statistically significant.
According to number of applications and diagnosis, the disapproval rate was higher when the number of applications was 3~6 among patients with mood disorder, mental retardation or others.
According to number of applications and facility, the disapproval rate was higher when number of applications was 4 or more among mental hospital patients, and when it was 6 or more among nursing home patients.
The factors most influential on the judgment of continuing hospitalization were facility, number of applications and diagnosis, and the disapproval rate was high among mental hospital patients, alcoholics, those with medical insurance, and those with low risk of injury.
Key words: Judgment of continuing hospitalization, Dissent rate, Mental health judgment board

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» NR6-086

PROJECT ANTI-BULLY: BULLYING IN MIDDLE SCHOOLS YEAR TWO SURVEY

Fabianna Pergolizzi, Fabianna Pergolizzi, Darren Richmond, Joseph Pergolizzi, M.D, and the Project Anti Bully Study Group

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to • Describe actions that constitute bullying, including cyberbullying in middle schools; • Understand the extent, and different types of, bullying within a culture of meanness; • Describe actions to resist bullying; and • Recognize the gender differences that exist related to bullying.

SUMMARY:

Background. In 2006, Project Anti-bully started a project to determine the prevalence of bullying in middle schools. Although bullying and victimization in the United States are first identified in elementary school, the problem becomes particularly acute, in terms of frequency and severity, in early adolescence. Yet our knowledge of bullies and victims and their peer affiliations during this period is limited. This poster presents the results of the 2007 surveys and their comparison to the first year's surveys. Anti-bullying legislation mandates anti-bullying education, the content for which will be based on surveys such as the one presented in this paper. Methodology. 7th-8th graders at 5 schools (Naples, FL; Miami Beach, FL, Palo Alto, CA (2 schools); Durham, NC) responded to 14 Child Abuse Prevention Services Survey items. Results. 631 surveys were analyzed. In 2006, about half of respondents reported that they, personally, had never been bullied in school. That number dropped in 2007 for both boys and girls.

However, the majority of respondents in both 2006 and 2007 found bullying was a problem at their school, and females found bullying more of a problem in 2007 than 2006 ($p<0.001$). When asked how safe children felt in school, most respondents found it was "safe" or "very safe," with boys finding rating school significantly more in the category "very unsafe" in 2007 than 2006 ($p=0.042$). Boys and girls differed in how they dealt with bullies. The main tactic used by girls in both 2006 and 2007 was to ignore the bully, closely followed by doing nothing. Boys were more likely to hit or push a bully in 2006 and 2007 (nearly unchanged) followed by ignoring the bully. Relatively few children of both genders asked for help from a friend or adult, but girls were more likely than boys to request help from their friends. However, when a child observed someone else being bullied, boys and girls had similar reactions with the vast majority reporting that they did nothing, followed by telling the bully to stop or talking to the victim. Far fewer observers of bullying behavior reported that they summoned help from a friend or adult. The majority of respondents did not report ever having been cyberbullied and there was no significant difference in cyberbullying scores year over year. Compared to the result of the 2006 surveys, there was an increase in bullying observed at school ($p<0.05$), bullying was more of a problem for females ($p<0.001$).

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» NR6-087

COMPARISON OF PERSONALITY DIMENSIONS IN BODY DYSMORPHIC DISORDER AND OBSESSIVE-COMPULSIVE DISORDER

Megan Kelly Ph.D., Nicole C. McLaughlin, Ph.D., Benjamin D. Greenberg, M.D., Ph.D., Katharine A. Phillips, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand differences in personality traits between body dysmorphic disorder (BDD) and obsessive-compulsive disorder. Participants should also be able to understand how these differences in personality traits have implications for patient care.

SUMMARY:

Background: Body dysmorphic disorder (BDD) and obsessive-compulsive disorder (OCD) have many similarities, including time-consuming obsessions and compulsions. While both disorders appear to have certain personality characteristics in common, no studies have directly compared personality traits in these disorders. Methods: BDD (n=100), OCD (n=93), and healthy control subjects (n=436) completed the NEO-Five Factor Inventory (NEO-FFI). NEO personality domain scores were age-adjusted. Results: BDD and OCD subjects were significantly higher in neuroticism than controls (both $p<.001$), with BDD and OCD subjects scoring in the very high range. Neuroticism scores for BDD and OCD subjects did not significantly differ. On extraversion, both BDD and OCD subjects had significantly lower scores than controls (both in the low range; $p<.001$). However, BDD subjects had significantly lower extraversion scores than OCD subjects ($p=.004$). Both BDD and OCD subjects were significantly less open to experience than controls (average range for BDD and OCD; $p=.002$ and $p<.001$, respectively); BDD and OCD scores did not significantly differ. On agreeableness, BDD subjects, but not OCD subjects, had significantly lower scores than controls (low range for BDD; $p=.01$), although BDD and OCD scores did not significantly differ (average range for OCD). Conversely, on conscientiousness, OCD subjects, but not BDD subjects, had significantly lower scores than controls ($p=.009$); BDD and OCD scores did not significantly differ (both in the low range). Conclusions: Both BDD and OCD patients have very high levels of neuroticism, but BDD patients are significantly less extraverted than OCD patients, consistent with some previous findings of greater social impairment in BDD. In addition, BDD patients—but not OCD patients—are less agreeable than normal controls. Conversely, OCD patients—but not BDD patients—are less conscientious than normal controls. These findings have implications for patient care.

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» NR6-088

PHYSICAL FUNCTIONING AND PHYSICAL HEALTH-RELATED QUALITY OF LIFE IN BODY DYSMORPHIC DISORDER

Katharine Phillips M.D., Megan M. Kelly, Ph.D., William Menard, B.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify characteristics and correlates of physical functioning and physical health-related quality of life in individuals with body dysmorphic disorder (BDD). Participants should also be able to understand the relative contribution of BDD severity, duration of BDD, and social anxiety to physical functioning and physical health-related quality of life.

SUMMARY:

Background: Physical functioning and physical health-related quality of life (QoL) appear to often be poor in patients with body dysmorphic disorder (BDD). However, no prior study has examined correlates of physical functioning/QoL in BDD. Methods: 176 individuals (mean age 32.5 ± 12.3, 71% female) with current DSM-IV BDD completed the SF-36 and Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q). Other clinical features were assessed. Results: The SF-36 Physical Component Summary (PCS) score (mean 51.8 ± 11.8) was 0.7 SD units poorer in BDD than U.S. population norms. Worse scores were associated with older age ($r=-.30$, $p<.001$), longer BDD duration ($r=-.30$, $p<.001$), receiving disability benefits ($r=-.37$, $p<.001$), and greater social anxiety ($r=-.19$, $p=.02$), but not number of Axis I disorders or BDD severity. However, greater BDD severity was associated with poorer QoL on the SF-36 Physical Functioning subscale ($r=-.17$, $p=.03$). On the Q-LES-Q, physical health-related QoL (mean score 50.4 ± 18.8) scores were 1.9 SD units poorer than community norms, with poorer QoL associated with more severe BDD symptoms ($r=-.33$, $p<.001$), a greater number of comorbid Axis I disorders ($r=-.26$, $p=.004$), and receiving disability benefits ($r=-.22$, $p=.01$). After accounting for age, gender, and disability status, BDD severity was significantly independently associated with Q-LES-Q physical health-related QoL. On the SF-36, in regression analyses BDD severity did not significantly contribute to PCS score but was significantly independently associated with the Physical Functioning subscale. Conclusions: Physical functioning and physical health-related QoL in BDD is poorer than for population/community norms. Our finding in some analyses that BDD severity, BDD duration, and social anxiety were associated with poorer functioning/QoL is consistent with clinical observations that many patients avoid medical care in part because of anxiety and shame about their appearance.

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» NR6-089

EYE-TO-EYE TELEPSYCHIATRY: UNLOCKING THE GOAL OF SPECIALIST PSYCHIATRIC TREATMENT ON A BROADER BASIS, TO A CHEAPER COST

Agneta Ekman M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to recognize the difference between the Teleworking/Video Presence project and ordinary videoconferencing equipment. The participant should further be familiar with the concepts of hybrid and mediated spaces and recognize their potential as an enabler of the delivery of high quality psychiatric treatment in new areas.

SUMMARY:

Psychiatric services delivered by telepsychiatry produces clinical outcomes equivalent to those provided face to face (1). In some aspects it has even been found superior "…videoconferencing enhanced the therapeutic relationship and … was less intrusive than [face to face] communication" (2). Additional benefits are decreased cost and access to specialist consultation (1). This study identified the key factors explaining why the technology was not broader used by conducting a comprehensive literature review on telepsychiatry. To test the assumption that the Video Presence project at KTH's conferencing equipment (ViPr) would address these issues a clinical trial involving 20 patients (7 men and 13 women, age 20-78) referred from GPs and psychiatrists was performed. Patients were diagnosed with MINI and their mood course followed with MADRS and evaluations of their subjective satisfaction with the sessions. Most common diagnoses were Major depression, Dysthymic disorder and GAD; four patients had Bipolar depression; 80% were treated with antidepressants and/or mood stabilizers and one patient with paranoid symptoms was given neuroleptics. The technique was CBT. Session duration was 50 minutes including tests.

The literature review identified the following factors as most likely explanations for why the use of the technology is not broader: Facial expressions cannot be read due to visual and auditory information lacking in richness, hampering emotional connections (3); there is a training need before psychiatrists can use telepsychiatry (4); and technical problems decreased credibility (2). The clinical study supported previous research in terms of clinical outcome; a 69% improvement in MADRS score between session 1 and 7. In addition the qualitative analysis suggests that the differentiating characteristics of the technology fully addresses the previously identified as limiting factors (2-4). A controlled study is hence recommended to verify these promising results.

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2) De Las Cuevas C. Arredondo MT, Cabrera MF, Sulzenbacher H, Meise U: Randomized clinical trial of telepsychiatry through videoconference versus face-to-face conventional psychiatric treatment. Telemed J E Health 2006; 12:341-350; Norman S: The use of telemedicine in psychiatry. Journal of psychiatric and mental health nursing 2006; 13:771-777; Wagnhild G, Leenknecht C, Zauher J: Psychiatrists satisfaction with telepsychiatry. Telemed J E Health 2006; 12:546-551

» NR6-090

RESEARCH ASSESSMENT OF DEPRESSION DIAGNOSIS AND SEVERITY: COMPARABILITY OF TELEPHONE AND IN-PERSON INTERVIEW

William Yavorsky Ph.D., Janet B.W. Williams, D.S.W.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand how the use of the telephone does not reduce a clinician's ability to reliably conduct and rate a diagnostic or severity assessment of depression. Concerns about data quality, disclosure of sensitive information by telephone and the ability to assess observable behaviors will be addressed.

SUMMARY:

Objective: Telephone-based assessment of depression has become more common in clinical and research contexts. Telephone assessment can provide more ready access to hard-to-reach populations and, for clinical trials, a more diverse sample. Despite these advantages, there are often questions about the tolerability of telephone interviews with depressed populations as well as the reliability of this administration mode. This review examines studies comparing the reliability and acceptability of telephone and in-person assessment of depression.

Method: Electronic databases were searched with a list of keywords that included: "telephone", "assessment" and "depression". The minimum criterion for inclusion was that the study compare telephone to in-person assessment of depression using a standard rating instrument.

Results: There were 84 articles reviewed with 14 meeting the narrower criterion for inclusion of comparing telephone to in-person assessment. Measures appropriate for comparison were reported in all studies, with intraclass correlation coefficients (ICC) reported in 36% (5/14), kappa reported in 43% (6/14), and 21% (3/14) used other methods to assess agreement, depending on the characteristics of the instrument studied. The range of ICCs (.80-.96) and range of kappas (.45-.96) demonstrate good agreement across multiple instrument types.

Conclusion: Telephone and in-person assessment of depression show similar reliabilities across most accepted instruments. Telephone assessment is acceptable to most individuals and may have certain advantages over in-person interviews, with some studies suggesting that the telephone interface affords a level of comfort and anonymity. The primary advantages of telephone assessment, however, are in terms of geography and economics: the ability to sample larger, more diverse groups using fewer resources.

Christian Yavorsky, Ph.D. is an employee of MedAvante, Inc. who provided funding for this research.

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1) Allen K, Cull A, Sharpe M: Diagnosing major depression in medical outpatients: acceptability of telephone interviews. J Psychosom Res 2003; 55:385-387

2) Kobak K, William JBW, Jeglic E, Salvucci D, Sharp I: Face-to-face versus remote administration of the Montgomery-Asberg Depression Rating Scale using videoconferencing and telephone. Depress Anxiety 2007; 25:913-919

» NR6-091

FREQUENCY AND PREDICTORS OF LAMOTRIGINE-RELATED SERIOUS RASH AND INFLAMMATORY REACTIONS: SYSTEMATIC REVIEW AND META-ANALYSIS

Laura Caldwell B.A., SN Ghaemi, M.D., M.P.H.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to appreciate the relative and absolute risks of serious acute inflammatory reactions with lamotrigine use, and be familiar with possible predictors of serious adverse outcomes with lamotrigine

SUMMARY:

Objective: Serious rash is a common side effect of lamotrigine, yet its predictors and preventive measures are poorly understood. Other acute inflammatory reactions, besides rash, are also underrecognized as adverse events with lamotrigine. In this systematic

review, we sought to examine the frequency, risk factors and preventive measures for these outcomes.
Method: We carried out computerized literature searches for English or foreign-language reports of lamotrigine and rash or inflammatory reactions, using the Medline, HealthStar, Current Contents, PsychInfo, CINAHL, National Library of Medicine, EMBASE, DARE, and Cochrane Library databases, for 1960 through March 2009. 171 articles were identified, of which about 20 articles met inclusion criteria. Full data analysis will be presented. Partial analysis is reported here.
Results: Overall risk of serious rash was low but notable, and overall risk of serious acute inflammatory reactions, other than rash, was about as frequent. Causes of heterogeneity will be explored. One predictor of rash appears to be baseline history of drug allergies. Multiple cases of serious rash or other inflammatory reactions also appeared to be related to presence of baseline autoimmune disorders.
Conclusions: It appears that acute inflammatory reactions, not related to rash, are an important serious risk with lamotrigine treatment. Predictors of serious outcomes appear to include baseline history of drug allergies and presence of autoimmune disorders. Final data will be presented at the conference.
Funding Source: None

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1) Ketter TA, Wang PW, Chandler RA, et al.: Dermatology precautions and slower titration yield low incidence of lamotrigine treatment-emergent rash. J Clin Psychiatry May;66(5):642-645, 2005.

2) Bavdekar SB, Muranjan MN, Gogtay NJ, et al.: Anticonvulsant hypersensitivity syndrome: lymphocyte toxicity assay for the confirmation of diagnosis and risk assessment. Ann Pharmacother 38:1648-1650, 2004.

» NR6-092

THE ROLE OF PATIENT ATTACHMENT STYLE IN PREDICTING TREATMENT RETENTION AND OUTCOME IN SHORT-TERM PSYCHOTHERAPY

Nivea Calico M.D.,Arnold Winston, M.D.,Catherine Eubanks-Carter, Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to examine the role of patient attachment style in predicting treatment retention and outcome in psychotherapy.

SUMMARY:

Introduction: To examine the role of patient attachment style in predicting treatment retention and outcome in a 30 session short-term psychotherapy. In the present study we set out to examine the correlation of trauma, locus of control, and introject with attachment status and the possibility of subjects initially scored as insecure attachment on the Relationship Scales Questionnaire later developing secure attachment after the completion of psychotherapy. Methods: A sample of 100 patients (73 completers and 27 dropouts) whose attachment styles had been measured by the Relationship Scales Questionnaire were randomly assigned to either cognitive behavioral therapy or brief relational therapy. Selection of patients was based upon the following Inclusion criteria: Patients diagnosed with personality disorder cluster C and NOS with cluster C features; and Exclusion criteria: Patients with psychosis, serious medical conditions and significant suicidal risk. Additional outcome measures were used in the study and will be described in full detail. Results: Although patients showed significant improvement with respect to symptoms, interpersonal functioning, and target complaints, they did not show change in attachment in either CBT or BRT. Conclusions: Preliminary results showed that there was no significant change in patient attachment style between CBT or BRT groups over the course of treatment.
While short-term treatments are helpful for achieving symptom relief, longer and more intensive treatments may be necessary in order to change attachment. styles.

REFERENCES:

1) Holmes J: John Bowlby & Attachment Theory. Edited by Laurence Spurling, Makers of Modern Psychotherapy, 1993.

2) Winston A, Winston B: Handbook of Integrated Short-Term Psychotherapy. American Psychiatric Publishing Inc.,2002

» NR6-093

TREATMENT PATTERNS BY RACE/ETHNICITY AND HOUSEHOLD INCOME AMONG ATTENTION-DEFICIT HYPERACTIVITY DISORDER SUBJECTS TREATED WITH STIMULANTS

Laura Christensen M.S., Heather Aeder, M.A., Rahul Sasané, Ph.D., Carolyn Harley, Ph.D., Paul Hodgkins, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the association between socioeconomic factors (race/ethnicity and household income) and treatment patterns (persistence, adherence) for attention-deficit hyperactivity disorder (ADHD) patients taking stimulant medications (amphetamine or methylphenidate).

SUMMARY:

Objective: Examine persistence and adherence by race/ethnicity and annual household income among those taking a stimulant medication (amphetamine (AMPH) or methylphenidate (MPH)) for ADHD.
Methods: Subjects were newly treated, aged >=6, diagnosed with ADHD and continuously enrolled in a commercial health plan 6 months prior and 12 months after their first prescription (Jan. 1, 2004 – Sept. 30, 2006). Persistence was defined as the number of days a subject remained on initial therapy (AMPH or MPH). Adherence was defined as the number of days of initial therapy supplied divided by persistent days. Means for each cohort comparison were analyzed using the F-test from one-way ANOVA.
Results: Differences in mean persistence and adherence among non-Hispanic Caucasians (NHC), Hispanics (H) and African Americans (AA) were studied. For children on MPH (n=10,004) or AMPH (n=7231), adherence was highest for NHC, followed by H and then AA ($p<0.0001$ for each drug, AMPH range: 0.46 -0.56, MPH range: 0.45 - 0.55). The same pattern was found in persistence among children on MPH ($p<0.0001$) and in adherence among adults on AMPH ($p=0.0004$, n=8552). There were no significant differences by race/ethnicity for persistence among children on AMPH, for persistence among adults on either drug, or for adherence among adults on MPH.
For children on MPH (n=11,841) or AMPH (n=8629), persistence and adherence were highest for households earning >$100k and lowest for those earning <$60k ($p<0.05$ for each). Among adults on MPH (n=5746), mean persistence was highest for households earning $60k to $100k (190 days) and lowest for <$60k (176 days, $p=0.01$) while there were no significant differences by income in persistence for AMPH (n=8904) or in adherence for either AMPH or MPH.
Conclusion: Persistence and adherence to stimulant medications differed by race/ethnicity and household income, with implications for the optimal management of ADHD.
Supported by funding from Shire Development Inc.

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2) Zuvekas SH, Vitiello B, Norquist GS. Recent trends in stimulant medication use among U.S. children. Am J Psychiatry 2006; 163: 579-585

» NR6-094

CLINICAL PATHWAYS FOR PSYCHIATRIC PATIENT CARE: STAFF OPINIONS AND CLINICAL OUTCOMES IN A TERTIARY PSYCHIATRIC HOSPITAL

Margaret Hendriks B.S.N., Rathi Mahendran, MBBS., MMed(Psych).,FAMS

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to 1.The participant will gain insight into the multidisciplinary team's perspective of the use of clinical pathways for patient care in a tertiary psychiatric hospital. 2.Recognize the value of clinical pathways to track patients' clinical outcomes.

SUMMARY:
Introduction: This research was conducted with multidisciplinary teams to assess their opinions on the usefulness of clinical pathways (CP) and reviews the clinical outcomes of patients placed on CPs from 2004 to 2007
Method: The research used a validated questionnaire in which Part 1 captured sociodemographic information of the participants and Part 2 had fourteen questions on the use of CP within the hospital, assessed the contribution of CPs to effectiveness of care, professional autonomy, quality care and professional collaboration. SPSS was used for analysis. In addition, datamining of patients placed on CPs was undertaken retrospectively and analyzed for clinical outcomes.
Results: Response rate to the research was 78.4%. Majority were nurses (83.2%), 13.1% doctors and 3.6% allied health staff. The findings were significant: 64.7% of doctors, 77.2% of nurses and 100% of allied health staff found CPs useful as a checklist. 47.1% of doctors, 42.1% of nurses and 100% of allied staff responded that CP was supportive in daily psychiatric decision-making. 35.3% of doctors, 41.2% of nurses and 80% of allied health staff concluded that CP use had improved their care of patients. Analyses of clinical outcomes of patients placed on CP revealed: Increased usage of CPs: In 2007, 3038 patients placed on CPs compared to 981 in 2003
Reduction of average length of stay for patients on CP: Dementia (28.3 days in 2005, 22.7 days in 2007), First Episode Schizophrenia (17.9 days in 2004, 15.3 days in 2007), Alcohol Dependence (20.4 days in 2004, 12.7 days in 2007), Relapsed Schizophrenia (21.1 days in 2004, 21.3 days in 2007).
Reduction in unplanned readmission rates for patients on CP: In 2006, First Episode Schizophrenia registered 3.6%, Relapsed Schizophrenia 4.8%, Alcohol Dependence and Opiate Dependence 3% each as compared to the hospital's KPI of 9%.
Conclusion: CPs support evidenced based care for patients and will assist in tracking and monitoring patients clinical outcomes.

REFERENCES:
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2) Dykes PC, Wheeler K. Evidence-based practice for nurse practitioners with clinical pathways. Clinical Excellence for Nurse Practitioners 1999; 3(5): 291-297.

» NR6-095

BURDEN OF ILLNESS AND COMORBIDITIES IN ADULT PATIENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER COMPARED TO PATIENTS WITH DEPRESSION

Rahul Sasane Ph.D., Leslie Montejano, B.A.,Paul Hodgkins, Ph.D., Dan Huse, M.A.

EDUCATIONAL OBJECTIVES:
The impact of Depression (DP) in the workplace has been thoroughly researched. Fewer studies have investigated the impact of adult attention-deficit hyperactivity disorder (ADHD) in the workplace. This study examined differences in direct healthcare expenditures, indirect productivity losses, and comorbidities among adult ADHD and DP patients. At the end of this poster, the participant should be able to identify burden of illness in adults diagnosed with ADHD benchmarked against DP.

SUMMARY:
Objective: The purpose of this study is to identify direct and indirect costs associated with adult ADHD benchmarked against DP.
Methods: Patients with =2 insurance claims with an ADHD diagnosis (n=29,965) were randomly matched 1:1 on gender, age, region, and capitated services use to patients with =2 DP diagnoses (n=29,965). All patients were aged =18 and enrolled in a health plan in all of 2006. ADHD and DP cohorts were compared on measures of 2006 direct healthcare costs, including hospitalizations, ER visits, outpatient services and prescriptions. Indirect cost measures included work absences (WA), short-term disability (STD), and worker's compensation (WC). Multivariate analyses controlled for differences between cohorts, including the presence of specific non-psychiatric and psychiatric comorbid conditions.
Results: Compared to DP patients, ADHD patients had lower healthcare costs ($4422 v $6383, P<0.0001), lower STD costs ($743 v $1310, P<0.0001), lower WC costs ($357 v $845, p=0.043), but no difference in WA costs ($3313 v $3536, P=0.2965) over 12 months. We estimated indirect costs were 50% of total costs of $8835 for ADHD patients and 47% of total costs of $12074 for DP patients. Except for injuries (P=0.009) and oppositional disorder (P<0.0001), DP patients had a higher prevalence of the selected comorbidities compared to ADHD patients. After controlling for differences between groups, total direct costs remained higher for DP patients; differences on indirect measures were not significant. The presence of comorbidities was a driver of costs.
Conclusion: ADHD patients incurred lower total costs than did DP patients. This may be related to the lower prevalence of specific comorbidities in ADHD patients. The higher proportion of indirect to total costs for ADHD patients relative to DP patients suggests that lost productivity is important when evaluating the burden of adult ADHD in the workplace.
Supported by funding from Shire Development Inc.

REFERENCES:
1) Secnik K, Swensen A, Lage MJ. Comorbidities and costs of adult patients diagnosed with attention-deficit hyperactivity disorder. Pharmacoeconomics 2005; 23: 93–102.

2) National Committee for Quality Assurance. The state of health care quality 2007. Washington, DC: 2007, 20-21.

» NR6-096

PERSONALITY DISORDER AND TREATMENT OUTCOME IN PATIENTS WITH UNIPOLAR DEPRESSION

Theresa Unger, Sabine Hoffmann, Stephan Koehler, Barbara Ross, MD., Arthur Mackert, Prof., Thomas Fydrich, Prof.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize how important it is to assess the presence of a comorbid PD, because the results of this study show that it has an impact on the treatment outcome in patients with MDD. Furthermore, the participants should be able to recognize how important it is to assess the PD appropriately.

SUMMARY:
Background: There is conflicting evidence about the influence of comorbid personality disorder (PD) on the treatment outcome in patients with major depression disorder (MDD).
Objective: The purpose of this naturalistic study was to compare the acute treatment outcome of depressed in-patients with and without PD.
Method: 67 patients diagnosed with MDD (58 % women; age: M=52.6, SD=12.5) were assessed before and after standard treatment of unipolar depression using Hamilton Depression Rating Scale (HAMD), Beck Depression Inventory (BDI), Brief Symptom Inventory (BSI) and Short-Form 12 (SF-12). Axis II diagnoses

were made using the Structured Clinical Interview for DSM-IV Personality Disorders (SCID-II).
Results:43.8 % of the patients met criteria for at least one comorbid PD. Both patients with and without PD showed significant symptomatic response to acute treatment of depression. Post treatment results indicate that patients with PD had a significantly worse outcome concerning the general psychopathology (BSI). This can be explained by their more severe symptoms at baseline. There were no significant differences in mean depression scores (HAMD, BDI) or psychological and physiological health (SF-12) at treatment termination.
Conclusions: Both depressed in-patients with and without comorbid PD showed a similar treatment response. Nevertheless, because of their more severe symptoms at baseline, patients with PD showed more general psychopathology at treatment termination. Furthermore, results of the impact of specific PD on the treatment outcome in patients with MDD and a dimensional approach to assess the personality will be presented.

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1) Brieger P, Ehrt U, Bloeink R & Marneros A: Consequences of comorbid personality disorders in major depression. J Nerv Ment Dis 2002; 190: 304-309.

2) Schiavone P, Dorz S, Conforti D, Scarso C & Borgherini G: The clinical implications of DSM-IV personality disorder comorbidity in depressed inpatients: a replication study in an Italian setting. Journal of Personality Disorders 2006; 20: 1-8.

» NR6-097

INCIDENCE OF METABOLIC SYNDROME AND RESPONSE TO METFORMIN TREATMENT IN PATIENTS ON ASSERTIVE COMMUNITY TREATMENT TEAMS

Caroline Williams M.D., Caroline Williams, M.D., David Lindy, M.D., Doreen Wall, R.N., MacDara O'Sullivan, MSW.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the risk factors and diagnostic criteria for metabolic syndrome as well as risks, benefits and possible indications for treatment with Metformin. In addition, the participant should be able to identify the rate of response to Metformin in the population studied.

SUMMARY:

Patients with severe and persistent mental illness (SPMI) have an increased incidence of metabolic syndrome, which is associated with increased risk of cardiovascular disease and type 2 diabetes. The National Cholesterol Education Program has proposed that 3 or more of the following clinical criteria define metabolic syndrome: abdominal obesity, elevated triglycerides, decreased HDL, elevated BP, and elevated fasting glucose. Metformin, an oral anti-diabetes drug, has been shown to be an effective treatment for metabolic syndrome. SPMI patients appear to be at risk for metabolic syndrome both because of their illnesses and the use of atypical antipsychotic medications as treatment. Assertive Community Treatment (ACT), a SAMSHA evidence-based practice for treating SPMI patients in the community, has been widely implemented nationally and internationally for SPMI patients who require more than standard care. Our study examines the incidence of metabolic syndrome in three ACT teams (N=68 x 3=204). Patients will be measured for abominal obesity, triglycerides, HDL, BP, and fasting glucose at baseline, three and six months. Patients with metabolic syndrome on one team (N=22) will receive metformin treatment for the six month study period, compared to the other two teams which will serve as comparison groups. We hypothesize that ACT patients will have higher rates of metabolic syndrome than the general SPMI population because they are more severely ill, that Metformin will effectively treat metabolic syndrome in ACT patients who comply with treatment, and that ACT teams will provide higher rates of Metformin compliance than standard SPMI care. Our poster will present data from six months of study.

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2) Wu RR, Zhao JP, Jin H, Shao P, Fang MS, Guo XF, He YQ, Liu YJ, Chen JD, Li LH: Lifestyle intervention and metformin for treatment of antipsychotic-induced weight gain: A randomized controlled trial. JAMA 2008;299:185-193.

» NR6-098

PRELIMINARY RESULT OF A PILOT STUDY ON RTMS TREATMENT OF BIPOLAR DEPRESSION

Guohua Xia M.D., Cameron S. Carter, M.D., Donald M. Hilty, M.D., David Whitney, PhD, Robert E. Hales, M.D., M.B.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know the most recent progress in rTMS treatment of bipolar depression, be able to formulate a comprehensive treatment plan that includes consideration of potential nonpharmacological treatment including rTMS, and better understand the necessity to further study the potential benefit of rTMS in treatment of related mental disorders.

SUMMARY:

Studies have shown the antidepressant effect of repetitive Transcranial Magnetic Stimulation (rTMS) in treatment-resistant major depressive disorder. Few studies have been done regarding rTMS treatment in bipolar disorders. This pilot study hypothesizes that 20Hz rTMS on the left dorsal prefrontal cortex (LDLPFC) may benefit bipolar depression with minimal side effects.
In an open trial, adult candidates with treatment resistant (failed >2 medications) bipolar depression by DSM-IV were recruited after signing consent. Patients who meet the enrollment criteria with Hamilton Depression Rating Scale (HAMD)>18 were treated with 3 weeks of 20 Hz rTMS at LDLPFC on weekdays while keeping same doses of psychotropic medications from 4 or more weeks before enrollment and through the end of the study. Outcome and other variables were assessed by standard psychological scales. Preliminary result of first 7 participants indicates significant improvement of depression. Mean total HAMD score decreases from 29 at baseline to 11 at the end of 3-week treatment (paired 2-tail T-tests: $p<0.001$), the significant deduction sustained through 2-week follow-up. The Self Report Inventory of Depressive Symptomatology shows similar statistically significant benefit. About 86% participants responded (HAMD drop =50%) and 57% reached remission (HAM-D21=7) during or at the end of 3-week rTMS. Monitoring of other mental condition via Hopkins Verbal Learning Test, Mini Mental State Examination, Symptom Checklist-90-Revised, and Young Mania Rating Scale did not show deterioration. Tolerable focal pain was observed among 3 patients but disappeared over the treatment course. No seizure or switch to mania occurred.
The data suggested antidepressant effects and reasonable safety of the 20 Hz rTMS on LDLPFC in treatment of bipolar depression. Due to the small sample size, placebo effect, and potential bias, randomized sham-controlled studies with a large sample are required for a conclusion.

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1) O'Reardon JP, Solvason HB, Janicak PG, Sampson S, Isenberg KE, Nahas Z, McDonald WM, Avery D, Fitzgerald PB, Loo C, Demitrack MA, George MS, Sackeim HA. Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. Biol Psychiatry. 2007 Dec 1;62(11):1208-16.

2) Nahas Z, Molloy MA, Hughes PL, Oliver NC, Arana GW, Risch SC, George MS. Repetitive transcranial magnetic stimulation: perspectives

for application in the treatment of bipolar and unipolar disorders. Bipolar Disord. 1999 Dec;1(2):73-80.

» NR6-099

EFFICACY OF QUETIAPINE IN ACUTE BIPOLAR I OR II DEPRESSION: A KOREAN MULTI-CENTER, PROSPECTIVE, OPEN-LABEL, 8 WEEKS OBSERVATIONAL STUDY

Bo-Hyun Yoon M.D., Won-Myong Bahk, M.D.,Ph.D., Duk-In Jon, M.D.,Ph.D., Myung-Kyu Kim,M.D.,Ph.D., Sang-Yol Lee,M.D.,Ph.D., Sang-Keun Chung, M.D.,Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to treat the patients with bipolar depression with appropriate atypical antipsychotics.

SUMMARY:

Objective: Although the randomized, controlled trials of quetiapine monotherapy in bipolar depressed patients were well published, Korean data on that were rarely found. The purpose of this study was to evaluate the efficacy of quetiapine in bipolar depression in the clinical setting.
Methods: Patients with DSM-IV diagnosis of bipolar I or II depression were included. They were treated with quetiapine and other mood stabilizers. The doses of quetiapine and mood stabilizers were flexible according to the clinical judgment. Clinical improvements were rated by severity of illness of Clinical Global Impression-Bipolar version (CGI-BP-S) and Montgomery-Asberg Depression Rating Scale (MADRS) at baseline, week 4 and week 8 after treatment.
Results: A total of 877 patients [bipolar I depression; N=577 (65.7%), bipolar II depression; N=301 (34.3%)] were recruited and 44 (5%) patients were dropped out during the study. The initial mean dose of bipolar I and bipolar II patients were 214.6±186.5mg/day and 157.4±174.6mg/day, respectively. The mean doses at week 4 and 8 of bipolar I patients were 362.7±234.3mg/day and 383.4±241.4mg/day and those of bipolar II patients were 262.1±231.2mg/day and 283.7±222.6mg/day. Doses of bipolar I patients were significantly higher than those of bipolar II patients. CGI-BP-S and MADRS were significantly improved at week 4 and 8 compared with baseline. Clinical improvements were not differed between bipolar I and II patients. The response and remission rate at week 8 of all patients were 60.1% and 54.2%, respectively and they were not differed between bipolar I and II patients. Only 8 patients (0.8%) were switched to manic at week 4.
Conclusion: Although there are limitations in this study, it suggests that quetiapine combination improves the depressive symptoms in both bipolar I and II depression patients with minimal incidence of manic switch and drop outs. So, it may be an effective and safe option in treating bipolar depression.

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» NR6-100

EFFECT OF QUETIAPINE ON THE SUBJECTIVE ESTIMATES OF SLEEP IN THE 8 WEEKS TREATMENT OF ACUTE BIPOLAR DEPRESSION

Bo-Hyun Yoon M.D., Won-Myong Bahk, M.D.,Ph.D., Duk-In Jon, M.D.,Ph.D., Myung-Kyu Kim, M.D.,Ph.D., Sang-Yol Lee, M.D.,Ph.D., Sang-Keun Chung, M.D.,Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the difference of subjective sleep estimate in bipolar bipolar depression.

SUMMARY:

Objective: Sleep disturbance is a characteristic feature of bipolar depression, and both the quality and quantity of sleep are typically adversely affected during depressive episodes. The purpose of this study was to evaluate the subjective estimate of sleep after quetiapine treatment in bipolar I and II patients.
Methods: Patients with bipolar I or II depression were included. They were treated with quetiapine and other mood stabilizers. The doses of quetiapine and mood stabilizers were flexible according to the clinical judgment. Clinical improvements were rated by severity of illness of Clinical Global Impression-Bipolar version (CGI-BP-S) and Montgomery-Asberg Depression Rating Scale (MADRS). Modified version of Leeds Sleep Evaluation Questionnaire (LSEQ) was used to assess the subjective measures of nighttime sleep and hangover, which included the factors covering four areas: i) getting to sleep (GTS), ii) quality of sleep (QOS), iii) awakening from sleep (AFS), and iv) behavior following wakefulness (BFW) or hangover during the next day. All assessments were done at baseline and week 4 and 8 after treatment.
Results: A total of 877 patients [bipolar I depression; N=577 (65.7%), bipolar II depression; N=301 (34.3%)] were recruited and 44 (5%) patients were dropped out during the study. CGI-BP-S and MADRS were significantly improved at week 4 and 8 compared with baseline. Clinical improvements were not differed between bipolar I and II patients. The nighttime sleep parameters (GTS and QOS) were more impaired in bipolar II patients at baseline. But, all sleep parameters of modified LSEQ were improved at week 4 and 8 without impairment of daytime hangover in both bipolar I and II patients and significant differences were not found at week 4 and 8 between two groups.
Conclusion: This result based on LSEQ suggests that quetiapine improved multiple dimensions of subjective estimate of sleep, including sleep quality and sleep duration, without daytime dysfunction

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1) Endicott J, Paulsson B, Gustafsson U, Schioler H, Hassan M. Quetiapine monotherapy in the treatment of depressive episodes of bipolar I and II disorder: Improvement in quality of life and quality of sleep. J Affect Disord 2008;111:306-319.

2) Riemann D, Voderholzer U, Berger M. Sleep and slee-wake manipulation in bipolar depression. Neuropsychobiology 2002;45(Suppl):7-12.

Wednesday, May 20, 2009

3:00 p.m. - 5:00 p.m.
Hall D, Exhibit Level,
Moscone Convention Center

NEW RESEARCH POSTER SESSION 7: NEW RESEARCH

» NR7-001

NEUROBIOLOGICAL CHANGES AFTER 40 DAYS OF FASTING:SELF-RESTRAINT AS A COGNITIVE BEHAVIORAL THERAPEUTIC MODALITY

Tunku-A.R. Ben ABUBAKAR M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize implications of biological changes as a result of Fasting.

SUMMARY:

Objective: To Study the Effects of Fasting on the Human Brain
Method: Subject fasted for 40 consecutive days. FDG Positron Emission Tomography of the Brain with simultaneous determination of 24 hour urinary excretion of Homovanillic Acid (HVA), main Dopamine (DA) metabolite was obtained at baseline and follow-up.
Results: Increased FDG uptake in specific regions of Prefrontal Cortex with preferential shift to Left Brodman's Area (BA) 9 & 10 (DLPFC, OFC) and Right BA 24 (ACC) accompanied by a reciprocal decrease in 24 hour urinary excretion of HVA was detected at follow-up compared to baseline.Above findings implicates potential role of DA and the plastic adaptive capacity of the dopaminergic system in altering synapticconnectivity and (possibly compensatory) upregulation of postsynaptic DA receptors secondary to diminished CNS circulating DA as a result of continuous fasting. Post Hoc finding of greater than fourfold (444%) increase in 24 hour urinary Androsterone excretion which correlates with DHEA (marker of Aging) represents intriguing theoretical basis for anti aging effects of fasting and calorie restriction.
Conclusion: Innovative case study findings represent fertile ground for future research to consistently replicate in well designed randomized (single blind, placebo controlled) prospective & crossover studies with a larger sample size to gain scientific validity.

REFERENCES:

1) Cummings, J.L. 1993. Frontal-Subcortical Circuits and Human Behavior. Archives of Neurology, 50:873-80.

2) McEwen, B.S. 1998. Protective and Damaging Effects of Stress Mediators. New England Journal of Medicine, 338:171-78. Mesulam, M.-Marsel. 2000. Principles of Behavioral and Cognitive Neurology, 2nd Edition. Oxford University Press, New York, pp.12.

» NR7-002

MICROMETER SIZED THREADLIKE AND/OR SPHERICAL PARTICLES IN CEREBROSPINAL FLUID (CSF) OF PATIENTS WITH BIPOLAR DISORDERS

Ullvi Båve M.D., Rolf Nybom, Mikael Landén, M.D. Ph.D., Lennart Wetterberg, M.D. Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that changes in cerebrospinal fluid, detected by scanning electron microscopy (SEM), may be found in both patients with schizophrenia and bipolar disorders (BD), but not in a non-psychiatric control material. The participant should also be able to recognize that thread-like particles previously not has been described, and to date only in this study in patients with BD.

SUMMARY:

Introduction: To date, the etiology of bipolar disorder (BD) as well as schizophrenia is unknown, although there are several clinical and pathogenic similarities between the two conditions. In an earlier report micrometer-sized particles were found in the cerebrospinal fluid (CSF) of patients with schizophrenia. The aim of this study was to examine the CSF of patients with BD in euthymic state in comparison to a control group of non-psychiatric patients, in whom CSF was sampled in connection to spinal anaesthesia before surgery. Material and method: Consecutive new outpatients referred for treatment and continuing patients at the bipolar outpatient unit were included in the study, after informed consent. CSF was obtained by lumbar puncture from 59 patients (30 females) with BD type I or II, and from 21 (11 females) controls. The structures in CSF were examined by scanning electron microscopy (SEM) after the CSF was filtered and dried by vacuum suction to eliminate the fluid component of the CSF. Results: 22/59 BP patients had thread-like structures not described previously, 42/59 had spherical particles (similar to those in schizophrenic patients) and 6/59 had threads with spherical particles closely attached. Eleven BP patients did not display any structures in their CSF. In total, 48/59 had either thread-like, spherical, or both types of structures, compared to none of the 21 non-psychiatric control patients. Conclusion: The particles detected in SEM, previously not described in patients with BD, could hypothetically be involved in the pathology of BD, either as an inducer or as a result of the disease process. Further research is required to understand the possible pathogenic role of these particles.

REFERENCES:

1) Wetterberg L, Nybom R, Bratlid T, Fladby T, Olsson B, Wigzell H. Micrometer-sized particles in cerebrospinal fluid (CSF) in patients with schizophrenia. Neurosci Lett. 2002;329(1):91-5.

2) Raedler TJ, Wiedemann K. CSF-studies in neuropsychiatric disorders. Neuro Endocrinol Lett. 2006 ;27(3):297-305.

» NR7-003

LEFT-RIGHT INFORMATION TRANSMISSION ASSESSED FROM BILATERAL ELECTRODERMAL ACTIVITY REFLECTS LEVEL OF HYPNOTIC EXPERIENCE

Petr Bob Ph.D., Marek Susta, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to demonstrate that during Stroop stimuli in hypnotic conditions the patients with higher hypnotizability display decreased level of interhemispheric information transmission measured by pointwise transinformation calculated between left and right records of bilateral electrodermal activity.

SUMMARY:

Recent findings indicate that interhemispheric interaction and information transition presents a general mechanism that the brain uses across different sensory modalities to increase information processing efficiency, most likely by splitting the load of processing between the two hemispheres (1). This process of splitting allows the information to be processed in parallel distributed mode which enables more efficient information processing (2). In this context it was proposed that interhemispheric interaction can modulate attentional capacity and selective attention mainly in conditions when attending to one stimulus needs to ignore another (e.g. Stroop task). These findings suggest a hypothesis that specific changes in selective attention and interhemispheric interactions during hypnosis could be reflected in left-right information transmission calculated from bilateral measurement. In the present

study we have performed bilateral electrodermal (EDA) measurement in 33 psychiatric outpatients (mean age 34.54) during Stroop task. The Stroop stimuli were presented in waking, during waking hypnosis and after hypnotic suggestion inducing black-white seeing. The results show that during Stroop stimuli in both hypnotic conditions the patients with higher hypnotizability (N=18) display decreased level of interhemispheric information transmission measured by pointwise transinformation (PTI) calculated between left and right EDA records. This relationship also confirms significant correlation between hypnotizability measured by Stanford scale SHSS:C and PTI during Stroop task in the period after hypnotic suggestion inducing black-white seeing ($r=-0.41$, $p<0.01$). In summary, these results indicate that patients with higher hypnotizability display lower information transmission in comparison the patients with lower hypnotizability, which is likely caused by increased ability of selective inhibition and disconnection related heightened processing efficiency in susceptible individuals.
Commercial Support - Funding for this work was provided by the Czech Ministry of Education within the projects MSM0021620849 and Centre for Neuropsychiatric Research of Traumatic Stress (1M06039).

REFERENCES:

1) Banich MT: The missing link: the role of interhemispheric interaction in attentional processing. Brain Cogn 1998; 36:28–57

2) Scalf PE, Banich MT, Kramer AF, Narechania K, Simon CD: Double take: parallel processing by the cerebral hemispheres reduces attentional blink. J Exp Psychol Hum Percept Perform 2007; 33:298-329

» NR7-004

STRESS, LIMBIC IRRITABILITY AND CHAOTIC PATTERNS OF HEART RATE DYNAMICS IN PATIENTS WITH UNIPOLAR DEPRESSION

Petr Bob Ph.D., Marek Susta, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to demonstrate that during Stroop stimuli the patients with higher level of complex partial seizure-like symptoms have increased chaos in heart rate dynamics.

SUMMARY:

According to recent findings stress represents significant condition in pathophysiology of depression and influences abnormal development in the brain. Repeated stress and cognitive conflict may also determine sensitization, limbic irritability and temporal-limbic epileptic-like activity (1). Because recent findings indicate that epileptiform processes are related to increased neural chaos (2), the aim of this study is to find relationship between neural chaos in autonomic responses reflecting brain activity during stress activation and temporal-limbic epileptic-like activity. For empirical examination of suggested hypothesis Stroop word-colour test, ECG recording, calculation of chaos indices i.e. largest Lyapunov exponents (LLEs) in nonlinear data analysis and psychometric measures of cognitive, affective and memory symptoms related to temporal-limbic epileptic-like activity called complex partial seizure-like symptoms (LSCL-33, structured interview CPSI), traumatic stress (TSC-40) and depression (BDI-II) in 60 patients with unipolar depression (mean age 33.5) and 50 healthy controls (mean age 32.4) were used. Significant correlation $r=0.59$ ($p<0.01$) between LLEs and LSCL-33, and significant correlation $r=0.58$ ($p<0.01$) between LLEs and CPSI found in the depressive patients indicates that degree of chaos in autonomic responses during conflicting Stroop task reflected by LLEs is closely related to limbic irritability. Correlation between LLEs and BDI-II ($r=0.35$, $p<0.01$), between LLEs and TSC-40 ($r=0.39$, $p<0.01$) were less significant. Similar correlations in healthy controls were not found. The result are in agreement with findings that epileptiform activity is closely related to neural chaos and potentially might provide explanation of neurobiological mechanisms underlying stress sensitization and predictive marker of anticonvulsant treatment of depression.
Commercial Support -Funding for this work was provided by grants MSM0021620849 and 1M06039.

REFERENCES:

1) Teicher M, Andersen SL, Polcari A, Anderson CM, Navalta CP, Kim DM: The neurobiological consequences of early stress and childhood maltreatment. Neurosci Biobehav Rev 2003; 27:3-44

2) Tirsch WS, Stude P, Scherb H, Keidel M: Temporal order of nonlinear dynamics in Human Brain. Brain Res Rev 2004; 45:79-95

» NR7-005

INHALED LOXAPINE RAPIDLY IMPROVES ACUTE AGITATION IN SCHIZOPHRENIC PATIENTS

James Cassella Ph.D., Dan Spyker, PhD,MD, Robert Fishman, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize acute agitation in a schizophrenic population and understand a potential new treatment method for that condition.

SUMMARY:

This Phase 3 randomized, double-blind, placebo-controlled clinical study assessed the efficacy and safety of inhaled loxapine in treating acute agitation in schizophrenic patients.Loxapine was administered via inhalation using the Staccato® system, which delivers thermally-generated drug aerosol to the deep lung for rapid systemic absorption with IV-like kinetics. Consenting male and female adults, 18 to 65 years of age, who met DSM-IV criteria for schizophrenia, presenting with a relevant degree of agitation at baseline, were enrolled in the study and randomly assigned to treatment. A total of 344 patients received a single inhalation of either 0 mg, 5 mg, or 10 mg of loxapine in an in-patient treatment facility.The primary efficacy endpoint was the absolute change in Positive and Negative Syndrome Scale Excited Component (PEC) score from baseline to 2 hours following treatment. The primary endpoint following 5 mg and 10 mg Staccato Loxapine vs. placebo was statistically significant and PEC scores were significantly improved for the 10 mg group vs placebo beginning at 10 min and continuing for the entire 24 hour assessment period. Clinical Global Impression-Improvement (CGI-I) at 2 hours post-dose and responder analysis for CGI-I were statistically significant for both the 5 mg and 10 mg doses vs. placebo. The time to first rescue medication was statistically significant for the active doses vs placebo. In conclusion, inhaled loxapine produced rapid and significant improvement in agitated schizophrenic patients in clinical settings. Statistically significant effects were observed as early as 10 minutes and continued through 24 hours post treatment with the higher dose. Staccato loxapine may provide a rapid, simple, less intrusive alternative for agitated patients.
This research was funded by Alexza Pharmaceuticals.

REFERENCES:

1) Allen MH, Currier GC, Grogg A. Use of Restraints and Pharmacotherapy in Academic Psychiatric Emergency Services. General Hospital Psychiatry, 2003, 26(1):42-49.

2) Allen MH, Currier GW, Carpenter D, Ross R and Docherty JP. Expert Consensus Guideline Series: Treatment of Behavioral Emergencies. Journal of Psychiatric Practice 2005;11(Supp 1):1-108.

» NR7-006

INHALED LOXAPINE RAPIDLY IMPROVES ACUTE AGITATION IN PATIENTS WITH BIPOLAR DISORDER

Robert Fishman M.D., Daniel A. Spyker, Ph.D. M.D., James V. Cassella, Ph.D., AZ-004 Study Group

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize acute agitation in a population with bipolar I disorder

and understand a potential new treatment method for that condition.

SUMMARY:

This second Phase 3 randomized, double-blind, placebo-controlled study assessed the efficacy and safety of inhaled loxapine in treating acute agitation in patients with bipolar I disorder. Loxapine was administered using the Staccato® system, which delivers thermally generated drug aerosol to the deep lung for rapid systemic absorption with IV-like kinetics. Consenting male and female adults, 18 to 65 years of age, who met DSM-IV criteria for bipolar I disorder (manic or mixed episodes) and presented with a relevant degree of agitation at baseline, were enrolled in the study and randomly assigned to treatment. A total of 314 patients received a single inhalation of either 0 mg, 5 mg, or 10 mg of loxapine in an in-patient treatment facility. Up to 2 additional doses of study drug were allowed beyond 2 h if required. The primary efficacy endpoint was the absolute change in Positive and Negative Symptom Scale, Excited Component (PEC) score from baseline to 2 hours after first dose. Both the 5 mg and 10 mg doses met the primary endpoint, with significant differences vs. placebo in the 2-hour change from baseline PEC. PEC scores were significantly improved for the 10 mg group vs. placebo beginning at 10 min and continuing for the entire 24-hour assessment period. Clinical Global Impression-Improvement (CGI-I) at 2 hours and responder analysis for CGI-I both showed statistically significant differences for the 5 mg and 10 mg doses vs. placebo. Differences in time to rescue medication were statistically significant for the active doses vs. placebo. Inhaled loxapine was safe and generally well tolerated. In conclusion, inhaled loxapine produced rapid and significant improvement in agitated patients with bipolar I disorder. Statistically significant effects were observed with the higher dose as early as 10 minutes post-treatment, and continued through 24 hours post-treatment. Staccato loxapine may provide a rapid, simple, less intrusive alternative to injections for agitated patients. This research was funded by Alexza Pharmaceuticals.

REFERENCES:

1) Allen MH, Currier GW, Carpenter D, Ross R and Docherty JP. Expert Consensus Guideline Series: Treatment of Behavioral Emergencies. Journal of Psychiatric Practice 2005; 11(Supp 1):1-108.

2) Allen MH, Currier GC, Grogg A. Use of Restraints and Pharmacotherapy in Academic Psychiatric Emergency Services. General Hospital Psychiatry 2003; 26(1):42-49.

» NR7-007

THE EFFECT OF IMAGERY OF WORD ON PRIMING EFFECT: A FMRI STUDY

Bumseok Jeong, Jeewook Choi, M.D., Ph.D., Ji-woong Kim, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know the effect of the degree of the imagery of prime word on semantic priming and it's neural correlates.

SUMMARY:

Background: Semantic priming is affected by the degree of both association and imagery of a word. In the association effect of word on semantic priming, perisylvian structures including bilateral inferior frontal gyrus, left middle temporal gyrus, supramarginal gyrus have been reported. Little is, however, known about the brain region of the effect of imagery of word on semantic priming.
Methods: Each 40 word pairs for high (HA)-, low (LA)- and non-association (NA), non-word (NW) conditions were presented. Each 40 association word pairs included of 20 high (HI) and 20 low (LI) imagery prime stimuli. A trial consisted of 30ms prime, 30ms mask, 500ms probe, 2~8s SOA. Brain activation was measured using functional MRI during word discrimination by subjects. Both behavioral and functional neuroimaging data were analyzed to explore the effect of degree of association and of imagery.
Results: The shortest response time (RT) was showed in HA, followed LA and NA. NW showed the longest RT ($p<.01$). RT was faster in HI than LI within HA, not LA condition ($p<.01$). Left superior temporal gyrus was more activated in HA than both LA and NA. Both right fusiform gyrus and left supramarginal gyrus were more activated in HI than LI within HA condition.
Conclusion: The present study indicated the effect of the degree of imagery on semantic priming is shown within word pair having high association and occurs the early stage of language process. Our paradigm might be useful to explore the semantic deficit in various psychiatric disorders.

REFERENCES:

1) McDermott KB, Roediger HL: Effects of imagery on perceptual implicit memory tests. J Exp Psychol Learn Mem Cogn 1994; 20:1370-1390.

2) Nakamura K, Dehaene S, Jobert A, Le Bihan D, Kouider S: Task-specific change of unconscious neural priming in the cerebral language network. Proc Natl Acad Sci U S A 2007;104:19643-19648.

» NR7-008

ABNORMAL CORTICAL EXCITABILITY IN OBSESSIVE–COMPULSIVE DISORDER

Jee In Kang, Deog-Young Kim, M.D., Kee Namkoong,Psy.D., Chan-Hyung Kim,Psy.D., Min Joon,M.D, Se Joo Kim,Psy.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to have information about paired pulse TMS measures of motor cortical excitability and understand alteration of cortical excitability in obsessive-compulsive disorder

SUMMARY:

Objective: The purpose of the present study was to compare cortical excitability in patients with obsessive-compulsive disorder (OCD) and normal controls. We hypothesized that OCD patients would have higher cortical excitability with shortened cortical silent period or reduced intracortical inhibition, considering their impairment of response inhibition.
Methods:We assessed the motor cortex excitability by measuring resting motor threshold (MT), cortical silent period, and intracortical inhibition (ICI) and intracortical facilitation (ICF) with paired transcranial magnetic stimulation (TMS) in 30 OCD patients and 36 age-matched normal controls. Paired TMS with subthreshold conditioning was used to test early ICI with interstimulus intervals (ISIs) 2 and 3 ms, and ICF with ISIs 10 and 15 ms.
Results:Regarding the cortical silent period, OCD patients revealed more shortened duration for bilateral hemisphere, compared to normal controls (Rt 175.2ms vs. 193.1ms, $p=0.003$, Lt.; 178.1ms vs. 193.9ms, $p=0.029$). In addition, OCD patients showed significantly less inhibitionat ISIs of 2ms and 3ms in only right hemisphere, compared to normal controls ($p=0.001$ for ISI 2, $p=0.004$ for ISI 3). No significant differences were found between OCD patients and normal controls for the mean resting MT.
Conclusions:These findings suggest that OCD may be associated with deficits of cortical inhibition.

REFERENCES:

1) Greenberg BD, Ziemann U, Cora-Locatelli G, et al. Altered cortical excitability in obsessive-compulsive disorder. Neurology 2000 Jan 11;54(1):142-147.

2) Gilbert DL. Motor cortex inhibitory function in Tourette syndrome, attention deficit disorder, and obsessive compulsive disorder: studies using transcranial magnetic stimulation. Adv Neurol 2006;99:107-114.

» NR7-009

COMMON EFFECT OF ANTIPSYCHOTICS ON BIOSYNTHESIS AND REGULATION OF FATTY ACIDS AND CHOLESTEROL SUPPORTS A ROLE OF LIPID HOMEOSTASIS IN SCHIZOPHRENIA

Christian Lavedan Ph.D., Simona Volpi, Ph.D., Louis Licamele, M.S., Shruti N. Mitkus, Ph.D., Kendra Mack, M.S., Andrew Thompson, B.S., Mihael H. Polymeropoulos, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to 1.Understand the impact of antipsychotics on the expression of the human genome; 2.Recognize that antipsychotics have a common effect on biosynthesis and regulation of fatty acids and cholesterol; 3.Recognize that the activation by antipsychotics of genes associated with lipid homeostasis is not just a off target effect of these drugs but rather a common mechanism by which they may achieve their antipsychotic activity.

SUMMARY:

Objective: For decades, the dopamine hypothesis has gained the most attention in an attempt to explain the origin and the symptoms of schizophrenia. While this hypothesis offers an explanation for the relationship between psychotic symptoms and dopamine kinetics, it does not provide a direct explanation of the etiology of schizophrenia which remains poorly understood. Consequently, current antipsychotics that target neurotransmitter receptors, have limited and inconsistent efficacy. To gain insights into the mechanism of action of these drugs, we studied the effect of antipsychotics on the expression of the human genome, and compared it to that of an extensive library of drugs used in a variety of disorders. Methods: The expression profile of 12,490 genes in a cell line treated with 11 typical and 7 atypical antipsychotics was analyzed with a Weighted Influence Model, Rank of Ranks method. The "antipsychotic signature" was compared to that of a library of 448 other compounds. Results: Nineteen of the first 20 ranked probe sets in the antipsychotic group profile correspond to 13 genes involved in fatty acids and cholesterol biosynthesis, or in phospholipid metabolism. Typical and atypical antipsychotics had a similar effect on lipid homeostasis, regardless of their metabolic or lipid-related adverse event profile. It was observed that antipsychotics not only activate genes involved in lipid homeostasis but do this preferentially from all other genes. Conclusions: We propose that the activation by antipsychotics of genes associated with lipid homeostasis is not just a common off target effect of these drugs but rather a common mechanism by which they achieve their antipsychotic activity. These results also support convergent clinical evidence for a lipid hypothesis of schizophrenia, and may help research aimed at the development of novel treatments for this devastating disease. Vanda Pharmaceuticals sponsored this study.

REFERENCES:

1) Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, Keefe RS, Davis SM, Davis CE, Lebowitz BD, Severe J, Hsiao JK: Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia. N.Engl.J Med 2005; 353:1209-1223

2) Reddy RD, Keshavan MS, Yao JK: Reduced red blood cell membrane essential polyunsaturated fatty acids in first episode schizophrenia at neuroleptic-naive baseline. Schizophr Bull 2004; 30:901-911

» NR7-010

ASSOCIATION OF ARACHIDONATE 12-LIPOXYGENASE (ALOX12) GENE AND SCHIZOPHRENIA IN KOREAN POPULATION

Jaejin Lee M.D., Jiyoung Song,Ph.D.,M.D., Ahrang Cho, Ph.D., M.D., Woojae Kim M.D., Tae Kim M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to assessed the genetic association between single nucleotide polymorphisms of ALOX12 and schizophrenia in Korean population.

SUMMARY:

Objective: ALOX12 has been reported to be related with fatty acid metabolism, glutamate-induced neurodegeneration, and inhibition of tyrosine hydroxylase. We assessed the genetic association between single nucleotide polymorphisms of ALOX12 and schizophrenia in Korean population.
Method: We recruited 278 patients with schizophrenia and 234 normal control subjects. Clinical information of the group with schizophrenia was obtained from medical records, the Brief Psychiatric Rating Scale (BPRS), the Scale for the Assessment of Negative Symptoms (SANS), and the Operational Criteria Checklist (OPCRIT). Three SNPs of ALOX12 gene were selected, including rs1126667, rs434473, and rs1042357. For the analysis of genetic data, SNPStats, SNPAnalyzer, and Helixtree programs were used.
Results: In ALOX12 gene, we also found genetic association of rs1126667 and rs1042357 with schizophrenia both in recessive model (P=0.015 and 0.015, respectively). A linkage disequilibrium block was found and a specific haplotype (G-A-C) showed a significant association with schizophrenia (P=0.0123). Among the items of OPCRIT, catatonia, negative formal thought disorder, restricted affect, and blunted affect have genetic association with rs434473 (P=0.040).
Conclusion: We concluded that rs1126667, rs1042357 of ALOX12 gene are associated with schizophrenia in Korean population

REFERENCES:

1) Association of a new polymorphism in ALOX12 gene with bipolar disorder. Fridman C, Ojopi EP Eur Arch Psychiatry Clin Neurosci. 2003 Feb;253(1):40-3.

2) Polymorphisms in genes involved in neurodevelopment may be associated with altered brain morphology in schizophrenia: Preliminary evidence. Gregório SP, Sallet PC Psychiatry Res. 2008 Dec 1

» NR7-011

THE NON-PHARMACOLOGICAL THERAPIES IN PSYCHIATRIC RESIDENCY TRAINING PROGRAMS IN KOREA IN 2008

Jae-jin Lee, SJ Moon, M.D., GH Bahn, M.D.,Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know about the current state of the difference of experienced non-pharmacological therapies among the residents during the psychiatric residency training.

SUMMARY:

Introduction: Although attention for non-pharmacological therapies is increasing recently, the hospitals charging psychiatric residency training do not provide various clinical experiences to the psychiatric residents. This study tried to set the level and the way of future education; to find a solution to the problem and improvement through the follow up study about the present condition of non-pharmacological therapies in fourth-year psychiatric residancy.
Methods: From June 13, 2008 to June 14, 2008, there was a questionnaire by distributing the survey and the agreement for fourth-year psychiatric residents who are working as psychiatric residancy across the country during fourth-year residents workshop.
Results: The total number of non-pharmacological therapy types what residents experienced in four years of training was 6 for average. It is significant decrease than 6.9 for average in the former study. In this study compared with the former one, the non-pharmacological therapy types what the residents experienced were distributed similar in general, but ECT and TMS items - have experienced 19.1% by asking the electrostimulation and neuromagnetic devices item in the previous study - were 53.6% and 24.7%, definitely increasing.
Numbers of residents and numbers of faculty members in the hospitals charging the residents training were positively correlated with the diversity of non-pharmacological psychiatric therapies. ($p<0.05$). The correlation with the number of the faculty members at a hospital of university but the fellows was appeared to be the

highest. ($p<0.01$).
Conclusions: It would be necessary for a standardization of training program as a level of the institute to minimize the difference of experienced therapies among the residents, especially, for an effort as a level of the institute considering an educational side and residents' interesting field.

REFERENCES:

1) Benjamin James Sadock, M.D., Virginia Alcott Sadock M.D. Kaplan & Sadock's Synopsis of psychiatry (10th edition)

2) Moon SJ. The current state of the application of non-pharmacological therapies in psychiatric residency training programs in Korea

(The Abstract was presented as Annual Meeting of American Psychiatric Association, Washington, 2007)

» NR7-012

EMOTIONAL AND COGNITIVE EFFECTS OF DEEP BRAIN STIMULATION FOR TREATMENT RESISTANT DEPRESSION

Mircea Polosan M.D., Lhommée E, Wauquiez G, Chabardes S, M.D.,Ph.D., Seigneuret E, M.D., Benabid AL; M.D., Ph.D., Bougerol T, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, , the participants will become familiar with deep brain stimulation effects in treatment resistant depression, especially the differences in terms of impact on cognitive and emotional symptoms of depression

SUMMARY:

Background: Despite various conventional antidepressant strategies, up to 20% patients develop treatment resistance. Recent data support the interest of deep brain stimulation (DBS) of the subgenual cingulate region (Brodmann Area 25) in these cases of disabling treatment resistant depression (TRD). As this region seems involved in fronto-limbic interactions, its dysfunction has cortical and subcortical repercussions underlying cognitive and emotional symptoms of depression. DBS mechanism in TRD is not fully elucidated, especially the modulation of the activity of these cortico-subcortical neural networks.
Objective: Assessment of emotional and cognitive changes in TRD treated by DBS of cingulate BA25 region.
Method: Measurements of memory, executive functions and attentional bias in emotional information processing have been analyzed in comparison with mood evaluations before neurosurgery and after 2 months of DBS in a TRD patient.
Results: Significant improvement of executive functions (TMT, Stroop, span test, CPT II) memory (Hopkins test) as well as alleviation of the attentional bias (emotional Stroop, facial emotions' recognition, memory of affective words) have been noticed before any significant stable mood improvement occured.
Conclusion: Subgenual cingulate DBS induces an initial cognitive positive impact before mood improvement occurs. This different evolution under DBS treatment suggests that cognitive symptoms are not secondary to mood disorders, but they are based on different frontal-limbic neural circuits.

REFERENCES:

1) Lozano AM, Mayberg HS, Giaccobe P et al. Subcallosal Cingulate Gyrus Deep Brain Stimulation for Treatment-Resistant Depression. Biol Psychiatry 2008 ; 64 : 461-467.

2) Mayberg HS, Liotti M, Brannan SK et al. Reciprocal Limbic-Cortical Function and Negative Mood: Converging PET Findings in Depression and Normal Sadness, Am J Psychiatry 1999; 156:675–682

» NR7-013

IL-6, DEPRESSION AND TRAUMATIC STRESS

Jiri Raboch M.D., Petr Bob, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to demonstrate that cytokine IL-6 is closely related to traumatic stress symptoms and depression.

SUMMARY:

Recent growing evidence indicates that various types of interactions among nervous and immune systems are important in pathogenesis of depression. These findings strongly suggest that proinflammatory cytokines such as IL-6 or IL-1 play a significant role in developing depression and can mediate its psychological, behavioral and neurobiological manifestations. Great importance of this cytokine hypothesis of depression is that the inflammatory process may be influenced by either external stressors related psychoneuroimmunological changes or organic inflammatory diseases or conditions or both (1, 2). These findings suggest a hypothesis that specific influences related to traumatic stress and dissociation could be found in close relationship to increased level of cytokine IL-6 that has been found in close relationship to depression. In the present study we have performed psychometric measurement of depression (BDI-II), traumatic stress symptoms (TSC-40) and dissociation (DES), and serum IL-6 in 40 inpatients with unipolar depression (mean age 42.3?6.8). The results show that IL-6 is significantly correlated to BDI-II (Spearman $R=0.47$, $p<0.01$), TSC-40 (Spearman $R=0.32$, $p<0.05$) but not to DES (Spearman $R=0.25$, $p=0.11$). In summary, findings of the present study indicate that increased level of IL-6 could be directly related to depression and symptoms of traumatic stress, and support recent findings on a role of cytokines in cognitive functions and psychopathology.
Commercial Support: Funding for this work was provided by the Czech Ministry of Education within the projects MSM0021620849 and Centre for Neuropsychiatric Research of Traumatic Stress (1M06039).

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» NR7-014

MULTIANALYTE BIOMARKER BLOOD TEST TO AID IN DIAGNOSIS, TREATMENT AND MANAGEMENT OF MAJOR DEPRESSIVE DISORDER

Perry Renshaw, MD, PhD, Director of Magnetic Resonance, Utah Brain Institute, Professor of Psychiatry, University of Utah School of Medicine;John Bilello, PhD, Chief Scientific Officer, Ridge Diagnostics, Bo Pi, PhD, Chief Technical Officer, Ridge Diagnostics;John Bilello, PhD, Chief Scientific Officer, Ridge Diagnostics

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, participants will have an understanding of newly developed biological markers associated with MDD. They will be able to apply information derived from these markers to clinical practice by way of a blood test to aid in diagnosing, managing and optimizing treatment of patients with MDD

SUMMARY:

The paradigm used for neuropsychiatric diagnosis and patient management is primarily based upon clinical interviews to stratify patients within adopted classifications. This paradigm has the caveat of not including information derived from biological or pathophysiological mechanisms. Our preliminary studies demonstrate the potential clinical utility of MDDtest?, a biological test based upon physiological changes associated with MDD. The test utilizes immunoassay technology and a novel diagnostic method called Biomarker Hypermapping. This approach uniquely includes the construction of a multianalyte hypermap versus analyzing single markers either alone or in groups. The HyperMap uses multiple markers from a proprietary human biomarker library,

translational medicine studies, iterative disease profiling and interrelated algorithms to achieve diagnostic values and to stratify patients. Using clusters of biomarkers reflective of different physiologic parameters (including neurotrophic factors as well as metabolic, HPA axis, and inflammatory protein markers); the patient's biomarker responses are mapped onto a multi-dimensional hyperspace. Distinct coefficients are used to create the hyperspace vectors for subsets of patients and normal subjects. Multiplex biomarker data from clinical samples are used iteratively to define the hyperspace map and provide clinically relevant information to aid in diagnosis and patient management. An initial study evaluated samples from over 100 subjects 18-70 years old half with a confirmed diagnosis (DSM IV: 293.3, 296.32, 296.33. 296.34, or 296.35, performed at a single site) and half normal control subjects (mean age 40 [MDD] vs. 37 [Control]). Seven to nine quantified serum biomarkers and the hypermap algorithm were used to generate diagnostic values with a sensitivity of 91% and a specificity of 82%. In a second clinical study, sera were evaluated from 50 patients and 20 age matched controls. The results of this study of otherwise healthy 20-50 year old subjects, confirmed the earlier data. Measurement of 9 serum proteins resulted in a sensitivity of 95% and a specificity of 88%. An additional longitudinal study is ongoing to evaluate the ability of MDDtest to monitor response to antidepressants during treatment.

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» NR7-015

EFFECTS OF PHOSPHODIESTERASE TYPE-5 INHIBITOR, TADALAFIL ON APOPTOTIC NEURONAL CELL DEATH AND CELL PROLIFERATION IN MATERNAL-SEPARATED RAT PUPS

Baek Sang-Bin M.D., Geon-ho Bahn, M.D., Ph.D., Chang-Ju Kim, M.D., Ph.D., Mal-Soon Shin, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that tadalafil alleviate the maternal separation-induced decrease of memory capability by suppressing apoptotic neuronal cell death and by enhancing cell proliferation in the rat pups.

SUMMARY:

Early adverse experiences resulting from maternal separation may lead to neuronal cell death and they can eventually cause memory impairment. Maternal separation has been used to create a valid animal model of early life stress and also for creating a depression-like syndrome. Phosphodiesterase (PDE)-5 inhibitor tadalafil is widely prescribed agents for the treatment of erectile dysfunction. In this study, we investigated the effects of tadalafil on the apoptosis and cell proliferation in the hippocampal dentate gyrus of rat pups following maternal separation. On postnatal day 1, pups were randomly distributed into six groups(n = 10 in each group). They were maternal care group, maternal separation group, four maternal separation groups with 0.01, 0.1, 1, 10mg/kg tadalafil-treated. The rat pups in the maternal separation groups were separated for 6 h/day and was carried out from postnatal day 1 to postnatal day 14. On postnatal day 15, we permanently removed pups from dam's cages for 14 days. The immobility time of forced swim test was increased in the maternal-separated rat pups, and tadalafil treatment decreased immobility time. The rat pups in the maternal separation group showed deceased memory capability compared to the rat pups in the maternal care group, and tadalafil treatment increased memory capability of the rat pups in the maternal separation group. Apoptotic neuronal cell death in the hippocampal dentate gyrus was significantly increased in the maternal-separated rat pups, and tadalafil treatment suppressed the maternal separation-induced apoptosis. In contrast, cell proliferation in the hippocampal dentate gyrus was significantly decreased in the maternal-separated rat pups, and taldalafil treatment increased cell proliferation. The present results demonstrated that tadalafil alleviated the maternal separation-induced decrease of memory capability by suppressing apoptotic neuronal cell death and by enhancing cell proliferation in the rat pups.

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1) Kalinichev M, Easterling KW, Plotsky PM, Holtzman SG: Long-lasting changes in stress-induced corticosterone response and anxiety-like behaviors as a consequence of neonatal maternal separation in Long-Evans rats. Pharmacol Biochem Behav 2002; 73:131-140

2) Wong ML, Whelan F, Deloukas P, Whittaker P, Delgado M, Cantor RM, McCann SM, Licinio J: Phosphodiesterase genes are associated with susceptibility to major depression and antidepressant treatment response. Proc Natl Acad Sci USA 2006; 103:15124-15129

» NR7-016

OXIDATIVE STRESS AND COGNITIVE ABILITY IN ADULTS WITH DOWN SYNDROME

Andre Strydom, Ph.D., Mark Dickinson, MRCPsych, Sima Shende, MD, Domenico Pratico, Ph.D., Zuzana Walker, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand some of the anti-oxidant enzyme changes associated with chromosome 21 triplication.

SUMMARY:

Aims: We aimed to study the hypothesis that high levels of superoxide dismutase (SOD1), previously reported in Down syndrome, would be associated with poorer ability on cognitive tests. Compensatory rises in the activity of glutathione peroxidase (GPx) was expected to be associated with better ability, so that a high ratio between SOD1 and GPx was hypothesized to be the best predictor of poorer cognitive performance.

Methods: 32 adults with Down syndrome between the ages of 18 and 45 years donated blood samples for SOD1 and GPx assays and urine for Isoprostane 8,12-iso-iPF2a-VI assay, a specific biomarker of lipid peroxidation in vivo. Informants rated functional ability and memory function for all participants, and those adults with DS that was able to, also completed psychometric assessments of language ability and memory.

Results: Neither SOD1 nor GPx were related to the elevated markers of lipid peroxidation previously described in living adults with DS, and our hypothesis that an increased SOD1/GPx ratio would be correlated with worse performance on cognitive or functional measures was not supported. Contrary to our hypothesis, we found that low SOD1/GPx ratios were associated with worse memory ability, which remained after controlling for confounders such as sex, age or nutritional supplements.

Conclusions: The antioxidant system in DS is implicated in the cognitive phenotype associated with the chromosomal disorder, but the variations in the phenotype could result from several possible gene or gene product interactions. Much further research is required before it will be possible to counteract the oxidative stress associated with DS.

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» NR7-017

THYROID HORMONE LEVELS AND GOITRE IN ACUTE PSYCHIATRIC IN-PATIENTS

Taner Tosun, Nesrin Tomruk, M.D., Timucin Oral, M.D., Nihat Alpay, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize the significance of thyroid hormone levels in psychiatric patients and identify the risk factors for thyroid diseases in psychiatric populations.

SUMMARY:
Introduction: Thyroid diseases are the most common endocrine diseases and can cause many psychiatric disorders; hypothyroidism mainly depression, psychosis and cognitive impairment and hyperthyroidism anxiety. Thyroid diseases are the most prevalent undiagnosed medical conditions in psychiatric patients. Also, thyroid hormone levels may be temporarily abnormal in acutely hospitalized patients, referred to as Euthyroid Sick Syndrome (ESS). It is reported to be 5-30% in acute psychiatric in-patients, the most frequent being high T4 and TSH levels.
Method: In 197 consecutive acute psychiatric inpatients thyroid hormone levels were measured with ECLIA (electrochemiluminescence immunoassay) and goitre was classified, according to ICD.
Results: 60.9 % of the patients were male, 39.1 % were female. The prevalence of thyroid disease was 4 %, the incidence was 1.5 %. ESS was found in 26.9% (low fT3 45.3 %, low fT4 25.4 %, low sTSH 17 %) and goitre was present in 41.7 % of the cases. The duration of hospitalization was significantly longer in ESS group (25.4 vs 20.4 days, p=0.03). Goitre was significantly more prevalent in ESS group (x2=5.83, p=0.015), affective disorder patients (x2=6.50, p=0.01), in cases on lithium (x2=4.14, p=0.04) and with history of thyroid disease (x2=5.07, p=0.02). In thyroid disease cases (5 hypothyroid, 3 hyperthyroid); other medical conditions (5/8 p=0.004), goitre (7/8 p=0.009), history of thyroid disease (5/8 p=0.0008) and ? 60 years of age (2/8 p=0.03) were significantly more frequent. Also in this group, lithium use and affective illness were almost statistically significant.
Conclusion: The relatively high prevalence of thyroid disease may be related to the endemic goitre geographic character of Turkey, which may also account for the discrepancy in ESS. Risk factors determined for thyroid disease were in line with literature to a great extent. Screening for thyroid hormone levels is essential at least in high risk cases.

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» NR7-018

POSITIVE CORRLATION BETWEEN BLOOD S100B PROTEIN AND CLOZAPINE CONCENTRATION IN SCHIZOPHRENIC PATIENTS

Sheng-Chang Wang M.D., Yu-Li Liu,Ph.D.,Yu-Ping Su,M.D.,Shi-Chin Guo,M.D.,Keh-Ming Lin,M.D.,M.P.H.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be able to recognize the correlation between clozapine and plasma s100B protein, a potential biomarker of schizophrenia.

SUMMARY:
Several studies have demonstrated S100B, a glia-derived calcium-binding protein to be involved in the pathophysiology of schizophrenia. To investigate the potential role of clozapine treatment on astocyte activation, psychopathology, plasma S100B protein and clozapine concentration were assessed in 70 clozapine-treated schizophrenic inpatients. The results indicated that there was significant correlation between plasma S100B protein and clozapine concentration(r=0.25, p=0.03). However, there was no significant association between psychopathology and plasma S100B.

REFERENCES:
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» NR7-019

ASSESSMENT OF CEREBRAL REGIONS ASSOCIATED WITH SEXUAL AROUSAL IN DEPRESSIVE MALES BEFORE AND AFTER ANTIDEPRESSANT TREATMENT USING BOLD-FMRI

Jong-Chul Yang M.D., Sang K. Chung, M.D., Hyeon Jeong, M.D., Soon-Ah Kang, M.A., Seog-Ju Kim, M.D., Sung-Jong Eun, Ph.D., Gwang-Woo Jeong, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be able to recognize the cerebral regions associated with sexual arousal in depressive males before and after treatment using blood-oxygenation-level-dependent (BOLD) functional magnetic resonance imaging (fMRI). Also, this presentation may help an understanding of neural mechanisms for male sexual functioning.

SUMMARY:
Objective: Many depressive males have difficulties in sexual functioning. In our previous neuroimaging study, there was a significant difference of brain activation between healthy and drug-naive depressive males during visual sexual stimulation. The purpose of this study was to assess the brain activation changes during visual sexual stimulation in depressive males following pharmacotherapy by BOLD-fMRI.
Method: Eight depressive males with sexual dysfunction (mean (SD) age, 35.6 (10.3): mean (SD) scores of BDI and HAMD-17, 35.1 (5.8) and 31.9 (5.7), respectively) underwent fMRI on a 1.5T MR scanner before and after treatment. The fMRI data were obtained from 7 oblique planes using gradient-echo EPI. Sexual stimulation paradigm began with a 1 minute black screen, 2 minutes sexual stimulation with an erotic video film, 1 minute black screen, 2 minutes sexual stimulation, followed by 1 minute black screen. The data were analyzed by SPM99 ($p<0.05$). All depressive males took the mirtazapine treatment (mean (SD) dosage, 37.5 (9.4) mg/day) for 8 to 10 weeks.
Results: After treatment, depressive mood was improved (mean (SD) scores of BDI and HAMD-17, 7.9 (3.5) and 5.3 (1.7), respectively) and subjective effects of visual sexual stimulation were increased. Brain activation following pharmacotherapy increased in the area of middle and superior temporal gyri, inferior and superior parietal gyri, postcentral gyrus, hypothalamus, cingulate gyrus, putamen, and caudate nucleus. On the other hand, in precentral gyrus, inferior frontal gyrus, precuneus, lingual gyrus, and parahippocampal gyrus decreased. Especially, the relative signal intensity changes of hypothalamus were significantly correlated with the subjective effects of visual sexual stimulation.
Conclusions: These cerebral regions, especially hypothalamus, may be associated with sexual dysfunction in depressive males. Furthermore, these findings may assist in understand neural mechanisms for male sexual functioning.

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NR7-020

LU AA21004: EFFICACY AT LOW SEROTONIN TRANSPORTER OCCUPANCY AT CLINICALLY EFFECTIVE DOSES - FROM ANIMAL STUDIES TO DEPRESSED PATIENTS

Johan Areberg Ph.D., Marianne Dragheim, M.D., Lise Brennum, M.Sc., Tine B. Stensbøl Ph.D., Arne Mørk, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant will be familiar with the pharmacological profile of the novel antidepressant Lu AA21004, a 5-HT3 receptor antagonist, 5-HT1A receptor agonist, and 5-HT enhancer that also increases levels of noradrenaline, dopamine and acethylcholine in certain regions of the brain, and its dose-related occupancy of the serotonin transporter.

SUMMARY:

Objective: To determine the clinical relevance of serotonin (5-HT) transporter (SERT) occupancy in healthy subjects as a function of plasma concentration of the novel antidepressant Lu AA21004 using positron emission tomography (PET), and to relate the outcome to results from preclinical studies in animals.

Methods: The relationship between SERT occupancy and 5-HT levels in the hippocampus measured by microdialysis was determined in rats receiving Lu AA21004 5 mg/kg per day for 3 days via subcutaneously-implanted minipumps. SERT occupancy was measured by in vivo binding using the radioligand (3)H-MADAM [1] in rats and (11)C-MADAM in healthy young men. 11 healthy subjects were given Lu AA21004 for 9 days at doses of 2.5, 10 or 60 mg/day. Baseline MRI and PET scan were performed. A second PET scan was performed on treatment day 9. SERT occupancy in the hippocampus was estimated as the difference in binding potentials between baseline and day 9, divided by the binding potential at baseline.

Results: In rats, 5 mg/kg per day Lu AA21004 resulted in 41% SERT occupancy and produced a significant increase (203%) in extracellular levels of 5-HT. In healthy men, 2.5, 10 and 60 mg/day resulted in SERT occupancy levels of 27%, 54% and 68%, respectively. From the relationship between the plasma concentrations of Lu AA21004 and SERT occupancy in the PET study, it was predicted that doses of 5 mg per day or higher would be clinically effective. This was confirmed in a phase II study in depressed patients, in which 5 and 10 mg per day was effective and well tolerated.

Conclusions: Clinically effective doses for Lu AA21004 were reliably predicted from increases in extracellular 5-HT and SERT occupancy measures in rats and a PET study in healthy men. Conventional antidepressants are clinically effective at 80% occupancy. Therapeutic effects of Lu AA21004 are achieved at a much lower SERT occupancy, which may reflect the unique mode of action of this compound [2].

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NR7-021

LIMBIC AND CORPUS CALLOSUM ABERRATIONS IN ADOLESCENTS WITH BIPOLAR DISORDER: A TRACT-BASED SPATIAL STATISTICS ANALYSIS

Naama Barnea-Goraly, M.D., Kiki D. Chang, M.D., Asya Karchemmskiy, M.S., Meghan E. Howe, M.S.W., Allan L. Reiss, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the results of a whole-brain, tract-based statistical analysis (TBSS) of white matter structure in adolescents with bipolar disorder as compared with controls. Specifically, the participant will be able to describe limbic and corpus callosum white matter changes in observed in adolescents with bipolar disorder as compared with controls.

SUMMARY:

Purpose: To investigate white matter structure in adolescents with bipolar disorder who also are offspring of, at least, one parent with bipolar disorder.

Content: Bipolar disorder (BD) is a common and debilitating condition, often beginning in adolescence. Converging evidence from genetic and neuroimaging studies indicate that white matter abnormalities may be involved in BD, yet there is little information of white matter integrity in adolescents with this disorder.

Methodology: We used Diffusion Tensor Imaging (DTI) and Tract-Based Spatial Statistics (TBSS), a whole-brain voxel-by voxel analysis, to investigate white matter structure in adolescents with BD, who also are offspring of at least one parent with BD, and age- and IQ- matched control subjects. Fractional anisotropy (FA) (a measure of directional diffusivity) and Trace values (average diffusivity) were used as variables in this analysis.

Sample size and characteristics: 39 adolescents were included in this study. 21 adolescents had BD, and also were offspring of at least one parent with bipolar disorder, 18 subjects were controls who were age-, gender-, and IQ- matched to the BD group.

Results: Adolescents with BD had lower FA values than control subjects in the fornix, the left mid-posterior cingulate gyrus, throughout the corpus callosum, in fibers extending from the fornix to the thalamus, as well as in parietal and occipital corona radiata bilaterally. There were no significant between-group differences in Trace values. Importance: These results suggest that alterations in white matter tracts that are important for emotional modulation and cognition are present early in the course of bipolar disorder.

REFERENCES:

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NR7-022

DULOXETINE MODULATES PAIN-RELATED BRAIN RESPONSE IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

Narcís Cardoner M.D., Marina López-Solá, Ph.D., Jesús Pujol, M.D., Rosa Hernández-Ribas, M.D., Joan Deus, Ph.D., Hèctor Ortiz, Laura López-Araquistain, M.D., Erica Martínez-Amorós, M.D., Carles Soriano-Mas, Ph.D., Jose M. Menchón, M.D., Ben J. Harrison, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize brain correlates of pain in MDD and to know the potential application of brain imaging techniques in psychopharmacological treatment monitoring.

SUMMARY:

OBJECTIVE: The purpose of this study was to use functional magnetic resonance imaging (fMRI) to examine brain response to painful thermal stimuli in patients with major depressive disorder before (baseline) and after antidepressant treatment (time-points 1 and 8 weeks) with duloxetine.

METHOD: Patients with major depressive disorder (N=13) and healthy comparison subjects (N=20) were scanned three times using fMRI and a block-design experimental pain paradigm. Painful heat stimulation was applied to the right volar forearm. Severity of depressive symptoms was evaluated at each time-point using

the HDRS-17. Functional MRI data were analyzed using general linear models in SPM5.
RESULTS: Both groups showed significant activation of the bilateral insulo-opercular region, anterior cingulate cortex and motor supplementary area during painful stimulation. At baseline, depressed patients showed greater activation than healthy controls in the right prefrontal cortex ($t=3.81$, $p>0.001$). After antidepressant treatment, the magnitude of activation of the right prefrontal cortex to painful stimulation was reduced in patients. This reduction was significant after one ($t=4.18$, $p>0.001$) and eight ($t=3.6$, $p<0.001$) weeks of duloxetine treatment compared to baseline. HDRS-17 score reduction was positively and significantly correlated with decreased activation of the right prefrontal cortex at both treatment time-points (1ST week $t=3.74$, $p>0.001$ and 8th week $t=4.01$, $p<0.001$). This correlation was stronger after eight weeks of treatment ($R2 = 0.56$ $p<0.001$).
CONCLUSIONS: Our findings are consistent with previous studies implicating the right prefrontal cortex in the pathophysiology of major depression disorder(Johnstone, van Reekum, Urry, Kalin, & Davidson, 2007) and a general role for this region in processing aversive stimuli (Davidson, 1992). Dysfunction of the right prefrontal cortex may lead to an impaired modulation of aversive or painful experience in major depressive disorder. Following antidepressant treatment with duloxetine, pain-related hyperactivation of the right prefrontal cortex was reduced in these patients and associated with general clinical improvement.

REFERENCES:

1) Johnstone T, van Reekum CM, Urry HL, et al.: Failure to regulate: counterproductive recruitment of top-down prefrontal-subcortical circuitry in major depression. J Neurosci 27:8877-8884, 2007.

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» NR7-023

FUNCTIONAL NEUROIMAGING EVIDENCE AND NEUROANATOMICAL MECHANISM FOR THE DISSOCIATION OF CONSCIOUS AND UNCONSCIOUS MEMORY

Sang-Keun Chung M.D., Jong C. Yang, M.D., Hyeon Jeong, M.D., Soon A. Kang, M.A., Seog J. Kim, M.D., Sung J. Eun, Ph.D., Gwang W. Jeong, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the evidence for the dissociation of conscious and unconscious memory. Also, this presentation may help an understanding of neuroanatomical mechanisms of memory impairments in depressed patients using blood-oxygenation-level-dependent (BOLD) functional magnetic resonance imaging (fMRI).

SUMMARY:

Objective: Memory is divided into explicit and implicit memory. Explicit memory reflects the intentional or conscious recollection of events or facts, while implicit memory is related to unconscious stored knowledge that does not require intentional conscious recollection. Some investigators have reported that depressed patients have memory impairment in explicit retrieval process, but intact implicit memory. However, there has been little research about evidence and mechanism for that. The purpose of this study was to identify the cerebral regions associated with memory impairments in depressed patients using BOLD fMRI.
Method: 13 depressed patients who met DSM-? criteria for major depressive disorder and 14 healthy controls matched for sex, age, and educational level underwent a BOLD fMRI during the memory tasks: encoding of two-syllable words, and explicit (cued recall test) and implicit (word completion test) retrieval of previously learned words under the levels with conceptual and perceptual processing. The activation paradigm consisted of a cycle of alternating periods of 30 seconds of stimulation and 30 seconds of rest. During the tasks we obtained fMRI data from ten slices (6 mm slice thickness, 1 mm gap) parallel to the AC-PC line. The data were analyzed by SPM 99.
Results: Depressive patients were impaired on explicit memory tasks in compared with healthy controls. During cued recall test, in hippocampus, parahippocampal gyrus, posterior cingulate gyrus, precuneous, and middle temporal gyrus, depressed patients showed significantly less cerebral activation ($p<0.001$). However, there was no significant difference on implicit memory tasks.
Conclusions: These results show the experimental evidence for the distinction between conscious and unconscious memory and neuroanatomical mechanism for explicit memory impairment in depressed patients, suggesting that the performance of explicit and implicit memory tasks involves different neural mechanisms.

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2) Burt DB, Zembar MJ, Niederehe G: Depression and memory impairment: A meta-analysis of the association, its pattern, and specificity. Psychol Bull 1995; 117:285-305.

» NR7-024

ALTERED HIPPOCAMPAL FUNCTIONAL CONNECTIVITY LINKS DEPRESSIVE SYMPTOMS AND MEMORY DEFICITS IN AMNESTIC MILD COGNITIVE IMPAIRMENT

Joseph Goveas M.D., Chunming Xie, M.D., Wenjun Li, B.S., Zhilin Wu, Ph.D., Jennifer L. Jones, M.S., Piero G. Antuono, M.D., Shi-Jiang Li, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the hippocampal functional connectivity network abnormalities that link depressive symptoms and memory impairment in geriatric patients with and without amnestic mild cognitive impairment.

SUMMARY:

Objective: Elderly with depressive symptoms and depressed amnestic Mild Cognitive Impairment (aMCI) patients have a higher risk of developing Alzheimer's disease (AD) than those without depression. Little is known about the neuropathophysiological link between depressive symptoms and cognitive impairment. The main objective of this study is to identify the neural correlates of depressive symptoms and memory deficits in resting-state hippocampal functional connectivity (HFc) network, among aMCI and normal (CN) subjects.
Method: The resting-state functional connectivity MRI method (3-T scanner) was employed to measure the hippocampal network abnormalities in 15 elderly aMCI and 18 age-matched CN subjects. The linear regression analysis was used to identify the neural correlates of HFc to the Geriatric Depression Scale (GDS) and Rey Auditory Verbal Learning Test (RAVLT) scores.
Results: GDS and RAVLT scores were inversely correlated. HFc was negatively correlated to RAVLT delayed recall scores in left dorsolateral prefrontal cortex (DLPFC), right fusiform gyrus, and middle temporal (MTG) and superior temporal gyri (STG), IPC, and cerebellum; positive correlations in left amygdala and parahippocampus. HFc positively correlated to GDS scores in left DLPFC, right fusiform gyrus, bilateral MFC, STG, MTG, PHG, and cerebellum. Overlapped regions included right fusiform gyrus and STG; left DLPFC; MTG and cerebellum bilaterally ($P<0.05$, corrected; cluster size 4048 mm3).
Conclusions: A competitive nature of the interactive neural link between depressive symptoms and memory functions was found in areas affected with AD neuropathology, in elderly with and without aMCI and depressive symptoms. This suggests that the presence of depressive symptoms could affect the neural connections in aMCI patients and may accelerate disease progression.
Funding Source: This work was supported by NIH Grant

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» NR7-025

DECLARATIVE LONG-TERM MEMORY NETWORK IN EARLY ALZHEIMER'S DISEASE

Shirin Meyer, Thomas Brauer, M.D., Markus Donix, M.D., Katrin Poettrich, Ph.D., Annett Werner, Ph.D., Ruediger von Kummer, M.D., Vjera A. Holthoff, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand alterations in the neural representation of declarative longterm-memory in early AD.

SUMMARY:

Objectives: The purpose of the present study was to compare the neural correlates associated with retrieval of autobiographical episodic memory in patients with early Alzheimer's disease (AD) and healthy controls (HC).
Methods: We performed fMRI in 14 patients with early AD (mean age 61.5 ± 7.4, MMSE mean 25, SD 2.1) and 14 HC (mean age 60.5 years, SD 5.7) and analysed neural activity related to memory content (episodic/semantic) and remoteness (remote events from the age of 5-15 years, recent events from the last 5 years). The stimuli used during the fMRI study were based on autobiographic episodic memory items that included recollection and re-experiencing context rich events of the participant's own life and were contrasted with the retrieval of public events of the same period.
Results: Comparison of activations during autobiographical episodic versus semantic memory retrieval in the controls led to significant bilateral activations of the parietal-temporal junction, left temporal pole, anterior cingulate, retrosplenial cortex and cerebellum, whereas AD patients activated a different network including middle left temporal cortex, left superior motor cortex and left precuneus cortex.
Conclusion: Our data revealed activation of alternative pathways during autobiographical episodic memory retrieval in early AD suggesting a loss of specificity in the network supporting long-term memory.

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» NR7-026

MAGNETIC RESONANCE IMAGING AND MAGNETIC RESONANCE SPECTROSCOPY IN DOWN'S SYNDROME

Diane Mullins M.D., Melissa Lamar, Ph.D., Eileen Daly, B.Sc., Andy Simmons Ph.D., Kieran C. Murphy, M.D., Ph.D., Declan G. Murphy, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognise that magnetic resonance imaging (MRI) is an important tool for the assessment of dementia in people with Down's syndrome. The participant will also learn the magnetic resonance spectroscopy (1H-MRS) metabolite changes which occur in Down's syndrome, their significance and the correlation between MRI and 1H-MRS findings in this disorder.

SUMMARY:

Objective: To compare Magnetic Resonance Imaging (MRI) and Magnetic Resonance Spectroscopy (1H-MRS) in people with Down's syndrome.
Background: People with Down's syndrome have an increased risk of developing Alzheimer's disease (AD). The hippocampus is involved in memory functioning and is one of the brain regions first affected by AD. MRI hippocampal volumetric measurement enables quantification of atrophy. 1H-MRS can measure concentrations of brain metabolites including myoinositol (mI) and N-acetylaspartate (NAA). NAA is a proxy measure of neuronal density. mI is a marker of gliosis and amyloid plaques.
Method: MRI scanning was performed on a 1.5 Tesla system. Demented subjects with Down's syndrome (DS+, n=15) were compared with non-demented subjects with Down's syndrome (DS-, n=21) and healthy controls (n=24). Manual tracing of hippocampal volumes was undertaken using Measure software. 1H-MRS voxels of interest were defined in the left and right hippocampi. A point-resolved spectroscopy pulse sequence clearly resolved NAA and mI peaks. Statistical analysis was undertaken using SPSS15.
Results:Hippocampal volume was significantly reduced in DS+ compared to controls and in DS+ compared to DS-. [NAA] was significantly reduced and [mI] was significantly increased in DS+ compared to controls. A positive relationship was noted between hippocampal volume and [NAA] for the DS+ group but for the DS- and control groups, there appeared to be a negative relationship. A positive relationship was found between hippocampal volume and [mI] for the DS- groups but for the DS+ and control groups there appeared to be a slight negative relationship.
Conclusions: DS+ is associated with decreased viable neuronal density/function (as measured by NAA) and a reduction in hippocampal volume associated with impaired cognitive functioning. Increased [mI] in DS+ may increase the risk for dementia.
We are grateful for funding from the Baily Thomas Charitable Fund and the Alzheimer's Research Trust.

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» NR7-027

A PET SCAN STUDY OF OLANZAPINE TREATMENT IN BORDERLINE PERSONALITY DISORDER

S. Charles Schulz M.D., Jose V. Pardo, Ann Romine, Jazmin Camchong, Kelvin O. Lim

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to demonstrate knowledge regarding the neuropsychiatric correlates of borderline personality disorder symptoms and the impact of atypical antipsychotic treatment on brain metabolism.

SUMMARY:

Introduction: A previous PET scan study of personality disordered patients demonstrated inverse correlations between metabolism in the inferior frontal and anterior temporal lobes with impulsive and aggressive behaviors. Olanzapine has shown efficacy in a number, but not all randomized controlled trials (RCTs). In order to better understand treatment mechanisms of BPD, a PET imaging study was designed in a fashion used by Mayberg and colleagues to study depression.

Methods: Patients with a diagnosis of BPD were eligible for the study. Patients underwent a medication free PET scan (Seimens Biograph). Subjects then entered an eight week, open label trial of olanzapine while receiving objective ratings. The target dose at the fourth week of the study was 7.5mg/qhs. At the end of the medication trial, the patients underwent a second PET scan. PET parameters at baseline were correlated with ZAN-BPD and BDHI. The first PET scan was subtracted from the second to examine change over time. PET findings were then corrected for multiple comparisons.
Results: Fourteen subjects who met criteria for BPD completed the eight week trial of olanzapine and underwent both FDG PET scans. All subjects were female with an average age of 26 years. A correlation of the baseline PET scan with behavioral measures reveals a statistically significant ($p<0.05$) association of high BDHI with low frontal metabolism. Also, a subtraction of the first to the second scan demonstrated a significant increase in frontal metabolism and successful treatment.
Conclusions: The use of PET imaging and psychopharmacology has opened new avenues for the understanding and treatment of depression. Similar techniques have been applied to BPD in this study and have the potential to point to the circuitry of the illness. Further, by analysis of PET and symptom ratings, the physiology of response can be approached.
This study was supported by an Investigator Initiated Grant by Eli Lilly to Dr. Schulz

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» NR7-028

THE EFFECT OF YOGA AND WALKING ON BRAIN GABA LEVELS

Chris C. Streeter, M.D., Theodore H. Whitfield, Sc.D., Robert B. Saper, M.D., M.P.H., Liz Owen, B.A., Nancy Turnquist, M.A., Maria Gensler, Aleksandra Yakhkind, B.A., Surya K. Karri, M.D., M.P.H., Andrew P. Prescot, Ph.D., J. Eric Jensen, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify that participation in both walking and yoga sessions were associated with increases in brain GABA levels, with the greatest increase associated with Iyengar yoga being in the thalamus and the greatest increase associated with walking being in the anterior cingulate gyrus.

SUMMARY:

Objective: Low brain gamma-aminobutyric acid (GABA) levels have been reported in depressed individuals, with increased levels being observed with effective treatment. Exercise and yoga have been associated with improved mood. The acute practice of yoga has been associated with increased brain GABA levels. This study evaluates whether increases in GABA levels are specific to yoga or also observed in exercise with a similar metabolic demand.
Methods: Healthy subjects with no significant medical/psychiatric problems, using no GABAergic medications participated in 2 interventions that offered 36 1-hour sessions over a 12-week period of either walking on a flat surface at 2.5 miles/hour or Iyengar yoga. After which, subjects participated in an imaging session where brain GABA levels were obtained immediately pre and post a 1-hour walking or yoga session determined by group assignment. Magnetic resonance spectroscopy was used to measure GABA/Creatine ratios (GABA/Cr). Results: 22 subjects were randomly assigned to the yoga group (YG) (n = 10) or the walking group (WG) (n = 11). The YG exhibited a borderline significant increase in thalamic (TH) GABA/Cr ($p = 0.08$), with no significant changes noted in the WG TH GABA/Cr ($p = 0.89$). The effect size of the change in TH GABA/Cr from pre- to post-intervention was much greater for the YG (0.015) than for the WG (0.001). The WG showed a significant increase in anterior cingulate (AC) GABA/Cr ($p = 0.004$), while there was no evidence of a change in the YG AC GABA/Cr ($p = 0.17$). There was a significant difference in the pre- to post-intervention change in AC GABA/Cr comparing the WG and YG ($p = 0.002$), with the effect size for the WG (0.015) greater than that of the YG (-0.006). Conclusion: Participation in either the YG or WG was associated with increases in brain GABA levels. However the regional patterns were different, with the greatest increase in the YG being in the TH, while the greatest increase in the WG was in the AC.

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» NR7-029

CREATIVITY INDUCED BY DOPAMINE AGONISTS IN PARKINSON'S DISEASE

Eugénie Lhommee, M.A., Alina Batir, M.D., Claire Ardouin, M.A., Valérie Fraix M.D., Eric Seigneuret M.D., Stephan Chabardes M.D., Alim-Louis Benabid M.D., Pierre Pollak M.D. and Paul Krack M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this poster, the participants should be able to recognize dopamine induced creativity as a part of the spectrum of dopamine-induced behavioural changes. Attendees will better understand the pathophysiology of psychiatric adverse reactions in the treatment of PD and the implication of the mesolimbic dopaminergic system in creativity. Clinicians will enhance their skills in the management of dopaminergic treatment which has not only negative, but also positive side effects.

SUMMARY:

BACKGROUND: PD is characterised by loss of cognitive function such as flexibility, conceptualisation and visuospatial abilities. Creativity results precisely from such cognitive skills. Case studies however show emergence or enhancement of creativity in the course of PD.
OBJECTIVES: 1/ to describe creativity as part of a spectrum of behavioural changes induced by dopamine replacement therapy (DRT) in PD and 2/ to show that it is preferentially modulated by dopamine agonists.
METHODS: By means of a newly developed behavioural scale for PD, we selected 11 creative (CR), compared to 22 control PD patients (CT) who all underwent STN DBS. CR selection was based on a recent (re)emergence of creativity. Artistic creativity started in 6/11 CR while on DRT. Cognition, behaviours and mood fluctuations were assessed before surgery and one year after.
RESULTS: Baseline characteristics and cognitive efficiency did not differ between groups. While there was no difference in total DRT, when only dopamine agonists are taken into account CR had a larger equivalent dopamine agonist dose (mean (SD) = 402 (71) mg/day) than CT before surgery (mean (SD) = 270 (131) mg/day) ($p= 0.01$). CR had higher scores for mania ($p<0.0001$), hobbyism ($p<0.0001$) and « on » euphoria ($p<0.0001$). They did not differ from CT in gambling, shopping, hypersexuality, irritability or addiction to DRT. Postoperative improvement in UPDRS motor score (52%), stimulations parameters and mean DRT reduction (68.6%) were the same in the two groups. Apathy increased in both groups ($p<0.005$). Only 1/11 CR was still creative after surgery.

CONCLUSION: we showed that creativity in PD is linked to dopamine agonist therapy. Creativity arises with other modifications belonging to a positive hyperdopaminergic spectrum, but not to impulse control disorders. As shown in other hyperdopaminergic behaviours, creativity disappears after STN surgery, when DRT is (too) drastically reduced.

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1) Ardouin, C., Voon, V., Worbe, Y., Abouazar, N., Czernecki, V., Hosseini, H., et al. (2006). Pathological gambling in parkinson's disease improves on chronic subthalamic nucleus stimulation. Mov Disord, 21(11), 1941-1946.

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» NR7-030

THE EFFECT OF SPONTANEOUS CREATIVE EXPRESSION ON ANXIETY AND DEPRESSION IN PSYCHIATRIC INPATIENTS

Joanna MacLean, Gabor Keitner, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that spontaneous creative expression may provide a non-verbal vehicle for psychiatric inpatients to constructively and tangibly express feelings and emotions, thereby leading to significant improvement in their symptoms of anxiety and depression.

SUMMARY:

Purpose: To assess anxiety and depression in a psychiatric inpatient population before and after participating in a spontaneous creative expression (SCE) activity, a non-creative activity (NCA), or in a control cohort not participating in either activity (NI). This study was designed to test the hypothesis that creative expression would improve symptoms of anxiety and depression in psychiatric inpatients. Method: The study included 65 patients admitted to a tertiary hospital psychiatric unit with a diagnosis of either mood disorder – unipolar or bipolar (N=51); or psychotic disorders – schizophrenia, schizophreniform, schizoaffective, or delusional disorder (N=14). Thirty five (35) patients were administered the Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) pre and post participating in a supervised individual exercise of non-directive SCE for 30 minutes, consisting of painting any image. Two control groups were included: 1) 15 patients were administered the BAI and BDI at 30 minute intervals with no intervention (NI) and 2) 15 patients were administered the BAI and BDI pre and post participating in a NCA of word searches for 30 minutes. Results: There was a mean 61% improvement (decrease) in BAI scores among the SCE participants compared to a 1% improvement among the NI control group (p=.002 SCE vs. NI) and an 8% improvement in the NCA control group (p=.005, SCE vs. NCA). Similarly, BDI scores decreased (improved) 37% among the SCE participants, vs. 6.5% increased (worsened) in the NI control group (p=.0001 SCE vs. NI) and decreased (improved) 2% in the NCA control group (p=.001 SCE vs. NCA). Neither the BAI nor BDI scores improved significantly in the NI vs. NCA control participants (BAI p=.35 and BDI p=.36). Conclusion: SCE may provide a non-verbal vehicle for psychiatric inpatients to constructively and tangibly express feelings and emotions, thereby leading to significant improvement in their symptoms of anxiety and depression.

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» NR7-031

ASSESSMENT OF VERIFIABLE OBSERVABLE EVIDENCE OF ANXIETY IS INHIBITED BY PSYCHIATRY RESIDENCY TRAINING

Conrad Swartz M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to explain differences between psychological (subjective) anxiety and somatic tension (observable) anxiety in assessment and treatment, and how available observable evidence is not integrated into diagnosis.

SUMMARY:

Introduction: In DSM verifiable observable evidence is not required for diagnosis except in diagnosing dementia or catatonia. This reflects separation of psychiatric diagnosis from the scientific method. Is this separation associated with training to avoid verifiably assessing observable evidence?
Hypothesis: Detailed systematic efforts will succeed in training psychiatry residents to assess observable evidence of anxiety.
Methods: In a didactic class on research methods five PGY3 and PGY4 psychiatry residents in good standing were trained in Hamilton Anxiety Scale ratings. This was for both the original version and versions modified for each of observable somatic tension and subjective psychological anxiety. First, good interrater reliability was achieved (kappa 0.77 to 0.78, p<0.002). Then, each resident blindly rated six pairs of video recordings of unstructured regular clinical outpatient visits before and during response to a long-acting CNS- active beta-blocker. These recordings had been edited to remove mention of drugs and session dates. With anxiety rating scores the investigator blindly distinguished sessions before treatment from those during treatment with 100% accuracy and regarded the differences as obvious.
Results: Overall, residents distinguished sessions before treatment from sessions during response to treatment correctly only 59% of the time, about the same as random (50%). Accuracy was similar among somatic tension (55%), psychological (59%) and standard Hamilton Anxiety (64%) ratings.
Conclusion: Detailed systematic efforts did not succeed in training senior residents to assess observable evidence of anxiety sufficient to distinguish between pretreatment (sick) and treatment-responding (well) states in the same patients.
Discussion: The results suggest that previous training interfered with acquisition of skills in assessing observable evidence of psychopathology. This points to a systematic flaw in psychiatric education.

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1) Swartz CM: Less Anxiety But More Violence? Psychiatric Times April 2004; 21(4): 49-52

2) Swartz CM: Knowing That We Don't Know. Psychiatric Times June 2004; 21(7): 53-54.

» NR7-032

DISSOCIATIVE CATATONIA: CLINICAL PRESENTATION AND RESPONSE TO BENZODIAZEPINES

Joseph Lee M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to diagnose dissociative catatonia, recognize its prompt response to benzodiazepines, and appreciate the inadequacy of current diagnostic systems in its diagnosis

SUMMARY:

Objective: Dissociative catatonia – catatonia secondary to a dissociative state - has been sparsely reported in the literature. This study of 15 episodes of dissociative catatonia examines its

symptomatology, longitudinal course, and response to benzodiazepines. Methods: Out of 149 episodes of catatonia prospectively identified using research criteria, 15 (7 male, 8 female) met modified criteria of the DSM-IVTR and ICD-10 for dissociative trance (including those occurring during the course of other disorders) or dissociative stupor (catatonic stupor not taken as an exclusion criterion). All received benzodiazepines. A chart review was conducted noting the psychological precipitants, dissociative and catatonic symptoms, sequence of symptom progression, associated psychiatric diagnoses, and responses to benzodiazepines. Results: All 15 episodes were brief in duration (mean=3days, 1- 9) and of sudden onset associated closely in time with psychological stressors. Dissociative stupor occurred in 3, dissociative trance 6, dissociative possession trance 2, and dissociative trance and stupor 4. Three developed during the course of schizophrenia and 1 of mania. Ten manifested in the retarded form of catatonia, 3 excited and 2 mixed. ICD-10 and DSM-IV TR provide no criteria for the differentiation between catatonic stupor and dissociative stupor. In 9 both catatonic and dissociative symptoms developed simultaneously, and in 6 dissociative symptoms first appeared evolving into a catatonic state. All showed prompt responses to benzodiazepines; both catatonic and dissociative symptoms (including psychotic-like manifestations) fully resolved. Conclusions: Catatonia may develop secondary to a dissociative state. The dissociative catatonic syndrome, promptly responsive to benzodiazepines, may occur as a primary condition or during the course of other disorders. Current diagnostic systems are inadequate in its diagnosis.

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» NR7-033

IMPACT OF SUBSTANCE USE DISORDER ON THE OCCURRENCE OF OTHER MENTAL DISORDERS

Sung Man Chang, Maeng Je Cho, M.D., Ph.D., Jin-Yeong Kim, M.D., Ph.D., Jun-Young Lee, M.D., Ph.D., Hong Jin Jeon, M.D., Ph.D., Bong-Jin Hahm, M.D., Ph.D., Seong-Jin Cho, M.D., Ph.D., Hae Woo Lee, M.D., Jae-Nam Bae, M.D., Ph.D. Yanghyun Lee, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the importance of mental substance comorbidity.

SUMMARY:

Most people with mental disorders are also affected by co-occurring substance use disorder. However, there have been few studies on the dual diagnosis among Korean population. The aims of this study are to analyze the comorbidity patterns of mental-substance disorders, and to find the sociodemographic factors associated with comorbidity, and furthermore to analyze the temporal sequencing of dual diagnosis.

The nationwide Korean Epidemiologic Catchment Area study Replication (KECA-R) was conducted between August 2006 and April 2007. A multistage, cluster sampling design was adopted. Face-to-face interviews, aged 18 to 64 years were conducted with the Korean version of Composite International Diagnostic Interview (K-CIDI) based on the DSM-IV (N=6,510, response rate=81.7%). In general, high associations were found between mental and substance use disorder. A majority of mental disorders, especially mood disorder and anxiety disorder are strongly associated with alcohol dependence or nicotine use disorder. Associated factors for dual diagnoses were low income, divorced/separated/widowed, unmarried and unemployment. Temporal sequencings were various according to the comorbid disorders. Major depression generally started at an later age than alcohol dependence, whereas nicotine use disorder started at an earlier age than major depression. In case of people with dual diagnosis, more functional disabilities were found compared with the people without dual diagnosis.

High levels of mental-substance comorbidity were also found in Korean general population. It was reported that most people with dual diagnosis have tendency to report their first mental disorder occurred at an earlier age than their first substance disorder. However, in Koreans it did not occurred in the same manners. Temporal sequencing of dual diagnoses was various according to the separate dual diagnosis conditions. The present study showed that dual diagnosis leads to more functional disability.

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» NR7-034

NEGATIVE ATTITUDES TOWARD HELP SEEKING FOR MENTAL ILLNESS IN TWO POPULATION-BASED SURVEYS FROM THE UNITED STATES AND CANADA

Amit Jagdeo M.D., Sareen J., M.D., Cox B.J., Ph.D., Stein M.B., M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe sociodemographic correlates of negative attitudes toward help seeking for mental illness in the United States and Canada.

SUMMARY:

Objectives: To determine the prevalence and sociodemographic correlates of negative attitudes toward help seeking for mental illness among the general population in the United States (U.S.) and Ontario (Canada).

Methods: Two contemporaneous surveys were analyzed: the U.S. National Comorbidity Survey (NCS: N=5,877) and the Mental Health Supplement to the Ontario Health Survey (OHS: N=6,902). A composite variable was derived from three questions assessing probability, comfort and embarrassment related to help seeking for mental illness. Multiple logistic regression analyses were used to examine the correlates of negative attitudes toward help seeking. Results Negative attitudes toward mental health service utilization were prevalent in both population samples. 15% of the OHS and 20% of the NCS respondents stated that they probably or definitely would not seek treatment if they had a serious emotional problem. Almost half the sample in both surveys stated that they would be embarrassed if their friends knew about their use of mental health services. Negative attitudes toward help seeking for mental illness were highest among young, single, lesser educated males in both Canada and the U.S. Substance abuse or dependence, antisocial personality disorder, and not having sought help in the past for mental illness were associated with greater negative attitudes in both countries

ConclusionsYoung people in Canada and the United States – especially low income, low education males who have never sought help in the past for mental illness and may have a substance abuse or dependence problem – are most likely to have negative attitudes toward help seeking for mental illness.

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» NR7-035

LIFETIME PREVALENCE AND RISK FACTORS OF SUICIDAL IDEATION, PLAN, SINGLE, AND MULTIPLE ATTEMPTS IN A NATIONWIDE SAMPLE OF KOREA

Hong Jin Jeon, M.D., Ph.D., Jun-Young Lee, M.D., Ph.D., Bong-Jin

Hahm, M.D., Ph.D., Jin Pyo Hong, M.D., Ph.D., Jae Nam Bae, M.D., Ph.D., Seong-Jin Cho, M.D., Ph.D., Hae Woo Lee, M.D., Maeng Je Cho, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the lifetime prevalence of suicidal behaviors(suicidal ideation, plan, and attempts)in Korean adults and Bipolar disorders were associated with suicide attempts, more stronly associated with multiple attempts.

SUMMARY:

Objective: To evaluate the lifetime prevalence and correlates of suicidal behaviors including suicidal ideation, plan, and attempts (single and multiple).

Method: Study design was face-to-face interviews through household visits. The participant was a national sample of 6,510 adults aged more than 18 years from the Korean Epidemiologic Catchment Area Study Replication (KECA-R).We used the Korean version of the Composite International Diagnostic Interview (K-CIDI), a fully structured lay-administered diagnostic interview, and the questionnaire for suicidal behaviors.

Results: Estimated lifetime prevalences of suicidal ideation, plan, and attempt were 15.3%, 3.3%, and 3.2% (single attempt 2.1% and multiple 1.1%) in South Korea, respectively. 'Female gender' was the only factor associated with suicidal ideation and all kinds of suicidal behaviors. 'Female gender', 'younger age', and 'divorced/separated/widowed' were significantly associated with suicidal attempts, and more strongly associated with multiple attempts. Mood disorders were the most strongly associated with all kinds of suicidal behaviors among mental disorders. In detail, bipolar disorder was the most strongly associated with both single and multiple suicidal attempts. Bipolar disorders, major depressive disorders, and posttraumatic stress disorder were significantly associated with suicidal attempts, and more strongly associated with multiple attempts. Age of first suicidal attempt was significantly later in those with lifetime mood disorders than those without, but it showed no significant difference with anxiety disorders.

Conclusions: Suicidal behaviors are highly prevalent in Koreans. Mood disorders, especially bipolar disorders, were associated with suicidal attempts, more strongly associated with multiple attempts, and mood disorders are associated with later onset of suicidal attempt.

REFERENCES:

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» NR7-036

PREVALENCE, COMORBIDITIES, AND QUALITY OF LIFE IN KOREAN ADULTS WITH INTERNET ADDICTION

Hae Woo Lee, M.D., Bong-Jin Hahm, M.D., Jae Nam Bae, M.D., Dong Woo Lee,M.D., Seong In Cho, M.D., Jong Ik Park, M.D., Sung Man Jang,M.D., Jun-Young Lee,M.D., Sang Bin Baek,M.D., Maeng Je Cho,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand prevalecne of internet addiction, DSM-IV psychiatric comorbidities in Korean Adults.

SUMMARY:

Aims: No previous reports about internet addiction have not included nationwide sample, but subpopulation. This study aimed to estimate the prevalence, psychiatric comorbidity, and influence on Quality of life of IA in a nationwide sample of Korean adults.

Method: Study design was epidemiological cross-sectional survey and participants were nationally representative sample of 6,510 korean adults aged 18-64. Face-to-face interviews were conducted with Young' Internet Addiction Test (20-items), the Korean version of Composite International Diagnostic Interview (K-CIDI), and EuroQol (EQ-5D).

Results: The estimated prevalence of internet addiction was 4.77% (male 5.85% and female 3.09%) in korean adults. Among symptoms of internet addiction, Question about tolerance was the highest mean value in internet addiction group and the items-mean value about negative repercussions higher in male than female. Internet addiction was the most strongly associated with 12-month diagnosis of DSM-IV mood disorders (Adjusted OR 3.07, C.I.1.78~5.28) followed by alcohol use disorders (2.32, C.I. 1.59~3.96). Especially, 12-month alcohol use disorders is significant in male (2.25, C.I. 1.62~3.90), not in female and 12-month anxiety disorders in female (2.25, C.I. 1.22~4.13) not in male. Subjects with internet addiction showed lower Quality of life than those without. The severe internet addiction group showed low quality of life in male, not in female.

Conclusions: Age and psychiatric comorbidities were important factors in subject with internet addiction. Male differed from female in most strongly related comorbidities (mood disorders in male, anxiety disorders in female) and reported lower quality of life in subjects with severe internet addiction.

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» NR7-037

PARENTAL AGE AT BIRTH: CONTRIBUTION TO PSYCHOPATHOLOGY

Jorge Lopez-Castroman M.D., Hilario Blasco-Fontecilla, M.D., Ph.D., David Delgado-Gomez, Ignacio Basurte Villamor, M.D., Ph.D., Antonio Artes, Maria A. Oquendo, M.D., Ph.D., Marta Reyes-Torres M, M.D., Enrique Baca-Garcia, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the current knowledge on the influence of parental age at birth in the psychopathology of the offspring and consider the differences in parental age among psychiatric diagnostic categories.

SUMMARY:

To date, Down's syndrome is consistently associated with advanced maternal age at the time of conception, while autism and schizophrenia are consistently associated with advanced paternal age. This study tested the hypothesis that advanced parental age at birth would be associated with diagnosis in F2 (Psychotic disorders) and F7 (Mental retardation) categories of the international classification of diseases in its 10th revision (ICD-10) when compared with other diagnostic categories. The study was conducted using a database with follow-up information for 30965 patients aged 18 or younger at their first visit to ambulatory psychiatric facilities in the Community of Madrid (Spain) between 1980 and 2008. Out of 94969 treatment episodes (follow-up periods with time gap between visits smaller than a year), 1696 (1.78%) attained last diagnosis of psychotic disorder (F2) and 1841 (1.93%) last diagnosis of mental retardation (F7). Maternal, paternal and mean parental age across diagnostic categories was compared through a multiple ANOVA test after Bonferroni adjustment. A logistic regression model was used to estimate the risk associated with increasing age. Our findings demonstrate that both maternal and paternal ages are elevated for patients diagnosed mental retardation (F7). However, those diagnosed with psychotic disorders (F2) did not show a difference in parental age when com-

pared with the rest of patients followed in Mental Health centers. The highest risk for mental retardation was found among patients whose mothers were 35-40 years of age (OR=1.64; p<0,001) or patients whose fathers were 35-40 (OR=1.60; p=0.0014) or 40-45 years of age (OR=1.75;p=0.0035) at the time of birth. The present study is limited by the absence of a parallel control population and the small sample size for F2 and F7 categories. Further studies are needed to clarify the effect of parental age at birth in the diagnosis of psychopathology.

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» NR7-038

THE PREVALENCE OF PSYCHIATRIC DISORDERS IN PRIMARY CARE IN CHILE

Benjamin Vicente M.D., Robert Kohn, M.D.; Sandra Saldivia, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the prevalence of mental illness in primary care and its associated risk factors.

SUMMARY:

Objectives: There are few comprehensive studies of the epidemiology of psychiatric disorders in primary care in Latin America. Most studies of primary care have only focused on affective disorders and have examined primarily demographic variables as risk factors.

Methods: The study was carried out in Concepcion, Chile among ten primary care centers that are part of the national health care program. Three thousand participants were randomly selected and interviewed in their homes using the Composite International Diagnostic Interview (CIDI). In addition the CIDI diagnostic interview, subjects were asked socio-demographic factors and personal factors including satisfaction with living conditions and presence of physical illness; financial strain; physical and mental well-being; alcohol and drug misuse; quality of relationships; family psychiatric history; history of childhood abuse; spiritual beliefs; safety of living environment; recent life threatening events and discrimination.

Results: Interviews were completed with 94.6% of the respondents, N = 2839. The rate of lifetime disorders were: major depressive disorder, 23.6%; bipolar disorder, 1.9%; dysthymia, 3.9%; obsessive compulsive disorder, 1.6%; post-traumatic stress disorder, 11.4%; panic disorder, 4.9%; agoraphobia, 4.5%; social phobia, 18.9%; generalized anxiety disorder; 22.9%; eating disorders, 1.0%; somatoform disorder, 8.4%; non-affective psychosis, 2.7%. The rate of 12-month prevalent disorders were: major depressive disorder, 11.0%; bipolar disorder, 1.1%; dysthymia, 2.7%; obsessive compulsive disorder, 0%; post-traumatic stress disorder, 4.3%; panic disorder, 4.0%; agoraphobia, 3.8%; social phobia, 22,9%; generalized anxiety disorder; `8.9%; eating disorders, 0.6%; somatoform disorder, 8.4%; non-affective psychosis, 1.4%.

Conclusions: The rate of psychiatric disorders in the primary care center in Chile is considerably higher than that found in the community. Improved detection of individuals at risk for psychiatric disorders is needed through by studying potential risk factors.

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» NR7-039

NO ASSOCIATION BETWEEN THE SEROTONIN TRANSPORTER GENE REGULATORY REGION POLYMORPHISM (5-HTTLPR)AND PERSONALITY TRAITS AND PERSONALITY TYPE

Ik-Seung Chee, M.D., Ph.D., Department of Psychiatry, Chungnam National University Hospital, 640 Daesa-dong, Jung-gu, Daejeon, 301-721, Korea; MK Lee, M.D., JL KIM, M.D., Ph.D, SK Wang, M.D., Ph.D., HJ Kim, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to get the information about association between genetic polymorphism and personality traits and personality type.

SUMMARY:

Introduction: Behavioral-genetic studies show approximately 40% heritability for neuroticism(emotional instability), a major dimension of human personality. Anxiety-related personality traits, such as, NEO personality inventory neuroticism and temperament and character inventory(TCI)/ tridimensional personality questionnaire(TPQ) harm avoidance have been shown to have significant genetic components. To date, however, there is no specific genetic variants that contribute to these traits that have been conclusively identified. Some studies have investigated a association between a functional serotonin transporter promoter polymorphism(5-HTTLPR) and anxiety-related personality traits, although subsequent replication researches have failed. Method: We studied the association between 5-HTTLPR polymorphism and Eysenck personality Questionnaire (EPQ) compared by ANOVA and Myers-Briggs Type Indicator (MBTI) compared by Fisher's-test in 281 Korean medical students.

Results: There were no significant differences between the score of EPQ (Psychoticism, Extraversion, Neuroticism, Lie, Addition, Criminality, Impulsiveness, Venturesomeness, Empathy) and MBTI (16 personality types) and the 5-HTTLPR polymorphism. In addition, no association was observed in this study between individuals grouped by short allele(s/s) and long allele(s/l+l/l) of 5-HTTLPR polymorphism and any of the personality dimensions and personality type measured by the EPQ and MBTI. Conclusions: These findings provided no evidence for an association between 5-HTTLPR polymorphism and personality taits, and personality type.

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» NR7-040

INTERACTIONS OF SEROTONIN-RELATED GENES WITH SHORT-TERM ANTIDEPRESSANT RESPONSE IN MAJOR DEPRESSIVE DISORDERS

Po See Chen, Eugene Lin,Ph.D., Hui Hua Chang,M.S., Po-Wu Gean,Ph.D., Hsin Chun Tsai, M.D.

EDUCATIONAL OBJECTIVES:

The study was to designed assess both main effects of single loci and multilocus interactions to test the hypothesis that serotonin system related genes may contribute to the pharmacogenomics of short-term antidepressant response independently and/or through complex interactions in a Taiwanese population with major depressive disorder (MDD) At the conclusion of this presentation,GMDR approach is a promising method to assess the gene-gene interactions in the drug efficacy of antidepressants.

SUMMARY:
Introduction: Four serotonin related genes including guanine nucleotide binding protein beta polypeptide 3 (GNB3), 5-hydroxytryptamine receptor 1A (HTR1A; serotonin receptor 1A), 5-hydroxytryptamine receptor 2A (HTR2A; serotonin receptor 2A), and solute carrier family 6 member 4 (SLC6A4; serotonin neurotransmitter transporter) are candidate genes for influencing antidepressant treatment outcome. In this study, our goal was to assess both main effects of single loci and multilocus interactions to test the hypothesis that these four serotonin related genes may contribute to the pharmacogenomics of short-term antidepressant response independently and/or through complex interactions in a Taiwanese population with major depressive disorder (MDD).
Materials and methods: There were 101 MDD patients, including 35 rapid responders and 66 non-responders. We genotyped four single nucleotide polymorphisms (SNPs), including GNB3 rs5443 (C825T), HTR1A rs6295 (C-1019G), HTR2A rs6311 (T102C), and SLC6A4 rs25533. To investigate gene-gene interactions, we employed the generalized multifactor dimensionality reduction (GMDR) method.
Results: Single locus analyses showed that the GNB3 rs5443 polymorphism was associated with short-term antidepressant treatment outcome. Furthermore, interactions involving GNB3, HTR2A, and SLC6A4 were suggested using the GMDR method. These results support the hypothesis that GNB3, HTR2A, and SLC6A4 may play a role in short-term antidepressant treatment outcome with MDD in an interactive manner.
Conclusions: We demonstrated that the GMDR approach is a promising method to assess the gene-gene interactions in the drug efficacy of antidepressants with MDD patients. Future research with independent replication in large sample sizes is needed to confirm the role of the GNB3 rs5443, HTR2A rs6311, and SLC6A4 rs25533 polymorphisms identified in this study.
Keywords: antidepressant response, gene-gene interactions, major depressive disorder, single nucleotide polymorphisms

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» NR7-041

THE INFLUENCE OF CHILDHOOD TRAUMA, GABRA2 AND THEIR INTERACTION ON ALCOHOL, HEROIN AND COCAINE DEPENDENCE IN AFRICAN AMERICAN MEN

Mary-Anne Enoch M.A., Colin A. Hodgkinson, Ph.D., Qiaoping Yuan, Ph.D., Pei-Hong Shen, M.S., David Goldman, M.D., Alec Roy, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should become aware of the importance of both genetic and environmental influences, and their interplay, on the development of addiction. They will see that stress exposure very early in life has a major impact, and the greater the stress the greater the likelihood of severe addiction. Finally, methods for dealing with issues of population stratification in genetic studies on admixed populations such as African Americans will be presented.

SUMMARY:
Objectives: Childhood trauma and genetic variation are risk factors for the development of substance dependence. The GABRA2 gene has been implicated in addiction and anxiety in humans. Early life stress alters GABRA2 expression in adult rodents. We hypothesized that childhood trauma, GABRA2 variation and gene x environment interactions would influence vulnerability to addiction.
Methods: The study sample comprised African American men: 635 inpatients with lifetime DSM-IV (SCID derived) single and comorbid diagnoses of alcohol, cocaine and heroin dependence, and 320 controls. The Childhood Trauma Questionnaire (CTQ) was administered. Ten GABRA2 haplotype-tagging SNPs and 186 ancestry informative markers were genotyped using the Illumina GoldenGate platform.
Results: Increased exposure to childhood trauma predicted substance dependence ($p < 0.0001$). Polysubstance dependence was associated with the highest CTQ scores ($p < 0.0001$). The African Americans had four common (frequency: 0.11 – 0.30) haplotypes within the distal GABRA2 haplotype block: two yin-yang haplotypes that correspond to those in Caucasians and Asians and two haplotypes not found in other ethnic groups. One of the unique haplotypes predicted heroin addiction ($p < 0.05$). In contrast, the other haplotype was more common in controls ($p < 0.05$) and appeared to confer resilience to addiction after exposure to severe childhood trauma. The yin-yang haplotypes had no effects. In addition, the intron 2 SNP rs11503014, not located in any haplotype block, was associated with addiction ($p < 0.05$), specifically heroin addiction ($p < 0.005$). An interaction between severe childhood trauma and rs11503014 variation influenced addiction vulnerability, particularly to cocaine ($p < 0.005$).
Conclusions: These results suggest that at least in African American men, childhood trauma, GABRA2 variation and their interactions may play a role in risk and resilience to substance dependence.

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» NR7-042

ASSOCIATION STUDY OF BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) GENE AND BIPOLAR DISORDER IN KOREA

Duk-In Jon M.D., Hye Ji Min, MD, Jeong-Ho Seok, MD, Ph.D., Eun Lee, MD, Ph.D., Hyun Sang Cho, MD, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand the role of BDNF in the pathogenesis of bipolar disorder in Korea.

SUMMARY:
BACKGROUND: Brain-derived neurotrophic factor (BDNF) plays an important role in cell survival, differentiation, and cell death as well as in neural plasticity. Recent studies have suggested that BDNF plays a role in the pathogenesis of bipolar disorder.
OBJECTIVES: The aim of this study was to investigate the association of the genetic variations of the BDNF gene with bipolar disorder in Korea. We also studied the possible association of these genetic variants with clinical features.
METHODS: Val66Met polymorphism of the BDNF gene were analysed using a polymerase chain reaction (PCR)-based method in 166 bipolar patients and 214 controls.
RESULTS: No significant difference was found between bipolar patients and controls in the genotype and allele frequencies for the investigated BDNF polymorphism. Also no significant difference in the clinical features such as age of onset, onset type, family history, and suicidal history was observed between the two groups.
CONCLUSIONS: Our results suggest that the investigated polymorphisms of BDNF gene are not major risk factors responsible for predisposition to bipolar disorder or its clinical features. However, replication studies with large samples are needed.

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2) Skibinska M, Hauser J, Czerski PM, Leszczynska-Rodziewicz A, Kosmowska M, Kapelski P, et al. Association analysis of brain-derived neurotrophic factor (BDNF) gene Val66Met polymorphism in schizophrenia and bipolar affective disorder. World J Biol Psychiatry. 2004;5(4):215-220.

» NR7-043

ASSOCIATION ANALYSIS OF HEAT SHOCK PROTEIN 70 GENE POLYMORPHISMS IN SCHIZOPHRENIA

Tae-Youn Jun M.D., Jun TY , Kim JJ, Lim HK, Pae CU, Serretti A, Paik IH

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognized heat shock protein 70 gene might be implicated in the development of schizophrenia.

SUMMARY:

Genes encoding heat shock proteins (HSPs) are a promising candidate gene in schizophrenia as they are believed to play a protective role in the central nervous system. Association between the three polymorphisms of HSP70-1 (HSPA1A), HSP70-hom(HSPA1L) and HSP70-2 (HSPA1B) and schizophrenia has been reported. Thus, this study investigated the association between an enlarged set of SNPs at HSP70 gene and schizophrenia. 294 patients with schizophrenia and 287 controls were enrolled in the study. Genotypings of 5 SNPs of HSP70 were performed using Pyrosequencing®. Haploview 3.2 was used to generate a linkage disequilibrium map and to test for Hardy–Weinberg equilibrium. Single locus and haplotype based associations were tested. Tests for association and multi-marker haplotypes were performed by using a COCAPHASE v2.403. Association of SNP markers and clinical variables were analyzed by analysis of variance. Significant association was detected at rs2075799 (allele A, v2 = 8.03, df = 1, P = 0.0046), but not at rs2227956 (P = 0.28), rs1043618 (P = 0.88), rs562047 (P = 0.47) and rs539689 (P = 0.32). In fact, the rs2075799*G/A genotype was more represented in patients with schizophrenia than in controls (v2 = 8.23, df = 1, P = 0.0041). Haplotype based associations were also detected (global P value 0.000003); the T-A-C-C-G haplotype was more prevalent among the patients (odds ratio, OR 5.95). Sliding windows analysis revealed a major contribution from rs2227956 and rs2075799 (global-P value 0.0075), with T-A haplotype significantly associated with schizophrenia. There was no evidence of an association between the clinical variables and schizophrenia across the genotypes. Our results raise the possibility that HSP70 gene might be implicated in the development of schizophrenia, although limited by rare haplotypic association with the disease. Hence further studies from different ethnics should be performed to confirm these results.

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» NR7-044

IS THERE PROTECTIVE HAPLOTYPE OF DYSBINDIN GENE (DTNBP1) 3 POLYMORPHISMS FOR MAJOR DEPRESSIVE DISORDER

Tae-Youn Jun M.D., Jun TY , Kim JJ, Lim HK, Pae CU, Serretti A, C Lee

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize dysbindin gene variants may have a role in the susceptibility to major depressive disorder.

SUMMARY:

Dysbindin gene (DTNBP1) gene on 6p22.3 has currently been recognized as one of the most eminent susceptibility genes for schizophrenia. In this study, we examined DTNBP1 in the Korean population to determine the association of DTNBP1 and major depressive disorder(MDD) in conjunction with clinical variables. 188 patients with MDD and 350 controls were investigated for 4 variants within the dysbindin gene (rs3213207 A/G, rs1011313 C/T, rs760761 C/T, and rs2619522 A/C). Genotyping of 4 variants of DTNBP1 were performed using Pyrosequencing® . Haplotype analyses revealed a strong association (global model: LRS=21.276, df=5, p=0.0007; Permutation analysis p=0.0014; SE=0.00053) with the haplotype A/C/T/A having the strongest protective effect. Carriers of this haplotype had a significant protective effect (OR=0.16, 95% Confidence Interval (CI)=0.06–0.70). Sliding windows analysis revealed that the major contribution was due to the rs760761 (C/T) and rs2619522 (A/C) haplotype (LRS=23.9172, df=3, p=0.000026), though single marker analysis did not reveal any association with diagnosis. No association was also observed with the other clinical variables such as age, age of onset, family history, number of admission, history of suicidal attempts and duration of illness. These results suggest a protective effect of some dysbindin gene haplotypes on the development of MDD. Our finding suggests that dysbindin gene variants may have a role in the susceptibility to MDD. Adequately powered further studies in different ethnic groups are warranted.

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» NR7-045

ASSOCIATION BETWEEN TRYPTOPHAN HYDROXYLASE-2 GENE VARIATIONS AND THE PERSONALITY TRAITS OF NOVELTY SEEKING AND HARM AVOIDANCE

Chan-Hyung Kim M.D., Yoon-Young Nam, M.D., Hong Shick Lee, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the possible relationship between personality traits and tryptophan hydroxylase-2 gene variations.

SUMMARY:

Personality traits have been related to central serotonin system. Tryptophan hydroxylase is the rate-limiting enzyme in the serotonin biosynthesis responsible for the regulation of serotonin levels. A newly identified second isoform of the tryptophan hydroxylase gene (TPH2) was found to be solely expressed in the brain. We hypothesized that variation at the TPH2 gene and its 5' upstream region may be associated with personality traits. Two hundred thirteen Korean healthy individuals (80 males and 133 females) participated in the present study. We analyzed three SNPs polymorphisms (rs11178997, rs4570625, rs7305115) of 5' upstream region and the TPH2 and four haplotypes (TGA, TGG, TTA, TTG) and their association with personality traits, as measured with the Temperament and Character Inventory (TCI). The rs4570625 and the rs7305115 was associated with Novelty Seeking (F=6.9, p=0.001; F=12.5, p<0.001) and Harm Avoidance (F=7.0, p=0.001; F=10.3, p<0.001) in the Korean healthy subjects. Moreover, haplotype showed an association with Novelty Seeking (F=7.9, p<0.001) and Harm Avoidance (F=8.5; p<0.001) respectively. Our findings suggest that TPH2 SNPs and haplotypes may modulate personality traits in Korean healthy subjects, but further studies are required.

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HJ, Bondy B, Ackenheil M. SNP and haplotype analysis of a novel tryptophan hydroxylase isoform (TPH2) gene provide evidence for association with major depression. Mol Psychiatry 2004;9:1030-1036.

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» NR7-046

PROTECTIVE EFFECT OF DYSBINDIN GENE (DTNBP1) TO SCHIZOPHRENIA IN KOREAN POPULATION

JUNG JIN KIM M.D., Chi Un Pae, M.D., Chang Uk Lee, M.D., Chul Lee, M.D., In Ho Paik, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the association of dysbindin gene(DTNBP1) and schizophrenia and a possible protective effect of dysbindin gene variants in schizophrenia.

SUMMARY:

Dysbindin gene (DTNBP1) has been consistently reported to be associated with schizophrenia. However data from East Asian population has been sparse and inconsistent till today. This study tried to replicate the genetic association of DTNBP1with schizophrenia in a large Korean sample, as well as analyzing the association of DTNBP1 with clinical variables. Nine hundred and eight (908) patients with schizophrenia and 601 controls were investigated. The high-throughput genotyping method using pyrosequencer was used for genotyping 4 SNPs (rs3213207, rs1011313, rs760761, and rs2619522). Symptomatology was assessed at admission using the Positive and Negative Syndrome Scale. Haplotype analyses revealed a significant association with schizophrenia ($p < 0.0001$) with the haplotypes A-C-C-C and A-C-T-A having an eminent protective effect toward schizophrenia. The major contribution to the difference in the haplotype distribution between patients and the controls was the rs760761 (C/T) and rs2619522 (A/C) haplotypes ($p < 0.0001$). No association of DTNBP1 with symptomatology and other clinical variables was found. In conclusion, the present study suggests a possible protective effect of rare DTNBP1 variants in schizophrenia, although subsequent studies in different ethnic groups are warranted.

Key words: Dysbindin; gene; haplotype; schizophrenia; Korean.

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» NR7-047

PATIENT AND PHYSICIAN SATISFACTION WITH PHARMACOGENOMIC TESTING FOR DEPRESSED INPATIENTS AT THE MAYO CLINIC MOOD DISORDERS UNIT

Simon Kung M.D., Joel G. Winner, M.D., Josiah D. Allen, B.S., Karen A. Snyder, B.S., Renato D. Alarcon, M.D., M.P.H., David A. Mrazek, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to discuss patient and clinician satisfaction of pharmacogenomics for optimizing antideprssant selection in an inpatient mood disorders unit.

SUMMARY:

OBJECTIVE: More awareness exists among patients and physicians regarding pharmacogenomic testing for individualizing antidepressant medication selection. We report patient and physician satisfaction with genotyping for depressed inpatients.
METHODS: Patients hospitalized at the Mayo Clinic Mood Disorders Unit for unipolar or bipolar depression who had genotyping performed were included in this retrospective study. Patients completed a questionnaire regarding their awareness of genotyping, how much they felt it would benefit them, and their satisfaction. Clinicians completed a questionnaire regarding genotyping turnaround time, whether medications were changed because of results, results usefulness, and satisfaction.
RESULTS: Between April and August 2008, 37 pairs of patients and clinicians completed questionnaires. Genotyping results were fully (57%) or partially (30%) available before discharge. Fourteen patients (38%) had been aware of genotyping prior to hospitalization. Patient impressions of how genotyping might help with optimal medication selection increased from 2.5 to 3.4 on a 1-5 Likert scale (1=unlikely, 3=may or may not help, 5=very likely) during hospitalization. Their satisfaction was 3.4 (1=least, 3=neutral, 5=very satisfied). From the physician viewpoint, 37% reported changing medications based on genotyping results. On similar 1-5 Likert scales, the usefulness of results was rated 3.6, turnaround time 3.4, and satisfaction 3.5.
CONCLUSIONS: Patients are becoming more aware of pharmacogenomic testing, and after further discussion with their physicians, report that it would be helpful in antidepressant medication selection. Patients and physicians reported their satisfaction with genotyping as better than average, and we expect higher satisfaction scores if results were available sooner as almost half (43%) were not available before discharge. Genotyping results influenced physician management in 37% of cases.

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» NR7-048

PILOT STUDIES FOR FINEMAPPING OF CHROMOSOME 18 IN METHAMPHETAMINE ABUSERS: MAPK4 AS THE CANDIDATE GENE FOR COMORBIDITY OF PSYCHOSIS AND ADDICTION

Byung-Dae Lee, M.D., Eun-Young Kim, M.D., Jung-Hyun Lee, M.D., Do-Hoon Kwon, M.D., Yang-Tae Kim, M.D., Byung-Kook Ryu, M.D., Moon-Jin Kim, Sung-Nam Cho, M.D., Young-In Jeong, M.D., Je-Min Park, M.D., Sung-Gon Kim, M.D., Cheol-Joong Kang, M.D., Ji-Hoon Kim, M.D., Young-Min Lee, M.D., Michael A. Escamilla, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the process of genetic finemapping for elucidating the mental illnesses' candidate genes. The participant also should be able to identify the meaning of candidate gene for comorbidity of psychosis and addiction based on psychopathological knowledge.

SUMMARY:

BACKGROUND: Psychosis and addiction are very serious social problems in the worldwide. Psychosis is a deviation from the reality and addiction is the final defense beyond psychosis leading to comorbidity. We previously suggested the malic enzyme 2(ME2) as the candidate gene for psychosis in finemapping of chromosome 18. Chromosome 18 is also one of the possible regions that can contribute to addiction. We performed pilot studies for finemapping of chromosome 18 in the methamphetamine abusers for elucidating the candidate gene for comorbidity of psychosis and addiction. METHODS: We have selected 30 unrelated controls(16 males, 14 females; age=59.8±10.4) and 37 male methamphetamine abusers(age=43.3±7.8). We analyzed 56 SNPs of 18 neuronal genes in chromosome 18 for DNA samples that was checked for

the data quality and genotype error. The association between the case-control status and each individual SNP was measured by using multiple logistic regression models(adjusting for age and sex as covariates). And we controlled false discovery rate(FDR) to deal with multiple testing problem.
RESULTS: We found 9 significant SNPs of 5 genes in chromosome 18(P-value<0.05; adjusting for age as covariate) in methamphetamine abusers compared to controls.(rs1071600,rs12605942,rs2230164:MYOM1; rs3794899, rs3794901:MAPK4; rs2849233:MRO; rs3810067,rs598866:EMILIN2; rs483547:SMCHD1) We also found 3 significant SNPs of 2 genes (P-value<0.05; adjusting for age and sex as covariates). (rs1557314:EPB41L3; rs3794899,rs3794901:MAPK4) Two SNPs in MAPK4 gene were significant in both statistical groups.
CONCLUSIONS: MAPK4, the gene for mitogen-activated protein kinase 4, is one of the final 6 candidate genes including ME2 in 18q12-21 in our previous finemapping for psychosis. Our results suggest that MAPK4 can be a candidate gene that contribute to the comorbidity of psychosis and addcition. Future following studies are expected with many limitations including very small sample size.

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» NR7-049

ASSOCIATION BETWEEN DRDS AND SCHIZOPHRENIA IN KOREAN POPULATION: MULTI-STAGE ASSOCIATION ANALYSES

Kyu Young Lee M.D., Eun-Jeong Joo, M.D., Ph.D., Yong Sik Kim. M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to find a result of a multi-stage analytic design for a comprehensive examination of the genetic association of schizophrenia with the five DRDs. This strategy suggested an increase of efficiency for large-scale association studies using SNPs from a public database.

SUMMARY:

The dysregulation of the dopaminergic system has been implicated in the pathophysiology of schizophrenia with DRDs targeted as the most promising candidate genes. We performed a genetic association study on the five DRDs and schizophrenia in a Korean population using multi-stage analyses. A total of 142 SNPs in DRD1-5 from the dbSNP were evaluated. Using pooled DNA samples from 150 patients with major psychosis (schizophrenia N = 117, DSM-IV) and 150 controls, we screened the associations of each SNP typed by MALDI-TOF mass spectrometry. Each of the suggested SNPs was then genotyped and tested for an association in the individual samples composing the pools. Lastly, the SNPs associated in the prior stage were genotyped in the extended sample (270 patients with schizophrenia and 350 controls). Among 142 SNPs, 88 (62%) in our Korean population were polymorphic. As found by the pooling stage, 10 SNPs (DRD1: 2, DRD2: 3, and DRD4: 5) were identified ($p < 0.05$). SNPs rs1799914 at DRD1 ($p = 0.046$) and rs752306 at DRD4 ($p = 0.017$) had significantly different allele frequencies in the individually genotyped samples composing the pool. These results were similar to those of the comparisons made between patients with schizophrenia and controls. A suggestive association with rs752306 was lost, but gained further significance ($p = 0.017$) with rs1799914 in the extended sample. From these large-scale multi-stage analyses, we were able to find a possible association between DRD1 and schizophrenia. These findings showed the potential of multi-step strategy for finding genes related to schizophrenia.

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» NR7-050

THE ASSOCIATION OF SEROTONIN 1A RECEPTOR POLYMORPHISM WITH RESPONSES TO MIRTAZAPINE IN MAJOR DEPRESSIVE DISORDER

Min-Soo Lee, M.D., Ph.D, Hwa-Young Lee, M.D, Ph.D., Rhee-Hun Kang, M.D., Ph.D., Hun Soo Chang, Ph.D., Jong-Woo Paik, M.D., Ph.D., Young-Hoon Ko, M.D., Ph.D., Hyang-Mi Kim, M.S.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the role of serotonin 1A receptor polymorphism in individual response to mirtazapine treatment.

SUMMARY:

The serotonin 1A receptor (HTR1A) plays key roles in serotonin system and in underlying mechanisms of NaSSA action. In this study, we focused on the association between mirtazapine response and serotonin receptor 1A genetic polymorphism. We enrolled 366 Korean patient with MDD and all subjects were examined using the Structured Clinical Interview for DSM-IV. The severity of depression was assessed using the 21-item Hamilton Depression Rating (HAM-D-21) scale. Only subjects with a minimum score of 18 on the HAM-D-21 scale entered the study. Prior to study entry, a 2-weeks-wash-out was performed. Their clinical symptoms were evaluated with the HAM-D-21 scales at baseline and after 1, 2, 4, 8 and 16 weeks of treatment. Polymorphisms on HTR1A (-1019C>G and +272G>A) were genotyped using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) assays. The proportion of G allele carriers on HTR1A-1019C>G were lower in non-responder than that in responder at 8 weeks after initiation of mirtazapine treatment (36.2% vs 49%, respectively: $P = 0.031$, $OR = 2.16$). In addition, at 16 weeks after treatment, the frequency of G allele carriers on HTR1A-1019C>G were lower in non-remitted than that in remitted MDD patients (39.8% vs 53.7%, respectively: $P = 0.04$, $OR = 2.07$). These results suggest that -1019C>G polymorphism on HTR1A gene may be useful biomarker for predicting response to mirtazapine treatment in MDD patients.

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» NR7-051

ASSOCIATION BETWEEN H111H POLYMORPHISM AND GENE EXPRESSION OF BETA ARRESTIN 1 GENE (ARRB1) IN MAJOR DEPRESSIVE DISORDER

Min-Soo Lee, M.D., Ph.D, Hun Soo Chang, Ph.D., Rhee-Hun Kang, M.D., Ph.D., Hwa-Young Lee, M.D, Ph.D., Jong-Woo Paik, M.D., Ph.D., Young-Hoon Ko, M.D., Ph.D., Yoo-Jung Jeong, M.S.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the role of beta-arrestin polymorphism in individual

response to mirtazapine treatment.

SUMMARY:

Beta-arrestin 1, which is encoded by ARRB1 gene located in chromosome 11q13, plays a critical role in desensitization of G protein-coupled receptor by interfering in G protein receptor interaction which has been known to be involved in the pathophysiology of mood disorders and in the mechanism of action of antidepressant and mood-stabilizing treatments. As a candidate gene approach, we investigated the association between ARRB1 gene polymorphisms and responsiveness to mirtazapine treatment in Korean patients with major depression. We discovered 39 SNPs on ARRB1 gene using direct sequencing for 24 Koreans. Among them, 7 SNPs were selected for large scale genotyping in 298 patients with depression regarding the location, minor allele frequencies and linkage disequilibrium of SNPs. The proportion of minor allele carrier on ARRB1 H111H locus was higher in responder than in non-responder at 2 weeks after mirtazapine treatment (p=0.028). The decreases of HAM-D score were smaller in patients possessing minor allele than in those having major allele on ARRB1 H111H locus in both 1 and 2 weeks after mirtazapine treatment (p = 0.012 and 0.003 at 1 week and 2 weeks, respectively). Peripheral blood mononuclear cells possessing T allele on ARRB1 H111H showed higher levels of beta-arresin 1 mRNA expression compared with those of PBMC having the C allele. These results suggest that ARRB1 polymorphism may affect on the responsiveness of patient with major depression to mirtazapine treatment and that the determination of genotype on ARRB1 H111H may be useful as a genetic marker for predicting response of patient with major depression to mirtazapine and for planning treatment strategies.

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» NR7-052

PHARMACOGENETIC STUDIES OF ZIPRASIDONE, OLANZAPINE AND PERAZINE IN PARANOID SCHIZOPHRENIA

Jerzy Samochowiec M.D., Tybura P, M.D., PhD., Justyna Pelka Wysiecka, M.D., PhD.

EDUCATIONAL OBJECTIVES:

[no data]

SUMMARY:

Literature data revealed that efficacy and side effects of antipsychotic treatment is influenced by multiple genes interactions. Pharmacogenetic studies will help to determine which drug and dosage are best for each individual patient (1). The aim of our study was to find: 1) Genetic markers influencing susceptibility of paranoid schizophrenia. The polymorphisms of DRD2 (-141C del/ins, Taq1A, egzon8), DAT, 5HT2a, 5HTT_LPR, COMT, MAO A and GRIK3 genes were studied. 2) Relationships between different gene variants and both: the treatment efficacy measured by the PANSS. The group of 117 patients with paranoid schizophrenia consisted of 58 men and 59 women. There were no significant differences between groups according to gender. Males patients had significantly earlier age of onset but duration of illness was similar in both gender groups. Patients were treated randomly with perazine, olanzapine or ziprasidone. The control group consist of 230 healthy volunteers ethnically, gender and age matched. Results: 1) No differences were found in the allelic distribution in investigated genes polymorphisms between the whole schizophrenics and the control group (2). 2) Associations between DAT: A9 allele, DRD2: del 141C allele, DRD2: Taq1A A1 allele, COMT: Met/Met genotype and MAOA: 4VNTR allele (males only) and GRIK3: SER allele with non responding patients were found. The study was conducted under the Pfizer Independent Research Grant no. 2005-0039.

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» NR7-053

POLYMORPHISMS OF HTR2C AND LEPTIN GENES AND METABOLIC SYNDROME AND WEIGHT CHANGE IN PATIENTS WITH SCHIZOPHRENIA TAKING CLOZAPINE MORE THAN ONE YEAR

Kang Shi Hyun M.D., Jongil Lee,M.D., Mina So,M.D., Gahee Lee,M.D., Kwonyoung Kang,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the association between metabolic syndrome and HTR2C polymorphism and weight change during clozapine treatment and LEP polymorphism

SUMMARY:

The use of atypical antipsychotics is associated with metabolic side effects, which put patients with schizophrenia at risk for cardiovascular morbidity. The high inter-individual variability in antipsychotic-induced metabolic abnormalities suggests that genetic makeup is a possible determinant. In this cross-sectional study, we investigated whether genotypes of HTR2C-759C/T (rs3813928), HTR2C-697G/C (rs518147) and LEP-2548A/G (rs7799039) are associated with the metabolic syndrome and weight change during clozapine treatment in patients with schizophrenia using clozapine more than at least one year.

One hundred one Korean patients using clozapine more than one year were genotyped for the HTR2C-759C/T, HTR2C-697G/C, LEP-2548A/G polymorphism and were examined the weight, body mass index, blood pressure, triglycerides, high-density lipoprotein–cholesterol, total cholesterol, glucose and waist circumference. Weight changes after clozapine treatment were extracted from the medical record retrospectively.

Carriership of the variant alleles of HTR2C-697G/C was associated with an increased risk of metabolic syndrome. Carriership of the G alleles of LEP-2548A/G was associated with an increased risk of =7 % weight loss group. Carriership of the A alleles of LEP-2548A/G was associated with an increased risk of =7 % weight gain group.

Our findings suggest that HTR2C-697G/C are associated with an increased risk of metabolic syndrome and variation in the leptin gene are associated with weight change in patients with schizophrenia on long-term clozapine treatment.

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NR7-054

ASSOCIATION BETWEEN THE SEROTONIN TRANSPORTER GENE AND MAJOR DEPRESSIVE DISORDER IN THREE MAJOR ETHNIC GROUPS IN MALAYSIA

Nor Zainal M.B.B.S, Zahurin M, Lian L Hoong, Vijaya L Raj, Elsa H M Mohamed, Loke A Chin

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to obtained new knowledge on serotonin transporter gene association with major depressive disorder in the multiracial population in Malaysia.

SUMMARY:

Serotonin transporter (5-HTT) gene is located on chromosome 17q11.1-17q12. Two polymorphisms of the 5-HTT gene have been identified: a variable number of tandem repeat (VNTR) of 17 base pairs (bp) in the second intron and a 44 bp insertion/deletion in the promoter region (5-HTTLPR). The aim of this study was to investigate the association between major depressive disorder (MDD) and the two polymorphisms of the 5-HTT gene in the three major ethnic groups (Malay, Chinese and Indian) in Malaysia. A total of 298 healthy volunteers (109 Malay, 118 Chinese and 67 Indian) and 239 patients with MDD (52 Malay, 118 Chinese and 70 Indian) were recruited in this study. Significant differences in genotypic frequency were observed in the Indian ethnic group between MDD patients and control subjects for the VNTR polymorphism [genotypes, ?2=8.38, degrees of freedom (df.)=2, P=0.015]. However there was no difference between MDD patients and control subjects with regards to the allelic distribution [alleles, ?2=0.28, df.=1, P=0.60] in the Indian population. No statistical significant difference was observed in the allelic and genotypic frequencies between the MDD patients and control subjects for VNTR polymorphism in Malays and Chinese. In terms of the 5-HTTLPR polymorphism, there was no significant association in either genotypic or allelic distribution between MDD patients and control subjects in all the three ethnic groups in Malaysia [Malay; genotypes, ?2=1.12, df.=2, P=0.57; alleles, ?2=0.93, df.=1, P=0.33; Chinese; genotypes, ?2=0.67, df.=2, P=0.71; alleles, ?2=0.001, df.=1, P=0.98; Indian; genotypes, ?2=2.41, df.=2, P=0.30; alleles, ?2=0.08, df.=1, P=0.78]. All polymorphisms were observed to be in the Hardy-Weinberg equilibrium (HWE) except the genotypic frequencies of the VNTR polymorphism which were not in HWE in Indian population. These preliminary studies indicate that VNTR polymorphism of the 5-HTT gene may confer susceptibility for MDD in the Indian population in Malaysia.

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NR7-055

PRESCRIBING PRACTICES AND SUBSEQUENT SECLUSION AND RESTRAINT: A FAILURE MODE EFFECTS ANALYSIS

David Goldbloom M.D., Ramin Mojtabai, M.D., Ph.D., Michael Serby, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify the role of early psychopharmacological intervention in minimizing the use of seclusion and restraint.

SUMMARY:

Introduction: Strategies and protocols aimed at early assessment and timely behavioral management may be preferable to the use of seclusion and restraint (S&R). Knight suggested that early psychopharmacologic consultation may significantly reduce the need for S&R. Our study seeks to explore the role which early psychopharmacological intervention plays in the subsequent need for S&R. Methods: The study is a case-control study based on retrospective review of existing medical records. Cases were 39 patients admitted on weekends to Beth Israel Medical Center in New York City from July 2001 to July 2006 who experienced a S&R outcome. 39 controls were drawn from patients admitted on the same evenings. For cases, S&R characteristics (need for, number of episodes of, and time to S&R) were recorded. Prescribing practices were classified according to whether prns were made available and whether standing medication was increased, decreased, or left unchanged during the first 48 hours of hospitalization. Analyses were conducted using the SPSS 16.0 software (SPSS Inc., 2007). Results: The age (t=2.6, p=.01) and sex (X2=5.2, df=1, p=.023) of those with S&R outcomes differed from the controls with young males more likely to require S&R. The LOS of those in S&R was longer compared to controls (t=-3.4, p=.001). Those patients whose standing medication was left unchanged during the first 48 hours of hospitalization were 5.5x times more likely to be in restraints than those whose medications were either increased or had medications started (p=.027). Those patients with “high-risk” diagnoses (i.e. Bipolar disorder, Psychotic disorders) were more likely to be in S&R than those with “low-risk” diagnoses (Depressive disorders, Anxiety disorders) (X2=14.2, df=1, p<.001). These “high-risk” patients were more likely to be written for prn medication for agitation (X2=8.8, df=1, p=.006). Lastly, those written for prns averaged 1.16 episodes of S&R while those not written for prns averaged 0 (t=-2.2, p=.032). Conclusions: The Beth Israel psychiatric emergency room and weekend treatment team are successfully identifying patients likely to require S&R by their age, gender, and diagnosis and ensuring that they receive prn medication. On the other hand, more aggressive use of standing medications in the first 48 hours may decrease episodes of S&R.

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NR7-056

ATTITUDE OF PATIENTS AND THEIR CAREGIVERS TOWARDS PSYCHOTROPIC MEDICATIONS: A STUDY FROM INDIA

Sandeep Grover, Subho Chakrabarti,M.D., MRCPsych.; Shikha Tyagi, Aarti Sharma

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the attitude of patients and their caregivers towards psychotropic medications.

SUMMARY:

Introduction: Treatment adherence is influenced by various factors. One of the important patient characteristic which has been reported to influence treatment adherence is their attitudes & beliefs towards medications. This study evaluated the attitudes & beliefs towards medication of patients and their primary caregivers. Methods: 200 patients and their caregivers attending a busy psychiatry outpatient Department of a general hospital psychiatric unit were evaluated on a self rated questionnaire for their attitudes & beliefs towards medication. Results: Most of the patients considered psychotropic medications to be the most appropriate method of treatment of psychiatric ailment (70.5%), considered them to cause more benefit then harm (66.5%), capable of preventing relapse of symptoms (71%) and considered them better then other treatment

modalities (78.5%). About two-third of them considered psychotropic medications were only capable of only calming down the patient (66%). About half of them considered them to be costly (53%). About one third of the patients considered psychotropic medications to be addictive (35.5%) and to cause abnormal level of dryness, heat or coldness of the body (28.5%). There was no statistically significant difference between the attitude of patients and their caregivers. Conclusion: Majority of the patients and their caregiver have positive attitude towards psychotropic medications. However, about one third of them have negative attitude towards psychotropic medications. Implications: it is important to identify and address the negative attitude towards psychotropic medications to improve treatment adherence.

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» NR7-057

PERSONAL AND OCCUPATIONAL CHARACTERISTICS OF WORKERS PRESENTING TO A SPECIALIZED WORKERS' COMPENSATION BOARD PSYCHOLOGICAL TRAUMA PROGRAM

Jennifer Hensel M.D., Ash Bender, MD., Jason Bacchiochi, Ph.D., Carolyn S. Dewa, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to discuss the importance of psychological sequelae following workplace trauma. The participant will also understand the role of a specialized Workers' Compensation Board psychological trauma assessment and treatment program and appreciate some of the characteristics of workers presenting to such a program.

SUMMARY:

Background: Traumatic events in the workplace can lead to disabling psychological sequelae which may impact an individuals' ability to return to work. The Psychological Trauma Program (PTP) in Toronto, Canada is a specialized provincial Workers' Compensation Board assessment and treatment program for workers who are experiencing psychological symptoms after a traumatic workplace event. Knowledge of the characteristics of the clients presenting to this program would be useful for service needs identification and intervention development. Purpose: This study will describe the diagnoses and injury severity of workers seen at the PTP. Methods: Data from the PTP were analyzed for all clients referred from 1999 to 2006 within one year of the traumatic event (n=593). Occupations were coded according to the Canadian Classification and Dictionary of Occupations (CCDO). Diagnoses were determined using the Structured Clinical Interview for DSM Disorders (SCID-I version 2.0). Descriptive statistics (ANOVA, Pearson Chi-square) were used. Results: The majority of clients were 25-55 years old (85.7%), male (75.7%), worked in construction (27.7%) or manufacturing (20.8%), had been at their event employer more than 2 years (57.8%) and had experienced an accident (69.8%). Diagnoses were primarily PTSD (47.5%) and mood disorders (27.3%). Diagnosis did not significantly differ across age, sex or occupation. Injury severity was significantly associated with diagnosis ($p<0.05$), occupation ($p<0.001$), weeks with event employer ($p<0.05$), event code (accident vs assault, $p<0.001$) and event type (single vs repeated, $p<0.01$). Conclusion: Most workers seen at the PTP have a diagnosis of PTSD. Event-related factors and occupation are important determinants of injury severity. Moreover, injury severity appears to be related to diagnosis. Future research will need to further characterize these clients and determine how these factors contribute to return-to-work outcomes.

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» NR7-058

ONE-YEAR HOSPITAL UTILISATION AND LONG-ACTING INJECTABLE RISPERIDONE: A MIRROR IMAGE STUDY WITH A NATIONAL CLAIM-BASED DATABASE IN TAIWAN

Su Kuan-Pin M.D., Kuan-Pin Su, M.D., Ph.D., Hui-Chih Chang, M.H.A., Shih-Jen Tsai, M.D., Chao-Hsiun Tang, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand RLAI treatment is associated with a reduction of hospital service utilization in Taiwan and acquire the knowledge of using the mirror image study design and the national claim-based database for pharmacoeconomic studies.

SUMMARY:

Poor compliance to antipsychotic medication, which would potentially lead to disease relapse, has been challenging for psychiatrists when treating schizophrenia. Long-acting injection of antipsychotics is an appropriate alternative since better compliance improves treatment outcomes. Risperidone long-acting injection (RLAI) is the first licensed long-acting injectable atypical antipsychotic agent and has recently been reported cost effective by reducing total admission number and in-patient days in a community-based in-patient setting. The national claim-based database has never been used in any mirror-image study for RLAI.

The data source used for this one-year mirror image study was the Psychiatric Inpatients Medical Claims Data (PIMC) from the National Health Research Institute (NHRI), Taiwan. The PIMC compiled all the health care utilization records during 1996-2006 for patients who had at least one psychiatric hospitalization during 1996-2001. Patients with schizophrenia who were continuously treated with RLAI for at least 12 months were included. The differences in number of acute admissions, hospital days, and emergency room visits between the pre- and post-RLAI periods were compared.

A total of 108 from 91104 patients met the inclusion criteria. As compared to the one-year pre-RLAI period, the total number of acute admissions was reduced by 55% (80 vs. 36 times, $p=0.0003$) and total hospital stays were reduced by 48% (4106 vs. 2126 days, $p=0.0002$) in the six-month post-RLAI period. A reduced number of emergency room visits was also observed (55 vs. 25 times) but was not significantly different ($p=0.13$).

The study design of mirror-image has advantages of assessing real-world practice and having patients as their own controls. However, the effect of long-acting injectable agents could be overestimated due to the selection bias and the exclusion of non-compliant patients.

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» NR7-059

NEEDS OF PATIENTS WITH SCHIZOPHRENIA: A STUDY FROM INDIA

Parmanand Kulhara M.D., Ajit Avasthi, M.D., Sandeep Grover, M.D., Pratap Sharan.,Ph.D., Parveen Sharma, M.D., Sameer Malhotra, M.D.,

Sapna Gill, M. Phil.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand the needs of patients with schizophrenia in Indian context and how do they compare to international literature

SUMMARY:
Introduction: Assessment of needs of patients with schizophrenia and their caregivers is closely linked to psychosocial rehabilitation, but data in respect of needs of patients from India are lacking. This study evaluates the needs of schizophrenia patients and also assesses perspective of the relatives of the patients with regard to the needs of the patients. Methods: Needs of 100 consecutive patients with ICD-10 diagnosis of schizophrenia were assessed by the Camberwell Assessment of Needs (CAN). CAN was also administered to the caregiver to assess their perception about the needs of the patients. Results: The mean number of needs reported by patients was 8.14 and that by caregivers was 6.59, out of which more than two-third were unmet needs according to the patients and their caregivers. The most commonly reported need by both patients and their caregivers was need for welfare benefits. There was difference in other commonly identified needs by the patients and their caregivers. The most commonly reported area of needs identified by the patients in decreasing frequency were need for psychotic symptoms, psychological distress, information about the condition and the treatment, money, company of others , occupation and intimate relationships. The most commonly reported area of needs identified by the caregivers in decreasing frequency were need for safety to self, intimate relationships, physical health, marriage, information about condition and treatment, psychological distress, and psychotic symptoms. Conclusions: Most of schizophrenia patients had needs regarding welfare benefits, education about illness and psychological distress and their relatives shared these endorsements. Help provided by the government or Non-governmental organizations (NGOs) in most areas was negligible. There are some differences between the needs of our patients and schizophrenia patients from Western countries. Small sample size is a limitation of the study.

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» NR7-060

METABOLIC TESTING RATES IN THREE STATE MEDICAID PROGRAMS AFTER FDA WARNINGS ON ANTIPSYCHOTIC DRUGS AND DIABETES

Elaine H. Morrato, Dr.P.H., M.P.H., Benjamin Druss, M.D. M.P.H., Daniel M. Hartung, Pharm.D., M.P.H., Robert J. Valuck, Ph.D., Richard Allen, M.S., Elizabeth Campagna, M.S., John W. Newcomer, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to understand trends in diabetes and dyslipidemia screening and choice of antipsychotic in fee-for-service Medicaid patients initiating second-generation antipsychotic drugs after the FDA warning.

SUMMARY:
Objective: In 2003, the Food and Drug Administration (FDA) required a warning on diabetes risk for second-generation antipsychotic (SGA) drugs. Our aim was to characterize associations between the FDA warning and baseline glucose and lipid testing and individual SGA drug selection.
Design: Interrupted time series analyses of trends in metabolic testing were performed across the three study periods (Pre-Warning, Warning, and Post-Warning) using laboratory claims for an incident cohort of fee-for-service Medicaid clients starting SGA medication in California, Missouri, and Oregon between 1/1/02 and 12/31/05 and compared to a propensity-matched control cohort of albuterol-treated patients. Changes in SGA prescribing practices were similarly evaluated for each drug using time series analyses.
Main Outcome Measures: Monthly rates of baseline serum glucose and lipid testing for SGA-treated and propensity-matched albuterol-treated patients; monthly share of new SGA prescriptions for each SGA drug.
Results: Initial testing rates for SGA-treated patients were low: 27% (glucose) and 10% (lipids). The warning was not associated with an increase in glucose testing among SGA-treated patients and only a marginal increase in lipid testing rates (1.8%, $p = 0.02$). Testing rates and trends in SGA-treated patients were not different from background rates observed in the albuterol control group. New use of olanzapine (higher metabolic risk) declined during the warning period (19.9% annual share decline, $p<0.001$). Changes in the use of aripiprazole, quetiapine, risperidone, and ziprasidone were not associated with the warning.
Conclusions: Baseline glucose and lipid testing for SGA-treated patients was infrequent and underwent little change relative to the FDA diabetes warning. The warning was associated with a change in SGA drug selection consistent with intentions to reduce metabolic risk.This research was supported by Pfizer, Inc.

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» NR7-061

PREDICTIVE FACTORS OF PSYCHIATRIC ADMISSIONS' LENGTH OF STAY AND EARLY READMISSIONS

Rosa Quelhas M.D., Tiago Rodrigues, M.D., Henrique Pereira, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should recognize the importance of integrating the impact of predictive factors of admissions' length of stay (LS) in early readmission (ER) risk. The participant should consider assessment instruments to identify subjects with higher risk for prolonged LS or ER, and acknowledge the importance of this assessment in targeting at-risk individuals that require enhanced therapeutic intervention, in order to prevent poorer clinical courses.

SUMMARY:
Objective The optimization of acute psychiatric inpatients' length of stay (LS) is one potential way to reduce the costs of mental health care services. Different factors have been associated with LS, including treatment-related factors. However, the reduction of the LS should not jeopardize patients' clinical stabilization, which may be assessed by the inpatient early readmissions (ER). The authors' main objective was to define predictive factors for both the LS, and the risk of ER (1-year after discharge) of patients admitted in a psychiatric inpatients unit of the Hospital Magalhães Lemos (HML), Portugal.
Method: This prospective longitudinal study includes social, clinical and institutional variables of inpatient admissions between January 2007 and March 2008. A clinical interview was performed on the first three days after admission. Patients were assessed with BPRS-A scale (and BDI or YMRS, if indicated). On the date of discharge, the psychiatrist filled in a patient's problems' checklist

report. Patients with discharge before October 2007 were followed up during 1 year to detect ER.
Results: Analysis included 200 subjects, with mean age of 41 years. Median of LS was 17 days. Multivariate analysis showed that the diagnosis and the illness severity were the strongest predictors of LS, followed by the presence of specific clinical/social problems, the number of previous admissions, the age or marital status, and the therapeutic team. On the other hand, short LS, "major mood disorder" diagnosis, the report of problems, and ambulatory visit non-compliance predicted a higher risk of ER.
Conclusion: The identification of patients at risk for increased LS or ER helps to target them for enhanced therapeutic interventions and better aftercare measures (e.g., psychoeducation). Authors suggest that the initial inpatient assessment should include an illness severity scale and a standardized problems' checklist, in order to guarantee individualized and focused intervention.

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» NR7-062

SPECIALTY CARE COSTS IN CONTINUOUSLY ENROLLED INDIVIDUALS WITH BIPOLAR DISORDER ARE HIGHER THAN THOSE WITH INDIVIDUALS WITH DEPRESSION OR DIABETES

Mark Williams M.D., Nilay Shah, Ph.D., Amy Wagie, Mark A. Frye, M.D., Douglas Wood, MD

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:
i. Identify the cost of bipolar disorder to employers.
ii. Compare costs of bipolar disorder to employers with that of patients with depression and those with diabetes, and
iii. Recognize that all specialty costs are higher in bipolar disorder than depressed or diabetic patients.

SUMMARY:

Background: A future goal of healthcare economics is quality care at reduced cost. Healthcare resource utilization has been an increasing focus in bipolar disorder.
Method: Administrative claims of individuals with bipolar disorder (BPD) who were continuously enrolled for four years (2004-2007) were identified. We compared resource utilization and costs for these BPD patients (n=127) to that of continuously enrolled individuals with depression (n=1344) and diabetes (n=1,376). Resource utilization (total costs, specialty care costs, specialty care visits, outpatient psych costs, and outpatient psych visits) was compared across groups using bootstrapping to account for skewed nature of cost and utilization data.
Results: Over the 4-year period, the BPD patients had significantly higher ($p<0.05$) mean total annual costs compared to the entire population. BPD patients had non significantly higher mean annual costs compared to the depression and diabetes patients.. However, BPD patients had significantly higher (34% and 29%) specialty care costs compared to those with a diagnosis of depression and diabetes respectively (both $p<0.05$). Interestingly, patients with BPD had more than double the spending for both inpatient and outpatient psychiatry care compared to patients with depression ($p<0.05$).
Conclusions: Bipolar disorder patients with continuous enrollment in an employer-based health plan may represent those less likely to be disabled, yet they still show significantly higher specialty costs than those patients with depression as well as patients with diabetes. This data suggests that an intervention aimed at improving care in mental health specialty areas may be fruitful, and it should be accompanied by attention to an exploration of all specialty costs for bipolar patients.

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» NR7-063

HISTORICAL EVOLUTION OF DISSOCIATION CONCEPT: ORIGIN OF MULTIPLE PERSONALITY

Agueda Rojo M.D., José L. Fernández, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to know the mecanism of dissociation that was proposed by Pierre Janet and to establish a correlation with dissociative identity disorder of nowadays. Knowing the context where this psychopathological concept arose and knowing the historical evolution of this concept, increases our psychopathological knowledge and this help us to understand the becoming that this disorder has undergone

SUMMARY:

Knowing the historical-political, cultural and philosophical context in which the Dissociative Identity Disorder (DID) emerged and the fate which took place all along the history of psychiatry, is necessary to understand the becoming of this disorder, as we call nowadays.
If we want to research the origin of this disorder, we have to go back to the beginning of the "First dynamic psychiatry" so called by Ellenberger, around mesmerism and the animal magnetism, that will provide the foundations of the later artificial sonambulism, basis of the hypnosis. Along a evolutionary and conceptual line, we would be able to shape, briefly, a trajectory following a path from mesmerism to hypnosis, doubling or splitting of personality and finally, the dissociation concept. This is ascribed to Pierre Janet, and his "désagrégation psychologique" concept, though there are others authors that defend the priority of Sigmund Freud.
in this research, the doubling concept (dédoublement) and the nature of personality in the 19th century are analyzed, as well as others psychopathological concepts arisen along the historical path going to the moment when pierre Panet stated the "memory law" and distinguished between the consecutive and simultaneous personalities. The core of this "désagrégation" is the emergence of two phenomena in the human nature. One of them is made up of the common personality; the other one is made up of an anormal personality, that can be divided into others personalities in turn, and that is different from and completely ignored by the first one. The origin of did goes back to the end of the 19th century, in France, when the "désagrégation" concept emerged. Nowadays, interest in this pathology which the psychological basis is the dissociation, is reborn and this disorder is conceived of the same way as Pierre Janet considered it, in fin-de-siècle.

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» NR7-064

SOFTWARE SUPPORTED SEMI-AUTOMATIC GENERATION OF LABORATORY REPORTS IN A NEUROCHEMICAL LAB

Anton Köstlbacher M.A., Anton Köstlbacher, Alexander Haas, Ralf Köber, Ekkehard Haen

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize that the most important part of writing meaningful lab reports in therapeutic drug monitoring (TDM) of psychotropic drugs is the interpretation of measured concentrations using relevant, valid and reliable information sources. This can be supported by new laboratory information systems.

SUMMARY:
A typical task of neurochemical laboratories is the therapeutic drug monitoring (TDM) of psychotropic drugs. Beneath the actual process of detection and estimation of drug concentrations in serum samples, the most important part is the interpretation of the analytically measured values which can be a major difficulty for attending physicians.
Aim of the presented project was to create a fully web based, easy to use laboratory information management system (LIMS) for research oriented neurochemical laboratories. The developed system represents the whole workflow of the lab with a strong focus on the creation of meaningful lab reports. It acts as a decision support system (DSS) and uses different data sources, e.g. a drug interaction database, a pharmaceutical database and patient data. The lab reports are created semi-automatically including a text comment, which is generated from text modules. The resulting report is always reviewed by physicians and pharmacists in the lab.
Now in production use, the software fulfils all requirements: It helps to manage the workflow including the methods and machines in the lab. It supports the staff with the creation of reports and provides additional relevant drug data. As it is web based the software allows time and location independent writing of reports, which is well adopted. The software also provides the anonymized export of all data (excel/SPSS) for later statistical analysis, which is especially of great importance for research oriented labs.
Ongoing development is mainly focused on integrating more data sources like a semantic wiki for additional pharmaceutical data and different drug interaction databases available on the market. The presented project is an interdisciplinary effort involving people from different domains like pharmacology, psychiatry, bioinformatics and information science.

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» NR7-065

COST EFFECTIVENESS OF RISPERIDONE LONG ACTING INJECTION IN SEVERE AND ENDURING PSYCHIATRIC DISORDERS: A 22 MONTH MIRROR IMAGE ANALYSIS

Utpal Goswami M.B.B.S, H. Rao, MBBS

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to identify and implement cost-conscious and effective strategies in the long term management of chronic and severely ill patients with psychoses, by promoting adherence.

SUMMARY:
Objective: Cost-effective prescribing is crucial in managed care of severe and chronic mental disorders. Though favoured by most guidelines, atypical antipsychotics are costlier than the typicals. While depot antipsychotics may help addressing non-adherence, multiple relapses and chronicity, risperidone long acting injection (RLAI) is the only atypical agent. We evaluated the cost-effectiveness of RLAI compared with the non-RLAI treatments.
Method: This was a study of 32 adult patients receiving RLAI who had a previous non-RLAI treatment phase with an oral and/or a depot antipsychotic for comparison ('mirror-image'). Data were collected from all available records. Cost effectiveness measures included direct cost for medications, number and length of hospitalisations, emergency care provisions, regular out-patient appointments, community multidisciplinary team services and care plan reviews. The cost for each parameter was calculated based on reference costs per unit of activity.
Results: The mean treatment period was 22.57 months for pre- and post-RLAI phases. During RLAI treatment phase there was a 3-fold reduction in the mean number of admissions (μ=0.53); nearly 5-fold reduction in the mean duration of inpatient stay (μ=11.4 days); increase in the community visits (μ=67.3). There was also a decline in emergency care components: Crisis Team call-outs (2.5 fold, μ=0.3), domiciliary visits (33%; μ=0.3) and mental health act assessments (nearly 4-fold; μ=0.18). During RLAI phase, the total cost per patient reduced annually from pre-RLAI £15944.59 (direct=£1367.52; indirect=£14577) to £6952.35 (direct=£2985.6; indirect= £3966.75), thus saving £8992.24 per patient per year.
Conclusions: RLAI still appears to be a cost effective treatment option in difficult to treat psychoses. Several measures in this study are proxy indicators of clinical effectiveness, though lack of baseline data precludes comparison.

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» NR7-066 - WITHDRAWN

» NR7-067

EXECUTIVE FUNCTIONS AS AN IMPORTANT TARGET OF INTERVENTION IN BRAZILIAN SAMPLES OF PATIENTS WITH SCHIZOPHRENIA

Arthur Berberian M.S., Alessandra G S Capovilla, Ph.D, Bruna T. Trevisan, José Ari C Oliveira, M.D., Ph.D., Ary G. A. Araripe Neto, M.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to learn that since cognitive impairment is a core feature of schizophrenia, being executive functions (EF) an important ability in this context, no intervention can be considered effective unless it also targets this domain. The present study revels that first degree relatives present similar but less severe patterns of executive deficits than patients. EF are an important target for the development of new strategies of intervent

SUMMARY:
Many studies show that cognitive deficits are core characteristics of schizophrenia, including executive functions. These deficits are present also in first-degree relatives of schizophrenic patients, probably related to a familial loading for schizophrenia. However few studies have replicated finds of specific patterns of impairments in a Brazilian sample. This study aimed to assess executive function in schizophrenic patients and their first-degree relatives with a set of tests comprising the specific components of executive function. Method: Seventeen outpatients were recruited from a Brazilian particular psychiatric clinic. All patients met the DSM-IV criteria for schizophrenia and were on atypical antipsychotic medications. Seventeen siblings and seventeen healthy control subjects participated, all nonpsychotic according to DSM-IV criteria. All participants were assessed using Computerized Visual

and Auditory Working Memory, Computerized Stroop Test, Computerized Semantic Generation Test, Trail Making Test – Form B, Tower of London Test and FAS Verbal Fluency Test. It was carried out two sessions of administration of the tests during the regular period of treatment. Results: Significant differences were found between performances of schizophrenic and control groups in auditory working memory, selective attention, and planning. The first-degree relatives reached a medium average between patients with schizophrenia and healthy control subjects. Conclusions: Since cognitive impairment is a core feature of schizophrenia, no intervention can be considered effective unless it also targets this domain. These findings show executive impairments in schizophrenic patients and that siblings present similar but less severe cognitive deficits. These results are consistent with other studies and might be useful for a better understanding of the cognitive problems which occur in schizophrenia. To our knowledge, this is the first study to compare specific executive function components between patients and siblings in Brazil.

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» NR7-068

TREATING DEPRESSION IN TEMPORAL LOBE EPILEPSY: A CONTROLLED CLINICAL TRIAL OF COGNITIVE BEHAVIORAL THERAPY VS PHARMACOTHERAPY

Daniel Crail M.D., Alberto Herrera-Melo, Psy.D., Mario López-Gómez, M.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the relevance of treating depression in patients with epilepsy. The participant should know the pertinent issues to consider cognitive behavioral therapy as an option for the treatment of depressive symptoms in patients with temporal lobe epilepsy.

SUMMARY:

The incidence of mood disorders is higher among patients with epilepsy. The combination of seizures with depressive symptoms could result in greater disability among patients with both burdens. Objective: To compare the efficacy of CBT with antidepressant medication for the treatment of depression in patients with temporal lobe epilepsy (TLE). Methods. We conducted a controlled clinical trial with TLE outpatients treated in the National Institute of Neurology and Neurosurgery of Mexico. Psychiatric diagnosis was established using the Mini International Neuropsychiatric Interview (MINI). Forty-two patients meeting the DSM-IV criteria for MDD, with no other axis I disorder excluding anxiety, were enrolled and assigned randomly to one of two therapeutic options. Twenty patients were assigned to receive 16 structured group sessions of CBT (Group 1); Group 2 (n=22) received an SSRI (sertraline, citalopram or fluoxetine). Beck Depression Inventory (BDI) and Quality of Life in Epilepsy Inventory (QOLIE 31) were completed by each participant at the beginning, at week 8 and at the end of the trial (week 16). Results: There were no significant differences in baseline characteristics between groups. Linear regression analysis for repeated measures showed a positive effect on depressive symptoms in both groups at 8 weeks (F 15.9; $p<0.000$), but CBT resulted in significantly greater improvement in depression severity ($p<0.000$) at the end of the study. The effect on global QL was similar for both groups ($p=0.31$), although the QOLIE´s subscale analysis reported significative differences in seizure worry, emotional well-being, cognitive effects and overall perception of QL in the CBT group. Conclusions: The current findings provide preliminary evidence that CBT may be helpful in improving depression and QL in patients with TLE. The better outcome of the CBT group could be explained by a poor treatment adherence and more side effects in the antidepressive group.

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» NR7-069

PHENOMENOLOGICAL DIVERSITY OF HUNTINGTON'S DISEASE WITH DOMINATING PSYCHIATRIC SYMPTOMS :CHALLENGES TRADITIONAL CONCEPTS IN NEUROLOGY AND PSYCHIATRY

Cho D.Hwan M.D., Ho-Joon Je, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand that the traditionally emphasized signs of huntington's disease, "chorea plus dementia," may be inadequately narrowed core features for diagnostic guidance in the early stages of the disease.

SUMMARY:

Purpose: This article is to present a case with huntington's disease with various psychiatric symptoms and multiple psychiatric diagnosis.

Methods(Case presentation) A 44-year-old right handed korean male patient was admitted because of anxiety, recent memory loss, difficulties of immediate retention and recall and dull headache after car accident at April 23 2003. Brain MRI, chest X-ray, EKG, EEG and chemical labs(CBC, LFT, electrolyte, UA) was checked. Brain MRI showed cerebral atrophy and retrocerebellar arachnoid cyst but other findings were normal range and there were no clinical corelation to his symptoms. No medication was given and observed. he was diagnosed 'Diagnosis or Condition deferred on Axis I', discharged and he stoped OPD follow up.

He revisited maryknoll general hospital at may 18 2006. He complained 'insomnia, slurred speech, irritability, anger burst out' and His mother and sister said he had abnormal monements as a choreatic hyperkinesia and a dysarthria, a seesaw gait disturbance for 1 months. He didn't recognize his abnormal movements and behave like a normal person and blame others. He was evaluated psychologically by Structured Clinical Interview for DSM-IV Axis I Disorder(SCID-I), MMPI, SCL-90R, SCT, BDI, STAI-I, STAI-II, K-MMSE, BGT, DAP, KTF, K-WAIS, Rey-Kim, Rorschach, TAT, Stroop and TMT and checked magnatic resonance imaging(MRI) of the brain and Electroencephalography repeatedly(18 may 2006, 22 oct 2008). Brain MRI shows cerebral atrophic change especially enlargement of both lateral ventricles and degeneration change on parietal lobe, caudate nucleus.

Result: Neurologist examined this patient and diagnosed 'Huntington's disease'. The patient showed a great variety of psychiatric symtptoms and Neuropsychological findings. Psychiatrists diagnosed anxiety disorder , dysthymic disorder, Major depressive disorder, single episode, Ganser syndrome, psychotic disorder NOS, Dementia due to huntingtom's disease. His medication was changed according to his symptom change(antidepressants-Paroxetine to antipsychotics-Risperidone). His psychiatric symptoms were relieved and the situation of his life was improved(social relationship and life quality).

Conclusion: Huntington's disease have a phenomenological diversity of initial stage. From this point of view, the traditionally emphasized signs of huntington's disease, "chorea plus dementia," may be inadequately narrowed core features for diagnostic guidance.

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» NR7-070

CORRELATIONS OF SOMATIC AND BRAIN METABOLIC ALTERATION IN NONHUMAN PRIMATES UNDER VARIABLE FORAGING DEMAND CONDITION

Dunyue Lu M.D., Jeremy D. Coplan, MD, John Kral, MD, PhD, Prakasi Chandra, MD, Aaron Pinkhasov, MD.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the corelationship between brain and somatic of metabolic changes after stress in monkeys.

SUMMARY:

Introduction: Stress has been postulated to cause the metabolic syndrome and our previous study has shown that variable foraging demand (VFD) rearing resulted in higher weight, BMI and abdominal circumferences. We have also shown an enduring effect of VFD rearing on magnetic resonance spectroscopy imaging (MRS) measures considered reflective of neuronal integrity and metabolism in brain regions. We hypothesized that stress-induced changes of neuronal metabolism in brain is related with somatic metabolic syndrome (such as obesity and insulin resistance).

Methods: Thirteen Bonnet Macaque male reared under variable foraging demand (VFD) conditions and 9 age- matched control subjects underwent magnetic resonance spectroscopic imaging (MRSI). Blood chemistry, morphometry and Clamps were conducted according to experimental design.

Results: On MRSI, VFD-reared monkeys exhibited significantly reduced NAA/Cr ratios in the right caudate nucleus in comparison to control ($p<0.007$). The relationship between caudate NAA and BMI is significantly stronger in Non-VFD than in VFD monkeys. ($p<0.05$). In VFD monkeys, the blood level of LDL is negatively correlated with the NAA level of right caudate nucleus. However, in normal monkeys, there was no similar finding. Insulin resistance was found in VFD monkeys.

Conclusion: These data demonstrate that stress-induced somatic metabolic changes may be mediated by the changes of stress-induced metabolic changes in neuronal circuits in the brain.

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» NR7-071

RELATIONSHIP BETWEEN SLEEP PATTERNS AND CLINICAL SYMPTOMS IN ELDERLY HOSPITALIZED PATIENTS WITH DEMENTIA

Kaloyan Tanev M.D., Marilyn Sablosky, M.S., Donal O'Hanlon, M.D., Caleb J. Siefert, Ph.D., John D. Matthews, M.D., Lawrence T. Park, M.D., Maurizio Fava, M.D., Adrienne O. van Nieuwenhuizen, B.A., Nelson Tauro, Andrew Winokur, M.D.,Adrienne O. van Nieuwenhuizen, B.A.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize that there are sleep/wake cycle abnormalities in hospitalized patients with dementia

SUMMARY:

Sleep/wake cycles are compromised in dementia. Most research on sleep in dementia has involved community dwelling and nursing home residents. We studied 26 dementia inpatients hospitalized for acute behavioral and psychiatric symptoms. We used activity monitors (actigraphs) and clinical symptom measures. We compared actigraphy-derived sleep parameters (sleep efficiency, total sleep minutes per down period or time in bed) to the neuropsychiatric inventory (NPI). For each patient, we chose the first time during hospitalization when sleep data were available on the night preceding the NPI data. We analyzed the results for significant correlations, setting the level of significance at P=0.05. Total sleep minutes (derived actigraphically) significantly correlated with the NPI subscales of nighttime behaviors (R= -0.46, P=0.02) and aberrant motor behaviors (R= -0.40, P=0.05); they correlated nonsignificantly with the NPI subscales of hallucinations (R= -0.31, P=0.13) and disinhibition (R= -0.32, P=0.11). Sleep efficiency significantly correlated with the NPI subscales of aberrant motor behaviors (R= -0.60, P=0.00), nighttime behaviors (R= -0.45, P=0.03) and disinhibition (R= -0.45, P=0.02); and nonsignificantly with the subscales of hallucinations (R= -0.30, P=0.14) and depression (R= 0.32, P=0.11). Sleep latency significantly correlated with agitation (R= 0.56, P=0.01), anxiety (R= 0.47, P=0.02), irritability (R= 0.42, P=0.04) and nighttime behaviors (R= 0.50, P=0.01). We also compared the first and last available NPI assessments. We found significant differences in the total NPI scores, and in subscales of delusions, hallucination, agitation/aggression, depression/dysphoria, apathy/indifference, and irritability. Aberrant motor behaviors and nighttime behaviors did not differ significantly. Similarly, actigraphy-derived total sleep minutes and sleep efficiency did not differ from beginning to end of hospitalization. We conclude that in hospitalized patients with dementia more significantly disrupted sleep patterns are associated with more significant clinical symptoms at the beginning of hospitalization. Whereas standard care led to improved clinical symptoms, it did not lead to significant change in sleep-related behaviors or actigraphy-derived sleep parameters.

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» NR7-072

IMPAIRED RECOGNITION OF EMOTIONAL PROSODY IN ADOLESCENTS WITH BORDERLINE PERSONALITY DISORDER: A COMPARATIVE STUDY

Stephanie COLIN M.D., PHAM-SCOTTEZ Alexandra, M.D., BERTOZ Sylvie, Ph.D., ROBIN Marion, M.D., CURT Florence, M.D., CORCOS Maurice, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to acknowledge the reduced capacity of borderline adolescents to recognize auditory emotional cues, to acknowledge that borderline personality disorder is a reliable diagnosis in teenagehood, and to address specific emotional defects while treating these patients with psychotherapy –based treatments.

SUMMARY:

Communication of one's emotions is achieved mainly through facial expression and voice prosody. Although emotional dysregulation is now acknowledged as a core characteristic of the borderline personality disorder (BPD), few findings have shown a deficit in emotion recognition capacities among these patients. These studies were mostly exploring facial expressions recognition, and none of them were realized in adolescent population.

Our study's aim was to explore the auditory emotion recognition capacities of adolescents with BPD. We therefore constructed a computerized paradigm using short sound samples of previously validated emotional sounds, exploring 5 emotions (disgust, fear,

sadness, happiness, anger) and a neutral condition. Half of the 96 sound samples were words and half were interjections.
We compared a group of 23 adolescents with BPD (mean age 16.7) to a group of 22 healthy adolescents (mean age 16.8), and compared their recognition of both facial and prosodic emotion recognition. In both groups, Axis I and II diagnosis were assessed using K-SADS and SIDP-IV, auditory recognition was assessed with the MultiSound Affect Recognition Task and facial recognition with the MultiMorph Affect Recognition Task.
Results show a significantly impaired global capacity of emotional prosody recognition in the borderline group. When emotions are studied separately, results show a specific significant impairement of the recognition of disgust in the borderline group.Moreover, when words and interjections are studied separately, borderline adolescents are found to have a significantly impaired recognition of words, compared to the healthy group.
These findings support the hypothesis of an impairment of emotional recognition in borderline personality disorder, and stress the importance of the auditory processes in emotion recognition.Specific impairement of the recognition of disgust in BPD is further discussed with clinical and theoretical lightnings.

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» NR7-073

DIRECT AND INDIRECT EFFECTS OF THE TEMPERAMENT AND CHARACTER ON ALEXITHYMIA: A PATHWAY ANALYSIS WITH DEPRESSION AND ANXIETY

Seog Ju Kim M.D., Yu-Jin Lee, M.D., Ph.D., In Hee Cho, M.D., Ph.D., Jee Hyun Ha, M.D., Ph.D., Jong-Chul Yang, M.D., Ph.D., Sang-Keun Chung, M.D., Ph.D., Seong-Jin Cho, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to 1) understand both trait-dependent and state-dependent concept of alexithymia, 2) understand the pathway from the temperament and character to alexithymia, 3) recognize the direct association between alexithymia and the temperament and character and 4) recognize the mediating effects of depression and anxiety on the relationship between alexithymia and the temperament and character.

SUMMARY:

Objective: Alexithymia has been conceptualized as a trait-dependent personality construct. However, it has also been suggested to be a state-dependent phenomenon closely related to common psychiatric symptoms such as depression or anxiety. We aimed to assess the pathway from the temperament and character to alexithymia using depression and anxiety as mediators in psychiatrically healthy subjects.Method: Among 379 community-based subjects, 334 subjects (130 male, 204 female, 42.8±13.7 years), whose psychiatric health was verified by SCID-IV, completed the Toronto Alexithymia Scale (TAS), the Temperament and Character Inventory (TCI), the State-Trait Anxiety Inventory (STAI) and the Center for Epidemiological Studies-Depression scale (CES-D). Based on the linear regression analysis, the schematic models for the pathway analysis from TCI scores to TAS scores were made using Amos program. Results: Low Reward dependence (RD), Self-directedness (SD), Cooperativeness (CO) and high STAI had direct effects on TAS total score. SD had also an indirect effect via STAI on TAS total score. On TAS factor 1 (difficulty in identifying feeling), RD, SD, Self-transcendence (ST), STAI-T and CES-D had direct effects. SD had also an indirect effect via STAI-T and CES-D on TAS factor 1. On TAS factor 2 (difficulty in expressing feeling), Novelty-seeking (NS), Harm avoidance (HA), RD, SD and CO had direct effects. On TAS factor 3 (externally oriented thinking), RD and SD had direct effects.
Conclusion: We report that low RD and SD had direct effects on all three factors of alexithymia and that low SD had also an indirect effect on alexithymia via anxiety or depression, especially on the identification of feeling. Current results suggest that although alexithymia is affected directly by trait-dependent personality, state-dependent psychiatric symptoms may also have mediating effects on the relationship between alexithymia and personality.

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» NR7-074

A LONGITUDINAL STUDY OF THE 10-YEAR COURSE OF IMPULSIVE SYMPTOMS IN BORDERLINE PERSONALITY DISORDER

D. Bradford Reich M.D., Mary C. Zanarini, Ed.D., Frances R. Frankenburg, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the different types of impulsive symptoms found in Borderline Personality Disorder and understand the expected course of these symptoms.

SUMMARY:

Objective: The purpose of this study was to determine the course (i.e. time-to remission) of the impulsive symptoms of borderline personality disorder (BPD).
Method: The study assessed the prevalence of the 17 individual symptoms contained in the Impulse Section of the Revised Diagnostic Interview for Borderlines (DIB-R) at baseline and then over 5 contiguous 2-year intervals in subjects meeting DIB-R and DSM III-R criteria for BPD (N=290) and in 72 subjects meeting DSM-III-R for another personality disorder (and neither criteria sef for BPD).
Results: Among borderline patients, all 17 symptoms studied showed sharp patterns of decline over time and were reported at 10-year follow-up by less than 15% of the patients who reported them at baseline. The median time-to-remission for 10 of 11 forms of impulsivity that tend to involve other people was sometime between baseline and two-year follow-up. These ten forms included: promiscuity, paraphilias, suicide threats, gambling sprees, physical fights, physical threats, physical assaults, property damage, reckless driving, and antisocial actions. In contrast, the median time-to-remission of five of the six potentially private forms of impulsivity was sometime between the two and four-year follow-ups. These five forms included: alcohol abuse, drug abuse, eating binges, spending sprees, and self-mutilation.
Conclusion: The results of this study suggest that all forms of impulsivity in BPD decline dramatically over time. They also suggest that impulsive symptoms that are interpersonal in nature tend to decline more rapidly than those that are more solitary in nature.

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NR7-075

INFLUENCE OF FAMILY HISTORY OF ASPD ON CLINICAL CHARACTERISTICS OF PSYCHIATRIC OUTPATIENTS

Lei Wei, D.O.,Elizabeth J. Nickel, M.A.,Elizabeth C. Penick, Ph.D.,Ekkehard Othmer, M.D., Ph.D.,Barry Liskow, M.D.,Marsha Read, Ph.D.,Ned Hunter, Ph.D.,William F. Gabrielli, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the importance of obtaining a family history of antisocial personality disorder when treating psychiatric outpatients.

SUMMARY:

Objective: To compare clinical characteristics of psychiatric outpatients with and without a family history of Antisocial Personality Disorder (ASPD) among first degree relatives.
Method: During a five-year period, all new outpatients in a large psychiatric outpatient service were administered a structured diagnostic interview, a psychosocial history that included a review of nine familial psychiatric disorders, and the Symptom Checklist-90-R before seeing a clinic physician.
Results: As expected, ASPD was more often reported among male first-degree relatives than female first-degree relatives by both male and female subjects. Psychiatric outpatients with a positive family history of ASPD (FH+ASPD; n=299) were significantly younger, less well educated and more likely to be separated/divorced than outpatients without a family history of ASPD (FH-ASPD; n=805). Overall, psychiatric comorbidity was greater among outpatients with a positive family history of ASPD. Antisocial personality disorder, Alcoholism, Drug Abuse and Mania were more prevalent in the FH+ASPD group, regardless of gender. Somatization disorder was significantly more prevalent in female FH+ASPD patients. Many current ratings of psychosocial functioning were significantly poorer in the FH+ASPD group, but no differences were noted in treatment history.
Conclusion: Psychiatric outpatients with a positive family history of ASPD appear to be a clinically distinct group along many relevant dimensions. These findings suggest that when a patient presents with a family history of ASPD, the clinician should be especially alert to the possibility of the presence of substance abuse and the more externalizing psychiatric disorders such as mania.

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NR7-076

ANALYSIS OF MENTAL HEALTH CARE POLICY IN MEXICO

Gabriel Sotelo M.D., Armida Granados,M.D.,Mirna A. Trancoso,M.D., Carlos Campillo,M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to analize international and Mexican Mental Health Care Policy.

SUMMARY:

In Mexico, prevalence of mental disorders is estimated at 28.6%; these disorders also account for about 14% of the total expenditure allocated for diseases by the government.
Objectives:Review international background, legal framework and National Program of Mental Health Care.
Design strategies aimed at strengthening the National Health System.
Methods:We reviewed references such as the Brazilian and Caracas Declarations, both proposed by the Pan-American and the World Health Organization. The Declarations are considered community-based services which can reduce hospitalizations and readmissions.
Mexican General Health Law, Article 74 is relative to the attention of mental illness.
National Health System strategy 5 is about organization and integration of service delivery action. Sub-strategy 5.9 highlights strengthen the National Mental Health Care.
Strategies are made for the Program of Action on Specific Mental Health.
Results: Strategies: 1.Promote the study of care in mental and psychiatric health while encouraging the update of associated legislative regulation. 2. Combat the stigmatism and discrimination associated with mental disorders. 3. Integrating promotional and prevention programs for mental disorders. 4. Develop systems and processes for planning, managing and evaluation of the national system of care for mental health. 5. Integrating mental health care in a community with general health services. 6. Standardize the processes of mental and psychiatric health care, to safeguard the integrity of the patient and avoid the occurrence of side effects and medical errors. 7. Establish alliances with other sectors and the community in caring for mental and psychiatric health care. 8. Include patients with mental disorder as primary beneficiaries of the Social Security System in Health. 9. Stimulate research into mental and psychiatric health care. 10. Develop human resources in mental health and community psychiatry. 11. Strengthen the operating financing by investing in mental and psychiatric health care.
Conclusions:In Mexico there is a legal basis for mental health care that gives greater weight to hospital care, minimizing outpatient care and rehabilitation.
There is a need to review and update regulations to strengthen policies for mental health care in communities.

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NR7-077

RECRUITING THE NEXT GENERATION OF PSYCHIATRISTS – THE EVALUATION OF A PSYCHIATRY RECRUITMENT PROGRAM

Kien Dang M.D., Lisa Andermann, M.D., Matthew Levy, M.D., Taylor Armstrong, M.D., Claire De Souza, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to:
1) List barriers to recruiting medical students into a career in psychiatry.
2) Identify what medical students find helpful in choosing a career in psychiatry.
3) Know how medical students evaluate various recruitment strategies into psychiatry.

SUMMARY:

Despite an ongoing need for psychiatrists, there continue to be barriers to recruiting medical students into psychiatry residency programs. Negative perceptions of psychiatry as well as limited exposure during pre-clerkship are a few barriers to recruitment. It has been suggested that positive undergraduate experiences in psychiatry, regular social gatherings with psychiatrists, meals with invited speakers, and career fairs may be helpful in the recruitment of medical students into a psychiatry residency program.
At the University of Toronto, a recruitment committee with the goals of encouraging and recruiting medical students into a career

in psychiatry has been implemented. The recruitment committee has organized a number of recruitment activities, and these activities have been evaluated by medical students. Qualitative comments about a Psychiatry Interest Group consistently demonstrated that students most appreciated the discussion with psychiatrists and psychiatry residents about the practice of psychiatry. Over 90% felt that the interest group was interesting, and increased awareness of psychiatry. Qualitative comments about Medical Student Dinners with psychiatrists also carried the theme of students benefiting from discussion with psychiatrists and residents. Evaluation of a week-long Medical Student Summer Institute showed that 10% undecided about psychiatry prior to the institute, decreased to 4%. 89% were interested in psychiatry as a career before the institute, 95% were interested afterwards. Over 90% found the week-long institute interesting, and relevant.
Lastly, the organization of an information day coinciding with residency interviews increased students' views of the University of Toronto from 72% favorable, to 83% favorable.
Overall, recruitment committee activities are appreciated by students for the opportunity to interact with psychiatrists and psychiatry residents, increasing their awareness about a career in psychiatry, and can influence their career choice.

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» NR7-078

A METHOD FOR EVALUATION OF COMPETENCY IN RISK ASSESSMENT FOR SUICIDE

Erick Hung, Dale E. McNiel, Ph.D., Samantha R. Fordwood, Ph.D., Stephen E. Hall, M.D., Renee L. Binder, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: (1) Discuss the need for developing competency-based measurement in education about suicide risk assessment; (2) Describe a new method for evaluating clinical competency in risk assessment for suicide; (3) Discuss application of the method in an observed structured clinical evaluation (OSCE) format; and (4) Discuss evidence regarding reliability, validity, and consumer satisfaction with the method.

SUMMARY:

The ability to assess and manage patients' risk for self-harm represents a core competency for mental health professionals. Although psychiatric residency training programs are increasingly expected to evaluate residents according to specific core competencies, few methods are available to measure competency in risk assessment for suicide. This presentation describes development and evaluation of a competency assessment tool (CAT) for suicide risk assessment. We developed the measure based on review of the literature on suicide and consultation with faculty focus groups in a large academic psychiatry department. The measure structures ratings covering interviewing and data collection, case formulation and presentation, treatment planning, and documentation. To evaluate the CAT, 31 faculty members used it to rate the performance of 31 trainees (12 PGY1s, 14 PGY2s, and 5 clinical psychology interns) who participated in an observed structured clinical evaluation (OSCE) of a standardized patient. After interviewing the patient, trainees presented the risk assessment findings to faculty observers. Using the CAT, faculty rated trainees' performance and gave feedback. The CAT showed good internal consistency reliability (Cronbach's alpha = 0.94). Evidence of criterion related validity included (a) more senior trainees performed significantly ($p<.05$) better on the CAT than more junior trainees, and (b) trainees with more hours of previous training in risk assessment and clinical experience with suicidal patients performed better than trainees with less previous training and experience ($p <.05$). Participants rated the CAT as helpful for evaluating competency in suicide risk assessment. On a scale ranging from one, not at all helpful, to seven, extremely helpful, the mean faculty rating of the CAT was 5.8 and the mean trainee rating was 5.9. Overall, the findings support the potential usefulness of a new method for evaluating competency in risk assessment for suicide.

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» NR7-079

DIURNAL VARIATION IN PLASMA BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) LEVEL IN HUMAN: GENDER DIFFERENCE

Joon-Ho Ahn M.D., Sam-Wook Choi, M.D., Sooyoung Bang, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to tell the difference between plasma and serum BDNF levels and to recognize the presence of a diurnal variation in BDNF level in men.

SUMMARY:

Diurnal changes of brain-derived neurotrophic factor (BDNF) mRNA and protein contents have been detected in the rat central nervous system. However, insufficient data is available on the diurnal variation of peripheral BDNF in human. We measured plasma and serum BDNF levels three times a day (AM9:00, PM1:00, PM5:00) in healthy men (N=14) and women (N=7). We detected significant diurnal variation in plasma BDNF level in men, but not in women. Men showed the highest plasma BDNF level in the morning, with a trend of decrease during the day. Comparing the plasma BDNF levels of the two sexes revealed that men showed significantly higher BDNF values than women at AM9:00 ($p<0.001$) and PM1:00 ($p=0.01$). No diurnal variation was found in serum BDNF level in both men and women.
In conclusion, we demonstrated that plasma levels could be a more sensitive marker of BDNF variation than serum levels and sex difference has a specific impact on diurnal variation in plasma BDNF level.

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» NR7-080

RESEARCH ISSUES IN SURVEY MEASUREMENT OF BEHAVIORS INDICATING DIVERSION OF PRESCRIPTION MEDICATIONS FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

Douglas Currivan Ph.D., Larry A. Kroutil, M.P.H., Jill Ruppenkamp, M.S., Scott Novak, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to

(1) understand methods for asking questions about attitudes and behaviors related to the potential for adults to divert prescription medications for the treatment of ADHD to others and (2) identify key themes in adults' attitudes and behaviors to be considered in further research aimed at designing campaigns to reduce the likelihood of diversion of prescription medications for ADHD.

SUMMARY:
Nonmedical use of prescription medication is a growing concern in the United States. Data from the 2007 National Survey on Drug Use and Health indicate over half of the nonmedical users of prescription pain relievers, tranquilizers, stimulants, and sedatives aged 12 or older got the drugs they used most recently "from a friend or relative for free." While prior research has focused on the characteristics of users, less is known about the attitudes and behaviors of those supplying diverted medications to users. In developing items for use in a national survey on the diversion of prescription medications for ADHD, we conducted 8 face-to-face cognitive interviews with adults aged 18 to 49 who had been prescribed ADHD medications in the past 12 months. Unlike most cognitive testing protocols, participants completed the survey items via a web-based demonstration instrument to simulate actual survey conditions. The interviewer observed each response and asked retrospective probes following each completed section, when the response tasks were fresh in participants' minds. These interview techniques allowed the researchers to identify key themes for understanding the diversion of ADHD medications, including situations in which participants might give away or sell their medications, and how the decision to divert their ADHD medications could be influenced by relationships to persons requesting medications. For example, participants indicated a greater willingness to share their medications with family members or close friends than with others. Participants also expressed greater confidence that others were not appropriating their medication when the prescription was strictly limited to 30 pills each month. The themes identified in this study provide a platform for further research to prevent the diversion of ADHD medications. Preliminary findings from the full-scale data collection also will be presented. This research was supported by Eli Lilly and Company.

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» NR7-081

QUALITY OF CARE AND THERAPEUTIC ALLIANCE IN EMERGENCY PSYCHIATRY: A NEW VALIDATE QUESTIONNAIRE

Coralie Lazignac M.D., Eric Adam, MSc., Salvatore Virgillito MSc., Adrian Coman, M.D., Cristian Damsa, M. D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize the critical points about quality of care in emergency psychiatry: rapid diagnose, application of validated clinical guidelines for emergencies, and focus on therapeutic alliance.

SUMMARY:
Data on the impact of a newly validated questionnaire about therapeutic alliance in emergency psychiatry will be discussed by an international emergency network [1]. Then, the presentation will focus on the most recent expert recommendations of rapid diagnose, validated clinical guidelines for emergencies and about therapeutic alliance. We developed a 10 items bidirectional therapeutic alliance scale adapted to emergency conditions, involving 5412 patients during 12 months (June, 2007 - June, 2008). The therapeutic alliance scale was independently fulfilled by each patient and by his emergency consulting psychiatrist. Surprisingly, during the use of this scale of therapeutic alliance, we found a significant decrease of percentage of not voluntary hospitalizations for the patients having consulted psychiatric emergencies ($p=0.00035$) and also a significant decrease of the number of involuntary injections ($p<0.05$). These findings suggest that the systematic assessment of the quality of the therapeutic alliance could stimulate the psychiatrists to improve the patient management, probably by the "Heisenberg effect" earlier described in our team [2]. Moreover, the reduction of non voluntary hospitalizations was related to fewer side effects and grave events than observed in the 12 months period prior to the utilization of this scale. The improvement of the therapeutic alliance was associated with a significant increase of the psychotherapeutic time spent with the patients ($p<0.05$). Further studies, as one running now in Belgium, should validate if the systematic use of this therapeutic alliance scale could have a similar effect in other emergency units.

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» NR7-082

A COMPARISON OF PSYCHIATRY AND INTERNAL MEDICINE: A BIBLIOMETRIC STUDY OF RESEARCH FOCUS

Karina Stone M.D., SN Ghaemi, M.D., M.P.H.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be aware of the kinds of research studies published in the most prominent psychiatric versus medical journals and appreciate the relative attention to biological versus clinical research in psychiatry versus internal medicine.

SUMMARY:
Objective: To determine what kinds of research studies are being published in the most prestigious American psychiatric journal compared to its equivalent journal in internal medicine. The distribution of types of studies published may reflect the conceptual values of contemporary psychiatry compared to internal medicine. Since internal medicine can be seen as more scientifically advanced in its disease knowledge base than psychiatry, we also compared the current psychiatric journal content to internal medicine content from 48 years ago.
Method: We reviewed table of contents and abstracts of all papers published in the calendar year 2008 in the most prominent and highly-cited non-specialty English-speaking psychiatric journal: The Archives of General Psychiatry. This was compared to its equivalent medical counterpart, The Archives of Internal Medicine, the latter being assessed in the calendar year 2008, as well as in the calendar year 1960.
Results: Partial data are provided here, these are tentative estimates. Full results will be presented. In the Archives of General Psychiatry in 2008, 120 papers were published, of which 50% were neurobiological (imaging/genetics/physiology), 30% were epidemiological, 5% pharmacological, 5% other treatments, and 5% miscellaneous. We will further analyze these data by other subcategories, and overall conceptual approach (biological vs psychosocial). In contrast, current Archives of Internal Medicine content tended to involve more clinical treatment and epidemiological studies. Past Archives of Internal Medicine will be presented.
Conclusions: If the most prominent psychiatric journal content reflects the main focus of contemporary psychiatric research, it

appears that genetic and neuroimaging studies are most valued. Compared to the main current internal medicine journal comparator, clinical studies are underrepresented in psychiatric research.
Funding Source: None

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» NR7-083

LONGITUDINAL CONSENT-RELATED ABILITIES AMONG RESEARCH PARTICIPANTS WITH SCHIZOPHRENIA: RESULTS FROM THE CATIE STUDY

Thomas Stroup M.D., Paul S. Appelbaum, MD, Hongbin Gu, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to identify predictors of change in decision-making capacity for research participation and recognize individuals who might be at risk of inadequate capacity or of losing capacity over time.

SUMMARY:

Objective: Research participants must have adequate consent-related abilities to provide informed consent at the time of enrollment. We sought to determine if research participants with schizophrenia maintain adequate consent-related abilities during a longitudinal study. If participants lose abilities during a trial they may not be able to judge and protect their interests. If reduced abilities are common or can be predicted, special protections can be targeted appropriately.
Method: We examined longitudinal consent-related abilities of participants in the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia study using the MacArthur Competence Assessment Tool-Clinical Research (MacCAT-CR) at protocol-specified times over 18 months.
Results: Of 1,158 research participants in this analysis, most (n= 650, 56%) had a stable pattern of Understanding scores, 235 (20%) improved substantially with no evidence of decline, 273 (24%) had at least one assessment with substantial worsening. Appreciation scores showed similar patterns; Reasoning scores had higher rates of worsening. During the course of the trial, 43 (4%) fell below the initial threshold for adequate capacity, which was predicted by lower Understanding scores, more severe positive symptoms, and poorer neurocognitive functioning at baseline, and by increases in negative symptoms and deteriorating global status.
Conclusions: Most participants in this long-term study had stable or improved consent-related abilities, but almost one-fourth experienced substantial worsening and 4% of participants fell below the study's capacity threshold for enrollment. Clinical investigators should monitor with special care individuals with marginal capacity at study entry and increased levels of psychotic symptoms during a study.

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» NR7-084

METHODOLOGICAL ISSUES IN RESEARCH OF EARLY INTERVENTION IN PTSD: ARE ADEQUATELY-POWERED PREVENTION STUDIES FEASIBLE?

Joseph Zohar M.D., Ehud Klein, M.D., Gavriel Schreiber, M.D., Arieh Y. Shalev, M.D., Zeev Kaplan, M.D., A. Cohen, Ph.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be able to identify the ways in which early intervention after trauma may lessen or prevent the development of PTSD. Following the talk, participants should appreciate the methodological and logistical problems that may arise in studies of early intervention in PTSD, and be able to discuss different methods of overcoming these difficulties.

SUMMARY:

The concept of "golden hours" in internal medicine highlights the "window of opportunity" that exists immediately after trauma for preventing further damage.
Since PTSD develops after a specific trauma, there may be a window of opportunity to intervene and prevent its development. However, the methodological obstacles to performing research in this field must first be identified and addressed.
In a unique setting in Israel, where psychiatrists are an integral part of the ER department, and provide the appropriate infrastructure, a multi-center study examined the preventive potential of escitalopram treatment, begun within 1 month of the trauma (i.e. before PTSD diagnosis). 10 research assistants contacted over 20,000 potential participants by telephone (leads based on ER visits), eventually recruiting 417 individuals. Participants were randomized into the treatment or the placebo group for 12 weeks, and the 205 participants who completed the treatment phase then had PTSD symptoms monitored for 13 months.
The significant dropout (only 37% of those who initially agreed to participate actually completed the study) illustrates the difficulties of retaining participants in such a study. However, no significant differences were observed between dropout and completers, in demographic or trauma measures.
Alternative preventive measures may need other considerations. In a short pilot study, 7 of 23 eligible patients agreed to single intervention (cortisol) when approached in the ER immediately (within 6 hours) after the trauma. Here, medication compliance would not be an issue (since only one dose is taken), but the logistics of recruiting participants within a short time frame are different.
The paper highlights the importance of early intervention in PTSD, draws up the conceptual and logistical framework for this, describes the tools and procedures used, and highlights the advances and drawbacks in this type of methodology.
This research was funded by a grant from Lundbeck.

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» NR7-085

GABAPENTIN ENACARBIL IMPROVES SLEEP IN SUBJECTS WITH MODERATE-TO-SEVERE PRIMARY RESTLESS LEGS SYNDROME (RLS)

Philip Becker M.D., Clete A. Kushida, M.D., Ph.D., Aaron L. Ellenbogen, DO., MPH., Daniel M. Canafax, PharmD., Eileen T. Monaghan, Ronald W. Barrett, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand the effects of gabapentin enacarbil treatment on Restless Legs Syndrome-associated sleep disturbance, as assessed by the Medical Outcomes Study sleep scale and the Post-Sleep

Questionnaire, in patients with moderate-to-severe primary Restless Legs Syndrome.

SUMMARY:
Introduction: Sleep disturbance is the primary complaint of patients with Restless Legs Syndrome (RLS)(1,2). Gabapentin enacarbil (GEn) is a nondopaminergic therapy under investigation for RLS. Self-reported sleep outcomes with GEn 1200mg compared with placebo in subjects with RLS were assessed.
Methods: XP052 was a 12-week double-blind multicenter study. Subjects with moderate-to-severe primary RLS were randomized to receive GEn 1200mg (n=114) or placebo (n=108) at 5pm with food. Co-primary endpoints: mean change from baseline in International Restless Legs Scale (IRLS) total score and proportion of responders (rated 'very much' or 'much' improved) on the investigator-rated Clinical Global Impression–Improvement (CGI-I) scale. Sleep disturbance was assessed using the Medical Outcomes Study (MOS) Sleep Scale and Post-Sleep Questionnaire (PSQ).
Results: GEn significantly improved mean IRLS total score vs placebo at Week 12 LOCF (adjusted mean treatment difference for change from baseline: –4.0; 95%CI: –6.2, –1.9; p=0.0003) and significantly more GEn subjects were CGI-I responders (76.1% vs 38.9%; adjusted odds ratio: 5.1; 95%CI: 2.8, 9.2; p<0.0001). GEn significantly improved all MOS Sleep Scale domains from baseline to Week 12 LOCF vs placebo (daytime somnolence: -17.4 vs -9.6, p=0.0018; sleep quantity: 0.8 vs 0.4 h, p=0.0084; sleep adequacy: 27.7 vs 13.4, p<0.0001; sleep disturbance: -29.1 vs -15.5, p<0.0001). GEn subjects reported higher overall sleep quality, greater ability to function, and fewer nights with RLS symptoms, nighttime awakenings and hours awake per night due to RLS symptoms vs placebo on the PSQ at Week 12 LOCF (each item p<0.05 for distribution of responses). The two most frequently reported AEs (GEn, placebo) were somnolence (27%, 7%) and dizziness (19%, 5%).
Conclusions: GEn 1200 mg once daily significantly reduces RLS symptoms and improves subject-reported sleep outcomes compared with placebo. Supported by XenoPort, Inc., Santa Clara, CA.

REFERENCES:

1) Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisir J: Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the Restless Legs Syndrome Diagnosis and Epidemiology Workshop at the National Institutes of Health. Sleep Med 2003; 4:101–119.

2) Hening W, Walters AS, Allen RP, Montplaisir J, Myers A, Ferini-Strambi L: Impact, diagnosis and treatment of restless legs syndrome (RLS) in a primary care population: the REST (RLS epidemiology, symptoms, and treatment) primary care study. Sleep Med 2004; 5:237–246.

» NR7-086

GABAPENTIN ENACARBIL RELIEVES PAIN ASSOCIATED WITH RESTLESS LEGS SYNDROME (RLS)

Daniel Canafax Pharm.D., Clete A. Kushida, M.D., Ph.D., Philip M. Becker, M.D., Aaron L. Ellenbogen, D.O., M.P.H., Eileen T. Monaghan., Ronald W. Barrett, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be aware of the data demonstrating that patients with Restless Legs Syndrome (RLS) symptoms may also experience RLS-associated pain, as well as understand the effects of gabapentin enacarbil in relieving pain associated with RLS, compared with placebo, in subjects with moderate-to-severe primary RLS.

SUMMARY:
Introduction: Painful symptoms are reported by ~60% of patients with RLS. Gabapentin enacarbil (GEn) is a nondopaminergic therapy under investigation for the treatment of moderate-to-severe primary RLS. The effect of GEn 1200mg on RLS symptoms and associated pain was assessed.
Methods: XP052, a 12-week double-blind multicenter study, randomized subjects with moderate-to-severe primary RLS to GEn 1200mg (n=114) or placebo (n=108) at 5pm with food. Co-primary endpoints: mean change from baseline in International Restless Legs Scale (IRLS) total score and proportion of responders (rated 'very much' or 'much' improved) on the investigator-rated Clinical Global Impression–Improvement (CGI-I) scale. Subjects recorded 'pain associated with RLS symptoms' in the last 24 h on an 11-point scale (0=no pain, 10=most intense pain imaginable) every morning for 7 days before assessment (Weeks 2, 4, 8 and 12). Those with other neurologic disease (e.g. diabetic neuropathy) or movement disorders were excluded.
Results: GEn improved mean IRLS total score vs placebo at Week 12 LOCF and more GEn subjects were CGI-I responders (both p<0.001). Baseline average daily pain scores of >0 and >=4 were reported by 89% and 51% of subjects, respectively. GEn significantly reduced mean (SD) pain scores vs placebo for subjects with baseline pain scores >0 (–2.5 [2.3] vs –1.3 [2.1]; AMTD: –1.1; p<0.0001) and >=4 (–3.7 [2.2] vs –1.9 [2.4]; AMTD: –1.7; p<0.0001) at Week 12 LOCF. Significantly more GEn-treated subjects reported a >=50% reduction in daily pain score vs placebo with baseline pain scores >0 (58.6% vs 35.2%; AOR: 2.6; 95%CI: 1.5, 4.5; p=0.0006) and >=4 (75.4% vs 33.3%; AOR: 6.9; 95%CI: 2.9, 16.5; p<0.0001). The two most frequently reported adverse events (GEn, placebo) were somnolence (27%, 7%) and dizziness (19%, 5%).
Conclusions: GEn 1200mg significantly improves RLS symptoms and reduces pain associated with RLS symptoms compared with placebo.Supported by XenoPort, Inc., Santa Clara, CA.

REFERENCES:

1) Allen RP, Walters AS, Montplaisir J, Hening W, Myers A, Bell TJ, Ferini-Strambi L: Restless legs syndrome prevalence and impact. Arch Intern Med 2005; 165:1286–1292.

2) Kushida CA, Becker PM, Ellenbogen AL, Canafax DM, Barrett RW. A randomized, double-blind, placebo-controlled study of XP13512/GSK1838262 in patients with restless legs syndrome. Neurology 2008; In Press.

» NR7-087

ASSOCIATION BETWEEN ANTIPSYCHOTIC-INDUCED RESTLESS LEGS SYNDROME AND TYROSINE HYDROXYLASE GENE POLYMORPHISM

Chul-Hyun Cho M.D., Seung-Gul Kang, M.D., Ph.D., Heon-Jeong Lee, M.D., Ph.D., Min-Soo Lee, M.D., Ph.D., Leen Kim, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize association between antipsychotic-induced restless legs syndrome and tyrosine hydroxylase gene polymorphism, especially tyrosine hydroxylase gene Val81Met SNP in female schizophrenia patients.

SUMMARY:
Objectives: The restless legs syndrome is presumed to be more prevalent in schizophrenia who take antipsychotics. Antipsychotic-induced restless legs syndrome is attributed to blocking of dopamine receptor by antipsychotics. We hypothesized that the genetic susceptibility to antipsychotic-induced restless legs syndrome differs among schizophrenic patients who take antipsychotics. The tyrosine hydroxylase is the enzyme responsible for catalyzing the conversion of L-tyrosine to dopa. The purpose of this study is to determine whether the tyrosine hydroxylase gene Val81Met polymorphism is associated with antipsychotic-induced RLS.
Methods: 190 Korean schizophrenic patients were evaluated by the diagnostic criteria of the International Restless Legs Syndrome Study Group (IRLSSG), IRLSSG rating scale for restless legs syndrome (IRLS), and Brief Psychiatric Rating Scale (BPRS). The genotyping was performed for tyrosine hydroxylase gene Val-81Met single-nucleotide polymorphism (SNP).

Results: Of the 190 schizophrenic patients, 44 (23.2%) were found to have restless legs syndrome. We detected significant differences in the genotype (?2=6.15, p=0.046), allele (?2=4.67, p=0.031) and allele M carrier (MM+MV vs. VV; ?2=5.76, p=0.016) frequencies of tyrosine hydroxylase gene Val81Met SNP between those with and without restless legs syndrome in female schizophrenia. Conclusion: These findings suggest that the tyrosine hydroxylase gene Val81Met SNP might be associated with antipsychotic-induced restless legs syndrome in female schizophrenia.

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1) Wetter TC, Brunner J, Bronisch T. : Restless legs syndrome probably induced by risperidone treatment. Pharmacopsychiatry 2002 May;35(3):109-111

2) Kang SG, Lee HJ, Choi JE, et al. : Association study between antipsychotics-induced restless legs syndrome and polymorphisms of dopamine D1, D2, D3, and D4 receptor genes in schizophrenia. Neuropsychopharmacol Biol Psychiatry 2007;31(5):1078-1083

» NR7-088

CAN AN INSOMNIA THERAPY TREAT SLEEP MAINTENANCE WITHOUT SUPPRESSING AROUSABILITY: EFFECTS OF DOXEPIN 1, 3, AND 6 MG ACROSS PHASE 3 TRIALS

H. Heith Durrence Ph.D., Philip Jochelson, M.D., Roberta Rogowski, BSN

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to evaluate the efficacy of 1 mg, 3 mg and 6 mg of doxepin on sleep maintenance measures for the treatment of chronic and transient insomnia.

SUMMARY:

This report reviews the sleep maintenance (SM) efficacy from three trials evaluating doxepin (DXP 1, 3, 6 mg), a selective H1 antagonist at the doses studied, in adult and elderly populations with either primary or transient insomnia.

SM endpoints from three double-blind placebo-controlled trials are reported. In two trials, patients meeting DSM-IV-TR criteria for primary insomnia were randomized for up to 12 wks of treatment. Study A was a 12-wk trial of elderly patients (N=240; DXP 1 and 3 mg vs. placebo (PBO)); Study B was a 5-wk trial of adults patients (N=221; DXP 3 and 6 mg vs. PBO). Study C was a single-night trial that used a model of transient insomnia to simulate sleep disturbance in healthy adults (N=565; DXP 6 mg vs. PBO). Efficacy was evaluated with polysomnography. SM endpoints included wake after sleep onset (WASO) and number of awakenings (NAW). Data from the first and final night (N; Study A=N85; Study B=N29) of the study are reported.

DXP 1 mg (Study A; $p<0.01$), 3 mg (Study A and B; $p<0.0001$) and 6 mg (Study B and C; $p<0.0001$) significantly improved WASO on N1 of all three trials, with improvements vs. PBO ranging from 17 (Study A, 1 mg) to 40 minutes (Study C, 6 mg). These significant improvements were maintained at the final timepoint. NAW were not improved vs PBO at any dose or timepoint in any trial.

DXP 1, 3 and 6 mg demonstrated significant improvement in WASO across three Phase 3 trials that was maintained at the final timepoint. Interestingly, SM efficacy was not accompanied by reductions in NAW, a finding inconsistent with the existing literature involving GABA-mediated hypnotic medication. These data suggest DXP is effective at treating SM insomnia in both transient and chronic insomnia populations, and in adult and elderly populations. Additionally, these data suggest that DXP 1, 3 and 6 mg may reduce time spent awake after nighttime arousals without suppressing arousability, though further evaluation is necessary.

REFERENCES:

1) Roth T, Rogowski R, Hull S, et al. Efficacy and Safety of Doxepin 1, 3 and 6 mg in Adults with Primary Insomnia. Sleep 2007;30: 1555-1561

2) Scharf, M, Rogowski, R, Hull S, et al. Efficacy and safety of doxepin 1, 3 and 6 mg in elderly patients with primary insomnia. J Clin Psyc. 2008;69:1557-1564

» NR7-089

GABAPENTIN ENACARBIL IMPROVES MOOD, QUALITY OF LIFE, AND FUNCTIONING IN SUBJECTS WITH MODERATE-TO-SEVERE PRIMARY RESTLESS LEGS SYNDROME (RLS)

Aaron Ellenbogen D.O., Philip M. Becker, M.D., Clete A. Kushida, M.D., Ph.D., Daniel M. Canafax, PharmD., Eileen T. Monaghan, Ronald W. Barrett, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to describe the negative impact of Restless Legs Syndrome (RLS) on mood, quality of life, and functioning, and understand the effect of gabapentin enacarbil treatment on these outcomes compared with placebo in subjects with moderate-to-severe primary RLS.

SUMMARY:

Introduction: Restless Legs Syndrome (RLS) symptoms may negatively impact subjects' mood, quality of life (QoL), and functioning (1, 2). The efficacy of gabapentin enacarbil (GEn), a nondopaminergic therapy under investigation for the treatment of RLS, on these outcomes was evaluated.

Methods: XP052 was a 12-week, double-blind, placebo-controlled multicenter study. Subjects with moderate-to-severe primary RLS were randomized to receive GEn 1200mg (n=114) or placebo (n=108) at 5pm with food. Co-primary endpoints: mean change from baseline in International Restless Legs Scale (IRLS) total score and proportion of responders (rated 'very much' or 'much' improved) on the investigator-rated Clinical Global Impression–Improvement (CGI-I) scale. Mood, QoL, and functioning were assessed using the Profile of Mood State (POMS), Mood Assessment Question (MAQ), Johns Hopkins RLSQoL questionnaire, and item 2 (ability to function in the past week) of the Post-Sleep Questionnaire (PSQ).

Results: GEn significantly reduced mean IRLS total score from baseline compared with placebo at Week 12 LOCF (adjusted mean treatment difference [AMTD] for change from baseline: –4.0; 95%CI: –6.2, –1.9; $p=0.0003$), and significantly more subjects were CGI-I responders (76% versus 39%; adjusted odds ratio: 5.1; 95%CI: 2.8, 9.2; $p<0.0001$). GEn significantly improved POMS total mood disturbance score (AMTD: –6.9; 95%CI: –11.1, –2.7; $p=0.014$), overall mood (MAQ; $p=0.0008$), mean RLSQoL overall life-impact score (AMTD [standard error]: 7.8 [1.86]; $p<0.0001$), and functioning (PSQ item 2; $p=0.0002$) versus placebo at Week 12 LOCF, compared with baseline. The two most frequently reported adverse events for GEn and placebo, respectively, were somnolence (27% versus 7%) and dizziness (19% versus 5%).

Conclusions: GEn 1200 mg once daily significantly improved RLS symptoms, as well as overall mood, QoL, and functioning.

Study supported by XenoPort, Inc., Santa Clara, CA.

REFERENCES:

1) 1. Abetz L, Allen RP, Follet A, Washburn T, Earley C, Kirsch J, Knight H: Evaluating the quality of life of patients with restless legs syndrome. Clin Ther 2004; 26:925-935.

2) 2. Allen RP, Walters AS, Montplaisir J, Hening W, Myers A, Bell TJ, Ferini-Strambi L: Restless legs syndrome prevalence and impact. Arch Intern Med 2005; 165:1286-1292.

» NR7-090

ARMODAFINIL IMPROVES WAKEFULNESS THROUGHOUT THE DAY IN PATIENTS WITH RESIDUAL EXCESSIVE SLEEPINESS ASSOCIATED WITH TREATED OSA

Max Hirshkowitz, Ph.D., Alan Lankford, Ph.D., Ronghua Yang, Ph.D., Gregory A. Rippon, M.D., M.S., Thomas Roth, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be able to discuss the efficacy and safety of armodafinil once daily for improving wakefulness throughout the day in patients with obstructive sleep apnea who experience excessive sleepiness with regular use of continuous positive airway pressure.

SUMMARY:
Objectives: Many patients with obstructive sleep apnea (OSA) have residual excessive sleepiness (ES) regardless of continuous positive airway pressure (CPAP) treatment. Armodafinil, the R- and longer-lasting isomer of modafinil, is a non-amphetamine, wakefulness-promoting medication. Armodafinil sustains higher plasma concentrations, the difference being greatest later in the day, compared with modafinil on a milligram-to-milligram basis, which may obviate the need to split or administer higher doses to maintain wakefulness throughout the day. A post hoc analysis of a 12-week, randomized, double-blind study was performed to assess the effectiveness of once-daily armodafinil in improving wakefulness throughout the day in patients with residual ES associated with treated OSA.
Methods: Adult patients were administered armodafinil 150 mg (n=131) or 250 mg (n=131), or placebo (n=130), once daily (before 8 am, or at 7 am on lab visits). Mean sleep latency (MSL) was assessed through the 30-min Maintenance of Wakefulness Test, performed every 2 h beginning at 9 am for a total of 6 tests at weeks 4, 8 and 12.
Results: At final visit, the MSL for the average of all 6 tests (9am-7pm) was significantly improved from baseline by 2.6 min in the armodafinil 150 mg group, 2.9 min in the 250 mg armodafinil group, and 2.7 min in the combined armodafinil groups relative to placebo (P<0.004 for all). Numeric separation in MSL was seen between each armodafinil group and the placebo group at the first 5 tests but not at the 7 pm test. Armodafinil was generally well tolerated.
Conclusion: In this post hoc analysis, armodafinil once daily was effective in improving wakefulness throughout the day, relative to placebo, in patients with residual ES associated with treated OSA.
FUNDING SOURCE: Sponsored by Cephalon, Inc.

REFERENCES:
1) 1. Dinges DF, Arora S, Darwish M, Niebler GE. Pharmacodynamic effects on alertness of single doses of armodafinil in healthy subjects during a nocturnal period of acute sleep loss. Curr Med Res Opin 2006;22:159-167.

2) 2. Roth T, White D, Schmidt-Nowara W, et al. Effects of armodafinil in the treatment of residual excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome: a 12-week, multicenter, double-blind, randomized, placebo-controlled study in nCPAP-adherent adults. Clin Ther 2006;28:689-706.

» NR7-091

EFFECTS OF DOXEPIN 1 AND 3 MG ON EARLY MORNING AWAKENINGS IN ELDERLY ADULTS WITH PRIMARY INSOMNIA

Philip Jochelson M.D., Roberta Rogowski, BSN, H. Heith Durrence, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to evaluate the efficacy of 1 mg and 3 mg of doxepin on measures of early morning awakenings for the treatment of chronic insomnia in elderly adults.

SUMMARY:
Early morning awakenings (EMA), waking too early and being unable to fall back to sleep, is often a key symptom of chronic insomnia. Though it is a core symptom of DSM-IV diagnosed insomnia, it is seldom addressed in clinical trials examining medication effects on sleep parameters. The present analysis examined the impact of doxepin (DXP 1, 3 mg), a selective H1 antagonist at the doses studied, on EMA in an elderly population with primary insomnia. Selected endpoints from a randomized, double-blind, placebo-controlled study of elderly adults with DSM-IV-TR defined primary insomnia are reported. Patients were randomized to 12 weeks of DXP 1 mg (N=77), 3 mg (N=82), or placebo (PBO; N=81). Efficacy was evaluated with polysomnography (PSG) data from the first and last time points of the study, nights 1 (N1) and 85 (N85). PSG endpoints of early morning awakenings included sleep efficiency (SE) in the last third-of-the-night (SE-LTN), SE last quarter-of-the-night (SE-LQN), and SE in hours 7 and 8. Next-day residual effects were assessed using the Digit Symbol Substitution Test (DSST), Symbol Copying Test (SCT), and a Visual Analog Scale (VAS) for sleepiness.
On N1, DXP 1 and 3 mg significantly improved SE-LTN (p=0.0007), SE-LQN (p=0.0011) and SE in hours 7 (p=0.0028) and 8 (p=0.0211), when respectively compared with PBO. These improvements were sustained at N85, with significance versus PBO maintained for 3 mg on all parameters except SE in hour 8 (p=0.06). There were no significant group differences in the DSST, SCT, or VAS at any timepoint during the trial.
In adults with chronic insomnia, DXP 1 and 3 mg significantly improved PSG parameters associated with EMA, a prevalent, bothersome, but neglected symptom. These improvements were sustained through the final hour of the night with no observed next-day residual effects. These data suggest that DXP 1 and 3 mg are effective at treating early morning awakenings without causing next-day residual effects.

REFERENCES:
1) Roth T, Rogowski R, Hull S, et al. Efficacy and Safety of Doxepin 1, 3 and 6 mg in Adults with Primary Insomnia. Sleep 2007;30: 1555-1561

2) Scharf, M, Rogowski, R, Hull S, et al. Efficacy and safety of doxepin 1, 3 and 6 mg in elderly patients with primary insomnia. J Clin Psyc. 2008;69:1557-1564

» NR7-092

CORRELATIONS OF SUBJECTIVE REPORTS AND POLYSOMNOGRAPHIC FINDINGS IN OBSTRUCTIVE SLEEP APNEA PATIENTS

Seong Hwan Kim M.D., Sang-Myung Chun M.D., Ph.D., assistant professor, Chul-Jung Kang, M.D., Ph.D., assistant professor, Jae-Hong Park M.D., Master.

EDUCATIONAL OBJECTIVES:
At the conclusion of this session, the participant should be able to recognize that subjective sleepiness scales may have little value in assessment of obstructive sleep apnea(OSA) and bed partner reports may be helpful in predicting OSA.

SUMMARY:
In South Korea, screening tools to assess sleep quality or obstructive sleep apnea(OSA) are subjective questionnaires which were developed in western country. However, these widely used sleep questionnaires were not yet verified in Korea. The purpose of this study was to examine correlations between patient's subjective symptom complaints and objective polysomnographic findings.
A retrospective chart review of 71 consecutive patients reporting snoring or observed apnea with or without daytime drowsiness was conducted. Patients and their bed partner accomplished the subjective sleep questionnaires (The Epworth sleepiness scale, Pittsburgh Sleep Quality Index, Global Sleep Assessment Questionnaire, Bed Partner Questionnaire) and underwent diagnostic overnight polysomnography(PSG).
There was no difference in sleepiness scales between patients with or without obstructive sleep apnea according to PSG study. But some questions about snoring or reports of bed partners of patients, such as "Does your bed partner complain about your snoring or apnea?", showed significant differences. The authors could not find differences in subjective reports according to severity of obstructive sleep apnea. However some complaints or reports of bed partners, including "How bothersome is patient's snoring to

you during last 4 weeks?", correlated well with sleep parameters in correlation analysis. This study showed bed partner report is more accurate than patient's subjective sleep questionnaire in predicting OSA.

REFERENCES:

1) Rosenthal LD, Dolan DC. The Epworth sleepiness scale in the identification of obstructive sleep apnea. J Nerv Ment Dis. 2008;196:429-31.

2) Nguyen AT, Baltzan MA, Small D, Wolkove N, Guillon S, Palayew M. Clinical reproducibility of the Epworth Sleepiness Scale. J Clin Sleep Med. 2006;2:170-4.

» NR7-093

LOW-DOSE ZOLPIDEM TARTRATE SUBLINGUAL LOZENGE (INTERMEZZO®) SAFELY AND EFFECTIVELY TREATS INSOMNIA FOLLOWING MOTN AWAKENING

Andrew Krystal, M.D., Russell Rosenberg, Ph.D., David Seiden, M.D., Milton Erman, M.D., Thomas Roth, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to acknowledge that it is feasible to treat insomnia characterized by difficulty returning to sleep after a middle-of-the-night (MOTN) awakening on an as-needed (prn) basis using a low dose of zolpidem tartrate.

SUMMARY:

Introduction: A binary buffer-containing low-dose zolpidem tartrate sublingual lozenge (ZSL) is being developed for prn treatment of insomnia characterized by difficulty returning to sleep after an MOTN awakening. This study evaluated the safety and efficacy of 3.5 mg ZSL when taken prn.

Methods: Adults (18 to 64 years, N=295) with DSM-IV primary insomnia characterized by MOTN awakenings were randomized to 4 weeks of prn double-blind treatment with either ZSL 3.5 mg or placebo, after a 2-week IVRS single-blind placebo screening. Subjects had to demonstrate at least 2 MOTN awakenings >30 minutes and 1 MOTN awakening >60 minutes per week to be eligible. Subjects called IVRS following an MOTN awakening and, if they had been awake > 10 minutes and had > 4 hours remaining in bed, were permitted to self-administer study medication.

Results: Compared to placebo, 3.5 mg ZSL significantly reduced latency to sleep onset after MOTN awakenings and improved sleep quality and next-day alertness ratings throughout the treatment period. Furthermore, ZSL significantly improved the post-MOTN sleep maintenance parameters of wake after sleep onset and number of awakenings versus placebo. The ZSL effect on post-MOTN total sleep time was significantly better than placebo at week 1 and 2; however, the difference at weeks 3 and 4 did not achieve statistical significance. Mean weekly intake was similar for ZSL and placebo. Placebo intake gradually declined from 4.8 in week 1 to 4.2 in week 4, while ZSL intake declined from 4.9 to 4.0 during the same period. All treatments were well tolerated.

Conclusions:These study findings confirm the utility of ZSL for prn treatment of insomnia characterized by difficulty returning to sleep after MOTN awakening.

Support:Funded by Transcept Pharmaceuticals, Inc., Pt. Richmond, CA.

REFERENCES:

1) Roth T, Hull SG, Lankford DA, Rosenberg R, Scharf MB; Intermezzo Study Group.Low-dose sublingual zolpidem tartrate is associated with dose-related improvement in sleep onset and duration in insomnia characterized by middle-of-the-night (MOTN) awakenings. Sleep. 2008 Sep 1;31(9):1277-84.

2) Ohayon MM. Nocturnal awakenings and comorbid disorders in the American general population. J Psychiatr Res. 2008 Nov;43(1):48-54.

» NR7-094

EFFECTS OF DOXEPIN 1, 3, AND 6 MG ON SLEEP EFFICIENCY BY HOUR FROM TWO LONG-TERM TRIALS OF CHRONIC INSOMNIA

Alan Lankford Ph.D., Philip Jochelson, M.D., H. Heith Durrence, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to evaluate the efficacy of 1 mg and 3 mg of doxepin on sleep effiency throughout the night for the treatment of chronic insomnia.

SUMMARY:

Currently approved insomnia medications that act as GABA modulators have not demonstrated efficacy lasting into the final hours of the night without significant next-day residual effects. This report reviews time spent asleep by hour and residual effects data from two long-term polysomnography (PSG) trials evaluating doxepin (DXP) for the treatment of insomnia.

Time asleep was evaluated in two double-blind, placebo-controlled trials; a 12-week trial of elderly patients (Study A; N=240; DXP 1 and 3 mg vs. placebo (PBO)) and a 5-week trial of adult patients (Study B; N=221; DXP 3 and 6 mg vs. PBO). Total sleep time (TST) was analyzed globally, in each of the 8 hours of PSG assessment, and in the final third and quarter of the night. Next-day residual effects were assessed using the Digit Symbol Substitution Test (DSST) and the Symbol Copying Test (SCT). Data from Night 1 (N1) are reported.

DXP 1 mg (Study A), 3 mg (Study A and B) and 6 mg (Study B) significantly improved overall TST in both trials compared with PBO. Significant improvements in the % of time asleep in the final third and quarter of the night, in the final hour, and in the majority of other hours across the night were also observed. In terms of next-day residual effects, there were no significant differences in the DSST or SCT at any dose in either trial.

In adult and elderly patients with chronic insomnia, DXP 1, 3 and 6 mg significantly improved the % of time asleep both globally and at most hours throughout the night, with the strongest effect in the last part of the night. Importantly, though low-dose DXP increased the amount of time asleep through the final hour of assessment (hour 8), efficacy was not accompanied by evidence of next-day residual sedation at hour 9. These data suggest histamine may be an integral part of a gating mechanism in the arousal system that allows transition from sleep to wake without residual sedation.

REFERENCES:

1) Roth T, Rogowski R, Hull S, et al. Efficacy and Safety of Doxepin 1, 3 and 6 mg in Adults with Primary Insomnia. Sleep 2007;30: 1555-1561

2) Scharf, M, Rogowski, R, Hull S, et al. Efficacy and safety of doxepin 1, 3 and 6 mg in elderly patients with primary insomnia. J Clin Psyc. 2008;69:1557-1564

» NR7-095

CLINICAL AND GENETIC CHARACTERISTICS OF OBSTRUCTIVE SLEEP APNEA SYNDROME AND NARCOLEPSY IN KOREAN PATIENTS

Hamin Lee M.D., Seung-Chul Hong, M.D., Ph.D., Jong-Hyun Jeong, M.D., Ph.D., Jin-Hee Han, M.D., Ph.D., Sung-Pil Lee, M.D., Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize and compare different clinical, polysomnographic, and genetic characteristics of obstructive sleep apnea syndrome and narcolepsy.

SUMMARY:

Objectives:To evaluate and compare clinical, polysomnographic, and genetic characteristics of obstructive sleep apnea syndrome and narcolepsy in Korean patients.

Methods: 226 subjects complaining of daytime sleepiness were

diagnosed as 1) Obstructive sleep apnea syndrome (OSAS), 2) Narcolepsy, and 3) Dual diagnosis of OSAS and narcolepsy using the revised ICSD-2 diagnostic criteria. Clinical evaluation, nocturnal polysomnography (NPSG) followed by multiple sleep latency test(MSLT), HLA typing, and cerebrospinal fluid(CSF) hypocretin-1 levels were assessed.
Results: All patients complained of excessive daytime sleepiness, as reported by Epworth Sleepiness Scale(ESS) and clinical interviews. ESS of patients with OSAS or narcolepsy did not differ from each other. Although dual diagnosis patients had higher ESS scores than patients with OSAS or narcolepsy, this finding was not significant. On NPSG, Patients with OSAS showed more stage 2 sleep, and less stage 3 and 4 sleep. On MSLT, patients with OSAS had longer mean sleep latency (SL), and less sleep-onset REM periods (SOREMPs) than patients with narcolepsy or dual diagnosis. On HLA typing, HLA DQB1*0602 frequencies were lowest in patients with OSAS than in narcoleptic or dual diagnosis patients. However, this value remained higher than that of the general population.
Conclusion: Nighttime sleep quality is worse in OSAS than in narcolepsy. OSAS manifests longer sleep latency and less SOREMP on MSLT. HLA-DQB1*0602 frequencies are lower in OSAS than in narcolepsy, but are higher than in healthy controls.
Our findings portray the different characteristics of OSAS and narcolepsy, which both present as pathologic daytime sleepiness.

REFERENCES:

1) American academy of Sleep Medicine: ICSD-2 International Classification of sleep disorders, 2nd ed.: Diagnostic and coding manual. Am Acad Sleep Med; 2005.

2) Johns MW: A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale.Sleep 1991; 14:540 -545

» NR7-096

EFFECT OF EPLIVANSERIN ON DRIVING AND COGNITIVE/PSYCHOMOTOR TASKS IN A STUDY OF PATIENTS WITH INSOMNIA CHARACTERIZED BY SLEEP MAINTENANCE DIFFICULTIES

Remi Luthringer Ph.D., Anne Floch, Pharm.D, Ph.D., Astrid Delfolie, M.S., Olivier Nicolas, Pharm.D., Ph.D., Aurelie Brunet, Pharm.D., Jean-Louis Pinquier. M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to understand that the novel sleep agent eplivanserin does not affect functioning in terms of driving a car and cognitive/psychomotor performance.

SUMMARY:

Introduction: Sleep maintenance insomnia is a prevalent condition [1]. Eplivanserin (EPL), an Antagonist of Serotonin Two A Receptors (ASTAR), being developed at 5 mg/day for chronic insomnia characterized by nocturnal awakenings, enhances slow wave sleep and slow wave activity [2]. It has no affinity for GABA receptors, unlike benzodiazepines. Objective: To assess driving and cognitive/psychomotor performance after repeated administration of eplivanserin to differentiate it from classical hypnotic agents, such as flurazepam 30 mg (active control), which may produce residual sedative effects due to their mechanism of action.
Methods: Randomized, double-blind, placebo- and active-controlled, double-dummy study. Patients (n=28) with sleep maintenance insomnia underwent a 3-way crossover with placebo, EPL and flurazepam (FLZ) 30 mg (a hypnotic with residual effects). Each 21-day treatment period was separated by a 3-week washout. After the final dose, from 2 to 23 h post-dose, a monotonous driving simulation evaluated the standard deviation of lane positioning (SDLP) and the number of lane crossings (NLC), and a driving test period with distractors tested the brake reaction time (BRT); cognitive/psychomotor performance was evaluated by a battery of tests, including body sway (BS), and using power of attention (PA) and quality of episodic secondary memory (QESM) composite scores.
Results: At any time over the 24-h test period, FLZ increased SDLP, while EPL did not significantly alter SDLP. Over the 24-h test period, FLZ produced significant impairment in NLC, BS, PA and QESM. EPL did not significantly alter NLC, BS, PA or QESM. Neither FLZ nor EPL affected BRT. The most common adverse events (AEs) were headache and somnolence; there were no deaths or serious AEs.
Conclusion: EPL 5 mg for 21 days at steady state did not alter driving or cognitive/psychomotor performance in patients with sleep maintenance insomnia. EPL was well tolerated. Supported by sanofi-aventis.

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2) Rinaldi-Carmona M, Congy C, Santucci V, Simiand J, Gautret B, Neliat G, et al. Biochemical and pharmacological properties of SR 46349B, a new potent and selective 5-hydroxytryptamine2 receptor antagonist. J Pharmacol Exp Ther 1992;262:759–768.

» NR7-097

RANDOMIZED PLACEBO- AND ACTIVE-CONTROLLED STUDY OF EPLIVANSERIN, A NOVEL SLEEP AGENT, ON NEXT-DAY PSYCHOMOTOR AND COGNITIVE TASKS IN HEALTHY SUBJECTS

Joelle Micallef-Roll Ph.D., Christine Roy, M.D.,Ph.D., Astrid Delfolie, M.S., Jean-Louis Pinquier, M.D., Olivier Blin, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to better understand the effects of eplivanserin on next-day psychomotor and cognitive performance on the last morning after repeated evening administration, using flurazepam as an active control.

SUMMARY:

Introduction: Eplivanserin, an Antagonist of Serotonin Two A Receptors (ASTAR)[1], is a novel sleep agent that, unlike benzodiazepines, has no affinity for GABA receptors. Eplivanserin increases slow wave sleep [2] and is being developed at 5 mg/day for chronic insomnia characterized by nocturnal awakenings. The objective of this study was to assess next-morning psychomotor and cognitive performance after repeated administration of eplivanserin to differentiate it from classical hypnotic agents, such as flurazepam 30mg (active control), which may produce residual sedative effects in the morning due to their mechanism of action.
Methods: A 2-part, double-blind, randomized, placebo-controlled, crossover study in 24 healthy subjects. Part A: Each subject received a single dose of flurazepam or placebo at bedtime and, after a 3-wk washout, received the opposite treatment. Part B: After 0-2 wk, each subject received either oral eplivanserin 5 mg or placebo for 21 days in the evening, and then the opposite treatment for 21 days. Next-day (7:05-7:29 AM) psychometric tests included: Critical Flicker Fusion (CFF) Frequency, Choice Reaction Time (CRT), Immediate and Delayed Recall of Supraspan Word Lists, Compensatory Tracking Task (CTT), and the Bond-Lader Visual Analog Scale (VAS).
Results: Part A: flurazepam exerted a significant deleterious effect on psychomotor/cognitive performance compared to placebo (p=0.0001). Part B: eplivanserin, compared to placebo, had no significant global effect on psychomotor/cognitive performance, including alertness, although CFF decreased (-1.01 Hz; p=0.0002), likely due to a slight miosis (a known effect of 5-HT2A antagonists). Both treatments were well tolerated; the most common adverse events were headache and somnolence/asthenia.
Conclusion: Flurazepam significantly impaired next-day psychomotor and cognitive performance in the morning, unlike eplivanserin, which showed no global effects.

Supported by sanofi-aventis.

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2) Hindmarch I, Cattelin F: Effect of two dose regimens of eplivanserin, a new sleep agent, on sleep and psychomotor performance of healthy subjects. Sleep 2008; 31:A33.

» NR7-098

EFFECT OF A PERIOD 3 (PER3) POLYMORPHISM ON SLEEP ARCHITECTURE IN PHASE ADVANCED TRANSIENT INSOMNIA

Shruti Mitkus Ph.D., Gunther Birznieks, M.S., Charles A. Czeisler Ph.D., M.D., Andrew Thompson B.S., Christian Lavedan Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to: 1.Understand that the PER3 4-5 polymorphism plays a role in regulating circadian rhythm 2.Recognize that individuals with the PER3 5/5 genotype may be protected against phase advanced transient insomnia associated with jet lag or some circadian rhythm sleep disorders 3.Recognize the possibility that transient insomnia patients with the PER3 non-5/5 genotype individuals may benefit from administration.

SUMMARY:

Objective: Insomnia is the most common sleep disorder and is also a symptom of circadian rhythm sleep disorders and other medical and psychiatric conditions. A 4-5 repeat polymorphism in a clock gene, Period 3 (PER3), plays a role in regulating the sleep-wake cycle. Although this polymorphism has been associated with delayed sleep phase syndrome, its role in transient insomnia is unknown. The effect of this polymorphism on polysomnographic sleep parameters was analyzed in individuals subjected to phase-advanced transient insomnia. Method: Transient insomnia was induced in healthy subjects, through a 5-hour phase advance protocol and a “first night effect”. Individuals (N=76) were genotyped by standard methods. Several sleep parameters were evaluated by polysomnography including sleep efficiency, total sleep time, latency to persistent sleep, wake after sleep onset, rapid eye movement (REM), non-REM, and slow wave sleep (SWS). Statistical analysis was performed using a generalized linear model for analysis of variance with pooled center as a covariate. Results: PER3 5/5 individuals had significantly greater sleep efficiency over an 8-hour sleep episode as compared to the non-5/5 individuals (6.2 vs. 5.3 hours, p=0.023). Rate of REM accumulation was faster in 5/5 than non-5/5 individuals (5.8 vs. 3.7 hours to accumulate 30 minutes of REM, p=0.000055), but non-REM and SWS accumulation rate did not differ between genotypes (p>0.05). Conclusions: PER3 5/5 individuals were significantly less disrupted by phase advance induced-transient insomnia than the non-5/5 individuals, suggesting that PER3 plays a role in regulating circadian rhythm. These results also suggest that genetic variations in PER3 may contribute to susceptibility to transient insomnia. This finding may have important implications for understanding the potential selective advantage of the PER3 5/5 genotype and its role in the pathophysiology of transient insomnia. Vanda Pharmaceuticals sponsored this study

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1) Rajaratnam S.M.W., Polymeropoulos M.H., Fisher D.M., Roth T., Scott C., Birznieks G. and Klerman E.B. Melatonin agonist tasimelteon (VEC-162) for transient insomnia after sleep-time shift: two randomised controlled multicentre trials. Lancet, in press.

2) Archer S.N., Robilliard D.L., Skene D.J., Smits M., Williams A., Arendt J. and von Schantz M. (2003) A length polymorphism in the circadian clock gene PER3 is linked to delayed sleep phase syndrome and extreme diurnal preference. Sleep, 26, 413-415.

» NR7-099

NIGHT 1/WEEK 1 EFFECTS OF DOXEPIN 1, 3, AND 6 MG ON SLEEP ONSET ACROSS PHASE 3 TRIALS OF TRANSIENT AND CHRONIC INSOMNIA

Roberta Rogowski B.S.N., Philip, Jochelson, M.D., H. Heith Durrence, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to evaluate the efficacy of 1 mg and 3 mg of doxepin on measures of early morning awakenings for the treatment of chronic insomnia in elderly adults.

SUMMARY:

This report reviews sleep onset efficacy from four Phase 3 trials evaluating doxepin (DXP 1, 3, 6 mg), a selective H1 antagonist at the doses studied, in adult and elderly patient populations with either primary or transient insomnia.

Sleep onset endpoints from four randomized, double-blind, placebo-controlled trials are reported. In three trials, patients meeting DSM-IV-TR criteria for primary insomnia were randomized for up to 12 weeks of treatment. Study A was a 12-week polysomnography (PSG) trial of elderly patients (N=240; DXP 1 and 3 mg vs. placebo (PBO)); Study B was a 4-week outpatient trial also with elderly patients (N=255; DXP 6 mg vs. PBO); Study C was a 5-week PSG trial of adult patients (N=221; DXP 3 and 6 mg vs PBO). The fourth trial (Study D) used a model of transient insomnia to simulate sleep onset disturbance in healthy adults (N=565; DXP 6 mg vs. PBO). Efficacy was evaluated with PSG and patient reports. Endpoints of sleep onset included sleep efficiency (SE) in hour 1 (Studies A, C and D), latency to persistent sleep (LPS; Studies A, C and D), and patient-reported latency to sleep onset (LSO; Study A and B). Data from the first assessment point are reported; this corresponds to night 1 for all LPS measurements; week 1 for LSO in Study A; night 1 for LSO in Study B.

In Study A, DXP 3 mg significantly improved SE at hour 1 and LSO. In Study B, DXP 6 mg significantly improved LSO. In Study C, DXP 3 mg significantly improved SE in hour 1 and LPS; DXP 6 mg significantly improved LPS. In Study D, DXP 6 mg significantly improved all onset variables.

DXP 3 and 6 mg significantly improved the majority of objective and subjective sleep onset parameters across four Phase 3 trials. These data suggest that DXP 3 and 6 mg are effective at treating insomnia characterized by sleep onset difficulty in both transient and chronic insomnia populations, in both adult and elderly patient populations.

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» NR7-100

EFFECT OF MELATONIN AGONIST TASIMELTEON ON SLEEP PARAMETERS AND ARCHITECTURE IN A PHASE ADVANCE MODEL OF TRANSIENT INSOMNIA

Russell Rosenberg Ph.D., Gunther Birznieks, M.S., Christin H. Scott, M.S., Paolo Baroldi, M.D., Ph.D., Mihael H. Polymeropoulos, M.D., Thomas Roth, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to be familiar with the efficacy of tasimelteon, a potent and specific melatonin agonist of MT1 and MT2 human receptors, in a 5hr-phase advance induced model of transient insomnia. The participant should be familiar with the data that emerged from a randomized, double blind, placebo-controlled, multi-center study of 412 healthy volunteers that received either 20mg, 50mg, 100mg

tasimelteon or placebo.

SUMMARY:
Objective: Tasimelteon is an investigational dual MT1/MT2 receptor melatonin agonist. The clinical efficacy and safety of tasimelteon using a model of transient insomnia induced by both "First Night Effect" and phase advance was studied in this Phase III trial.
Methods: A randomized, double-blind, placebo-controlled, multi-center study of 412 healthy adults was conducted. Transient insomnia was induced via a combination of stress inducement (first night in a sleep laboratory) and circadian rhythm disruption (5 hour bedtime advance). Subjects received 20mg, 50mg, 100mg tasimelteon or placebo 30 minutes prior to bedtime, and sleep measures were assessed using polysomnography (PSG) with post-sleep questionnaires to measure subjective sleep onset and sleep time.
Results: The primary outcome measure, LPS, significantly improved for all tasimelteon doses (21.5 min., $p<0.001$; 26.3 min., $p<0.001$ and 22.8 min., $p<0.001$) and improvements in WASO were observed (24.2 min., $p<0.02$; 33.7 min., $p=0.001$ and 17.5 min., $p=0.081$) at 20, 50, and 100mg respectively compared with placebo. The sleep increase in tasimelteon groups was primarily observed in NREM sleep. Significant improvements in subjective assessments of sleep onset and sleep time were also demonstrated.
Conclusion: Tasimelteon demonstrated sleep onset and maintenance effects both objectively as measured by PSG and subjectively by self-assessment. Given the combined first night effect and circadian challenge, efficacy may reflect the combined soporific and circadian effects of tasimelteon. Tasimelteon was safe, well tolerated, and no next-day residual effects were observed.
Vanda Pharmaceuticals sponsored this study.

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1) Rajaratnam S.M.W., Polymeropoulos M.H., Fisher D.M., Roth T., Scott C., Birznieks G. and Klerman E.B. Melatonin agonist tasimelteon (VEC-162) for transient insomnia after sleep-time shift: two randomised controlled multicentre trials. Lancet, in press.

2) Rosenberg R., Caron J., Roth T., Amato D. (2005). An assessment of the efficacy and safety of eszopiclone in the treatment of transient insomnia in healthy adults. Sleep Med. 6(1):15-22

» NR7-101

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF ARMODAFINIL IN PATIENTS WITH EXCESSIVE SLEEPINESS ASSOCIATED WITH JET LAG DISORDER

Thomas Roth, Ph.D., Richard Bogan, M.D., James Youakim, M.D., Ronghua Yang, Ph.D., Jane Tiller, F.R.C.Psych

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, participants should be able to describe the effects of armodafinil on wakefulness compared with placebo in otherwise healthy patients with excessive sleepiness associated with jet lag disorder.

SUMMARY:
Objective: Jet lag disorder is a circadian rhythm sleep disorder that affects approximately 66% of international travelers. This disorder can disrupt sleep patterns and lead to excessive sleepiness, fatigue, decreased alertness and concentration, and impaired daytime functioning. This study is believed to be the first reported clinical study of an intervention, specifically, armodafinil, the R-and longer-lasting isomer of modafinil, to improve wakefulness in this population. This study will evaluate whether armodafinil, a non-amphetamine, wakefulness-promoting medication, improves wakefulness in patients with ES associated with jet lag disorder.
Methods: This multicenter, randomized, double-blind, placebo-controlled study enrolled patients who have experienced ICSD-defined jet lag symptoms associated with a time zone change of ?6 hours on =1 occasion during the past 5 years. Baseline assessments, including overnight polysomnography and Multiple Sleep Latency Test (MSLT), were conducted at US centers to rule out pre-existing sleep disorders. Patients then took eastbound nighttime flights on private airplanes from the US to the European center (time zone change of 6 hours). Patients were randomized to receive armodafinil 50 or 150 mg or placebo once daily while staying at the center for 3 days. Primary outcome measures were mean sleep latency (MSL) from the MSLT and Patient Global Impression of Severity ratings averaged across days 1 and 2. On day 4, patients returned to the originating US center for final assessments. Patients were discharged and contacted 2 and 7 days later. Adverse events were monitored.
Results: Data regarding the effects of armodafinil treatment on wakefulness measured by daytime MSL and patient-reported condition will be presented. Secondary and tolerability outcomes will be reported.
Conclusions: This is the first study of the efficacy and tolerability of armodafinil in patients with excessive sleepiness associated with jet lag disorder.

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» NR7-102 - WITHDRAWN

» NR7-103

POOLED ANALYSIS OF THE EFFECTS OF RAMELTEON 8 MG ON LATENCY TO PERSISTENT SLEEP IN ADULTS WITH CHRONIC INSOMNIA CHARACTERIZED BY SEVERE BASELINE SLEEP

Sherry Wang-Weigand M.D., Louis Mini, M.D., Francis Ogrinc, Ph.D.

EDUCATIONAL OBJECTIVES:
At the conclusion of this presentation, the participant should be aware of the effects of ramelteon 8 mg on reduction of latency to persistent sleep in adults with chronic insomnia characterized by severe baseline sleep latency.

SUMMARY:
Introduction: Ramelteon is an MT1/MT2 melatonin receptor agonist approved for the treatment of insomnia characterized by difficulty with sleep onset. A previous pooled analysis found the mean reduction in latency to persistent sleep (LPS) at Nights 1 and 2 in adults with chronic insomnia taking ramelteon 8 mg to be approximately 13 minutes. The current analysis follows up on that study and evaluates the mean reduction in LPS at Nights 1 and 2 in subjects with more severe baseline sleep latency.
Methods: The current study was a pooled analysis of 4 randomized, double-blind, placebo-controlled clinical trials of ramelteon in subjects with chronic insomnia and a baseline LPS >60 min. The primary endpoint of each trial was LPS, measured by polysomnography (PSG). Adults (18-82 years) with chronic insomnia who took ramelteon 8 mg or placebo were included in the pooled analysis. Mean LPS from Nights 1 and 2 was evaluated.
Results: A total of 286 subjects who took ramelteon 8 mg (mean age 43.2 years) and 269 subjects who took placebo (mean age 44.9 years) were included in the analysis. Mean LPS at baseline was similar between the 2 groups (97.24 min placebo, 96.08 min ramelteon). At Nights 1 and 2, mean LPS was significantly lower in the ramelteon 8 mg group compared with the placebo group (39.53 min versus 56.75 min, $P<0.0001$); a difference of 17.22 minutes.
Conclusions: In this pooled analysis of 4 clinical trials, ramelteon 8 mg reduced mean LPS by approximately 17 minutes compared with placebo on Nights 1 and 2 of treatment in adults with chronic insomnia characterized by severe baseline sleep latency.
This study was supported by funding from the Takeda Pharmaceuticals Company, Ltd.

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» NR7-104

EFFECTS OF RAMELTEON ON SLEEP ONSET AND PHASE-SHIFT IN INDIVIDUALS WITH DELAYED SLEEP PHASE DISORDER

Phyllis Zee Ph.D., Sherry Wang-Weigand, M.D., Ph.D., Francis Ogrinc, Ph.D., Thomas Roth, Ph.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this presentation, the participant should be aware of the ability of various doses of ramelteon to reduce latency to persistent sleep and phase-advance dim-light melatonin onset in subjects with DSPD.

SUMMARY:

Introduction: Delayed sleep phase disorder (DSPD) is a circadian rhythm sleep disorder characterized by an inability to fall asleep and wake up at a desired time and is associated with sleep onset insomnia, difficulty waking up in the morning, and excessive daytime sleepiness. In previous clinical trials, ramelteon, a melatonin receptor agonist, has shown both phase-shifting and sleep-promoting effects. The current study evaluated the ability of ramelteon to advance sleep timing and melatonin phase in individuals with DSPD.

Methods: Adults (>18 years) meeting diagnostic criteria for DSPD were enrolled in a randomized, double-blind, placebo-controlled study. After an initial screening period, subjects were given ramelteon 1 mg, 4 mg, 8 mg, or placebo 30 minutes before desired sleep time nightly for 2 weeks, followed by a 1-week single-blind placebo run-out period. Latency to persistent sleep (LPS) was measured using polysomnography during the screening period and on Nights 6, 7, 13, and 14 of the treatment period. Complete endogenous melatonin profiles were collected during the screening period and after the 2-week treatment period. Dim-light melatonin onset time (DLMO) was compared between the screening phase and run-out phase to detect any phase shifts.

Results: A total of 132 individuals (32 placebo, 32 ramelteon 1 mg, 33 ramelteon 4 mg, 35 ramelteon 8 mg) were included in the study. There was a trend towards a reduction in mean LPS at Nights 6 and 7 with ramelteon 4 mg compared with placebo (P=0.084); however there were no statistically significant differences between any dose of ramelteon and placebo. A significant shift in DLMO (1 hour 50 min) was detected with ramelteon 1 mg compared with placebo.

Conclusions: In individuals with DSPD, ramelteon 1 mg significantly advanced the circadian rhythm of melatonin and there was a trend towards a reduction in LPS with ramelteon 4 mg compared with placebo.

This study was supported by the Takeda Pharmaceutical Company, Ltd.

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2) Zammit G, Erman M, Wang-Weigand S, Sainati S, Zhang J, Roth T. Evaluation of the efficacy and safety of ramelteon in subjects with chronic insomnia. J Clin Sleep Med 2007;3(5):495-504.

» NR7-105

SLEEP CORRELATES IN CHILDHOOD DEPRESSION: A STUDY IN AN EGYPTIAN SAMPLE

Tarek Asaad M.D., Yasser Abdel Razek, M.D., Ghada Abdel Razek, M.D., Mona Abdel Hady, M.D.

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the Characteristic sleep patterns of depressed children and adolescents and to identify the similarities and differences from sleep patterns of depressed adults.

SUMMARY:

Background: Sleep disturbances are prominent features of major depression. Characteristic sleep patterns have been described in adults with Major Depressive Disorder (MDD), but the sensitivity and specificity of such changes have been always a matter of great debate. REM sleep abnormalities , especially short REM latency, have been formerly thought as “specific” to depression. With more extensive studying , similar changes have been reported in other psychiatric and even non-psychiatric disorders, but the changes were ,of course, more robust in depression. Polysomnographic studies of children and adolescents with MDD failed to find objective conclusive results, comparable to adults.

The aim of the present study was to highlight this area, evaluating sleep profile in children and adolescents with MDD and how far it resembles , or differs from what has been previously described in adults.

Subjects & Methods :20 patients, with age range from 9 to 17 years, fulfilling DSM-IV criteria of MDD (according to SCID-I assessment) have been recruited from those attending outpatient department of Ain Shams University Psychiatric Institute , together with 10 age and sex matched healthy controls. Both patients and controls were subjected to physical and psychiatric examination, standardized sleep questionnaire for assessment of subjective sleep complaints in children and adolescents , as well as all-night polysomnography (repeated, when needed).

Results :Significant findings included : more difficulty in falling asleep , interrupted sleep ,shorter sleep duration , as well as increased nightmares in the patients group, regarding “subjective” sleep assessment. Significant polysomnographic findings were : prolonged sleep latency, short REM latency , decreased slow wave sleep (SWS) and decreased sleep efficiency. REM % and REM density were not significantly different.

Conclusion : MDD in children and adolescents shares some of the polysomnographic features described in adult major depression, which is in favour of considering it among the “continuum” of mood disorders ,rather than being a “separate” entity by itself.

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» NR7-106

TOTAL SERUM CHOLESTEROL AND SUICIDALITY IN MAJOR DEPRESSIVE DISORDER

Tarek Asaad M.D., Khaled Abdel Azim, M.D., S. Eid, M.D , Yasser Abdel Razek ,M.D

EDUCATIONAL OBJECTIVES:

At the conclusion of this session, the participant should be able to recognize the results of different studies about the relationship between serum cholesterol and Major depression with or without suicidal behavior.

SUMMARY:

Background: The relationship between serum cholesterol & depression & the risk of suicide have been an area of interest many years back. All the previous studies are controversial & conflicting.

Objectives: To determine the concentration of total serum cholesterol (or other cholesterol fractions) in different groups of patients

with major depression as an endeavor to answer the question: Can total serum cholesterol be used as a biological marker for depression & / or suicidal behavior? Subjects & methods: In this study we have studied three depressed patients groups (namely suicide attempters group; non-suicide depressed group & remission group) & one control group. They fulfilled the diagnostic criteria for major depressive episode according to DSM-IV. Socio-demographic & clinical variables (including Hamilton depression rating scale & Beck scale for suicide ideation) were correlated in all groups with total serum cholesterol (& its fractions namely, high density lipoprotein-cholesterol; low density lipoprotein-cholesterol& triglycerides). Results: no statistical differences were found between all groups regarding total cholesterol (or its fractions) even after adding of the gender effect. We conducted correlational analyses between lipid profiles & clinical variables inside the suicide attempters group & all results were insignificant statistically. Conclusion: Our findings did not confirm the hypothesis that low total serum cholesterol concentrations are significantly correlated to the severity of depression; phase of the illness or to the suicidality in depressed patients.

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