



Translating Mental Health Research into Practice: Accelerating the Pace

**49th Annual
NCDEU Meeting**
June 29 - July 2, 2009
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LATE-BREAKING RESEARCH REPORTS

9:00 a.m. – 12:00 p.m.

SSRI Use During Pregnancy and Preterm Birth

Katherine L. Wisner, M.D.

University of Pittsburgh, PA

Objective: Serotonin reuptake inhibitor (SRI) use during pregnancy incurs a low absolute risk for major malformations; however, other adverse outcomes have been reported. Major depressive disorder (MDD) also impacts reproductive outcomes. The objective was to determine whether: (1) minor physical anomalies (MPA), (2) maternal weight gain and infant birth weight, (3) rate of preterm birth, and (4) neonatal adaptation were affected by SRI or MDD exposure.

Methods: This was a prospective observational investigation with maternal assessments at 20, 30, and 36 weeks of gestation. Neonatal outcomes were obtained by blinded review of delivery records and infant examinations. Pregnant (N=238) women were categorized into mutually exclusive exposure groups: (1) no SRI, no MDD (N=131); (2) SRI (N=71), two subgroups (continuous=48 and partial=23); (3) MDD (N=36), two subgroups (continuous=14 and partial=22). The mean depressive symptom level of the Continuous MDD, no SRI group was significantly greater than all other groups, which demonstrates the expected treatment effect in the SRI group. Main outcome measures were MPA, maternal weight gain, infant birth weight, pregnancy duration, and neonatal characteristics.

Results: Infants exposed to either SRI or MDD continuously across gestation were more likely to be born preterm than non- or partially- exposed infants. Neither SRI nor MDD exposure increased the number of MPA or reduced maternal weight gain. Mean infant birth weights were equivalent. Other neonatal outcomes were similar (except 5 minute Apgar scores).

Conclusions: For pregnant women with MDD, both continuous SRI treatment and continuous untreated depression were associated with a >20% preterm birth rate.

Learning Objectives:

- Review reproductive outcomes impacted by SSRI exposure from this NIMH funded study
- Define the possible biological mechanisms for a relationship to preterm birth for both SSRI and MDD

Literature References:

Oberlander TF, et al. Neonatal outcomes after prenatal exposure to selective serotonin reuptake inhibitor antidepressants and maternal depression using population-based linked health data. Arch Gen Psychiatry 2006;63:898–906.

Suri R, et al. Effects of antenatal depression and antidepressant treatment on gestational age at birth and risk of preterm birth. Am J Psychiatry 2007;164:1206–13.

Wednesday, July 1, 2009

LATE-BREAKING RESEARCH REPORTS

9:00 a.m. – 12:00 p.m.

Selective Serotonin Receptor Inhibitor Pharmacotherapy Associated with Blood Transfusion in Depressed Patients Following Primary Total Knee Arthroplasty

Jason Ye, Sc.B.

Center for Hip and Knee Replacement, Columbia University Medical Center

Major depression is a common comorbidity in patients undergoing total knee arthroplasty (TKA). We examine the factors associated with blood transfusion following TKA in patients treated pharmacologically for depression.

Of 216 primary TKA patients with complete data sets (collected prospectively in our CHKR Registry), 45 patients were being treated with some type of antidepressant (20.8%). Of 45 TKA patients taking antidepressants, 25 (65.7%) took only selective serotonin receptor inhibitors (SSRIs) and 13 (34.2%) took only other antidepressants (OAD) during the peri-operative time period.

On univariate analysis, transfusion requirement was associated with SSRI therapy (as opposed to exclusive OAD therapy [$p=0.022$]), cardiac comorbidity ($p=0.027$), respiratory comorbidity ($p=0.025$), GI comorbidity ($p=0.008$), bilateral TKA (as opposed to unilateral TKA [$p=0.001$]) and use of Simplex P type acrylic bone cement ($p=0.033$). SSRI therapy was associated with transfusion requirement when controlling for bilateral versus unilateral TKA and respiratory comorbidity ($p=0.025$); bilateral versus unilateral TKA and cement type ($p=0.038$); bilateral versus unilateral TKA and GI comorbidity ($p=0.046$). The association of SSRI therapy with transfusion requirement did not reach significance when controlling for bilateral versus unilateral TKA and cardiac comorbidity ($p=0.121$). However, within the unilateral TKA sub-cohort, SSRI therapy was associated with transfusion requirement ($p=0.034$), while cardiac comorbidity was not associated with SSRI therapy ($p=0.119$) and cardiac comorbidity was not associated with transfusion requirement ($p=0.226$). On multiple linear regression, SSRI therapy was found to be a significant positive contributor to transfusion requirement (adjusted $R^2=0.603$, $\beta=0.22$, $\text{sig}=0.04$).

The association of SSRIs with bleeding during and after major surgery should be further investigated given prior implications of possible interference of normal platelet serotonin receptor function by SSRIs.

Learning Objectives:

- Understand data associating SSRIs with concrete measures of increased blood loss following major surgery
- Review multidisciplinary approach to determine whether or how SSRIs should be temporarily stopped prior to specific types of major surgery to prevent blood loss

Literature References:

Weinrieb RM, et al. Selective serotonin re-uptake inhibitors and the risk of bleeding. *J Clin Psychiatry* 2003;64:1502–10.

Turner MS, et al. Clinical impact of selective serotonin re-uptake inhibitors therapy with bleeding risks. *J Intern Med* 2007;261:205–13.

LATE-BREAKING RESEARCH REPORTS

9:00 a.m. – 12:00 p.m.

A Pilot Study of a Novel Drug Combination in Major Depressive Disorder

Maurizio Fava, M.D.

Massachusetts General Hospital, Boston

BCI-952 is a novel combination drug therapy, discovered using a proprietary pre-clinical neurogenesis platform (developed by BrainCells Inc., San Diego) that seeks to enhance the neurogenic profile of candidate drugs. We are reporting the first study to evaluate the clinical application of this unique drug development platform in a patient population. One hundred forty-two patients meeting DSM-IV criteria for Major Depressive Disorder (MDD) consented to participate in a 6-week double-blind, placebo-controlled, randomized study of BCI-952. Efficacy measures included the Clinical Global Impressions Scales for severity and improvement (CGI-S and CGI-I respectively), the Inventory of Depressive Symptoms (IDS-C30), and the patient-rated QIDS-SR16. Spontaneously reported adverse events were recorded.

Patients receiving BCI-952 achieved statistically significant improvement compared to the placebo on multiple measures of efficacy. For example, in a preliminary analysis, 39 of 67 (58%) BCI-952 patients achieved CGI-I scores ≤ 2 in contrast to only 12 of 33 (36%) placebo patients (Fisher's exact test; $p < 0.05$). Patients in the BCI-952 group revealed significantly greater improvement on the IDS-C30 than placebo patients ($p < 0.05$). Side effects were minimal and not different between any group.

We believe that this pilot study represents the first demonstration that rational drug discovery utilizing a pre-clinical neurogenesis platform can be applied to the treatment of MDD.

Learning Objectives:

- Learn the results of a placebo-controlled study of a novel combination therapy for depression
- Learn about the tolerability of this combination therapy in depression

Literature References:

Santarelli L, et al. Requirement of hippocampal neurogenesis for the behavioral effects of antidepressants. *Science* 2003;301:805–59.

Malberg J, et al. Chronic antidepressant treatment increases neurogenesis in adult rat hippocampus. *J Neurosci* 2000;20:9104–10.

Wednesday, July 1, 2009

LATE-BREAKING RESEARCH REPORTS

9:00 a.m. – 12:00 p.m.

Differential Response of Depressive and Manic Symptoms in Mixed States (MS) of Bipolar Disorder (BD)

Vivek Singh, M.D.

University of Texas Health Science Center at San Antonio

Background: Mixed states (MS), intrinsic and severe presentations of bipolar disorder (BD), constitute >50% of all syndromal episodes in BD and are associated with treatment refractoriness. Most reports of treatment efficacy in MS are post hoc analysis of clinical trials that included both manic and MS subjects. No study has reported separate outcomes on depressive and manic components of MS in either acute or prophylactic treatment. This presentation will focus on differential efficacy of adjunctive risperidone and lamotrigine on depressive and manic symptoms, acute and long term, and the predictors of sustained response in MS identified for each drug.

Methods: Results from two separate open label studies of adjunctive treatments in MS with risperidone (20 week duration; analysis completed) and lamotrigine (22 weeks duration; data collated and analysis in progress) in MS will be presented. Subjects in both studies were assessed with the Young Mania Rating Scale (YMRS) and Montgomery Åsberg Depression Rating Scale (MADRS). Primary outcome was measured by the proportion of subjects who attained sustained response (50% reduction on the MADRS or YMRS from baseline maintained over eight weeks without subsequent relapse) on either the depressive or manic component.

Results: In the risperidone study, a significantly higher proportion achieved sustained response on the manic compared to the depressive component, 40% (16/40) versus 15% (6/40) respectively (McNemar's Chi square 8.33, $p=0.004$). Higher elevated mood (T-test, unequal variance, DF 36.6, $t=5.42$, $p<0.0001$) and lower apparent sadness predicted (T-test, equal variance, DF 38, $t=2.51$, $p<0.016$). This finding indicates the need to assess outcomes on both manic and depressive components in patients with MS.

Learning Objectives:

- Understand the epidemiology of MS
- Understand differential response of manic and depressive symptoms in MS
- Understand predictors of acute and sustained response in MS

Literature References:

Suppes T, et al. The Texas implementation of medication algorithms: Update to the algorithms for treatment of bipolar I disorder. *J Clin Psychiatry* 2005;66:870–76.

Sachs G, et al. Risperidone plus mood stabilizer versus placebo plus mood stabilizer for acute mania of bipolar disorder: A double-blind comparison of efficacy and safety. *Am J Psychiatry* 2002;159:1146–56.

LATE-BREAKING RESEARCH REPORTS

9:00 a.m. – 12:00 p.m.

Sleep Actigraphy among Adolescents at Risk for Bipolar Disorder

Tina Goldstein, Ph.D.

University of Pittsburgh Medical Center, Western Psychiatric Institute and Clinic

Background: Dysregulated sleep is a classic symptom of both mania and depression in bipolar disorder (BP). Research also indicates that sleep disruptions often precede, and also precipitate, mood episodes in BP. Circadian system vulnerability is thus considered part of the biological diathesis for BP. It is therefore possible that circadian system abnormalities represent endophenotypes for BP that would allow for early detection/prevention efforts for those at-risk.

Objective: To examine sleep via actigraphy data among youth at-risk for BP.

Methods: Nine adolescents at-risk for BP by virtue of a positive first-degree family history of BP were recruited for a treatment development study of preventive Interpersonal and Social Rhythm Therapy (IPSRT). Demographic and clinical variables were measured at intake via interview with the subject and a parent. Subjects wore a multi-sensor armband (SenseWear Body Media) for four consecutive days (two weekdays, two weekend days) at study entry that collected continuous physiological data on sleep.

Results: Average total sleep time was 5.7 hours (SD=1.9); 75% of nights assessed were considered short sleep (<6.5 hours). Mean total nighttime sleep was similar on weekdays (M=5.7, SD=1.8) and weekends (M=5.6, SD=2.1). Average bedtime was 1:50 am on weekends and 11:54 pm on weekdays. Average wake-up time was 9:07 am on weekends and 7:27 am on weekdays. Subjects averaged 3.8 awakenings per night (SD=2.1); 75% of nights were characterized by at least three awakenings. Mean sleep efficiency was 75.7% (SD=14.2). Nearly 90% of nights were classified as low sleep efficiency (<90%).

Conclusions: Actigraphy data indicate that sleep patterns may be disrupted among adolescent offspring of BP parents. Specifically, we observed high rates of short sleep, low sleep efficiency, and frequent awakenings relative to normative data for this age group.^{1,2} These data indicate that an intervention targeting stabilization of sleep/wake cycles for those at-risk for BP may hold promise.

Learning Objectives:

- Understand the relationship between sleep and risk for bipolar disorder
- Become familiar with actigraphy data indicative of disrupted sleep patterns in adolescents at-risk for bipolar disorder

Literature References:

1. Carskadon MA, et al. Adolescent sleep patterns, circadian timing and sleepiness at a transition to early school days. *Sleep* 1998;21:871-81.
2. Wolfson AR, et al. Understanding adolescents' sleep patterns and school performance: A critical appraisal. *Sleep Med Rev* 2003;7:491-506.

Wednesday, July 1, 2009

LATE-BREAKING RESEARCH REPORTS

9:00 a.m. – 12:00 p.m.

A 15-Month, Random Assignment, Effectiveness Trial of Long-Acting Risperidone Injection versus Oral Atypical Antipsychotic Agents in Persons with Bipolar Disorder

Roy Chengappa, M.D.

University of Pittsburgh Medical Center, PA

Introduction: Medication gaps precede recurrences in persons with bipolar disorder (BD). Long-acting injectable antipsychotics have effectively addressed this problem in schizophrenia but are rarely used in BD. We hypothesized that BD patients receiving long-acting risperidone injections (LARI) would remain in treatment longer and experience fewer negative clinical events than those receiving oral atypical antipsychotic agents (AAP).

Methods: Moderately symptomatic (YMRS=16) BD patients were recruited to this 15-month naturalistic but randomized study. Patients were being switched from their existing antipsychotic agent or started on one. During a three month period, subjects were stabilized on oral risperidone followed by LARI (n=23) or an AAP (n=25); mood stabilizers continued unchanged. Patients that improved continued for one additional year. A board independent of the study declared clinical events that occurred among patients, and the treatment assignment (LARI or AAP) was concealed. Events (e.g., mixed episode, major depressive episode [MD]) were primary outcomes.

Results: Nine patients did not stabilize in three months leaving 39 patients in the one year follow-up (21 LARI, 18 AAP). Eleven patients (7 LARI, 4 AAP) had no clinical events. Forty-seven clinical events were recorded; fourteen LARI patients had 18 events [median=1, range 1-2] and 14 AAP patients had 29 events, [median=2, range 1-4], Mann-Whitney=141, p=0.037. Of the events, 36% were hypomanic or manic or mixed episodes; 21% were MD or sub-syndromal depressive symptoms; 32% were lapses in alcohol or drug dependence; five were miscellaneous. LARI patients remained 312 (\pm 158) days in the study versus 235 (\pm 171) days for AAP. 50% AAP subjects gained =7% baseline body weight compared to 33% of LARI.

Conclusions: LARI patients remained longer in treatment and experienced significantly fewer clinical events. LARI appears beneficial for BD patients; characterizing which BD subjects might benefit is worth exploring.

Learning Objectives:

- Review the role of long-acting injectable medications in the treatment of schizophrenia and the lack of data for bipolar patients
- Review the outcomes of a 15-month randomized trial comparing long-acting risperidone versus oral atypical antipsychotic agents

Literature References:

Schooler N. Relapse and rehospitalization: Comparing oral and depot antipsychotics. J Clin Psychiatry 2003;64.
Fleischhacker W. Treatment of schizophrenia with long-acting injectable risperidone: A 12-month open-label trial of the first long-acting second-generation antipsychotic. J Clin Psychiatry 2003;64:10.

LATE-BREAKING RESEARCH REPORTS

9:00 a.m. – 12:00 p.m.

A Double-Blind, Placebo-Controlled Study of Gabapentin Treatment of Cannabis Dependence

Barbara J. Mason, Ph.D.

Scripps Research Institute, La Jolla

Background: Cannabis dependence is the most prevalent illicit substance dependence disorder in the U.S., with characteristic disturbances in sleep, mood, and craving following cessation of use that may be motivational for relapse. There are no approved pharmacotherapies for cannabis dependence or withdrawal.

Objective: To gain an estimate of the efficacy and safety of gabapentin treatment of cannabis dependence and withdrawal.

Subjects: Fifty treatment-seeking outpatients meeting DSM-IV criteria for cannabis dependence. Exclusion criteria were dependence on substances other than cannabis or nicotine, pregnancy and, clinically significant medical or psychiatric disorders and current use of medications that might influence study outcomes.

Methods: Subjects were randomized to 12 weeks of double-blind treatment with 1200 mg/d gabapentin or matched placebo. Research assessments and manualized behavioral therapy occurred weekly. Multilevel analyses compared changes from baseline in measures of consumption, mood and sleep for gabapentin versus placebo.

Results: Subjects were 88% male, 76% Caucasian, and averaged 34 years of age. Subjects had an average of 12 years of daily marijuana (mj) smoking, and were smoking 11 grams per week (g/wk) and had urinary THC/creatinine of 673 at baseline. Subjects treated with gabapentin showed significant decreases in g/wk ($p < 0.01$) and in THC/creatinine ($p < 0.02$), relative to placebo. Gabapentin subjects showed significantly greater improvement in mj craving ($p < 0.01$), the Beck Depression Inventory ($p < 0.05$), and sleep quality, latency, duration, and daytime dysfunction on the Pittsburgh Sleep Quality Index, relative to placebo. Gabapentin was well tolerated.

Conclusions: These results provide support for the safety and efficacy of gabapentin treatment of cannabis dependence and withdrawal.

Importance: A withdrawal syndrome characterized by an aggregate of superficially mild symptoms may be particularly responsive to treatment with a neuromodulating drug like gabapentin. Thus, the development of gabapentin as a pharmacotherapy for cannabis dependence may have potential public health benefits.

Learning Objectives:

- Understand the clinical features of cannabis withdrawal
- Become familiar with methods of assessing and treating cannabis dependence

Literature References:

Budney AJ, et al. The time course and significance of cannabis withdrawal. *J Abnorm Psychol* 2003;112:393–402.
Huestis MA, Cone EJ. Differentiating new marijuana use from residual drug excretion in occasional marijuana users. *J Anal Toxicol* 1998;22:445–54.

Wednesday, July 1, 2009

LATE-BREAKING RESEARCH REPORTS

9:00 a.m. – 12:00 p.m.

Technology Assisted Behavioral Intervention (TABI) for Depression: Feasibility of Combining Telecommunications Technologies

David C. Mohr, Ph.D.

Northwestern University

Background: Telemental health aims to reduce barriers by providing effective treatment over large geographic distances and reducing costs. Trials to date have examined telemental health media in isolation. Internet interventions are efficient but produce extremely high non-adherence and dropout rates.^{1,2} Telephone psychotherapy produces good adherence and attrition of around 7%, but still requires substantial therapist time.³ The goal of this feasibility study was to develop a treatment model that combines the efficiencies of internet treatment with the telephone to enhance adherence.

Methods: Fifteen participants were enrolled with a PHQ-9>10, which is the MacArthur criterion for referral for psychotherapy.⁴ Treatment included access to “mood Manager,” an internet CBT program that contains learning modules and tools that are designed to be used on a frequent basis to support behavioral activation and cognitive restructuring. Participants also received weekly brief motivational interviewing (MI) phone calls. Depression was assessed using the PHQ-9 and telephone-administered Hamilton Depression Rating Scale (HAMD) at baseline, week 4, and week 8.

Results: One patient dropped out before starting the program, and 14 (93.3%) completed. The PHQ-9 dropped from 14.7±3.9 at baseline to 5.2±4.7 at week 8, $p<0.0001$. The HAMD dropped from a baseline of 19.1±6.5 to 10.3±6.7, $p<0.0001$. Patients logged in on average 2.6 times per week for 9.9 minutes each time. MI phone calls averaged 10.7 minutes per week.

Discussion: This feasibility study supports the use of multiple telecommunications channels aimed at providing both standardized skills training and outreach to enhance adherence. These results must be confirmed in a larger randomized controlled trial, which is currently underway.

Learning Objectives:

- Understand how telecommunications media can be integrated to improve efficacy
- Understand how telecommunications media can be integrated to improve adherence

Literature References:

1. Warmerdam L, et al. Internet-based treatment for adults with depressive symptoms: Randomized controlled trial. *J Med Internet Res* 2008;10:e44.
2. Clarke G, et al. Overcoming depression on the internet (ODIN) (2): A randomized trial of a self-help depression skills program with reminders. *J Med Internet Res* 2005;7:e16.
3. Mohr DC, et al. The effect of telephone-administered psychotherapy on symptoms of depression and attrition: A meta-analysis. *Clin Psychol Sci Pract* 2008;15:243–53.
4. The MacArthur Foundation's Initiative on Depression and Primary Care. The Macarthur initiative on depression and primary care at Dartmouth and Duke: Depression management toolkit. Hanover, NH: Dartmouth, 2004.

LATE-BREAKING RESEARCH REPORTS

9:00 a.m. – 12:00 p.m.

Randomized, Double-Blind, Placebo-Controlled Study with Armodafinil in Patients with Residual Excessive Sleepiness Associated with Treated Obstructive Sleep Apnea and Comorbid Depressive Disorders: Patient Characteristics and Treatment Effect

Andrew Krystal, M.D.

Duke University Medical Center

Background: Depression is a common comorbidity in patients with obstructive sleep apnea (OSA). However, the clinical implications of a comorbid depressive disorder on the treatment of residual excessive sleepiness (ES) in patients with treated OSA are unknown. Armodafinil, the R- and longer-lasting isomer of modafinil, is a non-amphetamine, wakefulness-promoting medication. This report characterizes patients in a study of armodafinil in patients with ES associated with continuous positive airway pressure (CPAP)-treated OSA who have a comorbid depressive disorder.

Methods: This is a multi-center, randomized, double-blind, placebo-controlled, parallel-group study. Patients had residual ES despite CPAP-treated OSA and a comorbid depressive disorder (met DSM-IV-TR criteria for major depressive disorder or dysthymic disorder) requiring antidepressant monotherapy. Inclusion criteria included a Clinical Global Impression of Severity (CGI-S) score of moderately ill or worse with regard to ES, an Epworth Sleepiness Scale (ESS) score of ≥ 10 , and a Hamilton Rating Scale for Depression (HAM-D-17) score of < 17 . A blinded, per-protocol baseline summary was conducted when 50% of the planned sample had completed the study. Efficacy data will be available for presentation.

Results: Of the 134 patients, 92% were diagnosed with major depressive disorder and 8% with dysthymia. 53% and 34% of patients were moderately or markedly ill for ES, respectively Clinical Global Impressions Scale for Severity (CGI-S). At baseline, the Maintenance of Wakefulness Test mean (SD) sleep latency (MSL) was 20.5(8.4) minutes and the mean ESS score was 14.7(3.2). The mean HAM-D-17 score was 6.7(4.3), indicating remitted depressive disorder. Mean worst fatigue score from the Brief Fatigue Inventory of 6.7(2.0) suggested moderate fatigue. Functional impairment was revealed by a mean score of 14.4(2.9) on the Functional Outcomes of Sleep Questionnaire. Primary outcomes of effects on wakefulness (change in MSL) and the proportion of patients with at least minimal improvement in ES for armodafinil versus placebo will be reported, along with secondary and tolerability outcomes.

Conclusions: Patients with treated OSA-associated residual ES and a comorbid depressive disorder report fatigue and functional impairment. This is the first study of armodafinil focused on this subgroup of the broader OSA patient population.

Learning Objectives:

- Understand the characteristics of patients with residual obstructive excessive sleepiness associated with sleep apnea who also have a comorbid depressive disorder
- Understand the efficacy and tolerability of armodafinil in this patient population

Literature References:

Roth T, et al. Effects of armodafinil in the treatment of residual excessive sleepiness associated with obstructive sleep apnea/hypopnea syndrome: A 12-week, multi-center, double-blind, randomized, placebo-controlled study in nCPAP-adherent adults. *Clin Ther* 2006;28:689–706.

Hirshkowitz M, et al. Adjunct armodafinil improves wakefulness and memory in obstructive sleep apnea/hypopnea syndrome. *Respir Med* 2007;101:616–27.

Wednesday, July 1, 2009

LATE-BREAKING RESEARCH REPORTS

9:00 a.m. – 12:00 p.m.

Randomized, Double-Blind, Placebo-Controlled, Crossover Study of the Efficacy and Safety of Lisdexamfetamine Dimesylate in Adults with Attention Deficit Hyperactivity Disorder: Novel Findings Using the Adult Workplace Environment Design

Matthew Brams, M.D.

Bayou City Research, Ltd.

Background: Duration of efficacy and safety of lisdexamfetamine dimesylate (LDX, Vyvanse®) were assessed in adults (18–55 years) with ADHD using the adult workplace environment (AWE).

Methods: Subjects entered a 4-week, open label, dose-optimization with LDX (30, 50, and 70 mg/d), then randomized to a two-week, double-blind, placebo-controlled crossover phase. Efficacy assessments included the Permanent Product Measure of Performance (PERMP) total score (attempted + correct) measured predose and 2, 4, 8, 10, 12, and 14 h postdose with scores averaged across postdose sessions (primary) and at each time throughout the day versus placebo (secondary) and ADHD Rating Scale (ADHD-RS) with adult prompts at baseline and crossover visits. Safety assessments included adverse events (AEs), vital signs, and ECG.

Results: 127 subjects were randomized (105 ITT, 103 completed the study). LS mean [SE] PERMP total scores were higher for subjects on LDX versus placebo when averaged across postdose sessions (312.9 [8.59] versus 289.5 [8.59]; $p < 0.0001$) and at all time points from 2 to 14 h postdose ($p < 0.005$ for all). During the crossover phase, ADHD-RS scores decreased ($p < 0.0001$) from baseline by mean (SD) -18.5 (9.88) and -7.8 (9.00) for subjects taking LDX and placebo, respectively. AEs (>10%) during dose-optimization were decreased appetite, dry mouth, headache, and insomnia; no AEs >10% were reported during crossover with LDX.

Conclusions: In adults with ADHD, LDX improved and maintained math test performance from the first (2 h) to last (14 h) postdose timepoint versus placebo. LDX was generally well tolerated.

Learning Objectives:

- The novel adult workplace environment (AWE) is designed to inform clinicians on aspects of ADHD treatment effect throughout the day in adults
- Duration of efficacy and safety of lisdexamfetamine dimesylate versus placebo in adults with ADHD in the AWE setting

Literature References:

Adler LA, et al. Double-blind, placebo-controlled study of the efficacy and safety of lisdexamfetamine dimesylate in adults with attention-deficit/hyperactivity disorder. *J Clin Psychiatry* 2008;69:1364–73.

Biederman J, et al. Lisdexamfetamine dimesylate and mixed amphetamine salts extended-release in children with ADHD: A double-blind, placebo-controlled, crossover analog classroom study. *Biol Psychiatry* 2007;62:970–76.