Full Abstracts for Poster Session

Wednesday, January 18, 2017

Session 1  |  1:00-1:50 pm
Session 2  |  1:50-2:45 pm
Brief Communications  |  3:00-4:30 pm
McLean Research Day 2017

Presenting Author: Ellen Finch, Research Assistant and Program Coordinator, BA

Co-Authors: John Gunderson, MD

Title: Learning Good Psychiatric Management (GPM): Preliminary Data

Key words: Good Psychiatric Management, Borderline Personality Disorder, GPM Questionnaire, GPM Trainers

Introduction: Borderline personality disorder (BPD) represents nearly 20% of psychiatric hospital and outpatient clinic admissions. Despite this prevalence, there are significant limitations in BPD training for psychiatrists and other mental health professionals. Recently, Good Psychiatric Management (GPM; Gunderson, 2011) was developed as an accessible, generalist model of treatment for BPD and, since 2012, over 3,100 mental health clinicians have been trained in GPM. As GPM is proliferated, the need for a reliable evaluation measure of GPM training effectiveness grows. To address this, John Gunderson, MD, in collaboration with GPM trainers Brian Palmer, MD, and Lois Choi-Kain, MD, recently developed the GPM Questionnaire. This poster presents preliminary data on GPM Questionnaire responses and explores its potential role in BPD treatment training.

Methods: A 100 item, true-false self-report questionnaire was developed in July 2016. Since then, the questionnaire has been filled out by mental health care professionals in various stages of training including GPM experts, experienced BPD treaters, and untrained medical residents. The questionnaires were scored by hand and the data analyzed in SPSS.

Results: GPM questionnaires are still being distributed and scored. Data available at this time shows scores increasing with BPD expertise, ranging from an average of 32.3% correct by inexperienced students to 100% correct by official GPM trainers. The poster will include data on mean scores of clinicians with varying levels of trainings, questions that are found to be most frequently correct or incorrect, and other significant findings.

Discussion: The significance of these preliminary findings are multifold. First, the large range in scores indicates that the GPM Questionnaire is capable of evaluating change and improvement in knowledge of BPD treatment among psychiatrists. Similarly, the consistent improvement of scores as level of training and experience increases indicates that the measure accurately reflects one’s competency in BPD treatment. Identifying which areas of GPM were most often incorrect and correct has strong implications for GPM trainers. This data will give GPM trainers the knowledge of what common sensical and may not require significant teaching, as well as areas that are not being taught adequately and require additional teaching. Furthermore, the average score of the inexperienced resident was still over 30%, supporting a central tenant of GPM: that good BPD treatment is largely common sense. These findings suggest that in the future, the GPM Questionnaire should be used before and after residency training as well as before and after GPM workshops to help determine the competency of clinicians, effectiveness of training, and areas of weakness that need more teaching. The questionnaire is currently one of the ways to evaluate people’s readiness to become and official GPM trainer. The questionnaire is currently being widely distributed and data is continuing to be collected. Special attention will beige to psychiatric residents and other students in future analyses that are planned.

Topic areas: Borderline Personality Disorder
McLean Research Day 2017

Theoretical/Commentary

Poster # 2
Time: 1:50-2:45pm

Presenting Author: Arthur Siegel, Director Internal Medicine

Co-Authors: Ross J. Baldessarini, M.D.

Title: Mitigating the Increased Risk of Suicide After Hospital Discharge: Can Psych Alert Technology Help?

Key words: Suicide, prevention, post-discharge, technology

Background: A Sentinel Event Alert prioritizing the need for improved detection and treatment of suicidal risk was issued by the Joint Commission in February, 2016 [1]. Psychiatric illnesses, especially mood disorders, present increased risk for suicide, especially following discharge from inpatient psychiatric care [2].

Observations: Olfson et al. [3] recently studied post-hospitalization suicidal risk in a nationwide US sample (2001–2007) of 1.86 M adult hospital discharges (41% psychiatric) involving 370 suicides [3]. They found an overall suicide rate within 3 months after discharge of 178/100,000 person-years, compared to an annual rate in the general population of only 12/100,000, which was 58% higher than overall suicide rates for the same disorders [3]. By primary diagnoses, 3-month post-discharge suicide rates ranked: major depressive disorder (MDD) ≥ bipolar disorder (BD) ≥ schizophrenia (Sz) > substance use disorders (SUDs) >> general medical diagnoses (Med) = general population (Genl Pop) rates. For all diagnostic groups, as expected, risks were 2–4-times higher among men than women [Figure 1].

Proposal: Recent research implicates inadequacies in the quality, timing, reliability, and consistency of post-hospital aftercare as contributing to suicidal risk [2]. In addition to improved planning and integration of post-hospital psychiatric aftercare, we recommend development and evaluation of a psychiatric variant (Psych Alert) of cell phone-based Medical Alert technology to mobilize an emergency response for patients seeking support at pre-suicidal moments [4]. Direct wireless contact with a known clinician via a necklace-type push-button call device should add protective benefit beyond accessing programs such as the National Suicide Prevention Lifeline (1–800–273–TALK [8255]). The proposed Psych Alert system requires design, implementation, and field testing of effectiveness, following the lead of comparable systems established for general medical applications [4,5].


Topic areas:
Addiction, Anxiety, Bipolar, Borderline Personality Disorder, Depression, Dissociative Disorders
The role of emotion regulation in treating severe pediatric OCD

Background: Emotion regulation (ER) is a transdiagnostic process that plays a key role in a wide range of psychopathology (Sheppes, Suri & Gross, 2015). Research has shown that those with anxiety disorders are more likely to experience difficulty managing their emotions and have a poorer understanding of emotions (Suveg & Zeman, 2004). Unfortunately, research specifically within pediatric obsessive-compulsive disorder (OCD) is limited. Advancing the understanding of emotion regulation within the context of both pediatric OCD and treatment outcome could provide more nuanced treatment approaches.

Methods: Data was collected from 44 children/adolescents and their families. The sample had an average age of 15 (SD = 1.75), presented with clinically severe OCD, and received treatment in a residential setting. The Children’s Yale Brown Obsessive Compulsive Scale (CYBOCS) was administered at intake and the child completed a self-report CYBOCS weekly and at discharge. Emotion regulation was assessed using the Difficulties in Emotion Regulation Scales (DERS; Weinberg & Klonsky, 2009).

Results: Youth receiving residential treatment experienced, on average, a 21% reduction in obsessive-compulsive symptoms (SD = 32%). After controlling for age and obsessive-compulsive severity at admission, hierarchical linear regressions revealed lower DERS Total Scores at admission (b = -10, t = -2.42, p < .05) and more improvements in DERS scores during treatment (b = .11, t = -2.19, p = .06) were both uniquely associated with a reduction in OCD symptoms. Together they explained 16% of the variance in outcome. Subscale analyses showed these effects may be due to limited access to emotion regulation strategies. Multi-level modeling indicated that during residential treatment (CBT-ERP), DERS Total Score, b = -.12, t = -2.38, p < .05, emotional awareness, b = -.29, t = -2.88, p < .05, and ER strategies, b = -.34, t = -2.19, p < .05, all significantly reduced during treatment.

Conclusion: Change in emotion regulation during treatment was uniquely associated with outcome, suggesting that emotional awareness and strategies may be important treatment components. The findings illustrate not only the importance of evaluating and teaching emotion regulation skills, they also suggest that exposure based treatment improves emotional awareness and regulation skills.

Topic areas:
Child/Adolescent
OCD
Presenting Author: Argyro Athanasiadi, Visiting Post Doctoral Research Fellow


Title: Axis I disorders in Adults and Adolescents with Borderline Personality Disorder

Key words: borderline personality, adolescents, complex comorbidity

Objective: Axis I psychiatric disorders often tend to co-exist with borderline personality disorder (BPD). This study’s first purpose is to determine the rates of comorbidity reported by adult and adolescent borderline patients. The second is to assess the rates of complex comorbidity in these two groups.

Method: A total of 104 adolescents (aged 13-17) and 290 adults (aged 18-35) with BPD were interviewed. We used the Structured Clinical Interview for DSM-III-R (SCID I) and the Structured Clinical Interview for DSM-IV Childhood Disorders (Kid-SCID) for the assessment of axis I disorders in adults and adolescents, respectively.

Results: Rates of PTSD and other anxiety disorders but not mood disorders were significantly higher among adult than adolescent patients with BPD. In addition, rates of eating disorders were significantly higher among adult borderline patients than adolescents (73.5% vs. 35.6%). A similar significant difference was found for substance use disorders (62.1% vs. 35.6%). Overall, a significantly higher percentage of adults with BPD than adolescents with BPD met criteria for complex comorbidity (i.e., a combination of disorders of affect (mood and anxiety disorders) and impulsivity, OR= 4.41, p < 0.001).

Conclusions: Taken together, the results of this study suggest that even though the patterns of comorbidity among adolescents with BPD are similar to those in adults, the rates of complex comorbidity significantly are lower in the younger group.

Topic areas:
Borderline Personality Disorder
Child/Adolescent
Perfectionism is often regarded as a transdiagnostic risk/maintaining factor for many disorders including eating disorders, social anxiety, depression, and obsessive compulsive disorder (OCD; Egan et al., 2011). Additionally, perfectionism has been implicated in body dysmorphic disorder (BDD), particularly in respect to one’s perceived appearance versus ideal appearance (Veale et al., 1996). However, there is little research directly comparing the role perfectionism may play in symptoms of BDD and OCD, especially across treatment.

Data were collected from 282 participants (57% male, average age=30) enrolled in intensive/residential treatment for OCD and related disorders. Participants with DSM 5 diagnoses of BDD (n=28) and OCD without BDD (n=254) were included in the study. Participants completed the Yale-Brown Obsessive Compulsive Scales (Y-BOCS; OCD symptom severity), the BDD modification of the Y-BOCS (BBD-Y-BOCS), the Almost Perfect Scale-Revised (APS-R), and the Obsessive Beliefs Questionnaire-44 (OBQ-44) upon admission and discharge from the program.

One-way ANOVAs revealed significant differences between those with BDD and those with OCD on the APS-R at both admission (F(1,247)=10.36, p=.001) and discharge (F(1, 247)=6.11, p=.014), along with the OBQ-44 perfectionism/certainty subscale at admission (F(1,276)=10.31, p=.001). Linear regression revealed BDD-Y-BOCS scores at admission were associated with scores on the OBQ-44 perfectionism/certainty subscale (β=.26, t(276)=4.50, p<.001), APS-R total score (β=.25, t(277)=4.17, p<.001), and APS-R discrepancy subscale (β=.29, t(278)=5.06, p<.001) when controlling for OCD symptom severity. Similar patterns were also seen at discharge.

This suggests that those with BDD had higher levels of perfectionism/perfectionistic beliefs than those with OCD, even at discharge from treatment. One’s perfectionistic beliefs, especially concerning discrepancy, may be a valuable treatment target in BDD. Further research should evaluate the impact of perfectionism in comorbid OCD and BDD, along with how these findings generalize to outpatient samples.

**Topic areas:**

OCD
**Title:** Exploring between-session change in CBM-I: How many sessions are sufficient?

**Key words:** cognition, anxiety, depression

**BACKGROUND:** Cognitive Bias Modification for interpretation bias (CBM-I) has demonstrated efficacy in shifting interpretation and clinical symptoms across multiple disorders. However, it is unclear how many sessions are required (e.g., multi-session protocols ranged from four to sixteen sessions). We used data from a randomized controlled trial to explore when shifts in interpretation and symptoms occurred.

**METHODS:** Participants (N = 43) were enrolled in an RCT testing whether CBM-I augmented partial hospital care. They completed daily sessions of a CBM-I, and number of sessions varied naturalistically based on the number of days they attended the hospital program. We examined between-session change in patients’ accuracy and reaction time scores, as well as a daily measure of depression and anxiety, over the course of the sessions.

**RESULTS:** Accuracy on the interpretation task improved significantly between sessions until after session 4. Reaction time improved between sessions until after session 5. Symptoms improved the most between session 1 and 2, and did not significantly differ between sessions thereafter. Number of sessions correlated with change in negative interpretations (r = .373, p =.033) on an assessment version of the task.

**CONCLUSION:** Patients appear to learn the contingencies of this task very quickly, only requiring a few sessions in order to achieve high performance. The data suggest improvement in performance plateaus after 5 sessions. It is unclear, however, if the repetition of high performance is necessary for long-term improvement. Future directions include experimentally testing different numbers of sessions and examining long-term effects on symptoms.

**Topic areas:**
Anxiety
Depression
Title: Deletion of CNTNAP2 and White Matter Changes in Schizophrenia

Key words: copy number variant, white matter, myelination, hiPSC, CNTNAP2

Background. Schizophrenia (SZ) is a severe mental disorder with heritability estimated at ~80%. Genetic variants in contactin-associated protein-like 2 (CNTNAP2) have been reported in SZ. This gene is critically involved in normal neuronal synchronization and myelin production. Deletions in this gene would therefore be expected to impact white matter (WM) integrity. Compromised WM integrity has been implicated in SZ and may also be a heritable biomarker. In order to help characterize the genetic components of WM changes in SZ, we examined two carriers of a large heterozygous deletion in CNTNAP2 with discordant clinical phenotypes.

Methods. A 59 year old female proband who met DSM-IV criteria for a diagnosis of schizo-affective disorder (depressed subtype), her clinically unaffected 90 year old father, and four unrelated non-psychiatric controls completed a diffusion kurtosis imaging protocol on a Siemens 3T system. Human induced pluripotent stem cell (hiPSC) lines from skin biopsies of both carriers were generated and differentiated in vitro to oligodendrocytes.

Results. The fractional anisotropy (FA) and radial kurtosis (RK) were reduced and the radial diffusivity (RD) was increased in the corona radiata and the genu of the corpus callosum (CC) in the proband compared with the father and controls. The clinically unaffected father closely resembled the controls in the genu of CC, but differed from them in the uncinate fasciculus and internal capsule. In the whole brain WM analysis, the FA and RK were reduced, and the RD was increased, in both the proband and the father compared with the controls, more substantially in the proband than in the father. Preliminary results from the in vitro differentiation suggest defective differentiation of patient-derived hiPSCs to oligodendrocyte precursor cells in the proband only.

Conclusions. These preliminary data suggest that WM integrity is compromised in both carriers, possibly due to a demyelinating process that may be associated with this specific mutation. More severe and widespread demyelination is present in the clinically affected proband than in the unaffected carrier father, suggesting that additional WM changes may be associated with SZ, possibly independent of this mutation. These findings complement the molecular and cellular phenotypes of the hiPSC neural cells derived from these carriers and support the role of brain imaging in helping to elucidate objectively measurable neuroanatomic phenotypic consequences of genetic variant susceptibility. This is one of the first studies to combine neuroimaging and hiPSC-based observations in carriers of the same mutation with discordant phenotypes, demonstrating the utility of both approaches in understanding pleiotropic clinical effects.

Topic areas:
Imaging
Schizophrenia
The past era of human neuroscience has focused on group-averaged data acquired from temporarily isolated or sparse samples of the brain and behavior. Mobile aspects of the human condition have been underexplored including dynamic responses to transient life stressors, illness, administered pharmacology, and unexplained variation that is characteristic of young adulthood and mental illness. Research focused on the group also emphasizes methods that may miss idiosyncratic features of the individual’s brain and unique path through life. In addition to leaving major areas of human neuroscience uncharted, these emphases contribute to the challenge of translating functional neuroimaging approaches into clinical tools. Psychotic disorders are classic examples of unstable biological conditions that would be particularly appropriate for longitudinal study. Changes in macroscopic brain anatomy and functional architecture over time in individuals suffering from these disorders would be particularly valuable to advance our understanding of which aspects of altered physiology are fixed vs. plastic, and which reflect idiosyncratic features of individual physiology and maturation. Until recently, longitudinal brain imaging coupled with dense behavioral characterization was not feasible due to the high burden of scanning and phenotyping instruments that depend on office visits. However, recent reports from Chen R et al (2012 Cell) and Poldrack RA et al. (2015 Nat Commun) provide proof-of-concept demonstrations that human biology, neuroimaging, and behavior can be intensely tracked over extended periods in the individual. Here we expand on these pioneering efforts by constructing and demonstrating a platform to extensively study individuals with over time using a combination of low-burden neuroimaging techniques that employ ‘micro-tasks’ and optimized brief acquisition sequences, real-world behavior and sleep tracking using active and passive features of smartphones and wearables, and daily recorded voice diaries. In six adults with a psychotic disorder (bipolar disorder with psychosis, schizoaffective disorder or schizophrenia), we obtained up to one year of continuous real-world behavior and up to 15 in-person study visits spaced to capture naturally occurring illness fluctuations. Each visit entailed a brief clinical interview and functional and structural MRI scan session (~45 min). During functional scans, a core battery of tasks, including visuomotor, face matching, rule switching, 2-back, mental rotation micro-tasks, and a passive fixation "rest" task were collected during simultaneous multi-slice fMRI (Siemens 3T Prisma, SMS=5, TE=32.6ms, TR=1.0s, vox=2.4mm) and continuous physiological monitoring. Overall, patients remained compliant with daily surveys and monthly scan protocols even during periods of low mood and motivation. Relationships between smartphone-derived metrics of mood, energy, and cognition were examined in relation to periods of exogenous stress, sleep, and changes in treatments. Several early insights are reported from this pilot, including effects of sleeplessness on network connectivity and cognition in psychotic individuals. This study demonstrates proof-of-concept for applying a deep dynamic phenotyping approach in individuals with mental illness, suggesting a powerful, and feasible, paradigm for evaluating the effects of interventions on brain structure and function, and ultimately behavior.
Title: Assessing the Effectiveness of Positive Mood Induction in Individuals with Low vs. Moderate Anhedonia

Key words: Anhedonia, Mood Induction, Depression

Background: Anhedonia, the inability to experience pleasure in previously pleasurable activities, is a debilitating symptom of Major Depressive Disorder. Little work has been done, however, to determine whether anhedonia precludes all positive mood experiences. It is possible that experiencing an acute positive mood induction could increase affect in anhedonic individuals. To this end, we implemented a positive mood induction in individuals with moderate and low anhedonia to assess the influence of anhedonic symptoms on the effectiveness of positive mood induction. We also implemented a pilot mood induction involving “milder” positive feedback to assess whether extent of mood increase scales with strength of the positive mood induction used.

Methods: Mood induction 1 involved 32 individuals (15 females, mean age 33.97 years) recruited from the Harvard study pool. Participants completed a “humor intelligence test,” comprising 18 cartoons from the New Yorker Cartoon Caption Contest with three captions underneath: participants were instructed to select which caption they thought won for being the funniest. In 14/18 trials, participants received feedback that their response was correct (positive feedback), and were shown their actual response time in the feedback screen, with text saying they were faster than prior participants by a random number of seconds. After the 1st nine cartoons, study staff “stopped” the task to say their performance was spectacular. After the second nine cartoons, study staff “stopped” the task again to tell participants their performance was so impressive the director of research wanted to speak with them. At that point, a pre-recorded Skype video of an actor playing the “director of research” congratulating them on their excellent performance was played. Mood ratings were assessed with a slider scale asking participants to rate how they felt in the moment, from very negative to very positive. Mood induction 2 involved 8 individuals (3 females, mean age 27.33 years). Participants experienced the same mood induction until the second “interruption” from study staff: at this point participants simply received another round of verbal positive feedback rather than seeing a video.

Results: In the first mood induction, mean mood-change in the 22/32 who believed the induction was 13.9 points +/- 10.54. In the second mood induction, mean mood-change in the 8/8 believers was 14 points +/- 15.09. The believers were split into “high-anhedonia” (n=14, anhedonia > 20) and “low-anhedonia” (n=16, anhedonia < 20) cohorts. There was a trend difference in mood-change between the two groups (t(28) = 1.29, p = .055), with anhedonic individuals increasing more. Further, it was found that there was a significantly greater mood-change in the high- vs. low-anhedonia cohort (n = 10) who had experienced mood induction 1 (n = 12; t(20) = 2.27, p = .035).

Conclusions: The present study extends understanding of the effect of anhedonic symptoms on positive mood induction. Specifically, it demonstrates that the presence of moderate anhedonia does not alter effectiveness of a positive mood induction, which holds significant implications for treatment as it denotes flexible affect in anhedonic individuals. These results could potentially help us identifying new reward-based therapeutic interventions.

Topic areas: Depression
Suicidal risks in long-term controlled trials of antidepressants for major depressive disorder

Introduction/Aims: It is widely assumed that risks of suicidal behavior in randomized, controlled trials of treatments for mood disorders are very low, based largely on standard screening procedures intended to exclude potentially suicidal participants and close clinical monitoring.

Methods: We tested this hypothesis with reports identified in our recent comprehensive review and meta-analysis of long-term, controlled trials of antidepressants and psychotherapies for major depressive disorder. We identified 17 reports (38% of 45 reviewed) with data pertaining to suicidal events among a total of 5458 acutely depressed subjects.

Results: Rates for suicidal behavior (cases per 100 person-years) were unexpectedly high: ideation 2.08 [CI: 1.72–2.48]; attempts 0.65 [0.46–0.90]; suicides 0.25 (0.15–0.44]. Pooled rates were higher in antidepressant- vs. placebo-arms of trials, but drug-arms included more subjects observed longer with fewer dropouts, tending to exaggerate the drug-placebo contrast. With exposure times adjusted for high dropout rates, the observed rate of suicides in trials was 360/year/100,000, compared to an international general population rate of 12.5 (29-fold lower), and approximately 50 (7.2-fold lower) in clinical samples of persons diagnosed with major depression in various states of illness and remission.

Conclusions: The findings are striking in indicating unexpectedly high suicidal risks in controlled trials. They encourage further efforts to limit potentially fatal risks in therapeutic trials and to improve the reporting of such adverse outcomes.

Topic areas:
Addiction
Depression
Presenting Author: Shelly Greenfield, Chief Academic Officer, McLean Hospital; Chief, Division of Women's Mental Health; Professor of Psychiatry, Harvard Medical School; Director, Clinical and Health Services Research and Education

Co-Authors: Dawn E. Sugarman, PhD, Brittany R. Iles, BS, Esther Dechant, MD, Thomas Weigel, MD, Patricia Tarbox, MSW, LICSW

Title: Feasibility and Satisfaction of the Women's Recovery Group for Patients with Co-occurring Substance Use and Eating Disorders

Key words: substance use disorders, eating disorders, gender

Aims: Despite the high rate of co-occurrence among women with substance use disorders (SUDs) and eating disorders (EDs), no integrated treatments exist. The Women's Recovery Group (WRG) is an evidence-based, gender-specific group therapy for women with SUDs. The goal of this study is to assess feasibility and satisfaction of the WRG for women with co-occurring SUDs and EDs.

Methods: Women admitted to ED residential treatment were included if they were > 18 years and had a co-occurring SUD. Craving to use substances and engage in ED behaviors, and motivation to abstain from substances and ED behaviors were assessed pre and post-treatment; satisfaction with the WRG was assessed at post-treatment.

Results: Of 19 participants enrolled, mean age=22 years (SD=2.7), 94.7% were white, and 77.8% attended some college. Alcohol was most frequently used (68.4%), then cannabis (52.6%), and prescribed stimulants (15.8%); mean EDE-Q score was 4.3 (SD=1.5; range 0-6). Those who completed follow-up (n=14, 73.6%) were moderately satisfied with the WRG (M=34.9, SD=9.1; range 14-56). Craving for substances (t=4.6, df=13, p<.001) and to engage in ED behaviors (t=3.3, df=13, p<.01) decreased from pre- to post-treatment; no significant changes in motivation to abstain were observed. Topics "How to manage triggers and high-risk situations" and "Can I have fun and not use drugs or alcohol?" were rated as most helpful. Participants wanted more information on EDs (92.9%), self-esteem/self-image (92.9%), skills building (64.3%), and PTSD symptoms (64.3%).

Conclusions: Participants reported moderate satisfaction and helpfulness with the WRG in its current form. Women expressed the importance of targeting both SUDs and EDs, and provided suggestions for future topics, thus supporting the need for modifications to the WRG to better integrate treatment for women with SUDs and EDs.

Topic areas:
Addiction
Eating Disorders
Women
Presenting Author: Elyssa Barrick, Clinical Research Assistant II

Co-Authors: Daniel G. Dillon

Title: The Impact of Depression on Brain Activity During Source Memory Retrieval

Key words: Depression, Memory, ERP

Background: Recollection is disrupted in Major Depressive Disorder (MDD), but this disruption can be minimized by focused attention at encoding and retrieval. The neural mechanisms responsible for these clinically important phenomena are unclear. Thus, we used event-related potentials (ERPs) to examine recollection in MDD.

Methods: Twenty-four unmedicated adults with MDD and 24 controls encoded words shown on the left or right (perceptual source) by making animacy or mobility judgments (conceptual source). ERPs were recorded during cued source retrieval, which depends on recollection.

Results: Mobility judgments prompted deeper encoding than animacy judgments, and memory accuracy was characterized by a Group x Cue x Encoding Task interaction: depressed adults were generally less accurate and less confident than controls, but they showed excellent conceptual source memory following deeper encoding. In parallel, a positive parietal ERP deflection that tracks recollection was globally reduced in depression, but sustained left parietal activation was seen during conceptual source judgments for deeply encoded words in MDD.

Conclusions: This study links two reliable effects of depression on recollection to electrophysiological activity over parietal cortex. First, accuracy and confidence were reduced in MDD, and the most reliable ERP correlate of recollection—a positive parietal deflection from 400-800 ms—was blunted. Second, depressed adults showed excellent memory when the encoding and retrieval tasks demanded sustained attention, and this combination elicited slasting left parietal activity. These results link the impact of depression on recollection to parietal circuits that communicate with the hippocampus, highlighting the need for further work on this important topic.

Topic areas:
Depression
Introduction: Functional impairment is one of the most enduring, intractable consequences of psychiatric disorders. Community functioning (e.g., meaningful daily activity or social interests) plays a key role in evaluating for prognosis and quality of life. It is also an important outcome measure for assessing the efficacy of treatments. Genetic determinants underlie much of the risk and expression of psychiatric disorders, but genetic studies of functional impairment in psychiatric disorders are scarce. To date, there is only one report of a genome-wide association study (GWAS) of functional impairment (McGrath et al 2013) and this study relied on a self-report questionnaire [SF-12] (Contopoulos-Ioannidis et al., 2009) to measure general physical and mental health status. In the present study, we collected data on real-life community functioning using the Multnomah Community Ability Scale (MCAS), an interview based assessment, in patients with psychotic spectrum disorders (schizophrenia, schizoaffective, bipolar) and healthy controls. Our goals are to: i) estimate the SNP-based heritability of two domains of real-life functioning: independent living/meaningful activity and social competence, ii) identify common genetic variants associated with these two domains of real-life functioning, and iii) examine the shared genetic components between real-life functioning and other related phenotypes (e.g., subjective well-being, cognitive function, schizophrenia, bipolar, major depressive disorder [MDD] risk).

Methods: The total sample consisted of 686 patients and 43 controls. After quality control and genotype imputation (described in Hall et al 2015), 508 participants were included in these analyses (494 patients and 14 controls, all European American) for whom clinical and genome-wide data were available. We carried out genome-wide association analysis and SNP-based heritability analyses for each domain of functioning, adjusted for psychiatric symptom severity (SCID, the Positive and Negative Syndrome Scale) and principal components for population stratification. We estimated genetic correlation between the measure for independence living domain functioning and subjective well-being (Okbay et al 2016), cognitive function (Rietveld et al 2013), and schizophrenia, bipolar, MDD risk (the Psychiatric Genomics Consortium, PGC) using LD score regression.

Results: No significant GWAS association was identified, but several regions with suggestive association trends (p-value < 10-6) were identified. For each domain of functioning, SNP-based heritability was estimated to be 1 (p=0.26) for independent living and 0 (p=1) for social competence, respectively. Genetic correlations of independent living with subjective well-being was estimated to be 0.31 (p=0.23), with cognitive function, -0.31 (p=0.23), with schizophrenia risk, -0.27 (p=0.13), with bipolar risk, -0.28 (p=0.24), and with MDD risk, -0.61 (p=0.15).

Discussion: Our preliminary results suggest that some genetic loci might be associated with real-life functioning, though studies with larger sample size are needed to confirm these GWAS associations. The domain of independent living/meaningful activity has higher SNP-based heritability than the social competence domain. Higher risk of schizophrenia, bipolar and MDD is genetically correlated with lower dependent domain functioning, whereas lower cognition and better subjective wellbeing are genetically correlated with higher independent domain. Among the five genetic correlations estimated, we observed the greatest shared genetic components between independent living functioning and MDD.

Topic areas: Psychotic disorders
**Title:** An Investigation of White Matter Integrity in Major Depressive Disorder

**Key words:** Depression, diffusion imaging, white matter integrity, fractional anisotropy

Major Depressive Disorder (MDD) is a pervasive, burdensome condition that may involve disruption of white matter tracts that connect brain regions important for emotion regulation, cognitive control, and memory. To test this hypothesis and extend prior work, we used diffusion tensor imaging to measure fractional anisotropy (FA), an index of white matter integrity, in 40 unmedicated adults with MDD and 58 healthy controls. We measured FA in seven core white matter pathways: the anterior internal capsule, medial forebrain bundle, cingulum-ACC bundle, cingulum-hippocampus bundle, corona radiata, uncinate fasciculus, and the genu of the corpus callosum. We also correlated FA in each pathway with severity of negative affect and anhedonic symptoms of depression. Relative to controls, the MDD group showed reduced FA in the genu, internal capsule, cingulum-ACC bundle, and uncinate fasciculus, all ps < .04. Moreover, lower FA in the uncinate fasciculus and genu was associated with greater negative affect and anhedonic symptoms in depressed adults (rs = -.224-.465, ps > .035). Also, lower FA in the cingulum-ACC was associated with greater anhedonia (r = -.420, p = .013). Overall, these findings replicate prior results indicating widespread white matter reductions in MDD and link those reductions to individual differences in depressive severity and anhedonia. Determining whether information about white matter abnormalities is useful for treating depression remains an important goal for future work.

**Topic areas:**
Depression
Imaging
Stress Inoculation: Preliminary Evidence that Exposure to Low-Levels of Early Adversity Protect Against the Psychiatric Consequences of Teenage Exposure to Maltreatment

Stress inoculation hypothesizes that manageable levels of stress during early development may protect against the effects of high levels of stress at a later time. Rodent and primate studies provide considerable support. However, according to Liu (2015), no study has directly assessed its relevance to clinically significant outcomes. We assessed in an online sample (n=1420, 66% female, 23.1 ± 1.6 years) whether a subject’s impression of their degree of exposure to childhood maltreatment (CM) during the first three years of life, when stress-response system are highly susceptible to programming, moderated the relationship between CM during teenage years and symptom scores. Exposure to 10 types of CM across each year of childhood was assessed using the MACE. Early exposure significantly moderated the association between teenage CM and ratings of anxiety, suicidal ideation, anger-hostility and dissociation. Teenage CM accounted for 7.3% (p < 10^-8, n=579), 2.2% (p ns, n=303), 8.3% (p=0.002, n=260) and 6.5% (p < 0.005, n=279) of the variance in anxiety ratings in subjects indicating no, low, moderate or high early exposure, respectively. Similarly, there were significant associations between teenage CM and suicidal ideation in all but the low early exposure group. These findings provide initial support for a protective role of exposure to low-levels of early stress.

Topic areas:
- Anxiety
- Child/Adolescent
McLean Research Day 2017

Original Research - Clinical

Poster # 16
Time: 1:50-2:45pm

Presenting Author: Nicole Benson, Psychiatry Resident

Co-Authors: Stephen J. Seiner, MD, Paula Bolton, MS, Robert C. Meisner, MD, Casey Pierce, BA, Garrett Fitzmaurice, ScD, Alisa B. Busch, MD, MS

Title: Electroconvulsive Therapy in Transitional Age Youth

Key words: Electroconvulsive Therapy, Transitional Age Youth, Substance Use Disorders

Background: Transitional age youth (TAY) constitute a unique clinical population with distinct psychiatric and neuro-developmental characteristics. Electroconvulsive therapy (ECT) is a highly efficacious, well-tolerated treatment for major depressive disorder (MDD) and psychosis in adults; however, little is known about the effectiveness of ECT in TAY. Objectives: To assess whether acute phase ECT in TAY is associated with improvements in clinical outcomes, and whether screening positive for a substance use disorder (SUD; alcohol or drug) is associated with differences in treatment outcomes compared to those screening negative for SUD.

Methods: All patients aged 16-25 years old (TAY) who received ECT at McLean Hospital between May 2011 and January 2016, and who, prior to starting ECT, completed self-reported SUD screens (AUDIT-C and a single-item drug screen) and the Behavior and Symptom Identification Scale-24 (BASIS-24) and who completed the BASIS-24 again after the fifth ECT treatment. For five of the BASIS-24 domains (i.e., all domains except SUD), longitudinal changes in mean BASIS-24 domain scores from baseline to the fifth ECT treatment were assessed; mean changes by SUD screening status were also examined using linear mixed models.

Results: A total of 186 TAY met inclusion criteria for the study. Sixty-one percent screened positive for SUD; the mean age was 21.2±2.6 years. Among all patients, ECT was associated with significant clinical improvement (score decreases) in all five BASIS-24 domains during the acute phase treatment: depression/functioning (-0.701±0.066, p<0.001), interpersonal relationships (-0.353±0.062, p<0.001), self-harm (-0.622±0.068, p<0.001), emotional lability (-0.284±0.061, p<0.001), and psychosis (-0.124±0.042, p=0.004). Compared to TAY screening negative for SUD, TAY with co-occurring SUD had greater improvement in depression/functioning (-0.411±0.129, p=0.002) and emotional lability (-0.314±0.121, p=0.010) domains after five ECT treatments.

Conclusions: ECT in TAY was associated with significantly improved clinical outcomes during acute phase treatment. TAY screening positive for SUD had better acute phase ECT outcomes in self-reported depression/functioning and emotional lability than TAY screening negative for SUD. More research is needed to further clarify TAY patient characteristics that may be associated with differential ECT outcomes, and to determine whether the differential improvement in depression/functioning and lability for TAY who screen positive for co-occurring SUD may be due to confounding factors, such as temporary abstinence from substances during treatment.

Topic areas:
Child/Adolescent
Background: Cognition and social adjustment are some of the top concerns for the path to recovery for patients with first episode psychosis (FEP) (Jordan, 2014). Cognition has been found to be predictive of functional outcome (Nuechterlein, 2011) and the social adjustment scale can be used to measure functionality (Jaeger, 1992). The goal of this study is to examine the relationship between cognition and social adjustment in FEP. We predict that cognition has a positive effect on social adjustment.

Methods: A total of 19 surveys and cognitive assessments were collected from patients at the OnTrack Program, a first episode clinic at McLean Hospital. FEP patients were categorized using the DSM-IV for a diagnosis of bipolar with psychosis, major depressive disorder with psychosis, schizophrenia, schizoaffective, or psychosis NOS. Patients were evaluated cross-sectionally when first exhibiting psychosis (baseline), one year after (Y1), and two years after (Y2). 5 FEP baseline, 7 FEP Y1, 9 FEP Y2, and 16 controls were collected. Due to small sample size, patients were pooled together in analysis. The MATRICS Consensus Cognitive Battery (MCCB) was administered along with a modified version of the Social Adjustment Scale, emphasizing on work/academic, social, and family areas, via survey to participants. Within the MCCB, the social-emotional score of the MSCEIT (MCCB-SOC), was evaluated along with the composite scores of the MCCB. Clinical scale scores from the Young Mania Rating Scale (YMRS), Montgomery Asberg Depression Rating Scale (MADRS), Multnomah Community Ability Scale (MCAS), and Positive and Negative Syndrome Scale (PANSS), were also evaluated to assess for clinical state. Specifically from the MCAS, item numbers 6, 7, 13, grouped MCAS_independent (MCAS_IND), and item numbers 9-12, grouped MCAS_social (MCAS_SOC), and the PANSS Insight score (P_insight) were compared as separate groups.

Results: The social adjustment survey was non-significantly correlated with the MCCB-SOC, MCAS, and P_insight. A negative partial correlation between MCCB-SOC and the YMRS was observed, controlling for MCAS total score, Social Adjustment survey score, P_insight score, and MADRS, (r=-0.7383, p<0.01). A positive trend between MCCB-SOC and the MADRS was also observed (r= 0.4482, p=0.163).

Conclusion: The social adjustment survey has no significant effect with cognition but preliminary results suggest that the YMRS is the largest predictor of the MCCB-SOC. Lower manic symptoms predict a higher social-emotional component indicating that the mood of an individual is significant in determining how much an individual can relate to social situations. Limitations of the study include a selection bias where the population of the clinic is not fully represented. The current sample size is small and we are collecting a larger sample. Future directions include stratifying the different year groups and looking at diagnosis specific relationships.

Topic areas:
Bipolar
Psychotic disorders
Schizophrenia
**Presenting Author:** Cara Bigony, Research Assistant

**Co-Authors:** Chuda Rijal, Jennifer Nguyen, Kimberly Cramer, Kerry James Ressler

**Title:** Psychometrics at McLean: Investigating Childhood Trauma and Transdiagnostic Components of Mental Health

**Key words:** PTSD, trauma, childhood, transdiagnostic, psychometric

**Background:** In addition to high rates of transdiagnostic comorbidity, research reflects many underlying components of mental illness that cut across DSM-5 and ICD-10 diagnostic categories. While childhood trauma is understood as a factor that causes distress and dysfunction in PTSD, dissociative disorders, and related disorders, it is rarely thoroughly considered in transdiagnostic psychiatric care. The Psychometrics at McLean initiative focuses on psychological and behavioral phenotyping of the Partners Biobank enrollees, allowing researchers to better understand transdiagnostic components related to mental health.

**Methods:** Patients (n=30), ages 18-65, receiving treatment for Axis I disorders were recruited for participation in this pilot study. During a stay on an inpatient unit at McLean Hospital, participants who had consented to the Partners Healthcare Biobank were administered a battery of self-report measures. The primary outcome measure was the Childhood Trauma Questionnaire (CTQ), a retrospective 28-item self-report inventory designed to screen for abuse and neglect. It measures emotional, physical and sexual abuse, as well as physical and emotional neglect, experienced throughout childhood.

**Results:** Twenty-six participants completed the Childhood Trauma Questionnaire. 30.2% of participants reported physical abuse. 61.5% of participants reported emotional abuse, and 34.6% reported some form of sexual assault. The means for each subscale were consistent with current research results: physical abuse (mean score=7.73, none to low), emotional abuse (mean score=11.69, low to moderate), sexual abuse (mean score=8.92, moderate to severe). With ongoing data collection, we anticipate >100 enrolled participants by the annual ADAA meeting.

**Conclusion:** The results of this pilot study support the need for trauma-informed mental health care, given the high rates of childhood trauma reported across psychiatric diagnoses, rates which are considerably higher than the general population. Further collection of these measures will allow for deeper analysis of underlying transdiagnostic components of childhood trauma and mental health. Increasing awareness of the prevalence of childhood trauma in adult psychiatric populations will help treaters recognize and respond to signs and symptoms of trauma histories.

**Topic areas:**
Dissociative Disorders
PTSD
Using Perceptions of Care Survey to Improve Interpersonal Aspects of Patient Care

The Perceptions of Care (PoC) is a patient self-report patient satisfaction survey designed specifically for use in a mental healthcare setting. PoC contains 21 structured questions that ask respondents to report on particular aspects of care, rate their overall care and rate how much they were helped by care. In addition to the 21 structured questions, there are two open-ended questions that provide useful feedback to clinical and administrative staff. The items of the PoC fall into four domains: Information Received, Interpersonal Aspects of Care, Continuity and Coordination of Care, and Global Evaluation of Care. The goal of this project is to use the PoC to establish and encourage discussion of best practices at McLean Hospital as well as develop a report to continually monitor and evaluate these efforts. The researchers examined a sample of PoC surveys completed by 53,421 McLean Hospital Inpatients between 2005 and 2015. Correlations and exploratory factor analyses were performed to determine the key driving factors which predict overall patient perceptions of care. The Interpersonal Aspects of Care domain was found to have the strongest correlations with the other domains and global satisfaction with care (r=0.76, p<.01). The Interpersonal Aspects of Care domain is made up of seven PoC items. The original Exploratory Factor Analysis of the PoC survey based on 6,972 cases found that the two items of the Interpersonal Aspects domain were “Did the staff treat you with respect and dignity?” (0.93) and “Did the staff listen carefully to you?” (0.76) (Eisen, et al, 2002). Correlations within the current dataset found that staff listening carefully (r=0.83, p<.001) and respect and dignity (r=0.82, p<.001) were the two items most strongly correlated with the overall Interpersonal Aspects of Care score, further confirming that these two items were the key drivers in determining the patient care experience. Thus, these two items would be the metrics used for monitoring and evaluating Interpersonal Aspects of Care on Mclean Hospital inpatient units. Frequencies of “Always” responses (best possible response option) for these key driver items were tracked longitudinally as well as against the top performing unit for two pilot units (South Belknap 1 and North Belknap 2). The results of these analyses were provided in a concise report, The “McLean Values Report,” to unit leadership as well as the Care Experience Committee with a focus on action items and continued improvement on making patients feel more respected and listened to. The staff on the pilot units as well as the members of the committee reported that the new report was useful, thought-provoking and lead to discussion and action on the unit. As a result, this new McLean Values Report has been included in all inpatient unit Quarterly Quality Improvement reports. Units continue to use these key drivers to monitor and actively improve the interpersonal aspects of care provided.

Topic areas:
Outcomes/Quality
Presenting Author: Lucy Bingham, Co-op Student

Co-Authors: Elizabeth T. Ryan, Justin M. Shepherd, Jane F. McNeil, Scott E. Lukas

Title: Impact of Food on the Absorption and Kinetics of Alcohol: Snacks versus Meals

Key words: alcohol, food, pharmacokinetics, blood alcohol levels, impaired driving

Alcohol-impaired driving has accounted for nearly two-thirds of motor vehicle related deaths since 2009. Efforts to reduce drunk driving have begun with research into the development of alcohol sensing devices for automobiles. Since alcohol absorption, distribution, and metabolism varies across different conditions, it is important to investigate how real-world drinking scenarios impact the measurement of blood alcohol levels (BAL). Food and alcohol are often consumed at the same time in the form of snacking at parties or during a full meal. Research has found that individuals who eat before drinking have lower BAL than those who drink on an empty stomach and will report diminished feelings of intoxication. The aim of the present study was to more accurately quantify the impact of food on the pharmacokinetics of alcohol by manipulating the type of meal and the pattern of eating and drinking. Healthy male and female volunteers who reported drinking on a social basis were recruited to participate in one of two scenarios: (1) Social Snacking (n=5), in which subjects received a snack along with a mixed drink every 30 minutes and (2) Full Meal (n=5), during which subjects ate a 2-course meal with drinks, consuming the first “cocktail” on an empty stomach. An intravenous catheter was used to continuously collect blood samples every 5 minutes. Participants received a dose of 0.9 g/kg of alcohol, (40% vodka with orange juice). Whole blood alcohol levels were determined by Gas Chromatography. A statistically significant interaction was found between Social Snacking and Full Meal and time on percent BAL, such that 40 minutes after consumption, participants in the Full Meal group had a higher BAL (M=39.7 mg/dL , SD=9.8) than those in the Social Snacking group (M=19.0 mg/dL , SD=6.8). This effect, however, did not persist as the Social Snacking BAL began to surpass the Full Meal group once the full amount of food and drink were consumed. At 115 minutes, the BAL of Social Snacking was higher than the Full Meal (114.1 mg/dL ± 24.5 versus 99.0 mg/dL ± 19.7), although this difference was not statistically significant. These results confirm that eating food while drinking affects the rate of absorption and peak BAL. The higher BAL in the Social Snacking group at 40 minutes indicates that eating a small snack while drinking will result in a slower absorption than drinking on an empty stomach, as the Full Meal group consumed their first drink without food. However, once the entire meal was consumed, the rate of absorption slowed and the BAL from the Social Snacking group continued to rise, surpassing the Full Meal group and maintaining a higher (non-significant) BAL for the remainder of the study. Our current sample is likely too small to observe significance, but findings suggest having a drink (on an empty stomach) before dining may result in higher BAL than if one engages in light snacking, whereas those who have a drink with a full meal may lower one’s peak BAL more than continuously snacking while drinking.

Topic areas:
Addiction
Pharmacology
Introduction: Case management has been shown to improve outcomes for a spectrum of addictive disorders. (1) Individuals in methadone programs who are assigned to additional case management miss fewer doses of medication, more regularly attend physician appointments and have a reduced number of substance positive urine drug screens. (2) Additionally, clients with low pre-morbid cognitive abilities and alcohol use are more successful in treatment with the assistance of a case manager. (3) However, the role of case management for opioid addiction has mainly been explored through its use in methadone programs. There is limited research regarding its use in outpatient buprenorphine or naltrexone treatment, and even less information about the demographics of those who are most likely to benefit from additional case management in these programs.

Aim: The proposed work will examine a series of patients who entered outpatient treatment in the buprenorphine and extended release injectable naltrexone programs at McLean Hospital over a six-month period from Jan-Jun 2016. The format of this tailored treatment includes an average of 16 weeks of twice-weekly case management with a Licensed Clinical Social Worker, in addition to weekly appointments with an Advanced Practice Registered Nurse who receives oversight by a Board Certified Addiction Psychiatrist. Referrals to the program are provided through multiple outlets, including intensive outpatient and partial hospitalization programs, residential programs and acute inpatient detoxification units. Demographic characteristics of age, gender, type of substance use, duration of use and referral source are used as descriptive variables. Outcome measures include adherence to treatment as determined by the number of no-shows to case management sessions or groups, and medication adherence as determined by attendance at monthly dosing for injectable naltrexone or by buprenorphine positive urine drug screens. Rates of abstinence are measured by the number of negative urine drugs screens. This project hopes to inform the allocation of case management resources.

Methods: Chart review for all patients that began treatment through the outpatient buprenorphine injectable naltrexone clinic at McLean Hospital from Jan-Jun was completed. A multiple case design will be utilized so as to allow comparison of outcome measures between patients receiving naltrexone versus buprenorphine. IRB approval was not obtained because the categorization of this study meets criteria as a quality improvement project. The online medical record system, Meditech, was queried for further demographic information of the patients selected for this case series. Clinigen/Burlington Labs, the laboratories contracted with McLean Hospital to provide services for quantitative urine drug screens was used to accurately report the number of positive versus number of negative results over the designated time period.

Conclusions: The projected outline for completion of results is 1/1/17
McLean Research Day 2017

Program Description

Poster # 22
Time: 1:50-2:45pm

Presenting Author: Paula Bolton, MS, CNP, ANP-BC

Co-Authors: Teresa Henderson, BSN, RN  Julianna Currier, BSN, RN

Title: Dispelling the Stigma: Development of an ECT Support Group Co-led by Nurses and Persons with Lived Experience

Key words: ECT, Stigma, Support, peer, Nurses

The media often does not give an accurate depiction of ECT and contributes to controversy about ECT. Nurses realize that this controversy is mostly based on misconceptions. Patients and family members usually change their opinions about ECT after they have had ECT or have seen its results. ECT is actually very different from what has been shown in movies and has very few side effects. Electroconvulsive therapy (ECT) is used to treat a number of psychiatric conditions, such as depression, mania, catatonia and some psychotic illnesses. ECT may be preferable for patients who do not respond well to medications, who are having excessive side effects from medication, or who are actively suicidal. The decision to use ECT is one that must be carefully weighed by the patient and their family. The possibility of memory problems or confusion is often the most worrisome for people. Group therapy is a powerful tool to provide support, education, social networking and decrease isolation and stigma associated with mental illness. Peers provide information about their experiences and help support and encourage one another. We developed a support group for patients undergoing ECT, their families and those considering ECT. The group is co-led by nurses and persons with lived experience to be able to integrate education, facts and support and social interaction among group members. The success of the outpatient ECT support group, as evidenced by the response of participants, led to the development of a support group for inpatients. PMH nurses, working with persons with lived experience, are uniquely qualified to lead ECT support groups to decrease stigma and facilitate treatment. ECT treatment programs should create similar ECT support groups involving patients, families and persons in recovery to better advance patient centered care.

Topic areas:
Bipolar
Depression
Geriatric
Psychotic disorders
Accumulating evidence suggests that the serotonin 5HT2C receptor agonist, lorcaserin (LOR), may be a promising candidate for the management of substance use disorders, including nicotine addiction. The present study was conducted to determine whether acute or continuous LOR treatment might decrease the abuse-related reinforcing effects of nicotine in a primate species. The effects of LOR on food-maintained responding and daily activity following drug administration also were assessed to evaluate selectivity of treatment effects. Adult rhesus monkeys (n=3-4) with an extensive history of nicotine self-administration (>2 years) responded for injections of nicotine (0.32-100 μg/kg i.v.) or food pellets under a fixed-ratio schedule of reinforcement during daily 100-min sessions. When responding became stable, LOR was administered either as an acute pretreatment (0.1-1.0 mg/kg, IM) or by continuous infusion via osmotic mini-pump (0.1 mg/kg/hr, SC for 3-5 days). Results indicate that acute LOR produced a dose-dependent decrease in nicotine-maintained responding (10.0 μg/kg/inj), and that the highest LOR dose (1.0 mg/kg) dramatically reduced nicotine-maintained responding across the full range of self-administered doses. Continuous LOR treatment produced a similar effect, with decreases to about 50% of baseline intake during self-administration of 10.0 μg/kg/inj nicotine. Food-maintained responding was largely unaffected in 3 of 4 subjects after acute administration and unaffected in all subjects during continuous treatment. Grouped data show that home cage activity was generally decreased to ≤50% of saline control values following acute LOR. Taken together, these data indicate that LOR greatly reduces the reinforcing effects of nicotine with some effects on food-motivated responding and general activity. Further research for LOR as a novel pharmacotherapy for nicotine dependence is warranted.
Title: Neural Markers Underlying Reward Dysfunction Predicts Depression in Adolescents

Key words: Adolescent, Depression, fMRI

Background: Major Depressive Disorder (MDD) is a debilitating disorder, and rates of MDD rise sharply during adolescence (Avenevoli et al., 2015). Prior research has shown that adolescent depression is characterized by a blunted neural response to reward (Forbes et al., 2009). However, it remains unclear whether abnormal reward processing precedes the onset of depression. To address this gap, the present study tested whether activation in the striatal regions prospectively predicts depressive symptoms in healthy youth.

Methods: The study included healthy female adolescents aged 12-14 years. Adolescents (n = 43) were administered clinical interviews and completed self-report measures of depression symptom severity. Additionally, functional magnetic resonance imaging (fMRI) data were acquired while youth completed a gambling task to probe differential neural response to wins versus losses. Then, participants completed a 3-month follow-up assessment of depressive symptoms. In line with prior research, we hypothesized that blunted activation in the nucleus accumbens (i.e., relatively reduced activation for wins versus losses) would prospectively predict depressive symptom severity, while controlling for baseline symptoms.

Results: Data collection remains ongoing, and preliminary whole-brain analyses examined a subset of the participants (n = 33). Parameter estimates were extracted following win and loss feedback (i.e., Win-Loss contrast) in the left (x = -14, y = 2, z = -14; cluster size = 66; p < 0.05, FWE corrected) and right nucleus accumbens (x = 10, y = 12, z = -4; cluster size = 106; p < 0.05, FWE corrected). Results indicated that increased depressive symptoms at the 3-month follow-up assessment were associated with blunted activation in the left (pr = -0.46, p = 0.01) and right (pr = -0.42, p = 0.02) nucleus accumbens after accounting for baseline symptoms. Future analyses also will examine fronto-striatal connectivity to better clarify risk for depression.

Conclusion: Neural response to feedback may have important implications for understanding MDD risk, and results from the current study are expected to advance our understanding of the neurobiological mechanisms that may underlie the onset of MDD in adolescence.

**Presenting Author:** Kristin Javaras, Assistant Psychologist / Assistant Professor

**Co-Authors:** Mary C. Zanarini, James I. Hudson, Shelly F. Greenfield, John G. Gunderson

**Title:** Functional Outcomes in Community-Based Adults with Borderline Personality Disorder

**Key words:** Borderline personality disorder, Functional Outcomes, Functioning, Impairment, Community

**Background:** Many patients with borderline personality disorder (BPD) exhibit occupational and social impairment. In the present study, we investigated whether BPD-associated impairments are also found in the community, by comparing individuals with and without BPD in (1) a community-based sample and (2) a sibling-only subset of the sample.

**Methods:** The overall sample included 165 BPD and 964 non-BPD participants (72 and 106, respectively, in the sibling-only subset) from a family study of BPD. BPD diagnoses and functional outcomes were based on well-accepted, semi-structured interviews. In the overall (sibling-only) sample, multinomial (conditional) logistic regression was used to model outcome categories as a function of BPD status and demographic covariates, with robust standard errors to address dependence between relatives and weights to address unequal selection probabilities. Model-fitting results were used to calculate the adjusted risk difference (ARD; the estimated outcome probability for BPD minus non-BPD).

**Results:** In the overall sample, the estimated prevalence of good overall functioning (steady employment and at least one good relationship) was 47.6% in the BPD group and 74.2% in the non-BPD group, yielding an ARD of -26.6% (95% CI: [-41.5%, -11.7%]; p < 0.001). In the sibling-only subset, the ARD was -38.3% (95% CI: [-65.5%, -11.0%]; p < 0.01). BPD was also negatively associated with good outcomes in specific domains of functioning (occupational, and relationships with partner, friends, and parents).

**Conclusions:** In the community, individuals with BPD are less likely to exhibit good occupational and social outcomes, even compared to their own siblings.

**Topic areas:**
Borderline Personality Disorder
Presenting Author: Dana Borkum, Clinical Research Assistant II

Co-Authors: Laura R. Magni, Ph.D., Garrett M. Fitzmaurice, Sc.D., Marianne Goodman, M.D., Mary C. Zanarini, Ed.D.

Title: Protective Childhood Experiences Reported by Psychiatrically Healthy Adolescents, Adolescents with BPD, and Adults with BPD

Key words: borderline personality disorder, childhood protective experiences, adolescents

Objective: The main purpose of this study was to report on the prevalence rates of protective childhood experiences reported by psychiatrically healthy adolescents, adolescents with borderline personality disorder (BPD), and adults with BPD.

Methods: One hundred and four subjects were adolescents between the ages of 13 and 17 who met DIB-R and DSM-IV criteria for BPD. Sixty were age matched psychiatrically healthy comparison subjects. Two hundred and ninety subjects were adults between the ages of 18-35 who met DIB-R and DSM-III-R criteria for BPD. All three groups were interviewed using the Revised Childhood Experiences Questionnaire (CEQ-R), a semi-structured interview which assesses pathological and protective childhood experiences.

Results: Psychiatrically healthy adolescents reported significantly higher rates of four out of 18 protective factors than adolescents with BPD, including playing a sport, participating in a leadership role, participating in household responsibilities, and having a parent who has various interests. Adolescents with BPD reported significantly higher rates of five of these 18 protective factors than adults with BPD. These factors were related to individual competence - having a strong academic performance, participating in household responsibilities, participating in extracurricular activities - and relationships - having a positive relationship with parents and having parents who have positive relationships with members of their family of origin. Adults with BPD were significantly more likely to endorse having a steady work record than adolescents with BPD.

Conclusions: Taken together, the results of this study suggest that adolescents meeting criteria for BPD have significantly fewer protective factors than psychiatrically healthy adolescents. They also suggest that they have significantly more protective factors than adults with BPD.

Topic areas:
Borderline Personality Disorder
Presenting Author: Kristen Perrelli and Jessica Lahens, MSW Clinical Interns

Co-Authors: Mark Longsjo

Title: Comparing the Effectiveness of Partial Hospitalization Programs on patients' depressive symptoms

Key words: Depression, Partial Hospitalization Programs, Effectiveness, Outcomes

Partial hospitalization programs (PHPs) are a broad category of services provided for symptoms as disparate as substance abuse, mental health, and eating disorders. In the behavior health world, they are available to clients experiencing an increase in symptoms and are often used as additional stabilization after a crisis or to avoid a potential crisis. They consist of structured psychoeducation, processing, and skill-building groups. As providers, we must hold ourselves to the minimal standard of providing effective treatment to our clients in both partial and other types of programs. The McLean Southeast program emphasizes the creation of individualized treatment plans to decrease acute symptoms and recognizes patients’ strengths and goals. At the PHP at McLean Southeast, a variety of assessment tools are used at intake and discharge to ascertain the level of symptoms of our clients. These tools measure anxiety, depression, PTSD, and overall functioning. With the present study, we compared the pre and post measures of depression from the QIDS inventory from McLean Southeast’s PHP to comparable programs from previously peer-reviewed research. Comparison data collection is still in progress.

Topic areas:
Depression
Introduction: The P3 event related brain potential (ERP) provides fundamental information on the neural underpinnings of cognition. P3 amplitude is thought to index brain activity that updates working memory and has two subcomponents: P3a and P3b. The P3a subcomponent has a frontal/central maximum amplitude distribution and is associated with the initial processing of a new stimulus and redirection of attention. The P3b subcomponent has a central/parietal maximum amplitude distribution and is associated with the subsequent memory comparison and is proportional to the amount of attentional resources devoted to a given task. P3 latency is a measure of cognitive efficiency. Thus, P3a and P3b are generated partially by different neural structures and are related to specific stimulus evaluation processes (Polich and Criado, 2006). P3b deficit is a widely studied neurobiological marker in patients with schizophrenia and affective psychotic disorders (Hall et al 2007, 2009). However, much less is known about the P3a ERP, especially in the first episode psychosis (FEP) patients. Also, few studies have examined the P3a/P3b ERPs in relation to social and role functioning. The present study explored the relationships between baseline P3 ERP components, clinical variables and social and role functioning in FEP patients as part of an ongoing longitudinal study of first episode psychosis.

Method: FEP patients (n=9) and age and sex matched healthy controls (n=13) completed a ‘3-stimulus’ auditory oddball paradigm (400 binaural tones; 50-msec duration, 5 ms rise/fall times) in which infrequent non-target (novel) stimuli (12% Dog barks or water drop sound) are inserted into the sequence of target (12% 1500 Hz tones) and standard stimuli (76% 1000 Hz tones) and assessments of social and role functioning using the Global Functioning Social and Role Scale (GF-Social & GF-Role). Patients also completed symptom scales including the Young Mania Rating Scale (YMRS), Montgomery-Asperg Depression Rating Scale (MADRS), and the Positive and Negative Syndrome Scale (PANSS). T-tests and Person partial correlations were used to compare group differences and explore associations between variables.

Results: Controls had a significantly higher GF-Social and GF-Role functioning than patients (p<.001, both). P3a amplitude in patients did not differ from controls (p=0.29) whereas P3b amplitudes were significantly reduced in patients compared to controls (t(20)=1.9047, p=0.036). No difference in either P3a or P3b latency was found. Within FEP patients, P3a amplitude is associated with the YMRS at trend level (partial r=0.75, p=0.085). The correlations of P3a amplitude with GF-Social and GF-Role functioning were estimated to be 0.75 (p=0.14) and 0.06 (p=0.93), respectively. The correlation of P3b amplitude with GF-Social and GF-Role functioning were estimated to be 0.56 (p=0.32) and 0.45 (p=0.45), respectively.

Discussion: Our preliminary results suggest that P3a amplitude may be associated with severity of mania symptoms and the both P3a and P3b amplitudes may be associated with functional ability, specifically social functioning. We are collecting larger sample to confirm these results.

Topic areas:
Bipolar
Psychotic disorders
Schizophrenia
Drug use before age 14 dramatically increases the risk of substance use disorder (SUD) compared to later initiation. Identification of early traits that predict SUD risk is critical if we are to reduce or prevent SUD. Poor working memory in teenagers is associated with greater risk-taking behavior. We hypothesized that poor working memory would be associated with less plasticity (as measured by low salivary brain-derived neurotrophic factor [BDNF]) and more cocaine SUD-related behaviors in adolescence and adulthood. On post-natal day (P)20, we assessed working memory using the novel object recognition task and collected saliva in male and female rats. From early adolescence through adulthood (P28-64), rats were allowed to intravenously self-administer either a moderately high (0.75 mg/kg/infusion) or moderately low (0.25 mg/kg/infusion) cocaine dose under a fixed-ratio (FR)1 schedule that gradually increased to FR5. After 30 days of abstinence, saliva was re-collected and rats underwent a cocaine-primed (10 mg/kg, intraperitoneal) relapse test on P94. Object discrimination positively correlated with salivary BDNF on P20 in males, suggesting good working memory is associated with high plasticity. The opposite relationship was observed in females, in whom object discrimination negatively correlated with BDNF. Males earned more cocaine infusions during FR5 and made more cocaine-seeking responses during relapse compared to females at the 0.75 mg/kg cocaine dose, but no sex differences were observed in 0.25 mg/kg cocaine self-administration. Object discrimination and salivary BDNF on P20 negatively correlated with cocaine intake and seeking in males self-administering 0.75 mg/kg and in females self-administering 0.25 mg/kg cocaine. Finally, to assess whether salivary BDNF reflects a stable trait, correlations were conducted between P20 and P94. Salivary BDNF positively correlated independent of self-administration history in males (r=0.46, p<0.05), but in females this relationship was mediated by cocaine intake. Results establish poor early working memory and low salivary BDNF as potential risk factors for cocaine SUD, and suggest adolescent females may be more sensitive to cocaine than males. However, further research is needed to understand interactions between early working memory, salivary BDNF, and cocaine use in females.
Presenting Author: Ralph Buonopane, PhD, Program Director, Instructor in Psychology  

Co-Authors: Carol Nash, MS, Victoria Joyce, BA, Anne Beauchamp, PhD  

Title: Predictors of Child & Adolescent Psychiatric Readmission  

Key words: Readmission, Social Support

It has been well documented that recently discharged psychiatric patients have a critically high risk of suicide and suicide attempts leading to readmission in the 30 days post hospitalization. However, understanding the factors related to psychiatric readmission of children and adolescents is essential to improving the quality of pediatric healthcare. Research on the influence of post-discharge care on hospital readmission is limited and findings from the existing studies are inconsistent. We conducted an exploratory study of readmission predictors that could be targeted for future intervention and support to improve post discharge outcomes.

We conducted a prospective exploratory study to examine the impact of a range of sociodemographic, clinical, family and treatment utilization variables on both transition outcomes and hospital readmissions. Parents provided information on their child’s outcomes 30-day after their child was discharged from the McLean Franciscan Child and Adolescent Inpatient Mental Health Program (n=12 readmitted, n=32 not readmitted).

Patients who were readmitted were more likely to be Caucasian or female and have longer length of stays. Parent’s perceptions of the ease or difficulty with which their child reconnected with family, friends and school was significantly predictive of the risk of readmission. Days to first outpatient appointment was not predictive of readmission. However, remaining in therapy at 30 days was a significant predictor of decreased readmission rate. Elevated ratings of parent perceived stress at discharge was a significant predictor of readmission for patients discharged to a PHP program, but not a predictor of readmission for those discharged to outpatient care.

Longer length of stay and discharge to a PHP are both proxies for symptom severity, functional decline and weakness of a patient’s support system. The lack of significance for time to outpatient therapy may be explained by the very efficient post-discharge appointment rate of our unit, averaging 4.74 days from discharge to first outpatient appointment, compared to a nationally accepted standard of 7-10 days. Finally, the significance of remaining in therapy at 30 days emphasizes the importance, not only of timely transition to outpatient care without gaps in treatment, but the importance of maintaining that engagement in outpatient care during the critical weeks post-discharge.

Topic areas:  
Child/Adolescent
Medication non-adherence is a significant clinical problem in chronic disease management. In particular, adherence to second generation antipsychotics (2GA) is a major determinant of outcomes in psychotic disorders. Factors that contribute to non-adherence include impaired insight, attitudes toward medication, and trust in clinical providers. We explored the relationship between these factors and treatment adherence in a serious mental illness (SMI) population as part of an ongoing study of cardiovascular health in SMI. We administered the Hogan Drug Attitude Inventory (DAI), VOILS Mental Health Medication (VOILS), Trust in Physician Scale (PT), and the Scale to Assess Unawareness in Mental Disorder (SUMD) to patients taking a (2GA) medication at four different clinic locations (McLean Hospital, MGH, and two DMH run clinics: Massachusetts Mental Health Center, and the Michael J. Gill Clinic). These questionnaires are used to assess self-reported perceptions and attitudes toward medications (DAI), medication adherence (VOILS), physician trust (PT), and insight into symptoms of mental disorder (SUMD). Participants complete a baseline visit, and are followed at approximately three-month intervals for one year. We computed Pearson’s correlation coefficients between scores from the baseline visit and adherence data (n=92) using PASW statistical software. A weak, positive correlation, r(92)=.251, p=.016 suggests that medication adherence may be associated with high trust in the physician. A weak, negative correlation r(92)=.235, p=.024 suggests that increased insight could result in a more positive attitude toward medication. Finally, a weak, positive correlation r(92)=.223, p=.032 suggests that a more positive attitude toward medication could result in higher medication adherence. Overall this analysis suggests that patients with increased insight and positive clinical relationships are more likely to be adherent to treatments, and therefore are more likely to have improved clinical outcomes. We plan to add to these analyses with longitudinal data on the value of extending interventions for bolstering adherence and insight within this population. Further research in this area may lead to interventions for increased provider support leading to improved medication adherence and ultimately patient outcomes.
Developing and implementing an electronic patient reported outcomes measurement using REDCap in usual care psychiatric settings.

Background: Finding ways to feasibly and cost-efficiently measure patient reported outcomes in psychiatric routine care settings is critical to facilitate patient engagement in care, improve patient outcomes, and assess the performance of our treatment programs. McLean Hospital began an electronic patient reported outcomes measurement program, the Clinical Measurement Initiative (CMI), in November 2010. The CMI aims to inform individual patient care, assist with quality assessment of clinical programs, and facilitate clinical research. The CMI uses Research Electronic Database Capture (REDCap), a free (but not open source) secure web application for building and managing online surveys. We designed a custom reporting module for individual patient reports to be available immediately at the point of care, and an online aggregate reporting tool for clinical teams to track survey completion rates and outcomes.

Objective: To describe qualitatively and quantitatively the implementation experience of the McLean CMI program. Methods: We calculated descriptive longitudinal statistics of admission and discharge survey administration, and developed qualitative information about implementation “lessons learned” based on discussions with clinical teams that have implemented the CMI as part of the ongoing evaluation and monitoring of the program. We also stratified the quantitative statistics based on patterns of admission and discharge administration completion rates.

Results: Over 22 programs representing 11 clinical psychiatric subpopulations have implemented the CMI; 16 programs remain active and as of June 30, 2016 there are over 13,357 episodes of care completed. All inpatient units (N=5), 1 partial and 1 residential program were unable to sustain the CMI in a way they found useful for clinical care and discontinued. Across active programs, completing admission assessment within 3 days of admission on average was easier for teams than completing discharge assessments (mean range across programs and over time: admission assessments—82%-98%; discharge assessments—56%-64%). Having at least one clinical champion at each program was a key driver for successful implementation, but champions were not always associated with immediate success regarding high survey completion rates. Champions served several needs: problem-solving successful new workflows, generating team enthusiasm, and setting team expectations for the importance of integrating the CMI information into clinical care. Teams that integrated the CMI into their clinical care with patients were also more successful in sustaining the CMI program.

Conclusions: Achieving electronic patient reported outcomes measurement in intensive treatment psychiatric settings using REDCap and custom reporting tools is feasible, but more easily accomplished in residential and partial hospital levels of care (compared to inpatient), where patient acuity is high but less severe and lengths of stay are longer. Clinical champions play critical roles in successful implementation and maintenance of electronic patient reported outcomes measurement, and can be successful independent of program level of care or patient acuity. Champions were sometimes “necessary but not sufficient” and even among teams with champions, workflow challenges in administering electronic patient reported outcomes measurement can be difficult to overcome.

Topic areas:
Outcomes/Quality
Presenting Author: Min Su Kang, Research Assistant

Co-Authors: Rachel Clegg, Blaise Frederick, Julie Van der Feen, Blaise Aguirre, Diego A. Pizzagalli, Roselinde Kaiser

Title: Anomalies in resting-state network connectivity in adolescent depression

Key words: Depression, fMRI, functional connectivity, Adolescent, resting-state

Despite growing evidence that resting-state functional connectivity is altered in adults with major depressive disorder (MDD), few studies have investigated similar processes in adolescent depression. Because adolescence is a crucial time for neural and emotional maturation, it is particularly important to examine functional changes during this critical developmental period. We recruited 16 adolescents with MDD (14 on antidepressants) and 19 age-matched healthy controls between the ages of 13 and 18. Using high temporal resolution functional magnetic resonance imaging (fMRI), we investigated resting-state functional connectivity of intrinsic connectivity networks that have been implicated in adult depression, such as the Default Mode Network (DMN), Salience Network (SN), and Central Executive Network (CEN). Regions-of-interest (ROI)-to-ROI connectivity analyses revealed that adolescents with MDD were characterized by aberrant patterns of connectivity in a frontoinsular network spanning regions of DMN and CEN. Findings from this study suggest that interactions among key intrinsic connectivity networks are altered in adolescent MDD. These anomalies may contribute to core symptoms of depression, and serve as a potential target for therapeutic interventions.

Topic areas:
Depression
Patients with Higher Levels of Dissociation Perform Better than Patients with Lower Levels of Dissociation on Measure of Attention and Executive Function

Acute and chronic exposure to traumatic stress can lead to the emergence of pathologic dissociative symptoms. Unfortunately, chronic traumatic dissociation is linked to debilitating conditions such as posttraumatic stress disorder (PTSD) and dissociative identity disorder (DID). In trauma-exposed populations, dissociation is reportedly associated with reduced performance across a range of cognitive domains including attention, executive functioning, working memory and verbal, visual and episodic memory. Prior studies have primarily included individuals exposed to military trauma; therefore, in the current study we investigated executive functioning and cognitive control in a cross-diagnostic cohort of women with histories of childhood abuse and neglect. Patients diagnosed with PTSD both with and without the dissociative subtype or DID (n=33) as well as a group of healthy control participants (n=13) were recruited. Using a median split of Multidimensional Inventory of Dissociation partially dissociated intrusion scores, low dissociation (n=17) and high dissociation (n=16) patient groups were created. All participants completed a neurocognitive battery, which included the Trail Making Test (TMT) and the Stroop Color Word Test. The TMT consists of two subtests, Trails A and Trails B; Trails A primarily assesses psychomotor speed while Trails B uses an alternating set demand to measure cognitive flexibility and executive function. The Stroop test consists of the three conditions and measures the ability to establish competing response tendencies, inhibit inappropriate responses, and resist interference. A subset of participants also completed the Multi Source Interference Task (MSIT), a complex measure of cognitive control comprised of control and interference trials, which has previously been used to distinguish patient groups. Results indicate that both low and high dissociators performed Trails B significantly more slowly and made more errors relative to control participants. Additionally, on the interference condition of the Stroop, both low and high dissociators performed significantly more slowly and made more errors relative to the control participants. Interestingly, on the MSIT, while both patient groups performed equally well on control trials compared to controls, low dissociators had significantly longer response times, more commission errors and total errors, and significantly lower accuracy on the interference trials compared to control participants. In contrast, high dissociators demonstrated only significantly longer response times compared to controls; no other performance differences were detected on the interference trials. Taken together, these data provide evidence of executive function and cognitive control deficits in trauma-exposed patients with histories of childhood abuse and neglect regardless of the severity of dissociative symptoms. It is of note that patients with higher levels of dissociative symptoms appeared somewhat less impaired than those with lower levels of dissociative symptomatology. As dissociation has been noted to contribute to reduced cognitive function, likely interfering with incoming information, it is possible that those with higher levels of dissociative symptoms are more accustomed to having to filter irrelevant information than those with lower severity of symptoms. Furthermore, it may be the case that higher levels of dissociation facilitate a compensatory strategy for those patients. Additional studies are needed to clarify the role of dissociative symptom severity on cognitive performance.

Topic areas:
Dissociative Disorders
PTSD
Predictors of Nonmedical Benzodiazepine Use in Adults with Alcohol Use Disorder

Key words: alcohol use disorder, benzodiazepines, nonmedical use, polydrug use, anxiety sensitivity

Background: Although benzodiazepines are effective for several conditions, such as anxiety disorders, seizures, and insomnia, they also possess a high abuse potential. The public health harm associated with nonmedical benzodiazepine use has dramatically escalated in the past 20 years. Of particular concern is the rate of overdose deaths involving these drugs, which more than quadrupled from 1996 to 2014. Nonmedical benzodiazepine use (i.e., use without a prescription or at a dose or frequency greater than prescribed) is of particular concern in populations with co-occurring substance use disorders, as use in combination with other central nervous system depressants, such as alcohol, increases the risk of fatal overdose. However, correlates of benzodiazepine misuse in populations with alcohol use disorder have not been studied. Understanding factors that contribute to the nonmedical use of benzodiazepines is necessary to identify markers of risk and ultimately to determine appropriate treatment for this population.

Methods: A sample of 458 participants (34.5% female; mean age=42 years) with a diagnosis of alcohol use disorder was recruited from an inpatient detoxification unit and completed a battery of self-report questionnaires, including the Brief Addiction Monitor, the Anxiety Sensitivity Index, and the Brief Pain Inventory. A multivariable linear regression was used to evaluate predictors of past-month benzodiazepine misuse, including sociodemographic, psychiatric, and substance use variables.

Results: Results indicated that the following variables were associated with more days of benzodiazepine misuse: more days of marijuana use, other sedative/tranquilizer use, cocaine use, stimulant use, and heroin use. This model predicted 38% of the variance in nonmedical benzodiazepine use (F[17, 388]=13.94, p<.001). However, these results differed by gender. For women, greater anxiety sensitivity was associated with days of nonmedical benzodiazepine use, along with days of cocaine use and days of "other" (i.e., uncategorized) drug use. For men, days of marijuana use, sedative/tranquilizer use, stimulant use, and heroin use were associated with days of nonmedical benzodiazepine use. These models predicted 33% and 44% of the variance in days of benzodiazepine misuse, respectively. The gender by Anxiety Sensitivity Index interaction term was significant (B=-0.02, SEB=0.01, p=.003), suggesting that gender significantly moderated the association between anxiety sensitivity and nonmedical benzodiazepine use.

Conclusions: Our findings in a sample of inpatients with alcohol use disorder suggested that the misuse of benzodiazepines in this population may be consistent with a general pattern of multiple substance use. The finding that anxiety sensitivity was associated with nonmedical benzodiazepine use in women but not men is consistent with previous findings in patients with opioid use disorder. Interventions to reduce benzodiazepine misuse, especially in high-risk groups such as multiple substance users, may be indicated to reduce the risk of overdose.

Topic areas:
Addiction
Anxiety
Women
Background: Recent findings indicate that individuals with major depressive disorder (MDD) display blunted reinforcement learning due to an impaired reward responsiveness. In addition, childhood sexual abuse (CSA) has been linked to later life MDD. Amisulpride is a substituted benzamide neuroleptic, which at low doses, has been shown to increase DA synthesis and release due to presynaptic autoreceptor blockade, and have prohedonic effects. The current poster presents behavioral data from three groups (MDD, MDD with CSA, healthy controls) examining the effect of a single low dose of amisulpride (50 mg) on reinforcement learning, using a probabilistic selection task with both positive and negative feedback.

Methods: Data from 32 subjects in total were analyzed. These consisted of 9 MDD patients and 7 healthy controls who received amisulpride and 9 MDD patients and 7 healthy controls who received the placebo. Among MDD patients, amisulpride was balanced across MDD only and MDD with CSA. We assessed behavioral group differences in positive and negative reinforcement learning using accuracy scores from a computerized probabilistic selection task.

Results: A repeated measures ANOVA with a within subjects’ factor of learning type (positive or negative feedback) and between subjects’ factors of drug administration (amisulpride or placebo) and diagnosis (MDD or healthy control) revealed a significant drug x learning type interaction (p= .046). There were no significant interactions with diagnosis. Subsequent one-way ANOVAs examining the effect of amisulpride on each learning type separately revealed a trend effect of amisulpride on learning from negative feedback (p= .063), with the amisulpride group having higher accuracy (75%) than the placebo group (61%), regardless of diagnosis. Follow-up analyses including additional factors such as CSA and anxiety scores did not yield any further significant interactions (all p> .05).

Conclusion: These preliminary results indicate that amisulpride enhances learning from negative feedback and that this effect is not modified by MDD diagnosis or history of CSA. Results run counter to prior research findings that have found amisulpride to primarily enhance positive reinforcement learning. However, it is very important to consider that in this analysis the small sample size may be responsible for a false positive and in fact, when other factors such as CSA and anxiety scores were included in the analysis, the drug x learning type interaction was no longer significant. Further data collection is necessary to examine how CSA (with and without MDD) may modulate the effects of amisulpride on reinforcement learning.

Topic areas:
Depression
Pharmacology
Women
PACAP Alters Fear-Related Behavior and Increases Arc Expression in the CeA and BNST After Fear Conditioning in Rats

Pituitary adenylate cyclase-activating polypeptide (PACAP) is a highly conserved neuropeptide, with shared amino acid sequence homology among rats, mice, and humans. Alterations in the PACAP system are associated with stress and may play a role in psychiatric conditions such as post-traumatic stress disorder (PTSD). We have previously shown that PACAP modulates learning and memory and induces both amnestic (early) and hypermnesic (late) behavioral phenotypes in animals treated with PACAP prior to fear conditioning (Meloni et al., 2015). In those studies, immunohistochemistry for the immediate early gene c-Fos revealed PACAP-dependent effects in the central nucleus of the amygdala (CeA), but not basolateral amygdala (BLA) or dorsal hippocampus (DH), brain areas implicated in consolidation of fear learning. Here, we examined PACAP’s effects on synaptic plasticity in these brain areas by measuring changes in activity-regulated cytoskeleton-associated protein (Arc) expression, a biomarker of synaptic activity that could uncover plasticity-dependent effects not revealed by c-Fos in earlier studies. Male Sprague-Dawley rats were implanted with intracerebroventricular (ICV) cannula for infusion of either vehicle (VEH) or PACAP-38 (1.5 ug) followed 30 min later by fear conditioning; rats received two pairings of a 30 s, 75 dB tone co-terminating with a 0.6 mA footshock. Rats were perfused 1 hour after conditioning, and brain sections were processed for Arc immunoreactivity. There was a highly significant increase in Arc-labeled neurons in the CeA but not the bed nucleus of the stria terminalis (BNST) or DH (dentate gyrus) in PACAP-treated animals. In the CeA, double labeling immunohistochemistry indicated no co-localization between Arc and corticotropin releasing factor (CRF)-containing neurons in PACAP-treated animals. Arc staining in the BLA or dendritic fields of the CA1-CA3 of the DH were not significantly different between VEH and PACAP-treated rats. These results indicate that the CeA is a primary brain area involved in PACAP’s modulation of neuronal plasticity induced during fear conditioning. Because the CeA receives heavy PACAPergic innervation from the brainstem, stress-induced elevations in this neuropeptide - as is seen in some patients with PTSD (Ressler et al., 2011) - may facilitate consolidation of emotional memories through Arc-dependent pathways. Hence, understanding the neurobiology of PACAP systems may help reveal how stressful experiences such as exposure to trauma stress and exposure to trauma converge to promote psychiatric illness, and facilitate the development of more effective strategies to treat or prevent stress-related illness.

Topic areas:
PTSD
McLean Research Day 2017

Original Research - Clinical

Poster # 38
Time: 1:50-2:45pm

Presenting Author: Simone Chad-Friedman, Clinical Research Coordinator

Co-Authors: Simone Chad-Friedman, BA, Marie Forgeard, PhD, Courtney Beard, PhD, Thröstur Björgvinsson, PhD, ABPP

Title: Changes in Openness to Experience are Associated with Treatment Outcomes in a Partial Hospital Setting

Key words: Openness to Experience, Transdiagnostic, Adult, Depression, Anxiety

Background: Openness to experience (O), a dimension of the Five-Factor model of personality, is defined as the willingness to engage with new experiences and information. O is related to cognitive exploration as well as creativity and flexibility in cognitive processing. Past research has shown that O is a protective factor for mortality and is associated with improved decision making and resilience to stress. In addition, recent investigations indicate that O shows significant within-person variability and can change over short periods of time. Related to this, it is possible to increase O through training, yet few studies have examined the extent to which O changes during existing mental health interventions, and whether changes in O are associated with changes in mental health. In the present study, we examined whether O changed during brief intensive cognitive-behavioral treatment. We also tested whether changes in O were associated with changes in mental health.

Methods: We collected data from 271 adult patients (Mage = 34.09 years, 52% female, 87.1% White) enrolled in a partial hospital treatment program. At both admission and discharge, participants completed the PHQ9, GAD-7, and BASIS-24 to assess current symptoms. In addition, participants rated themselves on O during the past 24 hours in three domains (relationships, daily life activities outside of treatment, and treatment) (α = .95) (based on Goldberg, 1992).

Results: O increased significantly from admission to discharge from the program (T1 M = 4.16, SD = 1.29; T2 = 4.51, SD = 1.31, Cohen’s d = .27). O at admission was negatively associated with depression (r = -.24), anxiety (r = -.16), depression/functioning (r = -.33), relationship difficulties (r = -.16), and positively associated with psychosis (r = .20) and substance use (r = .13) (all ps < .05). Regression analyses (controlling for symptom severity at admission), changes in O during treatment were associated with changes in anxiety (β = -.13), depression/functioning (β = -.24), relationship difficulties (β = -.16), emotional lability (β = -.20), and psychosis (β = -.13) (all ps < .05).

Conclusion: The personality state of openness to experience is meaningfully associated with clinical characteristics as well as treatment outcomes of individuals presenting for partial hospitalization. At baseline, higher levels of O were associated to lower levels of depression, anxiety, and relationship difficulties, but also higher levels of psychosis and substance use. Changes in O were however consistently linked to improvements in treatment outcomes. This study was limited by the use of self-report measures and a naturalistic design; more research is needed to examine whether increasing O during treatment leads to enhanced treatment outcomes.

Topic areas:
Anxiety
Depression
Theoretical/Commentary

Poster # 39
Time: 1:00-1:50pm

Presenting Author: Kathryn Kieran, MSN, Director of Nursing Operations at Hill Center

Co-Authors: Patricia Mangones, MSN, PMHNP-BC

Title: Trauma Informed Prescribing

Key words: trauma, informed, care, polypharmacy, prescriber

Trauma informed care is increasingly recognized by all specialties as central to successful care of patients with histories of trauma (Muskett, 2014; Reeves, 2015). Psychiatry should lead at the forefront of these efforts, due to the inherent power differential in one-way sharing of feelings, voluntary and compulsory inpatient hospitalization, and voluntary and compulsory medication administration (Anai-Otong, 2016). Accentuated meaning of power dynamics exists for patients with trauma histories and there are additional considerations for prescribing psychiatric medication in this population. Patients with trauma histories overwhelmingly struggle with polypharmacy due to increased risk of medical illness, and comorbid mood and substance use disorders (Felitti et al., 1998; Kessler, Sonnega, Bromet, Hughes & Nelson, 1995). A predisposition towards somatization, and the potential for medical self-neglect as part of experiences of dissociative or avoidant symptomatology, increase provider-patient misunderstanding (Collett et al., 2016; Resnick & Acierno, 1997). Patients may believe that in order for their trauma or symptoms to be validated or “real,” their medication list must reflect severe debility by its length. Patients may also believe that any medication management can discount their trauma as “all in their head,” and subsequently resist efforts at symptom management via medications. Patients may have reactions along a spectrum of these beliefs, or hold these beliefs simultaneously. Many prescribing clinicians find, therefore, that the road to rational pharmacotherapy is paved with miscommunication and struggle. Prescribing strategies borrowed from gerontology, in particular the deprescribing model, are discussed as a potential way forward (Gupta & Cahill, 2016). The general stance of a clinician in these cases is one of compassionate listening, with frequent validation of the reasonable origin of traumatic beliefs, given the circumstances under which they arose. This compassion must be interwoven with firm boundaries, clearly outlined treatment goals and plans, and acknowledgement of patient choice whenever possible. At times, lower than therapeutic doses or brief, targeted use of doses at the upper limits of typical treatment ranges must be considered and implemented to gain or maintain a relationship (Loewenstein & Goodwin, 1999). Maintaining rational pharmacotherapy in the face of obstacles both within and without the treatment is addressed. Strategies for the frontline clinician to implement brief cognitive restructuring of medication beliefs are outlined. Guidelines for initiating a deprescribing model, and for addressing nonadherence to the prescribed regimen, are provided.

Topic areas:
Borderline Personality Disorder
Dissociative Disorders
Pharmacology
PTSD
Women
Presenting Author: Gabriele Chelini, Postdoctoral Research Fellow

Co-Authors: Harry Pantazopoulos, Sabina Berretta

Title: Role of the non-cell autonomous transcription factor OTX2 in the pathology of schizophrenia and bipolar disorder

Key words: OTX2, Schizophrenia, Bipolar Disorder, Neurodevelopment, Perineuronal Nets

Recently, several studies unveiled the pivotal role of the Orthodenticle homeobox 2 (Otx2) transcription factor to guide both pre and postnatal development. Interestingly, these studies demonstrated that cell-autonomous Otx2 plays a major role to determine neuronal destiny during embryonic life, while non-cell autonomous Otx2 specifically promotes postnatal experience-dependent maturation of Parvalbumin positive cells (PVcells). As a part of this maturation process, Otx2 induces the aggregation of Perineuronal Nets (PNNs), an extracellular matrix structure responsible for many cellular processes, including synaptic plasticity and circuit’s re-arrangement. In turn, PNNs have the ability to attract and maintain Otx2 into the cell, establishing a reciprocal relationship with this transcription factor. Previous postmortem findings from the Translational Neuroscience Laboratory, that have showed a reduction of PNNs in several brain regions of subjects with schizophrenia (SZ) and bipolar disorder (BD). We hypothesize a role of Otx2 decreased availability in the pathophysiology of SZ and BD. Notably, during postnatal life, Otx2 is mainly expressed in the Choroid Plexus (ChP), a periventricular encephalic area that may be directly impaired by the well-documented enlargement of ventricles reported in SZ patients. Our preliminary investigations suggests a significant reduction of Otx2 protein in SZ cerebrospinal fluid and amygdala, a limbic area where PNNs were found to be significant reduced in SZ and BD. Taken together these findings suggest a lack of postnatal brain maturation as a major cause for SZ pathophysiolo, opening the possibility for new diagnostic and therapeutic tools, as well as a very specific time-window for the intervention.

Topic areas:
Bipolar
Schizophrenia
Background: HIV-Transactivation of Transcription (Tat) protein, which plays a crucial role in viral replication, exerts damaging effects in the brain including oxidative stress. We previously reported brain gray matter density reductions and learning and memory impairments in GT-tg bigenic mice which can be induced to express Tat protein by doxycycline (Dox) activation of a tat transgene. In this study, we used in vivo proton (1H) magnetic resonance spectroscopy (MRS) to assess neurochemistry and temperature in the medial frontal cortex (mFC) of GT-tg bigenic mice administered Dox as well as in saline-treated control mice. The mFC was selected because it is an area involve in cognitive control, performance monitoring, error detection and behavioral adjustments through learning from adverse outcomes, which can be adversely affected by HIV-Tat protein expression. Methods: Adult male GT-tg mice were treated with saline (N=15) or Dox (N=15, 100 mg/kg, i.p.) for 7 days to induce Tat protein expression. Mice underwent 9.4T proton MRS of the mFC 1 day later. MRS spectra were acquired using an ultra-short-echo-time STEAM sequence with following parameters (TR = 4s, TE = 3s, 4096 complex points, 5000 Hz acquisition bandwidth, 1 ms 90 excitation pulse). Five partial acquisition sets of 128 water-suppressed free induction decays (FIDs) were acquired. After each water-suppressed partial acquisition, a separate water-unsuppressed spectrum (4 FIDs) also was acquired. All 640 FIDs from water-suppressed spectra were summed and used to obtain GSH values. Each water-suppressed and water-unsuppressed spectrum pair was used to obtain a brain temperature value, by comparing chemical shift of the water resonance (unsuppressed spectrum), which changes with temperature, to chemical shift of the N-acetylaspartate (NAA) resonance in the suppressed spectrum, which is temperature insensitive. All spectra were fitted using LCModel, and chemical shift frequencies were identified using MNova software. Results: Dox-treated mice expressing Tat exhibited higher glutathione (GSH) levels (p = 0.0036) and temperature (p = 0.040) than saline controls. Pearson correlation analysis found a positive association between GSH levels and temperature during the first partial acquisition (r = 0.51, p <0.01). Conclusion: These data suggest that conditional Tat protein expression increases mFC GSH levels. As GSH is the principal endogenous antioxidant, this effect may reflect a compensatory response to Tat-induced oxidative stress. While increased brain temperature could be caused by neuronal hyperactivation, inflammation, and/or oxidative stress, all of which are triggered by Tat protein, the correlation we found between GSH and temperature suggests that Tat-induced oxidative stress may be at least partially responsible.

Topic areas:
Imaging
Major depressive disorder (MDD) is a common neuropsychiatric disorder that affects more than 350 million people of all ages worldwide. In the United States alone, roughly 20 million people suffer from it every year. While MDD is typically characterized by persistent sad mood, loss of interest or pleasure in activities, feelings of worthlessness and hopelessness, and decreased energy, MDD can also affect cognition. Deficits in executive functioning, attention, and memory are some of the cognitive symptoms that have been described in MDD. In addition, it has been found that the severity of cognitive deficits correlates with the severity and length of depression. While the etiology of MDD is unknown, it has been discovered in genetic mouse models that deficits in inhibitory signaling via gamma-aminobutyric acid (GABA) and its type A receptor (GABAAR) are sufficient to induce depression-like behavior. Previous studies from our lab have shown that the mice lacking the GABAAR alpha2 subunit display anxiety- and depressive-like behaviors. As these studies examined acute forms of stress, we then wanted to investigate whether the knockdown of the alpha2 subunit gene would alter the susceptibility to more chronic forms of stress. To do this, we performed the chronic social defeat paradigm and examined changes in social interaction behavior following 10 and 5 days of social defeat stress in wild-type (WT) and homozygous alpha2 knockout (KO) mice. We found that 10 days of defeat stress produced a ceiling effect in the one-chamber social interaction test, as both defeated WT and KO mice exhibited reduced sociability. However, following 5 days of defeat stress, only the KO mice exhibited reduced sociability. Given these findings, we examined the effect of alpha2-containing GABAARs and 5 days of defeat stress on negativity bias, a cognitive symptom of MDD. Negativity bias is the tendency to interpret ambiguous or neutral information as negative, and we examined this symptom using the ambiguous cue discrimination paradigm. We hypothesized that 5 days of defeat stress would lead to an increase in freezing response to the ambiguous cue in KO mice but not in WT mice. Interestingly, while we did not see any difference between WT and KO mice in freezing response to the ambiguous cue at either baseline or after 5 days of defeat stress, we saw a genotype effect in the control group, where control KO mice showed increased freezing to the ambiguous cue whereas control WT mice did not. Since these mice were single housed whereas the mice tested at baseline were group housed, we concluded that the mild stress induced by 5 days of single housing is sufficient to elicit negativity bias in KO but not in WT mice, providing evidence for a potential gene-environment interaction. In summary, our studies suggest that alpha2-GABAARs may interact with stressful environments to prevent depressive-like behaviors in the chronic social defeat paradigm and to prevent negativity bias in the ambiguous cue discrimination paradigm.
**Title:** Treatment Response Disparities in LGBTQ Patients Receiving Intensive CBT Partial Hospital Care

**Keywords:** LGBT, CBT, disparities, outcomes

**Introduction:** Lesbian, gay, bisexual, transgender, and queer identifying (LGBTQ) individuals face higher risks for mental health issues, including depression, suicidality, and substance use, compared to the general population (King et al., 2008; McCabe et al., 2009; Reisner et al., 2016). Efforts in the literature to examine appropriate interventions have been few, and mostly include individual case studies (Safren & Rogers, 2001), or outcome research with culturally adapted CBT protocols for LGBTQ patients (e.g: ESTEEM: Pachankis et al., 2015; Mind Over Mood: Ross et al., 2008). However, it is currently unclear whether or not such LGBTQ-specific interventions are needed because the vast majority of treatment outcome studies do not report on participant sexuality or trans and nonbinary gender identities (Heck et al., 2016; Flentje, Bacca & Cochran, 2015). Studies specifically focusing on LGBTQ individuals’ treatment response are needed to determine to what extent existing evidence based treatments generalize to queer and trans populations. The current study compared patients identifying as lesbian, gay, bi, trans, and/or queer to straight and cisgender patients on clinical characteristics upon admission to an intensive CBT partial hospital, as well as treatment outcomes.

**Method:** Data were obtained from a deidentified database including clinical outcome measures completed by patients (n=447) attending an intensive CBT-based partial hospital program (M treatment days=8) between January and July of 2016. Of those patients, 64 (14%) self-identified as lesbian, gay, bi, trans, and/or queer on their admission form. Patients received individual and group CBT-based treatment, focusing on learning skills such as behavioral activation, cognitive restructuring and self-assessment. Patients also completed self-report questionnaires at admission and discharge, including the Patient Health Questionnaire (PHQ-9), Behavior and Symptom Identification Scale (BASIS-24), and Clinical Global Improvement Scale- self report (CGI).

**Results:** LGBTQ patients did not significantly differ from non-LGBTQ patients on most clinical characteristics upon admission, including depression severity, substance use, self-harm and suicidal ideation, quality of life, and motivation for treatment. LGBTQ patients did report significantly more prior inpatient hospitalizations (2.9 vs 1.7, t(429)=3.19, p=.002). Regarding treatment outcome, groups did not differ in their self-reported global improvement. However, there was a trend for LGBTQ patients to report less improvement in depression symptoms (PHQ-9: t(341)=1.86, p=.065). Finally, LGBTQ patients experienced significantly less improvement in self-harm (BASIS-24: t(342)=2.74, p=.007).

**Conclusion:** Unlike what is reported in much of the literature, LGBTQ patients in this naturalistic sample had comparable baseline clinical characteristics to the rest of the patient population. However, LGBTQ patients showed less improvement in depressive symptoms, and no improvement in measures of self-harm. This indicates that current CBT treatments may need to be modified to better address mental health issues in this population. For example, the partial hospital from which the current data were obtained is developing a group protocol to specifically address how patients’ identities (including gender and sexuality) affect their mental health and treatment. Further studies in different settings are needed to replicate the current findings with standard CBT protocols, as well as studies comparing standard CBT to culturally focused CBT.

**Topic areas:**
Addiction
Depression
Presenting Author: Rachel Clegg, Clinical Research Assistant II

Co-Authors: Roselinde Kaiser, Franziska Goer, Miranda Beltzer, Pia Pechtel, Alexis E. Whitton, Gordana Vitaliano, David P. Olson, Laurie A. Scott, Emili Cardenas, Diego A. Pizzagalli

Title: Effects of Early Life Stress on Corticolimbic Function and Cortisol Reactivity

Key words: amygdala, cortisol, early life stress

Introduction: Previous research has shown that experiencing early life stress (ELS) can lead to significant neurobiological and cognitive changes in adulthood, including changes in cortisol response to stress. For example, research comparing individuals with a history of ELS to non-stressed controls has revealed abnormalities in functional and structural connectivity between brain systems involved in regulating attention and emotion (e.g., lateral prefrontal cortex, LPFC) and systems involved in processing emotional salience (e.g., the amygdala). Individuals with ELS have also been shown to have a decreased cortisol response to stressors. However, research in this area is often inconsistent – with some studies showing hyperconnectivity, while others show hypoconnectivity between the amygdala and LPFC – and rarely combines multiple levels of cognitive and neurobiological analysis in a theoretically driven model of risk.

Aim: To investigate the association between ELS and corticolimbic functioning, we focused on resting-state functional connectivity (RSFC) of the amygdala (measured with fMRI). Additionally, we examined cortisol response to a psychosocial stressor. Finally, to probe putative relationships between ELS, cortisol reactivity, and corticolimbic dysfunction, we tested a model in which the association between ELS and amygdala RSFC was mediated by cortisol reactivity.

Methods: The study included 30 women with a history of childhood adversity (ELS group: sexual, physical, emotional, or verbal abuse, or witnessing domestic violence) and 11 non-stressed control women (control group: with no significant stress history). Presence of childhood stress was determined by the clinician-administered Traumatic Antecedent Questionnaire (TAQ). fMRI resting state data were acquired using a 3T Tim Trio scanner and a 32-channel head coil. Saliva samples were obtained before and after Maastricht Acute Stress test (MAST) and used to test for cortisol levels.

Results: Women with ELS exhibited more extreme negative RSFC between the left amygdala and LPFC compared to non-stressed control women. Women with ELS were also found to have blunted cortisol response to MAST, with the most significant difference in cortisol 20 minutes after stressor. A partial mediation was found to be trending towards significance, with cortisol reactivity partially mediating the relationship between ELS and corticolimbic dysfunction.

Conclusion: These findings suggest that ELS exposure was associated with more extreme antagonism between the amygdala and the LPFC, highlighting abnormally amplified down-regulation of limbic systems at rest and in the absence of emotional load. Additionally, history of ELS was correlated with blunted cortisol response to stressful situations in adulthood, suggesting endocrinological differences in response to stress. Finally, the results suggest a potential partial mediation in that blunted cortisol reactivity may underlie the relationship between ELS and abnormal corticolimbic connectivity. Collectively, the preliminary findings indicate that the presence of early life stress may skew neuroendocrinological development in ways that alter neurological systems.

Topic areas:
Imaging
**Program Description**

**Presenting Author:** Monika Kolodziej, Director of Psychological Services, McLean Fernside & Instructor in Psychology, Department of Psychiatry, Harvard Medical School

**Co-Authors:** Kenneth Gilman, Jennifer Keller, Kathryn McHugh, Elsie Uffelmann, Anna Munro, Emily Volpe, Rocco Iannucci

**Title:** Characteristics and Treatment Outcomes of Patients Seeking Residential Treatment for Co-Occurring Substance Use and Psychiatric Disorders

**Key words:** addiction, co-morbidity, residential, assessment, treatment

The McLean Fernside treatment program is a 30-day residential program for patients with co-occurring substance use and psychiatric disorders, many of whom also have chronic medical conditions such as diabetes, sleep apnea, and headaches. As a Signature Recovery service offered by the Alcohol and Drug Abuse Division of McLean Hospital, Fernside provides comprehensive, multidisciplinary services that include diagnostic assessment, psychopharmacology evaluation and treatment, medical and nursing exams, individual psychotherapy, evidence-based group interventions, psychoeducation, peer recovery engagement, family education and support groups, and holistic approaches in the areas of expressive therapy, fitness, and yoga. The goal of this quality improvement initiative is to examine in detail sociodemographic and diagnostic characteristics of patients seeking treatment at Fernside, and to relate those to a) self-report substance use and psychiatric symptom assessments conducted at admission, in the middle of treatment, and at discharge, and b) post-discharge phone interviews that inquire about substance use outcomes. Through this endeavor, we aim to deepen our understanding of how background and diagnostic characteristics relate to psychiatric symptoms reported during treatment and to substance use post-treatment. The findings will be used to inform our program development and quality improvement efforts, and to contribute to broader knowledge regarding residential treatment progress and outcomes of patients diagnosed with co-occurring disorders, which are often accompanied by chronic medical conditions.

**Topic areas:**

Addiction
Impact of childhood trauma on alcohol consumption and motivation to change in adolescent patients with co-occurring substance use and psychiatric disorders

There is growing evidence of a link between childhood trauma and heavy episodic drinking in adolescence. Given that this pattern of alcohol consumption emerges during adolescence, a crucial period of ongoing brain development, studies have begun to investigate correlates and predictors of adolescent alcohol use disorders. The purpose of the present study was to examine the role of childhood trauma in alcohol consumption and alcohol use disorders. Participants included two hundred and thirty-nine patients from the McLean Hospital Acute Residential Treatment (ART) and Landing programs for adolescents with co-occurring disorders. As part of a clinical quality assurance initiative, patients underwent a structured clinical interview (MINI-KID) to establish psychiatric diagnoses, and completed symptom severity scales, the Childhood Trauma Questionnaire (CTQ), and assessments of alcohol and drug use. Patients were divided into trauma (N=94) and non-trauma (N=145) groups using a previously established cut-off from a healthy adolescent cohort. Both groups met criteria for multiple other psychiatric and substance use disorders, as is typical of the patient population studied. The trauma group reported significantly greater alcohol consumption (frequency over the last year, p=.001) and incidence of binge drinking (p=.001) compared to the non-trauma group. While the trauma group also demonstrated significantly greater mood (p=.003) and anxiety (p=.013) symptoms, the effect of childhood trauma on alcohol consumption was not moderated or mediated by the presence of current mood or anxiety diagnoses. These findings suggest a strong influence of childhood trauma on alcohol consumption in adolescent patients with co-occurring psychiatric and substance abuse disorders. Given that childhood adversity represents a major risk factor for drug addiction and other psychiatric disorders persisting into adulthood, health professionals may benefit from utilizing screening tools for better assessing alcohol use patterns in adolescent patients known to have a history of childhood trauma.
Presenting Author: Joanna Korecka, Instructor in Psychiatry, HMS


Title: Dysregulation of ER stress response and calcium homeostasis in human iPSC-derived neurons carrying the LRRK2 G2019S mutation.

Key words: Parkinson's disease, human iPSC-derived neurons, LRRK2, G2019S mutation, endoplasmic reticulum

The Leucine-Rich Repeat Kinase (LRRK2) G2019S gain of function gene mutation is one of the most prevalent mutations contributing to Parkinson’s disease (PD) pathogenesis. The increased kinase activity alters mitochondrial health, axon outgrowth, intracellular trafficking and autophagy. We have previously shown that human LRRK2 G2019S iPS-derived neurons exhibit increased vulnerability to PD associated cell stressors and modify mitochondrial dynamics, which can be rescued by LRRK2 inhibitors (Cooper et al., 2012, Sci Transl Med. 20 12, 4;4(141):141ra90.). Human iPS-derived neurons carrying LRRK2 G2019S mutation and challenged with the endoplasmic reticulum (ER) calcium (Ca2+) uptake blocker thapsigargin (THP) show significantly decreased ER stress responses accompanied by neurite collapse when compared with healthy subject controls. As THP blocks ER Ca2+ influx via sarco/endoplasmic reticulum Ca2+ ATPase (SERCA) and induces ER stress, this indicates that iPS neurons carrying LRRK2 G2019S mutation exhibit an altered capacity to regulate Ca2+ homeostasis. Indeed, we further discovered that after THP-induced SERCA block human iPS-derived neurons carrying the LRRK2 G2019S mutation exhibit an increase in depolarization-induced calcium influx into the cell and modified calcium decay (interpreted as buffering capacity), when compared to healthy subject control neurons. This phenotype is diminished by treatment with antisense oligonucleotides targeting LRRK2 G2019S mutation. These data indicate that the LRRK2 G2019S mutation alters intracellular calcium homeostasis and ER stress response, phenotypes that could contribute to PD neuronal dysfunction.

Topic areas:
Geriatric
Background: Establishing the genetics underlying human pathology is crucial to fully understanding the mechanisms of disease and in identifying more effective treatments. Blood-based biomarkers are integral to research and therapy for a number of medical conditions. McLean Hospital participates in the Partners Healthcare Biobank, a multi-institution research initiative that provides researchers with material necessary to investigate the genetic factors in disease. Using the Biobank, McLean Hospital has established a research program seeking to reveal genetic factors in psychiatric conditions.

Methods: Patients with diverse psychiatric diagnoses are recruited to participate in the Biobank from inpatient units specializing in: depression and anxiety, psychotic disorders, obsessive compulsive disorders, and geriatric psychiatry. Consenting to the project grants the Biobank access to patient health information. Genetic material is collected and patients complete a battery of psychometric and lifestyle inventories. Current research intends to establish potential relationships between these self-report measures and psychometric data and genomic data.

Results: Since January 2016, McLean Hospital has enrolled 622 patients in this program. The Partners Biobank has provided samples or data to more than 90 research studies. More than 50,000 patients have consented to participate in the greater Partners Biobank. The Partners Biobank aims to consent 75,000 patients by 2018. McLean anticipates further unit expansion within the hospital.

Conclusions: These preliminary data suggest that the Partners Biobank will be an important component of a comprehensive program to discover genomic factors in psychiatric disorders.

Topic areas:
- Anxiety
- Depression
- Geriatric
- OCD
- Psychotic disorders
- Schizophrenia
Presenting Author: Ashley Lambros, Clinical Research Assistant II

Co-Authors: Kelly A. Sagar, M. Kathryn Dahlgren, Rosemary T. Smith, Korine B. Cabrera, Staci A. Gruber

Title: Snap, Crackle, and Pot: Exploring the Use of Marijuana Concentrates and Dabbing

Key words: Recreational Marijuana, Concentrates, Butane Hash Oil, Dabs

Background: As medical and recreational marijuana (MJ) use expands across the country, novel products, including MJ-based concentrates, are flourishing. Compared to conventional marijuana products, concentrates contain very high levels of Δ9-tetrahydrocannabinol (THC), the main psychoactive constituent of MJ and offer users a faster and more intense high. These potent forms of MJ are created by extracting cannabinoids from plant matter and are categorized as either solvent-based or solvent-less. Solvent-less concentrates include kief, resin, and different types of hash, while solvent-based products consist mainly of dabs, oils and tinctures. Novel modes of MJ use have also evolved. Dabbing is the process of inhaling a vaporized concentrate, colloquially known as a “dab”, with a modified water pipe and butane torch. Butane Hash Oil (BHO) is the end product of a butane extraction and a popular choice for dabbing. It is also the basis of numerous other concentrates including wax, budder, shatter, oil and more, all of which vary in potency and consistency. While these products have become increasingly popular, research is limited regarding the composition and overall impact of concentrate use. A recent analysis of 48 concentrates detected residual solvents in 83.3% of samples; these products also had an average THC level of 60.3% with some approaching 75%. This stands in stark contrast to the national average THC potency in flower products, which is approximately 12%. Many marijuana users report a preference for concentrates, as fewer hits are required to achieve a stronger and longer lasting high. However, while some users suggest concentrates help with relaxation and sleep, others report significant negative side effects, including passing out, feeling a loss of control over one’s body, or vomiting. As little is known about concentrate use, including motivation for use, overall effect, and impact on function, we developed a comprehensive internet-based survey study.

Methods: Survey content includes questions addressing demographics, substance use history, concentrate use, and two questionnaires: the Marijuana Motives Measure (MMM) and the Severity of Dependence Scale (SDS). Hosted by Survey Monkey, a link is advertised to targeted groups via Facebook and promoted to those with a history of liking marijuana or concentrate related pages (e.g., High Times Magazine or Cannabis Culture). A two-day testing period provided the ability to assess general response to the marketing strategy and functionality of the survey prior to initiating the full 30 day study. Data is collected daily, routinely checked for quality assurance and exported to a back up hard drive for storage.

Results: Pilot survey data collected from our ongoing studies of recreational MJ revealed that 67% of queried participants reported a history of concentrate use. Overall, concentrates were perceived as a less safe form of MJ consumption compared to flower and edible products. This preliminary study will present survey data and discuss the importance of obtaining clear definitions, descriptions and patterns of use in order to acquire valid data. Data will be used to characterize concentrate use in MJ users and help elucidate potential differences those who do and do not use concentrates.

Topic areas:
Addiction
Presenting Author: Erjing Cui, Academic Credit Student


Title: Distress Tolerance, OCD and Trauma

Key words: Distress Tolerance, OCD, Trauma

Introduction: There has been limited examination of the relationship between a trauma history and OCD diagnosis (Shavitt, 2009), especially within intensive/residential treatment (IRT) samples. On one hand, it is becoming increasingly common that individuals who had traumatic experiences suffered from low distress and emotion tolerances (Fetzner, 2014; Marshall, 2010). On the other hands, the severity of individuals’ distress tolerance (DT) is also known to be linked with obsessions (Cougle, 2011). While Hawthorne et al. (2013) found a significant relationship between OCD symptom severity and endorsement of trauma symptoms in those with primary OCD, no studies have examined the impact of trauma symptoms on distress tolerance ability in individuals with OCD. Thus, this research aims to evaluate differences in distress tolerance ability between individuals who have OCD with and without significant traumatic symptoms.

Methods: In this current study, 271 patients from an OCD residential treatment program. They were administered the PTSD Checklist (PCL-6), Yale-Brown Obsessive Compulsive Scale (Y-BOCS), and Distress Tolerance Scale (DTS) at admission and discharge. The suggested cut-off of ≥14 was used to split the sample into high vs. low PTSD symptom groups. Pearson correlations and one-way ANOVA analyses were conducted.

Results: In line with previous research, scores on the PCL-6 and Y-BOCS were positively correlated. At the admission time point, DTS total score and all DTS subscales were negatively associated with PCL-6 scores at admission. The pattern replicated at the discharge time point. When looking across treatment, DTS total score at admission is correlated with PCL-6 (r (148) = -.345, p < 0.001). However, at discharge, only the DTS Tolerance (r (124) = -.181, p < 0.05) and Appraisal (r (124) = -.212, p < 0.05) subscales were significantly associated with PCL-6 discharge scores. Results from the one-way ANOVA demonstrated that DTS scores at admission differed significantly between the high and low PTSD symptom groups (F (1, 146) = 8.285, p ≤ 0.05). The two groups did not differ significantly on DTS scores at discharge or change in DTS scores from admission to discharge.

Discussion: The result suggests that the endorsement of PTSD/trauma symptom was associated with lower ability to tolerate distress for individuals with severe/complex OCD both before and after treatment. This pattern was found to be stable across all four distress tolerance subscales. Further, those with elevated severity of PTSD symptoms had significantly lower ability to tolerate distress at admission. Interestingly, there were no significant differences between these two groups following treatment and severity of trauma symptoms at admission were not significantly associated with the ability to tolerate distress at discharge. Further, there were no significant differences in the degree to which individuals’ DTS scores changed across treatment between the high vs. low trauma group. This may suggest the presence of trauma symptoms is not an attenuating factor for increasing DT in OCD through IRT. Future longitudinal research should evaluate if the presence of trauma symptoms may impact an individuals’ process/trajectory of change in DT and overall OCD symptom reduction.

Topic areas:
OCD
PTSD
McLean Research Day 2017

Original Research - Pre-Clinical

Poster # 51
Time: 1:00-1:50pm

Presenting Author: Victoria Lawlor, Student Visitor

Co-Authors: Elyssa Barrick, B.A., B.S., Daniel G. Dillon, Ph.D.

Title: Piloting a Behavioral Assessment of Dopamine Capacity

Key words: dopamine, memory, erp, p300

Background: Dopamine (DA) is implicated in numerous psychiatric disorders, but it is difficult to measure in humans. Precise assessments can be made with positron emission tomography (PET), but PET is expensive and involves radiation. We sought to determine whether a battery of three non-invasive assessments, each with an established relationship to DA levels as measured by PET or in non-human primates, could be combined to provide an inexpensive estimate of DA.

Methods: Twenty healthy participants performed three tasks in an electroencephalography (EEG) recording booth. First, they completed a listening span task, as PET studies reveal a positive correlation between listening span and striatal DA levels. In this task, participants listened to increasingly long sets of sentences, trying to remember the final word in each sentence and answering questions about their content. Listening span corresponded to the longest set size with at least two correct answers. Second, we used electroculography to measure spontaneous blink rate, as work in non-human primates and patients with schizophrenia strongly links blink rate to global DA levels. Third, we probed working memory updating while recording EEG data. In our updating task, participants viewed sets of three letters that changed repeatedly. On “confirm” trials, participants simply had to indicate which letter was currently visible. On “retrieve” trials, they had to indicate which letter was previously presented in a given location. On “update” trials, they had to retrieve the previously presented letter in a given location and then update that representation by advancing along the alphabet by two letters. Given an extensive literature linking working memory updating with DA-based corticostriatal signals, we took accuracy and response time (RT) on update (relative to retrieve) trials as an indirect index of DA levels. We also expected to observe the strongest P300 ERP response on update trials.

Results: Consistent with prior literature, the modal span was 4.0. The mean number of blinks per minute was 19.3, similar to previous results, but the range was wide (0.5-70.5). Accuracy was highest and RT longest on update relative to retrieve and confirm trials, respectively (one-way ANOVAs on Condition, Fs > 7.73, ps < 0.003). However, performance was near ceiling (overall accuracy: 96.94±0.04), limiting our ability to detect individual differences. Moreover, the updating task elicited numerous blinks, making it difficult to extract reliable ERPs (Condition effect on P300 amplitude, F = 1.71, n.s.). We found no significant correlations between span, blink rate, and either RT or P300 amplitude on transform trials, |rs| < 0.40, ps > 0.12.

Conclusions: A non-invasive approach to DA assessment holds considerable promise, but the tasks used here appear suboptimal. In particular, the updating task elicited numerous eye movements, contaminating the EEG data, and blink rates were excessively variable, possibly due to the use of a fixation cross and the EEG cap. This pilot test constituted a useful first step, but a more stable blink metric and a cleaner measure of working memory updating are needed.

Topic areas:
Depression
**Presenting Author:** Rachel Doyle, Research Assistant, B.S.

**Co-Authors:** Jack Bergman

**Title:** Exponential Model of Demand Applied to Simple and Second Order Schedules of Reinforcement

**Key words:** Behavioral economics, Methamphetamine, Self-administration, Second order schedule, Exponential model of demand

**Rationale/Objectives:** The exponential model of demand has been used to compare the reinforcing strength of psychoactive drugs including psychostimulants like methamphetamine under simple fixed-ratio (FR) schedules of intravenous (i.v.) self-administration. The current study aims to compare the reinforcing strength of methamphetamine that is self-administered under simple and second-order FR schedules of reinforcement.

**Methods:** Adult male squirrel monkeys self-administered i.v. methamphetamine (0.001-0.1 mg/kg/inj) under an FR10 schedule. After dose response curves were generated, the reinforcing strength of a single dose of methamphetamine (0.01 mg/kg/inj or 0.032 mg/kg/inj) was determined under a simple FR schedule. The FR value initially was set at 10 and, after two sessions with stable intake (within 10%) was periodically increased by quarter-log units (i.e. FR10 to FR18 to FR30) until an FR value was reached at which zero injections were self-administered. Subsequently, subjects were trained to self-administer methamphetamine under a second order FR10(FR5:S) schedule. Under these conditions, every fifth response produced a light flash (conditioned reinforcer) and every 10th conditioned reinforcer was accompanied by an injection of 0.01 mg/kg methamphetamine. Once responding was reliably maintained under these schedule conditions, the reinforcing strength of methamphetamine was determined again by increasing the number of conditioned reinforcers per injection using the same stepwise procedure described above; i.e., the FR:S was periodically increased by a quarter-log unit (i.e. FR10:S to FR18:S to FR30:S).

**Results/Conclusions:** Dose response curves for methamphetamine self-administration under the FR10 schedule of reinforcement described an inverted U shape, with peak intake maintained by 0.01 mg/kg/inj. The number of reinforcers per session decreased as FR size increased under both simple and second-order schedule conditions, whereas the number of responses increased up to a peak value and then decreased. These patterns of responding across sessions with increasing FR costs mirror those seen in other studies and reliably fit exponential demand curves. Behavioral responses can be modulated by changes in the FR size under both simple and second order schedules of reinforcement.

**Topic areas:**
- Addiction
- Pharmacology
Assessing Traits as Endophenotypes in Clinically Unaffected Relatives

Key words: endophenotypes, antisaccades, schizophrenia, genetics

A number of traits associated with schizophrenia aggregate in relatives of schizophrenia patients at rates much higher than that of the clinical disorder. These traits, considered candidate endophenotypes, may be alternative, more penetrant manifestations of schizophrenia risk genes than schizophrenia itself. In order for an endophenotype to potentially increase the power of genetic analyses, not only should the distribution of the quantitative trait be heterogeneous in unaffected relatives, but the trait must also be found in unaffected relatives at a higher rate than in the general population. We have previously demonstrated that thought disorder with schizophrenic features meets these criteria. Here, we apply this approach to another provisionally identified endophenotype: antisaccade error rate. Performance on the antisaccade task is a widely studied candidate endophenotypes. We show that, while there is significant heterogeneity in performance on this task in unaffected relatives, we do not find evidence of a higher rate of antisaccade errors in unaffected relatives compared to normal controls. This finding provides further support for the utility of this approach for evaluating the suitability of a given trait as a candidate endophenotype and suggests that antisaccade error rate may not be useful as a schizophrenia endophenotype.
Presenting Author: Kelly Dumais, Postdoctoral Research Fellow

Co-Authors: Kelly M. Dumais, Amy C. Janes

Title: Sex differences in default mode network suppression during exposure to salient stimuli

Key words: Default mode network, sex differences, reward, salience

There are robust sex biases in the prevalence of neuropsychiatric disorders. Such sex differences can be generalized to women having higher rates of internalizing disorders, such as depression and anxiety, and men having higher rates of externalizing disorders, such as anti-social personality disorder. Sex differences in neural processes that control self-referential or attentional processes may predispose each sex to these categories of mental illness. One neurobiological target is the default mode network (DMN), which is a network of brain regions thought to underlie self-referential processing. During task performance, the DMN is typically suppressed to allow for external instead of internal focus. Therefore, we investigated whether DMN suppression is different in men and women during exposure to salient stimuli, such as reward and loss. To determine if sex differences in DMN activity would be specific to processing salient stimuli or to cognitive processes in general, we also investigated DMN suppression during a working memory task. We used a large sample of healthy control individuals from the Human Connectome Database (men=117, women=223) that had underwent functional magnetic resonant imaging during exposure to rewards and losses (gambling game) and during a working memory n-back task. We extracted beta weights from the DMN using a region of interest from Smith et al., 2009. In comparison to men, women show increased DMN suppression during the reward > baseline (p=0.034) and loss > baseline (p=0.023) contrasts. These sex differences were specific to salient stimuli, as there was no sex difference in DMN activity during the working memory task. As DMN suppression is associated with greater attention to external stimuli, our findings could reflect greater attention to reward/loss stimuli in women. Greater suppression of the DMN in women could also result in the need for greater suppression of self-referential thoughts during exposure to salient stimuli. Sex-specific neural processing of valenced stimuli may give insight into the neural mechanisms regulating sex biases in internalizing and externalizing psychiatric disorders.

Topic areas:
Gender Differences
First responders and active duty military service members are exposed to potentially traumatic events repeatedly while on the job. Given the high frequency and severity of these traumatic exposures, it is not surprising that first responders are at an increased risk for developing posttraumatic stress disorder (PTSD). Lifetime prevalence for PTSD in first responders has been estimated to be within 10% among an international sample (Berger et al., 2010) and 32% among a sample within the United States (Fullerton et al., 2004). In contrast, approximately 7% to 12% of adults in the U.S. will develop PTSD at some point in their lifetime (Kessler, 2010; Kolkow et al., 2007). Prior trauma, including childhood abuse and neglect, has been found to be a risk factor for the development of PTSD among first responders and veterans (Bremner et al., 1993, Beslau et al., 1999; Dougall et al., 2000, Follette et al., 1996). As such, providing a thorough assessment of PTSD, including a comprehensive understanding of trauma experiences, is a critical first step in providing care to emergency responders. Our objective is to highlight the importance of thorough assessment of PTSD for emergency responders, including symptoms of dissociation, in order to make appropriate treatment recommendations. Over the past two years, clinician administered assessment data have been collected from 103 men (N=97) and women (N=6) who qualify as LEADER patients. Trauma consultations were completed using the Clinician Administered PTSD Scale (CAPS-5) (Weathers et al., 2013). Of the LEADER patients who received trauma consultation, 75% met criteria for PTSD according to the CAPS-5. Approximately 48% of those individuals endorsed both work-related traumas and childhood abuse and neglect, including childhood sexual abuse (14%). Of note, 35% of the individuals who endorsed childhood trauma also met criteria for the dissociative subtype of PTSD. These findings emphasize the importance of comprehensive trauma assessment for first responders, including assessment of dissociative symptoms, and the important treatment implications that assessment data will yield.

**Topic areas:**
- Dissociative Disorders
- PTSD
Presenting Author: Erika Esposito, Clinical Research Assistant II

Co-Authors: Jeremy G. Stewart, PhD, Nina M. Lutz, Randy P. Auerbach, PhD, ABPP

Title: Reward Deficits in Depressed Adolescent Self-Injurers

Key words: Depression, Adolescents, Non-suicidal Self-Injury, Reward

Background: Prior research has shown that adolescent depression (Auerbach et al., 2014) and suicidality (Auerbach et al., 2015) are characterized by reward-related deficits. However, few studies have examined reward processing in the context of non-suicidal self-injury (NSSI). To address this unmet gap, the present study tests whether depressed adolescents reporting NSSI exhibit deficits in goal-directed behavior in the presence of uncertainty.

Methods: Participants include 95 depressed adolescents (57 female) aged 13-19 years (M = 15.84, SD = 1.417): (a) depressed acute self-injurers (i.e., at least 5 NSSI behaviors in the past month; n = 38) and (b) depressed adolescents without any lifetime self-injury (n = 57). All participants were administered clinical interviews assessing Axis I diagnoses, NSSI, and suicide history. Additionally, participants completed the Effort-Cost Computation Task (ECCT), a computerized behavioral task that probes differences in reward pursuit when outcomes are certain (i.e., 100% probability of reward receipt) versus uncertain (i.e., 50% probability of reward receipt) (Gold et al., 2013). We hypothesized that, relative to non-injurers, self-injurers would more often choose high-value options when outcomes were uncertain. However, no between-group differences would emerge during certain trials.

Results: A repeated measures ANOVA revealed a significant Group (NSSI, No NSSI) x Value ($3, $4, $5, $6, $7) interaction when the receipt of reward was uncertain, F(2.28, 212.31) = 3.31, p = .03, η2p= .03. Compared to the non-injurers, self-injurers selected the high-value (versus low-value) option more frequently when the outcome was uncertain. Consistent with hypotheses, no significant differences emerged on certain trials (p = .85).

Conclusion: Presently, the etiology of NSSI behaviors is not well understood. Our findings highlight reward-related deficits that may underlie NSSI behavior, and consequently, may provide important targets for novel treatments.

Topic areas:
Child/Adolescent
Depression
Pituitary adenylate cyclase-activating polypeptide (PACAP) and its cognate receptor (PAC1) have been associated with numerous psychiatric illnesses triggered by exposure to stress, including post-traumatic stress disorder and major depressive disorder. In rats, exposure to repeated variate stress increases PACAP and PAC1 expression in brain regions implicated in anxiety- and depression-like behaviors, and stress responsiveness. PACAP signaling is both necessary and sufficient to produce many of the behavioral and molecular consequences of stress. As such, it is conceivable that changes in PACAP signaling contribute importantly to the symptoms of mood and anxiety disorders as well as frequently co-morbid conditions, such as alcohol use disorder (AUD). In the current studies, we treated male C57BL/6J mice with intracerebroventricular (ICV) PACAP (0.0μg/μl, 0.02μg/μl, 0.1μg/μl, 0.25μg/μl, and 0.5μg/μl) and examined social interaction behavior and anxiety-like behavior on the elevated plus-maze. Due to the ability of PACAP to influence motivated behavior (e.g., intracranial self-stimulation), we also characterized the interaction between alcohol consumption and PACAP signaling in mice utilizing two voluntary alcohol consumption paradigms that result in steady-state or escalated alcohol consumption, respectively. Finally, considering that sleep architecture is altered in many psychiatric illnesses, we monitored EEG/EMG activity following ICV PACAP infusion utilizing implantable wireless telemetry devices. Specifically, we examined the impact of PACAP infusion on the various stages of sleep (slow-wave sleep and paradoxical sleep) as well as activity and temperature. Implications for the interactions among these systems and the mechanism for these PACAP induced effects will be discussed.

**Topic areas:**
- Addiction
- Anxiety
- Depression
- PTSD
Title: Associations between Childhood Maltreatment, Symptom Severity, and Response to Partial Hospitalization in Adulthood: Preliminary Findings

Key words: Childhood, Trauma, Anxiety, Flexibility, Treatment

Background: Childhood maltreatment (CM) is an encompassing term referring to a variety of potentially adverse/traumatic experiences including emotional, physical, or sexual abuse, and emotional or physical neglect (Bernstein et al., 2003). Past research has examined how these experiences relate to adult psychological conditions. Adult depression has been associated with childhood emotional abuse (Chapman et al., 2004; Mandelli, Petrelli, & Serretti 2015), emotional neglect (Infurna et al., 2016), and physical abuse (Comijs et al., 2013). CM has been associated with anxiety disorders (Cougle et al., 2008) and poorer cognitive flexibility (Spann et al., 2012). CM has also been negatively associated with disease course in a depressed adult sample (Miniati et al., 2010). Past research has not examined whether CM is meaningfully related to symptom severity and response to treatment among a transdiagnostic population during partial hospitalization in adulthood. Examining CM at this level of care is important given that patients in partial hospitals are at high risk for hospitalization and relapse (Beard et al., 2016).

Methods: Ninety-two patients (51.1% female, M age = 33.77 years) from the Behavioral Health Partial Hospital Program (BHP) at McLean Hospital completed the Patient Health Questionnaire (PHQ-9; Kroenke, Spitzer, & Williams, 2001) Generalized Anxiety Disorder Scale (GAD-7; Spitzer et al., 2006), the Behavior and Symptom Identification Scale (BASIS-24; Cameron et al., 2007), the Cognitive Flexibility Inventory (CFI; Dennis & Vander Wal, 2010), upon admission (T1) and discharge (T2) from the BHP. Additionally, 82 participants completed the Childhood Trauma Questionnaire (CTQ; Bernstein et al., 2003) on their third day of treatment; the other 10 opted out of completing this measure. Regression analyses assessed whether types of CM (emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect) were associated with symptom severity at admission (controlling for age, sex, and ethnicity), as well as changes in symptoms during treatment (controlling for age, sex, ethnicity, and baseline levels of symptoms). Follow-up analyses of variance examined differences between both CTQ groups.

Results: At admission, emotional abuse was associated with anxiety (β=.28, p=.04); physical abuse was associated with emotional lability (β =.29, p =.04); sexual abuse was associated with depression/functioning (β =.23, p =.05). In addition, emotional (β =-.39, p =.01) and physical (β =.34, p =.03) neglect were associated with changes in cognitive flexibility during treatment. Compared with those who completed the CTQ, those who opted out had higher levels of anxiety (p =.03) at baseline. They also had higher levels of depression at baseline; this difference only approached significance (p =.07).

Discussion: Results of the present study confirmed that CM is associated with symptom severity and disease course in a transdiagnostic sample of individuals experiencing acute psychopathology, though findings differed according to the type of maltreatment and outcomes. The diagnostic characteristics of those who opted out of taking the CTQ indicate that the results may be partly influenced by self-selection. These results shed light on the potential relationship of CM to symptom severity and to response to treatment, and underscore the importance of assessing CM to inform treatment.

Topic areas: Anxiety, Child/Adolescent, Depression
Presenting Author: Yan Li, Instructor of Psychiatry
Co-Authors: Raül Andero, Kerry J. Ressler, and Vadim Y. Bolshakov
Title: PACAP modulates amygdala-BNST interactions in control of anxiety
Key words: PACAP, BNST, amygdala, anxiety, synapse

Previous studies provide experimental evidence for the role of pituitary adenylate cyclase-activating polypeptide (PACAP)-mediated signaling in regulation of anxiety in both experimental animals and human subjects. It has been demonstrated that PACAP may regulate anxiety-related behavioral processes through its actions in two interacting brain regions, the amygdala and the bed nucleus of the stria terminalis (BNST). However, synaptic and network mechanisms of PACAP-mediated effects in the brain are poorly understood. In this study, we addressed specific questions about the nature of PACAP-induced synaptic and network-level modifications in BLA-BNST circuits, contributing to control of anxiety states. We expressed channelrhodopsin-2 (ChR2) under control of the neuron-specific promoter CaMKIIα in BLA neurons and photostimulated the corresponding fibers synapsing on neurons in two BNST subdivisions, ovBNST and adBNST, known to regulate anxiety in opposite directions — activation of ovBNST was shown to induce anxiety, whereas activation of adBNST is anxiolytic. Consistent with our finding that PACAP-containing fibers were observed in ovBNST only, we found that PACAP potentiated excitatory synaptic responses at inputs to ovBNST but not at inputs to adBNST, selectively increasing the synaptically-driven spike output of ovBNST neurons in response to activation of projections from the BLA. The enhanced firing of ovBNST neurons resulted in inhibition of adBNST, since ovBNST neurons, projecting to adBNST, are GABAergic. By using a combination of retrograde tracing, immunohistochemistry and in vivo optogenetics, we demonstrated that neurons in the parabrachial nucleus (PBN) in the brainstem are the source of PACAPergic innervations of the ovBNST. Thus, we showed that neuropeptide PACAP contributes to regulation of anxiety states by differentially affecting synaptic efficacy at BLA projections to different BNST subdivisions, and, therefore, modifying the signal flow in BLA-ovBNST-adBNST circuits in such a way that adBNST is inhibited. This would explain the ability of PACAP in BNST to trigger anxiety, as direct optogenetic inhibition of adBNST was shown to be anxiogenic.

Topic areas:
Anxiety
Presenting Author: Carl Lin, PI and assist prof

Co-Authors: Z. Lin, Y. Zhou, G. Sørensen, N. Xiong, X. Chen, N. Li, Y. Zhao, J. Yu, S. Li, H. Qing, T. Wang, E. Onaivi, B. Caine

Title: EIF3F Genetics of Substance Abuse

Key words: addiction, stressor, dopamine, genetics

In a functional genetic study of the human dopamine transporter gene (hDAT or SLC6A3), we have cloned the eukaryotic translation initiation factor 3 subunit F (EIF3F) as the first allele-selective and stressor-sensitive transcription factor (TF) for hDAT. EIF3F binds preferably to allele B of an intronic dinucleotide polymorphism (DNPi A/B) of hDAT, and this binding activity is enhanced by an acute stressor. Secondary analyses of dbGaP GWAS datasets show that single nucleotide polymorphisms (SNPs) next to DNPi interact significantly with the EIF3F gene in Caucasian substance abuse: meta-analysis P-values are down to 3.9 x 10^-15 with odds ratios between 0.17 and 6.5 by logistic regression. In a mouse study, one copy deletion of the EIF3F gene blunts cocaine self-administration selectively. Based on these genetic and other neuropharmacologic findings, a current dopaminergic model integrating genetics with stress effects is presented.

Topic areas:
Addiction
Excessive use of alcohol accounts for much of the public health burden related to alcohol use disorders, including fetal alcohol syndrome, fatal motor crashes, accidents, and homicides. For most, problematic drinking will not be brought to the attention of Primary Care Professionals and so many go untreated. This is precisely where an OTC herbal product could have the greatest impact. We have patented an extract of kudzu (Pueraria lobata) and McLean Hospital licensed its use to Natural Pharmacia International under the name Alkontrol-herbal. Over the past 20 years, our team has extensively studied this kudzu extract and demonstrated its safety and efficacy in healthy control subjects as well as in heavy binge drinkers. Most recently, we completed a modest outpatient safety and efficacy study in heavy drinkers (n=20) and demonstrated that a single dose of kudzu reduces alcohol consumption in a binge drinking paradigm. In a placebo-controlled, double-blind, between-subjects design experiment (n=10/group), a single dose of kudzu (520 mg active isoflavone) or placebo was administered 2.5 hours before the onset of a 90-minute afternoon drinking session, during which participants had the opportunity to drink up to 6 beers. The placebo group consumed 2.7 ± 0.78 beers during the baseline session and 3.4 ± 1.1 beers after treatment with placebo, whereas the group treated with kudzu significantly reduced their intake from 3.0 ± 1.7 at baseline to 1.9 ± 1.3 beers after treatment. Additionally, kudzu-treated participants drank at a much slower rate. There are no uniformly effective pharmacotherapies for treating alcohol use disorders and, while there are some promising medications, many gaps remain. The use of complementary and alternative therapies has rapidly increased by individuals across a wide variety of demographic variables. Thus, a product that reduces alcohol consumption for problematic drinkers would be well received by the public. Individuals will have access to a non-prescription and adherence to a medication such as Alkontrol-herbal may be boosted because of the low incidence of side effects and rapidly achieved results. To date, we have studied non-treatment-seeking moderate or binge-drinkers who are typically younger and have not been drinking for exceptionally long periods of time. What remains is to explore how kudzu extract might fit into a more comprehensive treatment program aimed at treatment-seeking alcohol-dependent persons. However, nutraceutical and herbal products are notoriously prone to variable potency, poor quality control, and are often mislabeled. Our project, funded by a Small Business Technology Transfer program, will fill this important vacuum with its two-prong approach by developing and producing (under GMP) a high quality, standardized kudzu extract for commercialization, followed by a clinical trial to assess the efficacy of Alkontrol-herbal in reducing alcohol use in treatment-seeking alcohol-dependent individuals. This is a two-phase study: Phase I will be focused on scaling up production of Alkontrol-herbal, while the clinical trial will be the major milestone of Phase II. Collectively, successful completion will pave the way for the commercialization of Alkontrol-herbal which will fill a gap as a viable adjunct to existing alcohol treatment strategies.

**Topic areas:**
Addiction
Pharmacology
Objective: BPD is a serious psychiatric disorder for which significant stigma persists amongst lay people and clinicians alike. Recent evidence suggests that brief training in Good Psychiatric Management (GPM) decreases stigma amongst clinicians and improves feelings of competence related to treating BPD (Keuroghlian et al., 2016). We sought to extend and replicate these findings.

Method: 94 clinicians (psychiatrists, social workers, psychologists, nurses) completed self-report questionnaires before and after a 1-day GPM training. Questions were related to clinicians’ attitudes about people with BPD, their willingness to treat patients with BPD, and their beliefs about BPD.

Results: After completing GPM training, participants endorsed positive attitude change about BPD, with changes in the expected direction on nearly all items. In general, treaters reported an improvement in understanding of BPD and more willingness to treat patients with BPD. More specifically, treaters reported an increase in confidence in their ability to diagnose BPD accurately after GPM training ($t(91) = -4.90$, $p < 0.001$). Treaters indicated feeling more professionally competent to care for BPD patients after training ($t(92) = -6.38$, $p < 0.001$). Ultimately, there was a significant improvement in treaters’ willingness to provide treatment to BPD patients after GPM training ($t(92) = -5.11$, $p < 0.001$). Additionally, there was a marginally significant decrease in treater desire to receive more training in the management and treatment of BPD after training ($t(93) = -1.29$, $p = 0.06$). In addition, treaters’ responses showed no significant difference in opinion about the effectiveness psychotherapy for treating BPD after completing GPM training ($t(93) = -1.29$, $p = 0.20$). A one-way ANOVA shows no significant effect of medical discipline (with all disciplines included) on average change score (across all items, $F(7, 93) = 1.16$, $p = 0.33$). However, greater experience was related to less change in willingness to treat BPD ($t(80) = -0.27$, $p = 0.02$) and feelings of competency in treating BPD ($t(80) = -0.25$, $p = 0.02$), suggesting that experience may crystallize willingness and competence such that they are less amenable to new training.

Conclusions: In replication of findings by Keuroghlian et al. (2016), we found that brief GPM training has a positive influence on clinicians’ BPD-related attitudes. Clinicians indicated stronger confidence in their ability to diagnose BPD, as well as greater compassion for BPD patients following training. The finding that more years of experience was related to decreased changes in attitude towards competency in BPD treatment and feelings about BPD patients may suggest less amenability due to well-formed views of psychiatric disorders, or could be due to ceiling effects. Overall, our findings provide evidence for the widespread efficacy of GPM training on improving treaters’ attitudes about BPD. Follow-up data collection is underway to examine whether attitude change persists 6 months after training. Additionally, the influence of specific clinician discipline will be examined.

Topic areas:
Borderline Personality Disorder
Presenting Author: Antonia Seligowski, Psychology Intern/Clinical Fellow

Co-Authors: Erin M. Bondy, Holly K. Orcutt, Kerry J. Ressler, Randy P. Auerbach

Title: The Relationship between the Late Positive Potential and Fear-Potentiated Startle

Key words: startle, PTSS, ERPs

Background: Posttraumatic stress symptoms (PTSS) are associated with significant impairment across multiple domains of functioning. Within the Negative Valence System, PTSS is represented by the acute threat construct. One way in which to measure acute threat is with fear-potentiated startle (FPS) paradigms. The FPS paradigm is based on classical conditioning principles, whereby an aversive unconditioned stimulus (US) is repeatedly paired with a conditioned stimulus (CS+; evokes the FPS response), and a conditioned response (CR) is observed (the eyeblink startle response). FPS is defined as the relative increase in startle response to an auditory stimulus when it is presented during a CS that predicts the US. Individuals with PTSS exhibit increased emotional arousal and poor fear discrimination, as evidenced by higher FPS to a CS+ and a lowered ability to discriminate between danger (CS+) and safety (CS-; presented without US) cues, respectively. A neurophysiological marker of emotional arousal is the late positive potential (LPP), an event-related brain potential that is potentiated among individuals with PTSS. Presently, it remains unclear whether FPS and LPP are related to one another, and further, if the LPP may be used as a neurophysiological marker of fear discrimination. Aim: As a first step in this research, the current study examined relations between LPP and FPS variables and compared LPP area for a CS+ and CS-.

Method: Participants included 54 undergraduate students (Mage = 20.26, SD = 2.61) enrolled at a large Midwestern university. The FPS response was measured via electromyography of the right orbicularis oculi muscle. The startle probe was a 108-decimal 40-millisecond burst of noise with near instantaneous rise. The US was a 250-millisecond airblast directed at the larynx. Conditioned stimuli consisted of different colored shapes presented on a computer monitor. Electroencephalogram (EEG) was used to obtain the LPP. EEG was recorded during the FPS session from 9 International 10–20 system sites with a tin-electrode cap. The LPP was computed as the average area at the Cz site 600-1200 ms poststimulus for each stimulus type.

Results: LPP area was more pronounced for the CS+ compared to the CS-, t(50) = 2.998, p = .004, and the observed effect size was small-to-moderate (d = .420). Additionally, the difference score for LPP to the CS+ versus CS- (higher score indicative of greater discrimination) was significantly related to FPS scores for the CS- (r = -.31, p = .034).

Conclusions: Results suggest that differences in LPP area may be indicative of fear discrimination, and that enhanced discrimination between danger and safety stimuli was related to better fear inhibition (indicated by lower FPS to the CS-). Overall, these findings indicate that the LPP may have potential as a neurophysiological marker of fear discrimination. Future research with clinical samples is needed to determine if LPP differences are indicative of symptom severity.

Topic areas: PTSD
Heavy marijuana use (high THC content and daily or near-daily use) by adolescents and young adults is associated with a higher prevalence of adverse effects, including schizophrenia. Conceivably, marijuana-induced changes in dopamine signaling contributes to its adverse effects as heavy marijuana users display reduced dopamine release, self-report blunted reward (less “high”) and heightened negative responses (anxiety, restlessness) following a dopaminergic challenge. This pilot study interrogates a novel hypothesis, that THC in marijuana dysregulates expression of the dcc receptor gene in prefrontal cortex, which interferes with normal dopamine signaling and conceivably contributing to the psychotomimetic effects of marijuana. The hypothesis is based on reports that aberrant prefrontal cortical dopamine innervation is implicated in psychosis, that DCC is a primary guidance molecule for dopamine innervation of the prefrontal cortex during adolescent brain development and decreased DCC expression in mice (dcc+/-) increases dopamine innervation and improves specific behaviors. Intriguingly, the dcc gene is implicated in schizophrenia. We measured the effects of THC on mRNA expression of dcc, dopamine receptors and other axonal guidance molecules in prefrontal cortex and other brain regions in adolescent rats treated intermittently with THC for three weeks (or vehicle), and then withdrawn for two weeks. Similarly, we measured the effects of THC given daily to adult rhesus monkeys for 24 days (n=3). Another group of monkeys were treated with THC combined with similar doses of cannabidiol, a putative anti-psychotic cannabinoid. Repeated THC increased expression of genes encoding dcc, D1, D5 dopamine receptors, and the dopamine transporter in rat prefrontal cortex after a drug-free period. Parallel findings were observed in nonhuman primates treated daily with THC for 24 days. If combined with THC, cannabidiol (CBD) blocked THC-induced up-regulation of dcc and D1 dopamine receptor genes in prefrontal cortex of nonhuman primates. Other brain regions showed similar, but not identical regulatory changes. These exciting pilot data suggest that up-regulation of dcc conceivably contributes to THC-induced neuroadaptive changes in dopamine signaling in prefrontal cortex. CBD blockade of THC effects on dcc may be relevant to the therapeutic potential of cannabidiol for schizophrenia. The findings also highlight potential mechanisms by which varying THC:CBD ratios may affect the molecular and psychoactive properties of marijuana. In view of the robust and parallel findings in two species, investigation of the role of dysregulated dcc in the psychoactive and psychotomimetic effects of marijuana is warranted.
Comorbid Depression and Alcohol Use Disorders in Dually Diagnosed Adolescents: Treatment Outcomes Related to Improvements in Self-Efficacy

Background: Self-efficacy, an integral component of emotional well-being, has been suggested to be a possible causal mechanism explaining symptom change in the integrated treatment of depression and substance use among adolescents. Accordingly, the objective of this study was to examine self-efficacy relative to symptom change in adolescents enrolled in a residential program for treatment of dual-diagnoses.

Methods: The current study examined adolescent 376 patients (ages 13-19, 17.0 ± 1.2 yrs., 49% female), stratified by psychiatric diagnoses of major depressive disorder (MDD) and/or alcohol use disorder (AUD), established using the MINI-Kid Structured Clinical Interview. Resulting subgroups included: MDD/AUD (n=125), MDD (n=116), AUD (n=70), and a psychiatric comparison group with diagnoses other than MDD or AUD (PCG, n=65). Within 48 hours of intake and within 24 hours of discharge, participants completed a battery of clinical assessments and self-report measures that included the Center for Epidemiologic Studies Depression Scale (CESD), the Difficulties in Emotion Regulation Scale (DERS), the Multidimensional Anxiety Scale for Children (MASC), and the General Self-Efficacy (GSE) Scale.

Results: MDD/AUD and MDD groups had similarly high levels of depressive symptoms at baseline (p<.001) compared to non-MDD groups, as well as a greater reduction of depressive symptoms over the course of treatment (39.1% compared to 26.7%). For emotion regulation, having a diagnosis of MDD or AUD was associated with higher baseline levels of difficulties (p<.001), but a greater magnitude of improved emotional regulation, 9.6% compared to 5.1%, compared to groups without MDD or AUD. There were no subgroup differences for anxiety symptoms at baseline, but a significant reduction of anxiety symptoms (7.6%) was observed regardless of group over the course of treatment. An interaction between MDD and AUD was observed only for GSE, with the MDD/AUD group demonstrating the lowest GSE at baseline, and the greatest improvement in GSE at discharge (10.6%) compared to all other groups. Notably, change in GSE over treatment was a significantly robust predictor of reduced depressive symptoms across all groups (r=-.330, p<.001), but did not predict improved emotional regulation in the PCG or reduced anxiety in any group.

Conclusion: The results of this study indicate unique patterns of relationships between clinical symptom improvement and self-efficacy over the course of residential treatment in adolescents with comorbid depressive and alcohol use disorders. Dysfunctional self-efficacy could be an underlying construct of depression and AUD that is responsive to treatment, and suggests that adolescents with MDD and AUD merit particular clinical attention because of markedly low self-efficacy. To this end, adolescents with these comorbid conditions may benefit from interventions targeted at improving self-efficacy to optimize treatment outcomes.

Topic areas:
Addiction
Anxiety
Child/Adolescent
Depression
Presenting Author: Allison Margolis, Clinical Research Assistant

Co-Authors: Allison Margolis, Dost Öngür, Ann K. Shinn, K. Eve Lewandowski, Kirsten Bolton

Title: Parental grit and caregiver burden in first episode psychosis

Key words:

The emergence of psychosis in young adulthood introduces persistent challenges for caregivers. Caregiver burden (CB), the stress that accompanies caring for a patient, negatively impacts caretaker and patient well being. As the magnitude of CB varies between individuals, we are interested in the influence of personality traits on the degree of CB following a child’s first episode of psychosis. We specifically examine “grit,” the disposition to persevere through setbacks and challenges over time, often when efforts are rarely rewarded. As psychotic disorders are chronic and caregivers’ efforts seldom yield explicit returns, grit is especially relevant to this population. Grit has been widely studied in the context of education and achievement; however, it has not, to our knowledge, previously been applied to the domain of psychosis. We administered the Burden Assessment Scale and the Short Grit Scale to parents whose children had recently experienced their first psychotic episode. A moderate, negative correlation, r(33)=-.29, p=.05, suggests that grit may be associated with decreased CB. Interestingly, the magnitude of the correlation was found to be larger among mothers than fathers, r(23)=-.37, compared to r(6)=-.05, despite similar levels of grit and CB in each group. In the future, we hope to clarify the nature of sex differences in the relationship between grit and CB, examine the influence of time, child diagnosis, and illness severity on CB, and determine the value of extending interventions for bolstering grit to this population. Further research in this area could allow for improved caregiver support.

Topic areas:
Bipolar
Psychotic disorders
Schizophrenia
Title: Role of underlying Conscience-Related Factors such as Guilt and Locus of Control in the Treatment of Obsessive-Compulsive Disorder (OCD)

Key words: Guilt, Treatment, OCD

Introduction: Previous research indicates that people with OCD experience excessive guilt, which is associated with increased OCD symptom severity (Shapiro & Stewart, 2011). Furthermore, research shows that when compared to other disorders, OC patients report having a more external Locus of Control (LOC), and are therefore less likely to attribute their life events as being under the control of others or chance (Kennedy, Lynch, and Schwab, 1998). While previous research has examined the relationship between LOC and the psychopathology of other disorders such as depression, similar research in OCD is scarce. A better understanding of this relationship can be very helpful, especially considering the importance given to motivation for gaining control over particular emotions, thoughts, and life events, as well as fearing loss of control over thoughts and actions in the development/maintenance of OCD symptoms (Moulding & Kyrios, 2007). There is also very limited research addressing the relationship between guilt and Locus of Control on OCD treatment outcome, especially in Intensive/Residential Treatment (IRT) samples. Most previous studies have utilized non-clinical samples or those with mild/moderate severity.

Methods: The overall objective of this study was to assess whether unaddressed conscience-related factors (C-RFs) such as guilt and LOC contribute to refractory OCD and its treatment. More specifically, this study aims to examine the effects of guilt, locus of control and their interactions on the general obsessive-compulsive (OC) symptomatology as well as treatment outcome. Fifty-three patients receiving IRT for severe OCD completed the Interpersonal Guilt Questionnaire, Rotter’s Locus of Control questionnaire and the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), at admission/discharge.

Results: Linear regression analyses indicated that omnipotent guilt (β=.386, t(51)=2.959, p=.005) was significantly associated with overall symptom severity at admission. Further, omnipotent guilt was significantly associated with Y-BOCS residual change scores (β=.519, t(33)=2.342, p=.026). These associations were not replicated for survivor guilt. Results also showed LOC was a potential prognostic factor as a more internal LOC at admission was associated with Y-BOCS residual change scores (β=.376, t(33)=2.296, p=.028). The moderating role of guilt on this relationship was evaluated; however, there was no significant interaction between LOC and guilt as it related to Y-BOCS residual change score. Therefore, guilt does not play a moderating role.

Discussion: This study highlights the important role that LOC may play in the treatment process, implicating it as a potential prognostic factor. LOC was also associated with clients’ reported experience of guilt. Interestingly, the relationship between guilt and OCD may vary based on type of guilt, with omnipotent guilt playing a larger role. Overall, this suggests guilt and LOC may independently impact treatment outcome and serve as potential treatment targets in IRT.

Topic areas:
OCD
Title: The Holistic Student Assessment: Evaluating the role of summer learning in the social-emotional development of youth

Key words: holistic, evaluation, social-emotional, adolescent, education

Introduction: Out-of-school time (OST) programs aim to increase social-emotional skills and other protective factors that can reduce the risk of developing mental illness. However, few programs use evidence-based tools to measure the level of impact they may have on social-emotional development (SED). The PEAR Institute at McLean Hospital is a translational center that bridges theory, research, and practice in order to support school districts and youth-serving organizations in their efforts to increase social-emotional skills and resilience in the service of academic and life success. In the summer of 2016, PEAR collaborated with a network of youth development programs in The Greater Boston Area to examine the impact of summer learning on SED.

Methods: The Holistic Student Assessment (HSA) was administered to youth participating in one of 19 summer programs in Boston. The HSA is a 61-item self-report survey, which measures 14 subscales that fit into three dimensions of behavior: Resiliencies, Relationships, and Learning & School Engagement. At the start of the program, participants completed the baseline survey (HSA-Pre), responding on a 4-point Likert scale (1=Not at all to 4=Almost Always). HSA subscales were standardized by gender and grade and converted to Z-scores (i.e., standard deviation scores). Students who scored 1 or more standard deviations (SD) in either direction from the mean (i.e., zero) were assigned a strength or a challenge score of 1 based on the direction of the attribute for each of the 14 subscales. Students were then categorized by need based on the number of strengths and challenges they exhibited: low, moderate, or high need. At the end of the program, participants completed a retrospective self-change version of the survey (HSA-R), responding on a 7-point Likert scale (1 = Much less than before, 4 = About the same, 7 = Much more than before). Students rated how they felt their thoughts and feelings have changed since the beginning of the program.

Results: Participants were 826 youth (60% female) in Grades 5 to 12. The average number of strengths was 2.9 (SD = 3.4) and the average number of challenges was 2.4 (SD = 2.9). The HSA identified 17.4% of students as high need and 41.5% as low need. At the end of the summer, participants reported statistically significant positive change (i.e., mean scores significantly greater than 4, “about the same”) on all 14 HSA-R subscales, including Reflection, School Bonding, and Critical Thinking. These are the subscales in which students reported frequent challenges on the HSA-Pre.

Discussion: OST programs, including summer opportunities, offer a new paradigm for learning—learning that is relevant, sustained, aspirational, and anxiety-free, with mentoring and social-emotional support. Our findings indicate that participation in a youth development summer program fosters social-emotional skills, including areas where youth tend to report challenges. Importantly, research demonstrates that social-emotional skills are related to academic achievement, school attendance, and student engagement. Evidence-based surveys, such as the HSA, demonstrate that the strategies used in summer settings can help bolster resilience among youth.

Topic areas:
Child/Adolescent
Alcohol-impaired driving is a major problem in the U.S., accounting for 31% of motor vehicle fatalities. As part of an effort to engineer alcohol sensing devices for automobiles to reduce drunk driving, blood alcohol levels (BAL) are being examined in a number of simulated real-world drinking scenarios to quantify how the body absorbs, distributes, and metabolizes alcohol. Drinking and exercise (e.g., dancing) occur together frequently, but research into the effects of exercise on BAL is inconclusive: some evidence suggests alcohol elimination increases during exercise, but other studies have failed to find a clear relationship. “Last call” is another common occurrence at bars, involving a last-minute drink (or more) consumed at a rapid pace prior to the bar closing and potentially driving home. There are major gaps in our understanding of how BAL is impacted by either of these scenarios and subsequent driving abilities. The aim of the present research was to simulate these real-world scenarios in a controlled laboratory setting to determine their impact on alcohol pharmacokinetics. Healthy male and female “social drinkers” were recruited. Individuals participated in one of three scenarios: (1) Exercise (n=4), during which individuals used a recumbent elliptical machine for 16 minutes immediately after drinking; (2) Last Call (n=4), during which individuals drank two-thirds of the full dose at the beginning, followed by the last third after approximately one hour; and (3) Bolus Drinking (n=4), the control condition, during which individuals drank the full dose and remained stationary throughout. On study day, blood samples were collected every two minutes through an intravenous catheter. The alcohol dose was 0.9 g/kg (40% vodka). Whole blood alcohol levels were determined by Gas Chromatography. A mixed ANOVA was conducted to compare differences in BAL from Bolus Drinking to both Exercise and Last Call. No statistical significant differences were found, likely due to the current small sample size. It was observed, however, that BAL levels in Exercise were numerically higher than those in Bolus Drinking (120 mg/dL ± 11.3 versus 109.9 mg/dL ± 15.7) and achieved at a more rapid pace (72 versus 82 minutes). The peak BAL achieved in Last Call was less than Bolus Drinking (100 mg/dL ± 28.1), however, the Last Call subjects hovered at around 70 mg/dL until their last drink, which caused them to rise rapidly to the peak. While the BAL-time profiles between scenarios appear to demonstrate differences in the absorptive phase and achieved peak BAL, the sample size prevented us from finding statistically significant differences. The results, however, may suggest that alcohol is absorbed more rapidly during exercise than when remaining stationary. In the Last Call scenario, participants consumed a final drink after their BAL had stabilized (distribution phase) and, while the peak BAL was lower than the Exercise and Bolus drinking scenarios, it is important to note that the BAL was still rising for 30–60 minutes after the “last call” was consumed — placing the individual at greater risk for alcohol-impaired driving after the bar closes.
McLean Research Day 2017

Original Research - Clinical
Poster # 70
Time: 1:50-2:45pm

Presenting Author: Yasmin Mashhoon, Assistant Professor of Psychiatry; Neuroscientist
Co-Authors: Jennifer Betts, Stacey Farmer, Scott Lukas

Title: Thicker frontal lobe regions associated with impulsivity and craving in smokers

Key words: cortical thickness, nicotine, smoking, frontal lobe, neuromaturation

Background: Dynamic neuromaturational refinements in the brain take place throughout adolescence and the early twenties that are associated with improved executive cognitive processing, particularly in prefrontal regions. As nicotine use is typically initiated during adolescence, the current objective was to investigate the impact of chronic nicotine use on frontal lobe cortical thickness in adult smokers relative to healthy non-smokers.

Methods: Five cigarette smokers (aged 33.7 ± 6.7; 3 females) and three non-smokers (aged 28.8 ± 4.5; 0 females) underwent high-resolution magnetic resonance imaging at 3 Tesla. Cortical surface reconstruction and preliminary analyses of frontal cortex thickness were performed using Freesurfer pipelines to measure bilateral anterior cingulate (ACC) and posterior cingulate (PCC) cortices as well as frontal and frontopolar gyri thickness estimates. The Barratt Impulsiveness Scale and Questionnaire on Smoking Urges were used to assess subjective impulsivity and smoking craving.

Results: Cortical thickness was significantly higher in smokers than non-smokers in the left hemisphere (LH) ACC (p≤0.05) and mid-PCC (p≤0.04) and the opercular inferior frontal gyrus (oIFG; p≤0.05) and middle frontal gyrus (MFG; p≤0.05). Cortical surface thickness was also higher in right hemisphere (RH) frontopolar gyrus (p≤0.05). Thicker mid-PCC correlated with greater reported motor (p≤0.05) and total (p≤0.03) impulsivity. Furthermore, thicker ACC, mid-PCC, oIFG, and MFG were correlated with greater reported cigarette craving (p≤0.05).

Discussion: While the sample size is small, preliminary analyses revealed significantly thicker frontal lobe regions in adult cigarette smokers, relative to non-smokers. This finding suggests that persistent cigarette smoking during adolescence and young adulthood may have interfered with normal GM maturation and synaptic pruning processes in the frontal lobe, which could affect regulation of executive cognitive function.

Topic areas:
Addiction
Imaging
Title: Attitudes about Evidence-Based Psychological Treatments based on Demographic Characteristics

Key words: Dissemination, CBT

Background: Despite huge advances in the development and demonstrated efficacy of evidence-based psychological treatments (EBPTs) in recent decades, progress in disseminating and implementing EBPTs has been gradual (Santucci, McHugh, & Barlow, 2012). Direct-to-consumer (DTC) marketing approaches may have the potential to promote EBPT treatment participation (Gallo, Comer, & Barlow, 2013). However, there is currently a lack of research investigating familiarity with and preference for EBPTs, as well as whether consumer attitudes and behaviors vary by demographic factors. This study aimed to examine the relationship between patients’ demographics (e.g., age, gender, education level) and their level of familiarity with and overall impression of specific EBPTs.

Methods: Participants included 297 adult patients at McLean Hospital’s Behavioral Health Partial Hospital Program (BHP). Participants completed a computerized questionnaire that assessed awareness of and attitudes toward EBPTs (including CBT, DBT, and ACT) at admission to the program.

Results: Women were more likely to prefer a combination of medication and psychotherapy, whereas men were more likely to prefer psychotherapy only ($\chi^2(3,288) = 11.85, p =.008$). When making decisions about mental health treatment, Asian patients were more likely than patients of other ethno-racial backgrounds to prefer treatment that research suggests is most effective over recommendations from treatment providers ($\chi^2(2,279) = 15.59, p <.0001$). Once referred to the BHP, women, individuals with college degrees or higher, and patients older than 35, were more likely than men to look up information about the program on the internet ($ps< .012$). Women and patients age 35 and older were more familiar with DBT than men ($\chi^2(3,295) = 20.56, p <.0001$; $\chi^2(12,295) = 28.75, p = .004$). Females reported more prior hours of CBT than males ($F(1,246) = 5.31, p =.022$).

Discussion: Patient demographics were related to familiarity with and beliefs about EBPTs. Therefore, different strategies may be required to target consumers based on demographics. Future research should examine what other resources people use to learn about and access mental health services, and whether or not individuals view themselves as consumers of mental health care. We will also present secondary analyses related to diagnoses, insurance providers, and patients’ primary care physicians.

Topic areas:
- Anxiety
- Depression
- Gender Differences
Borderline personality disorder (BPD) and post-traumatic stress disorder (PTSD) have high rates of co-occurrence. In one nationally representative sample, 30.2% of individuals with BPD also met criteria for PTSD (Pagura et al., 2010). This raises important questions about treatment strategies, including whether one disorder should be given treatment priority. Past longitudinal work examining the interplay of BPD and PTSD over 10 years has suggested that the two disorders should be treated concurrently (see Keuroghlian et al., 2015). However, little work has examined how treatment for either BPD or PTSD influences symptoms of the other disorder on a shorter timescale. Here we examined symptoms of PTSD and BPD during residential treatment designed to target BPD. The residential treatment is primarily DBT-oriented and includes elements of MBT. Notably, no specific trauma interventions are employed. 110 female patients completed measures related to PTSD (including the PCL-C) and BPD (including the ZAN-BPD and the MSI) at admission and at 2-week intervals during residential treatment. As defined by Monson et al. (2008), a reliable and significant change in PCL-C score was achieved within 2 weeks (mean change = 5.6), and a clinically significant change was achieved within 8 weeks (mean change = 11.44). These findings suggest that treatment that targets BPD may also treat PTSD. Further analyses will include hierarchical linear modeling (HLM) to examine differences in treatment trajectory across patients and whether changes in PTSD symptoms are temporally related to changes in BPD symptoms. Discussion will include implications for treatment. Additionally, discussion will include insights gained from measuring PTSD within this sample using self-report. For example, use of the PCL may be limited by a tendency to label events as traumatic that would not typically be labelled traumas under strict DSM criteria (e.g., “being born into a human body”, “the general world situation at the moment”).

**Topic areas:**
Borderline Personality Disorder
PTSD
The Impact of Anhedonia on Cognitive Behavior Therapy for Depressed Adolescents

Background. Major depressive disorder (MDD) is a debilitating disorder that frequently develops in adolescence (Avenevoli et al., 2015), and 74% of depressed adolescents report anhedonia (Yorbik et al., 2004). Previous research indicates that anhedonia severity negatively influences treatment response. Spijker and colleagues (2001) found the presence of anhedonia increased rates of treatment dropout and led to worse treatment outcomes while McMakin and colleagues (2012) reported that among treatment-resistant depressed adolescents, anhedonia predicted longer remission time and fewer depression-free days. In light of this prior work, the current study tested the impact of anhedonia on treatment response in a sample of adolescents receiving 12-weeks of individual cognitive behavioral therapy (CBT) for depression.

Methods. The study included depressed female adolescents (n = 27) aged 13-18 years. At baseline, participants were administered a clinical interview and completed self-report measures of depression and anhedonic symptoms. A subset of participants (n = 15) endorsed anhedonia, as operationalized by satisfying 3 or more criteria on the self-report anhedonia instrument. All participants then received 12 weeks of individual CBT. Based on previous research, we hypothesized that compared to non-anhedonic depressed youth, anhedonic depressed adolescents would report higher post-treatment depression severity.

Results. Preliminary results indicated the following. At baseline, there were no differences in reported depression between anhedonic and non-anhedonic participants, t(25) = 0.79, p = 0.44, d = 0.31. However, anhedonic depressed youth reported higher post-treatment depression severity relative to non-anhedonic depressed adolescents, t(21.34) = 1.71, p = 0.10, d = 0.64. Further, across participants, higher baseline anhedonia severity, predicted higher post-treatment depression severity while accounting for baseline depressive symptoms, b = 0.33, p = 0.047, R2 = 0.15.

Conclusion. In summary, anhedonia severity contributes to poor treatment outcomes among depressed adolescents receiving CBT, and thus, may suggest that alternative interventions that target these symptoms may be more effective.

References
McLean Research Day 2017

Presenting Author: Maria Mavrikaki, Postdoctoral Research Fellow

Co-Authors: Mavrikaki Maria, Pravetoni Marco, Page Sarah, Potter David and Chartoff Elena

Title: Oxycodone self-administration in male and female rats

Key words: Opioids, Self-administration, Sex differences, Reward, Addiction

The prescription opioid oxycodone is one of the most widely prescribed painkillers in the US. However, its use is complicated by high abuse potential. Since sex differences have been described in most stages of drug addiction, the present study tests if there are sex differences in oxycodone intravenous self-administration, a rodent model of drug addiction. Male and female Sprague-Dawley rats were implanted with jugular vein catheters and trained to self-administer oxycodone (0.03mg/kg/infusion). Rate of acquisition and maintenance of self-administration behavior on fixed ratio 1 (FR1), FR2, and FR5 schedules of reinforcement were measured. In addition, sensitivity to the reinforcing effects of oxycodone (dose response), and motivation to work for oxycodone (progressive ratio) were measured. In a separate cohort of rats, distribution of oxycodone to plasma and brain were measured after intravenous delivery. On an FR1 schedule of reinforcement, male rats self-administered more oxycodone than females. On FR2 and FR5 schedules, no significant sex differences in drug intake were observed, although females had significantly more inactive lever presses than males. In the dose response experiment, females tended to self-administer more oxycodone across doses. Similarly, there was a trend for females to work harder for oxycodone in the progressive ratio experiment. No significant sex differences were observed in plasma or brain oxycodone levels, suggesting that sex differences in oxycodone self-administration behavior are not due to pharmacokinetics. Taken together, our results suggest that there are sex differences in abuse liability of oxycodone, which has ramifications for the treatment of oxycodone dependence and abuse.

Topic areas:
Addiction
**Presenting Author:** Rosemary Smith, Senior Clinical Research Assistant

**Co-Authors:** Kelly A. Sagar, Mary Kathryn Dahlgren, Korine B. Cabrera, Ashley M. Lambros, Staci A. Gruber

**Title:** Reduced Pain and Improvements in Quality of Life and Cognition in Patients with Chronic Pain Following Three Months of Medical Marijuana Treatment

**Key words:** Medical marijuana, Chronic pain, Quality of life, Executive function

**Background:** Currently, 25 states and Washington D.C. have passed full medical marijuana (MMJ) programs, while 18 states allow limited access to non-psychoactive MMJ products. Chronic pain is among the most common indications for MMJ use. Marijuana (MJ) contains a variety of cannabinoids that primarily modulate the activity of the body's endocannabinoid system, which is involved in regulating mood, appetite, memory, and pain. Although the endocannabinoid system has been implicated in both anti-inflammatory processes and analgesia, few studies assessing the effects of cannabinoids on pain have been conducted thus far.

**Methods:** Patients certified for MMJ use who had not yet begun treatment were recruited. A subgroup of these patients who noted chronic pain as their primary indication completed measures assessing pain symptoms, clinical state, and quality of life at baseline (prior to beginning MMJ treatment) and following three months of treatment. Further, patients completed a neuropsychological battery at both visits, which included several measures assessing executive functioning.

**Results:** Following three months of treatment, patients reported primary symptom reduction evidenced by diminished self-reported pain ratings on the Visual Analog Scale (VAS), Numerical Rating Scale (NRS), Pain Distress Scale (PDS), and Neuropathic Pain Scale (NPS). In addition, patients reported improved quality of life with regard to physical health, general health, energy, and social functioning on the World Health Organization Quality of Life scale (WHOQOL-BREF) and the Short Form 36-Item Health Survey (SF-36). Further, on the Patient Global Impression of Change (PGIC) scale, which assesses patients’ beliefs about treatment efficacy, patients reported that activity limitations, symptoms, emotions, and overall quality of life improved after beginning MMJ treatment. Patients also reported reductions in depressive symptoms on the Beck Depression Inventory (BDI), although significant changes in other aspects of clinical state, including anxiety, were not observed. After three months of treatment, patients also tended to perform better on several measures of executive function, demonstrating improvements on measures of working memory (Letter-Number Sequencing, Digit Symbol Substitution Test), cognitive flexibility (Wisconsin Card Sorting Task), and selective attention (Stroop Color Word Test).

**Conclusions:** MMJ patients reported reduced pain, fewer depressive symptoms, and improved quality of life after three months of MMJ treatment. Further, they exhibited improved performance on measures of executive functioning, which may result from the reallocation of cognitive resources previously devoted to processing chronic pain and related symptomatology, as these symptoms appeared to have been ameliorated. These findings suggest that further work is needed to examine the specific effects of MMJ on clinical state, quality of life, and cognition in those with chronic pain, particularly in light of the current opiate epidemic. MMJ may prove to be a valuable substitute for traditional opiate-based therapies in patients with chronic pain, as these medications often do not provide full symptom relief and come with a host of associated side effects.

**Topic areas:**
Addiction
McLean Research Day 2017

Presenting Author: Katherine McHugh, Fitness & Activities Coordinator

Co-Authors: Katherine M. McHugh, Jennifer L. Buchholz, Lynne Kopeski, Marie Forgeard, Courtney Beard, Thröstur Björgvinsson,

Title: Integrating Yoga with Cognitive Behavioral Therapy: Perceived Benefits, Acceptability, Feasibility and Associated Changes in Mood in a Partial Hospital Setting

Key words: CBT, Yoga, Affect, Acceptability, Mood

Yoga enhances not only bodily health but also the health of the mind. Studies have demonstrated its efficacy in treating anxiety and several severe mental disorders including schizophrenia, depression, PTSD, and other anxiety disorders. The present study is the first examination of yoga as a complement to cognitive behavioral therapy (CBT) treatment in a partial hospital setting with a diagnostically heterogeneous sample of patients. The objective of this investigation was to study the feasibility of a yoga group as complementary treatment in a behavioral health partial hospital setting. In Phase 1, qualitative and quantitative reports of participants’ satisfaction supported yoga as a highly acceptable and feasible intervention within the partial hospital program. In phase 2, we investigated patient perceptions and recorded positive and negative affect before and after a brief yoga intervention designed to support mental health across a range of psychiatric diagnoses. A certified yoga instructor and a community residence counselor led 50-minute sessions of guided mindfulness, meditation, and physical movement. This Yoga for Wellness group was integrated into the Behavioral Health Partial CBT program once weekly. The instructor introduced clinical concepts during the yoga sequence which connected the physical practice to the mental health healing process, and contextualized yoga in order to begin to establish an evidence-based treatment program. In phase 2, participants reported a statistically significant increase in positive affect after the group. Participants also experienced a significant decrease in negative affect over the course of the group. Our data demonstrate a high level of patient satisfaction, coupled with improvements in mood, indicating a promising role for yoga as a complementary treatment with CBT for a diagnostically diverse population. Future research should investigate the mechanisms of change that lead to improvement after yoga interventions.

REFERENCES

Topic areas:
Anxiety
Depression
During adolescence, the frontal cortex undergoes the most substantial structural and functional changes during adolescence, although significant developmental changes also occur in hippocampus. These regions are notably vulnerable to alcohol use, particularly during adolescence, thus identifying neurodevelopmental vulnerabilities associated with early and escalating alcohol use during adolescence is critical. In the current study, brain activation using blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI), was acquired at 3 Tesla, during performance of a virtual version of the classic Morris Water Maze task, on retrieval (hidden platform) and motor control (visible platform) conditions. Participants included healthy adolescents, aged 13-14 years who are alcohol and drug naïve, and who exhibit no psychiatric symptoms or conditions, recruited locally to participate in a three year longitudinal study of adolescent brain development. Data from the baseline (year 1) visit demonstrate increased activation in the hippocampus during the retrieval condition when participants used cues in the environment (memory) to navigate to a hidden platform, compared to the motor condition, when no cues were present and participants navigated to a visible platform. In contrast, increased activation was observed in the default mode network during the motor condition, when cognitive task demands were minimal. Activation of the anterior cingulate cortex also was observed when the retrieval condition was compared to a probe trial, in which navigation occurred in the retrieval environment, however unbeknownst to participants, the platform had been removed. These are the first fMRI data to be reported from an adolescent cohort using this translational memory task, known to be sensitive to detecting alcohol and drug-related effects on memory performance. These preliminary findings are consistent with hippocampal and prefrontal activation patterns observed during memory retrieval in a prior adult study. Given that the age of onset of alcohol use often occurs during this crucial period of brain development, data acquired using this task at a baseline visit, when adolescents are alcohol and drug naïve, may provide a neurobiological signature of risk for use initiation. These data may also shed light on the impact of early alcohol and drug use on memory performance and developmental alterations in neuronal resource utilization.

Topic areas:
Addiction
Child/Adolescent
Gender Differences
Imaging
Determining the Effects of a Missense Variant in SLC39A8 on Serum Metals and Protein Glycosylation in Schizophrenia; Biomarker Development and Possible Novel Therapeutics.

**Key words:** Schizophrenia, Manganese, Glycosylation, Fucosylation, GWAS

A genome-wide association study (GWAS) published in 2014 identified over 100 genes associated with schizophrenia. One variant with high prevalence in the general population (~5%) and a strong correlation to schizophrenia (p < 8x10^-15) is a missense mutation in the zinc/manganese transporter SLC39A8. Manganese (Mn) is a critical cofactor for enzymes regulating the post-translational addition of sugar polymers to proteins through glycosylation, especially galactosyltransferases and fucosyltransferases. Fucosylation in neurons effects neuronal connectivity and cognitive processes including memory formation in rodents. Review of the 2014 GWAS data reveals multiple genes regulated by Mn or involved in glycosylation, suggesting a novel group of genes conveying risk for schizophrenia. Using the Partners Biobank, a repository of biological samples linked to the electronic medical record and genomic data, we plan to stratify controls and patients with schizophrenia into groups based on the SLC39A8 missense mutation. Serum from these individuals will be analyzed for Mn and Zn levels, as well as protein glycosylation patterns using mass spectrometry. A complementary assay of protein fucosylation from fresh peripheral blood mononuclear cells, a highly sensitive and specific test for changes in glycosylation, will then be performed in a subset of patients, as this would be predicted to be decreased in those with decreased Mn or dysfunctional glycosylation. Analysis will be aimed at determining if clinical characteristics and genotype can be correlated with peripheral heavy metal ion concentration or protein glycosylation patterns as potential biomarkers. If preliminary data support a role of manganese or glycosylation in the etiology of this disease, future studies will include a clinical investigation of dietary supplementation with manganese, fucose, galactose, and uridine as a potential treatment for schizophrenia.

**Topic areas:** Schizophrenia
A number of interacting factors determine the risk of Alzheimer’s disease (AD). Among the better-studied pathophysiologic pathways, the "amyloid cascade hypothesis" proposes that AD is an accumulation of Aβ-containing plaques and tangles of hyperphosphorylated tau (p-tau). This hypothesis has not been uncontroversial, and is best supported for familial/early-onset forms of AD (EOAD) pathology and less so for sporadic/late-onset forms (LOAD). Rather, accumulation of toxic Aβ and p-tau may not be the initial cause of LOAD and may instead be consequences of other causative factors. Because it is well documented that cellular, including neuronal, energy metabolism changes with age, one of the possibilities is that disturbed bioenergetics and resulting metabolic deficits are contributing mechanisms underlying LOAD. Thus, changes of bioenergetics and metabolism may be at the core of determining the survival capacities of brain cells with age and under stress, with these processes influenced, in turn, by genetic predisposition, epigenetics, environment, and lifestyle. Bioenergetic anomalies may trigger other pathological processes, such as resistance to growth factor/insulin signaling, neuroinflammation, cell membrane changes, and microvascular disease, which all contribute to age-related neurodegeneration, including AD. We address the concept that the pathogenesis of LOAD prominently includes accumulating metabolic dysfunction based on the hypothesis that aged neurons exhibit an "inverse Warburg effect" with an increase in oxidative phosphorylation (OxPhos) due to mitochondrial damage and dysfunction, resulting in an increased demand for lactate which is produced by astrocytes through elevation of their glycolytic capacity. These energy production abnormalities in combination with accelerated mitochondrial damage in neurons may be at the core of many, if not all, subsequent events in AD pathology. In support of this hypothesis we found in fibroblasts from LOAD patients (n=10) and control subjects (n=20) that AD cells shift their energy production to glycolysis possibly due to impaired mitochondrial respiration. To test this concept in AD-relevant neural cell populations we have designed an experimental approach using LOAD patients’- and control individual-derived induced pluripotent stem cells (iPSC) that are differentiated to neurons and astrocytes and cultured long-term, as an in vitro model of aging. The aging cells will be systematically analyzed for changes in their bioenergetic and metabolic profiles, and the accumulation of AD-associated neurotoxic factors. We expect that this “personalized cell system” will reveal a core mechanism in aging and the pathogenesis of LOAD, which could lead to the development of novel diagnostic and/or therapeutic strategies.

**Topic areas:**
Alzheimer's/Dementia
Increasing evidence suggests a role for inflammatory processes in autism spectrum disorders (ASDs). Some individuals with ASDs show elevated inflammatory markers and neuroimmune responses, as well as epidemiological association with familial autoimmune disorders. These findings raise the possibility that there is a subtype of ASD that is immunological in origin. Previous research in mice has shown that immune insults during critical developmental periods can result in a phenotype that reproduces some of the core features of ASD. We have recently developed a “multiple hit” immune model, whereby mice are exposed to repeated perinatal immune insults. In this model, pregnant mice are injected with the viral mimic poly(I:C) (20 mg/kg) on gestational day 12.5 in accordance to an established model of maternal immune activation. A subset of these offspring receives a second injection of LPS (lipopolysaccharide) (10 mg/kg) to induce a robust innate immune response on postnatal day 9. We have previously found that this model leads to a pronounced ASD-like behavioral phenotype with mice displaying deficits in social and communication behavior, increased repetitive behavior, as well as inducing a state of ongoing immune activation that persists into adulthood. Here, we examine this multiple hit immune activation model on two physiological measures that are commonly dysregulated in individuals with ASD, sleep and electroencephalography (EEG) epileptiform activity. Using a remote telemetry system, a transmitter was implanted at postnatal week 6 and measurements of EEG, electromyography (EMG), activity, and temperature were made for multiple weeks. During this period levels of activity, sleep, and circadian rhythm were analyzed. Prenatal poly I:C and postnatal LPS resulted in decreased daily temperature fluctuations and altered patterns of sleep. Considering that epilepsy is found in a higher percentage of individuals with ASD than in the general population and there is evidence for increased in epileptiform activity even in the absence of epilepsy, we examined EEG recordings from perinatal immune activated mice for the presence of epileptiform activity. Analysis revealed that a subset of the mice that received postnatal LPS displayed heightened levels of epileptiform activity, which included the presence of spike-wave discharges during sleep. In sum, perinatal immune activation resulted in alterations in sleep and epileptiform activity resembling aspects of ASD, further supporting a potential immunological involvement in ASD.
**Presenting Author:** Sivan Subburaju, Assistant Molecular neuroscientist

**Co-Authors:** Anna W. Sromek, John L. Neumeyer

**Title:** Preclinical validation of novel high affinity dopamine D2 receptor agonists: potential for treatment of Parkinson disease

**Key words:** D2 Receptor agonist, PET, MCL 536, MCL524

The D2high receptor is thought to be the functional form of the D2 receptor to which endogenous dopamine (DA) binds. Elevation of D2high receptors has been demonstrated in various neurological disorders in which the dopaminergic system is affected. In Parkinson’s disease (PD), the loss of dopaminergic neurons causes a shift of remaining D2 receptors into the high affinity state. Evidence for this is supported by the fact that medications used to treat PD have been shown specifically to target the D2high receptor. We recently reported the synthesis and receptor binding for D1high, D1low, D2high, D2low, and D3high receptors of a series of fluorinated aporphines, and identified two highly promising high affinity D2high ligands as potential tritiated radioligands for applications in in vitro receptor binding assays and autoradiography studies, MCL-524 and MCL-536. These agonists exhibited no affinity or low affinity for other receptors tested, including serotonin, a and b-adrenergic, benzodiazepine, GABAA, muscarinic, sigma, kappa, and mu opioid receptors, as well as dopamine, serotonin, and norepinephrine transporters and translocator protein. In the present study, we evaluated the radioligands [3H] MCL-524 and [3H] MCL-536 in a saturation binding study and competition binding studies against an agonist (N-propylnorapomorphine, NPA) and an antagonist (raclopride). First we evaluated [3H] MCL-524 and [3H] MCL-536 in a saturation assay in human D2long (EMD Millipore), the isoform of the D2 receptor found at the postsynaptic terminal. We determined [3H]MCL-536 to have a Kd value of 0.24 nM. In a competition binding assay with R-(-)-N-propylnorapomorphine (NPA) as the competing ligand NPA had a Ki binding affinity of 0.16 nM. When [3H] MCL-524 was used, NPA was found to have a Ki value of 0.99 nM. However, we did not observe a biphasic curve corresponding to D2high and D2low states when evaluating the results of these experiments. This is likely due to the fact that we were working within the concentration range which binds to the high-affinity state of the D2 receptor. In summary, the radioligands [3H] MCL-524 and [3H] MCL-536 display subnanomolar binding affinity to human D2long and have proven to be superior radioligands for in vitro evaluation in receptor binding assays. MCL-524 and MCL-536 will be developed as PET radiotracers and also have potential to replace the current standard therapies, as a lower-dose, oral medication for PD.

**Topic areas:**
- Addiction
- Depression
- Imaging
- Pharmacology
- Psychotic disorders
Presenting Author: Emery Mokler, Technical RA II, BA

Co-Authors: Abigail J. Alexander, Samantha M. Landino, Beate C. Finger, Yan Li, Vadim Bolshakov, Galen Missig, Christopher J. McDougle, William A. Carlezon Jr.

Title: Interactions between prenatal and early postnatal immune challenges in a mouse model of autism

Key words: Maternal Immune Activation (MIA), Autism Spectrum Disorder (ASD), Perinatal Immune Insults, Mouse Model, Sex Specific Differences

The role of immunological responses in the etiology of autism spectrum disorder (ASD) has long been hypothesized. A “multiple hit” model whereby multiple exposures to early life immune insults may contribute to the development of ASD. We developed a repeated immune challenge mouse model where pregnant mice were injected with the viral mimic poly(I:C) (20 mg/kg) on gestational day 12.5 of pregnancy. A subset of the offspring was injected with lipopolysaccharide (LPS) (10 mg/kg) on postnatal day 9 to induce a second robust innate immune response. A battery of behavioral assays were performed to characterize the behavioral phenotype of this model in relation to the core symptoms of ASD: deficits in communication and social interaction, and increases in stereotyped behaviors. To assess communication-related behavior, ultrasonic vocalizations (USVs) were recorded from male pups during a maternal separation test on postnatal days 10-16 and from adult males at seven weeks evoked from the presence of urine from a female in estrus. In both LPS treated pups and adults there were altered number of evoked USVs suggesting a dysregulation of communication. To measure social behavior, a one-chamber social interaction test was performed at 8 weeks. In males, postnatal LPS decreased social preference. To evaluate for the presence of stereotypic or repetitive behavior, mice were tested on a Rotarod at 7 weeks and were placed in a Y-Maze at 10 weeks to observe spontaneous alternations. Anxiety-like behaviors were measured from both males and females at 10 weeks in the open field test. There was heightened anxiety-like behavior for both sexes that received postnatal LPS. In sum, postnatal LPS was sufficient to produce a robust ASD-like behavioral phenotype, producing alterations in communication, social preference, stereotypic, and anxiety-like behavior. However, following prenatal poly(I:C) treatment we did not observe a reliable ASD-related behavioral phenotype, and found that the combination of poly(I:C) plus LPS produced only modest differences from the behavioral phenotype seen with postnatal LPS alone. Our findings provide evidence that perinatal immune insults can produce behavioral changes in mice resembling those found in ASD and lend further support to a potential immunological involvement in ASD.

Topic areas:
Child/Adolescent
Gender Differences
There are significant sex differences in the epidemiology, physiology, and treatment course of substance use disorders (SUDs). Evidence shows that gender-responsive treatment approaches lead to enhanced treatment outcomes for women with SUDs. Women-only treatment programs address the need for gender-responsive services for women with SUDs, but are limited in number and the majority of women receive treatment in mixed-gender settings. Few mixed-gender SUD treatment programs contain women-specific components. To address this gap, this study aimed to (1) develop a gender-responsive, computerized psychoeducational intervention (GRCP) to be delivered in a mobile format for women with SUDs, and (2) pilot test the GRCP as an addition to treatment as usual in a mixed-gender, inpatient SUD treatment program. Evidence supports the use of women-specific psychoeducational material and computerized delivery of psychoeducation for a variety of mental health problems. The GRCP was developed by adapting psychoeducational material from three modules of the Women’s Recovery Group, an evidence-based, women-focused, single-gender group therapy for women with SUDs. Three topics that are of key relevance to women with SUDs were selected for the GRCP: (1) The Effect of Drugs and Alcohol on Women’s Health, (2) Managing Mood, Anxiety, and Eating Problems without Using Substances, and (3) Women and their Partners. Modifications for a computerized format focused on presenting material in an engaging, interactive style accessible by women of varying literacy levels. Women enrolled in mixed-gender inpatient treatment at McLean Hospital’s Alcohol and Drug Abuse Treatment Program were included if they were (a) 18 years of age or older, and (b) able to read and provide informed consent. Women with an acute psychiatric or medical condition, or cognitive impairment that would impair the ability to complete study procedures were excluded. The GRCP intervention and all assessments were delivered on a study iPad. Patient satisfaction with the GRCP and attitudes about the relevance of gender-responsive components of the GRCP to SUD treatment were measured post-intervention. Twenty women (mean age = 40.7, SD=14.0; 95% white; 20% married) completed the study. Results show a high level of satisfaction with the GRCP (M=34.6, SD=4.8; maximum possible score = 40). The elements of the GRCP that were rated as the most relevant to recovery (Likert scale 0-4; 4=extremely relevant) were: the effects of substance use on self-care (M=3.7, SD=0.5), the symptoms of depression (M=3.7, SD= 0.6), and the influence of a partner on recovery (M=3.6, SD=0.5). All 20 women rated the GRCP as easy to navigate and 95% (n=19) found the interactive knowledge-check questions helpful. The ease of administration and high satisfaction ratings of the GRCP suggest that it has the potential to be a highly sustainable strategy for increasing gender-responsivity, even in settings with limited staff and financial capacity to offer specialty services.
McLean Research Day 2017

Original Research - Pre-Clinical

Poster # 84
Time: 1:50-2:45pm

Presenting Author: Elena Molokotos, Graduate Student
Co-Authors: Molokotos, E. Janes, A.C. Jerram, M.W.

Title: Differences in association for surface area and thickness within functional brain networks between monozygotic and dizygotic twin pairs

Key words: Brain Structure, Heritability, Twins, Human Connectome Project

Heritability rates of cortical surface area (SA) and thickness differ regionally. Whether these patterns correspond with functional brain networks is unclear. Such a link is plausible as network activation is heritable and brain function and structure are coupled. To determine the heritability of primary resting state networks (RSNs), we evaluated the SA and thickness of the default mode network (DMN), central executive network (CEN) and salience network (SN). The Human Connectome Project collected magnetic resonance imaging data for monozygotic (MZ, n = 72) and dizygotic (DZ, n = 60) twin pairs. Following a standard freesurfer pipeline, total network SA and thickness were calculated by summing the values of individual regions known to comprise these RSNs. Pearson correlation coefficients were calculated for thickness and area of RSNs in MZ and DZ twin sets. To demonstrate a genetic influence, correlation coefficients were z-transformed and compared between MZ and DZ sets. Relative to DZ twins, MZ twins showed stronger correlations for SA of the SN (p = .002), CEN (p = .001), and DMN (p = .001) and thickness for the CEN (p = .001) but not the other networks. The heritability of network anatomy is congruent with prior work showing strong heritability of global brain structure. These findings suggest that, while SA is heritable across networks, thickness is only heritable within the CEN. It is hypothesized that SA and thickness are mediated via different genetic mechanisms and the results suggest that the CEN structure is more broadly genetically determined than other RSNs.

Topic areas:
Imaging
**Title:** Comorbidity of Bipolar Disorder and Alzheimer’s Disease: A Neuropathological Study

**Key words:** Alzheimer’s Disease, Bipolar Disorder, Dementia, Lithium, Neuropathology

**Introduction:** Growing evidence suggests that individuals with bipolar disorder (BD) have an increased risk of developing dementia compared to the normal population (Kessing, 2003; Nunes et al. 2007) However, it is not yet well known whether these clinical observations underlie increased severity of neuropathological changes typical of Alzheimer’s disease (Neurofibrillary tangles; senile plaques) and other contributors of dementia (vascular pathology). Notably, results from clinical studies and experimental animal models suggest that chronic lithium exposure may decrease the neuropathology of dementia due to its potential to exert a neuroprotective effect (Forlenza et al. 2014). The present postmortem studies tested the hypothesis that BD subjects may present with increased severity of AD pathology with respect to control subjects matched by age and gender. Lithium exposure in BD subjects was expected to be inversely correlated to the severity of neuropathology.

**Methods:** BD subjects (n=75) and healthy controls (n=81) were matched by age and gender. Neuropathological data such as presence of neuritic plaques, neurofibrillary tangles, non-neuritic plaques, microinfarcts, and atherosclerosis and arteriosclerosis were collected from neuropathology reports. Medication history was collected for BD subjects (n=55). Lifetime exposure to lithium was recorded. Potential confounds such as age, gender, brain weight, and cause of death were tested using stepwise regression analysis.

**Results:** Presence of neuritic plaques in the neocortical grey matter was significantly higher in BD subjects compared to controls. Out of BD subjects who had neuritic plaques, the amount of lifetime lithium exposure was found to be inversely proportional to the severity. Presence of neurofibrillary tangles and non-neuritic plaques in neocortical grey matter was not significantly different in BD subjects compared to controls. Out of BD subjects who had non-neuritic plaques, the amount of lifetime lithium exposure was not significantly correlated. A positive trend was observed in the prevalence of microinfarcts in the neocortical grey matter in BD subjects compared to controls. There is no significant difference between BD subjects and controls in the presence of either arteriosclerosis and atherosclerosis.

**Conclusions:** Our findings support our hypothesis that at least one measure of dementia-related pathology, neuritic plaques, is increased in bipolar disorder and this is consistent with clinical findings. Our prediction that lithium exposure in BD subjects was expected to be inversely correlated to the severity and prevalence of dementia-related neuropathology was accurate for one aspect evaluated; non-neuritic plaque severity. Although preliminary, these results suggest that chronic exposure to lithium may have some protection against dementia-related pathology.

**Topic areas:**
Alzheimer’s/Dementia
Bipolar
Geriatric
Altered lysosomal stress markers in idiopathic Parkinson’s disease and following pharmacological-induced lysosomal dysfunction via glucocerebrosidase inhibition

Key words:

GBA1 encodes for the lysosomal hydrolase, glucocerebrosidase (GCase), and heterozygous mutations in GBA1 dramatically increase the risk for developing Parkinson’s disease (PD). Our data shows that sporadic PD (with no GBA1 mutation) mirrors GBA1 haploinsufficiency, given that GCase activity is reduced in several brain regions including the substantia nigra, and levels of the glycolipid substrate, glucosylsphingosine (GluSph), are elevated. Moreover, similar alterations to GCase activity and glycolipid levels occur in the brain of healthy subjects and mice in normal aging, and we hypothesize that disrupted glycolipid homeostasis and lysosomal function may precipitate degenerative processes in vulnerable neurons and lower the threshold for developing PD. Our current studies aim to determine the effect of modulating GCase activity and glycolipid levels in vivo on relevant cell biological mechanisms, including markers of lysosomal integrity and stress. To model altered glycolipid homeostasis in mice, we use pharmacological inhibition of GCase with conduritol-β-epoxide, CBE, a selective, irreversible inhibitor of GCase. A 28-day systemic treatment with CBE in wildtype mice leads to PD-relevant neuropathological changes including significantly elevated brain levels of the glycolipids GluSph and glucosylceramide (GluCer), aggregation of α-synuclein in the substantia nigra, and altered levels of proteins involved in the autophagy lysosomal pathway (Rocha EM et al, Antioxid. Redox Signal., 23(6) 550-564, 2015). As a readout of cellular responses to elevated glycolipids, we have performed analysis of levels of glycoprotein non-metastatic B (GPNMB), which is a transmembrane protein expressed in the brain in neurons and glia. GPNMB levels are elevated in the brain and CSF in lysosomal storage disorders that accumulate glycolipids, including neuronopathic Gaucher disease and Niemann-Pick Type C, and a SNP variant in the GPNMB gene has been associated with idiopathic PD risk. Our data shows that GPNMB levels are increased in the brain in CBE-treated mice, as well as in the substantia nigra in sporadic PD. Ongoing analyses will determine the relationship between GPNMB and lysosomal stress, and will evaluate additional markers of lysosomal function in models of altered glycolipid homeostasis. These data show the remarkable overlap between lysosomal storage diseases and age-dependent idiopathic PD.

Topic areas:
Neurology
Weekly Cognitive-Behavioral Therapy (CBT) with Exposure and Response Prevention (ERP) has been demonstrated as an evidence-based treatment for several pediatric anxiety disorders and Obsessive-Compulsive Disorder (OCD; Silverman, Pina, & Viswesvaran, 2008; Storch et al, 2007). For children with anxiety disorders who are not completing their activities of daily living, however, attending traditional weekly CBT may be insufficient. Intensive CBT may allow children to return to their daily routines in an expedient manner. Existing evidence from research settings has demonstrated that daily CBT with ERP can be effective (e.g., Storch et al, 2007); however, it remains to be seen if an intensive treatment for pediatric anxiety can be implemented effectively in a clinical milieu. Moreover, because data also suggest that group-based weekly CBT for youth anxiety produces results commensurate to individual weekly CBT (Silverman et al, 2008), an intensive group-based treatment may help more children improve simultaneously. We will present data from the McLean Anxiety Mastery Program (MAMP), an intensive group-based CBT program for pediatric anxiety disorders and OCD that requires a minimum of four weeks of treatment four times per week (Boger, Sperling, Potter, & Gallo, 2016). Independent evaluators administer the Anxiety Disorders Interview Schedule Child Version (ADIS-C), with Clinical Severity Ratings (CSR) assigned at baseline and discharge. Participants complete the Spence Children’s Anxiety Scale--(SCAS; Parent and Child Versions), and the Center for Epidemiologic Studies Depression Scale (CES-D), at each assessment and once per week while in treatment. Participants have historically completed The Child Anxiety Impact Scale (CAIS) at baseline and have recently begun completing the CAIS at discharge. Data have been collected on N=83 participants to date, and analyses at the time of the presentation will incorporate data from additional participants recruited in the coming months. Planned analyses include comparisons of baseline and post-treatment data from the Spence Children’s Anxiety Scale (SCAS) and the Center for Epidemiologic Studies Depression Scale (CES-D), and for a subset of participants, the Anxiety Disorders Interview Schedule Child Version (ADIS-C). The program’s goal is to fill current treatment gaps by reaching more children through group treatment and improving symptoms and functioning at a faster pace with its intensive design. Therefore, through analyses we aim to expand on initial findings that suggest decreases in children’s self-reported anxiety and lower CSR ratings at post-treatment compared to reports made a baseline.
Presenting Author: Olga Nazarenko, Clinical Research Assistant

Co-Authors: J Eric Jensen, Elizabeth A Olson, Matthew O Thomas, Scott L Rauch, Isabelle M Rosso

Title: Individual differences in discriminatory fear conditioning predict anterior insula GABA in adults with and without PTSD

Key words: fear, insular cortex, GABA, posttraumatic stress disorder, individual differences

Background: Posttraumatic stress disorder (PTSD) is associated with enhanced fear conditioning and deficient differentiation of danger and safety signals. Functional imaging studies have consistently implicated the anterior insula (AI) in the acquisition of conditioned fear, and there is emerging evidence that the AI may be involved in discriminative fear learning. In PTSD and anxiety disorders, the right AI is thought to contribute to anticipating future aversive physiological responses to conditioned stimuli, and to predicting how the relative value of stimuli might affect bodily states. In this study, we examined whether differential fear conditioning differed between adults with PTSD, trauma-exposed non-PTSD controls (TENC), and healthy comparison (HC) subjects. We also tested the hypothesis that individual differences in autonomic indices of differential fear conditioning would be associated with right AI neurochemistry, specifically markers of excitatory (glutamate) and inhibitory (GABA) metabolism using magnetic resonance spectroscopy (MRS).

Methods: This sample included 35 PTSD, 27 TENC, and 31 HC adult participants who completed single-voxel 3T MRS and a two-day fear conditioning paradigm. All participants were interviewed using the Structured Clinical Interview for DSM-IV, and PTSD and TENC participants also received the Clinician Administered PTSD Scale. MRS data were collected from a 2 X 2 X 3 ml right anterior insula voxel using MEGAPRESS for detection of GABA, and 2DJPRESS for glutamate (Glu). Both metabolites were normalized to creatine (Cr). The fear conditioning paradigm involved an acquisition phase with 16 paired presentations of conditioned stimuli (CS+) with the unconditioned stimulus (US, shock), and 16 trials of another conditioned stimulus (CS-) never paired with the US. Skin conductance response (SCR) was recorded as a peripheral indicator of conditioned fear; differential fear conditioning was defined as differential SCR to the CS+/CS- trials of the conditioning phase.

Results: Differential fear conditioning did not differ significantly between groups. PTSD patients had significantly lower GABA/Cr than HC (p<.05) but not TENC participants. In addition, differential SCR was significantly correlated with GABA/Cr (r=0.35, n=93, p=.0007) in the sample as a whole, such that participants whose SCRs showed stronger differentiation between CS+ and CS- trials had higher right AI GABA. Follow-up analyses identified similar effect sizes when this correlation was examined separately in PTSD patients (r=0.34, n=35, p=.05), TENC subjects (r=0.40, n=27, p=.04), and HC participants (r=0.30, n=31, p=.10). Glu/Cr was not significantly associated with the SCR index of differential fear conditioning.

Discussion: Higher anterior insula GABA measured by MRS was associated with greater differential fear conditioning in adults with and without PTSD. These findings support a role for the right AI in the detection and encoding of stimulus relevance that is acquired through differential fear learning, and are consistent with this region’s broader role in the anticipation of aversion. Combined examination of behavioral indices of fear learning and insula neurochemistry may help detect individual differences in vulnerability for PTSD.

Topic areas:
PTSD
Presenting Author: Christina M. Temes, Clinical and Research Fellow, Ph.D.

Co-Authors: Laura Magni, Ph.D., Garrett Fitzmaurice, Sc.D., Marianne Goodman, M.D., Mary C. Zanarini, Ed.D.

Title: Prevalence and Severity of Childhood Adversity in Adolescents with BPD, Psychiatically Healthy Adolescents, and Adults with BPD

Key words: borderline personality disorder, adolescence, abuse, neglect, childhood adversity

Objective: Existing research has demonstrated that both adolescents and adults with borderline personality disorder (BPD) report higher rates of childhood adversity than their same-age peers. In the present study, we directly compared the prevalence rates and reported severity of multiple forms of abuse and neglect in adolescents and adults with BPD, as well as in a group of psychiatically healthy adolescents.

Methods: The adolescent participant groups consisted of 104 adolescents (aged 13-17 years) with BPD recruited from inpatient units at McLean Hospital and Mount Sinai Medical Center, and sixty age-matched, psychiatically healthy controls recruited from the community. Additionally, a total of 290 adults with BPD were recruited from inpatient units at McLean Hospital. In addition to diagnostic evaluations, all participants completed an interview that assessed the presence and severity of multiple forms of childhood abuse and neglect.

Results: A significantly higher percentage of adolescents with BPD than psychiatically healthy adolescents reported 5 of 12 pathological childhood experiences, including physical abuse and several forms of neglect. Adolescents with BPD also reported more severe abusive experiences than their psychiatically healthy peers. In comparison to adolescents with BPD, a significantly higher percentage of adults with BPD reported nearly all forms of childhood adversity. Adults with BPD also rated these pathological childhood experiences as more severe than their adolescent counterparts.

Conclusions: Taken together, the results of this study suggest that adults with BPD report more severe profiles of abuse and neglect than adolescents with the disorder. They also suggest that adolescents with BPD report more childhood adversity than healthy peers.

Topic areas:
Borderline Personality Disorder
Child/Adolescent
Effect of comorbid anxiety disorders on response to partial hospital treatment

Background: Major depressive disorder (MDD) and anxiety disorders frequently co-occur. Although many studies have examined the effect of a comorbid anxiety disorder on treatment of another anxiety disorder, few studies have investigated the effect of comorbid anxiety on treatment of MDD. In particular, to our knowledge, no studies have examined this issue in a partial hospital setting, which provides brief, intensive transdiagnostic treatment.

Methods: Participants (N = 1162) were patients attending a CBT-based partial hospital. Participants completed self-report measures of symptom severity and functioning upon admission and discharge, and a structured diagnostic interview on their second day of treatment. We analyzed differences in self-report measures upon discharge between MDD patients with and without a comorbid anxiety disorder while controlling for baseline symptom levels.

Results: Compared to patients with MDD and no anxiety comorbidity, patients with a comorbid anxiety disorder did not show significant differences in treatment outcomes on measures of depression, self harm and general mental health. However, patients with a comorbid anxiety disorder did show greater reduction in general anxiety symptoms in response to treatment than patients with MDD alone (t=4.42, p < .001), likely due to greater anxiety severity upon admission.

Conclusions: Overall, comorbid anxiety disorders did not affect treatment outcome in this partial hospital setting. Any potential detrimental effects of a comorbid anxiety disorder may have been attenuated in this treatment setting due to its intensity and transdiagnostic nature. Future studies should conduct a more fine-grained analysis to determine whether specific comorbidities (e.g., PTSD) affect outcome. Differentiating the outcomes of patients presenting with varying comorbid anxiety disorders can serve to inform clinicians and partial hospitalization programs on success probabilities.

Topic areas:
Anxiety
Depression
Title: Social-emotional strengths and challenges of children and adolescents recommended for intervention services

Key words: Holistic, Intervention, Evaluation, Social-Emotional, Adolescents

Introduction: Teachers, administrators, and student support teams, including psychologists, counselors and social workers, struggle with understanding the social-emotional strengths and challenges of the students who arrive in their schools each fall. While 13 percent of children ages 8-15 have had a diagnosable mental disorder within the previous year and 20 percent of youth ages 13-18 have a severe mental disorder (NAMI, 2016), most teachers depend on their own intuition and previous experiences with teaching and learning to support their students. To address some of these challenges, self-report assessments are growing in popularity as a means of providing information to educators and student support staff about the academic, behavioral, and social-emotional needs of their students. It is essential that such measures demonstrate both utility and validity for identifying students in need of support services.

Method: The present work evaluated whether a student survey called the Holistic Student Assessment (HSA) could differentiate between responses of students who have been referred to Tier 3 intervention services (INT group) from a comparison group of students who did not receive intervention services (COM group). The HSA is a 61-item self-report assessment validated for use by students in Grade 5 and above. Students respond to questions about themselves, which are organized into 14 coherent scales that fit into three dimensions of behavior: Resiliencies, Relationships, and Learning and School Engagement. Students rate responses on a 4-point Likert scale ranging from “Not at All” to “Almost always.” Students are categorized as having a strength or struggle on a particular subscale based on transforming the 14 scales in z-scores. Based on the combination of strengths and challenges, students are categorized as low need (Tier 1), moderate need (Tier 2) and high need (Tier 3).

Results: A total of 1,835 students (48.5% female) in grades 6-12 completed the HSA during Fall 2015 (INT, n=99 and COM, n=1,736). Results demonstrated that the INT group had fewer strengths (M=1.38, SD =1.73) compared to COM (M=2.91 , SD=3.41). The INT group also had more challenges (M=3.75, SD=3.29) compared to the COM group (M=2.56, SD=3.17). Moreover, INT students had significantly higher scores in Assertiveness compared to COM students but significantly lower scores on 11 other scales including Emotion Control, Trust, Empathy, Reflection, and Optimism (all p’s <.05). The HSA identified a higher percentage of students as high needs in the INT group (36.4 %) compared to the COM group (20%).

Discussion: There is considerable value in using surveys that can reliably measure each child’s social-emotional strengths and challenges. This is because much research indicates that social-emotional skills, such as normative levels of empathy, play a central role in the development of prosocial orientations and the reduction of problem behaviors across development. Our findings show that the HSA differentiates results from students in crisis from those who are not. Developmentally sensitive assessments, like the HSA, can tailor intervention strategies to fit the developmental needs of children and adolescents.

Topic areas:
Child/Adolescent
Presenting Author: Emily Oot, Academic Credit Student

Co-Authors: Emily N. Oot, Kayle S. Sawyer, John E. Jensen, Marlene Oscar-Berman, Riya B. Luhar, Marisa M. Silveri

Title: Association of Anterior Cingulate Metabolite Levels with Neuropsychological Measures in Alcohol Use Disorder: The Role of Gender

Key words: Alcohol, MRS, Gender, Anterior Cingulate, Neuropsych

Purpose: Alterations in brain metabolites, as measured by magnetic resonance spectroscopy (MRS), have been reported in current alcohol drinkers as well as in recently detoxified alcoholics. Short-term abstinence has been associated with the recovery of metabolite levels and some cognitive functions, but it remains unclear what associations exist between these measures after long-term abstinence. Given that executive functions and memory are highly vulnerable to alcoholism, the purpose of the present study was to explore associations between alcoholism status, duration of abstinence, metabolite levels, and neuropsychological performance. Furthermore, given that there are gender differences in factors related to alcohol use across several domains (such as the phenomenon of “telescoping” in women, where there is more damage to health occurring over a shorter duration and at lower levels of alcohol consumption in women versus men), this study assessed whether gender plays a role in these associations.

Methods: The participants were 40 abstinent alcoholics (ALC, 18 men) and 50 non-alcoholic age-matched comparison subjects (NC, 24 men). Proton MRS was employed at 3T (PRESS; TE/TR=30ms/2s; voxel=2x2x2cm; spectral-width=2000Hz) to acquire metabolite data from a single obliqued voxel placed in the dorsal anterior cingulate cortex region. Proton metabolites were quantified using LCModel and normalized to creatine levels. Neuropsychological performance on the domains of memory, executive functioning, and affect were examined.

Results: There were no significant ALC vs. NC group differences in metabolite levels. The ALC group, however, exhibited significantly worse performance on all memory indices from the Wechsler Memory Scale (except for immediate memory) compared to the NC group. While no gender-specific interactions were observed for those measures, in ALC women higher glutamate levels were negatively associated with a shorter duration of abstinence and predicted worse visual memory and visual working memory. These associations were not observed in any other group.

Conclusions: These data provide preliminary evidence of relationships of anterior cingulate glutamate levels with both neuropsychological performance and duration of abstinence. This pattern of findings is consistent with evidence that recovery of brain metabolites is associated with increasing lengths of alcohol abstinence and restoration of some cognitive functions. Importantly, given that these relationships were observed only in alcoholic women, these data could shed light on factors underlying gender differences in risk factors for developing alcohol use disorders and neurobehavioral consequences of alcohol use.

Topic areas:
Addiction
Gender Differences
Imaging
**Title:** Rostral anterior cingulate cortex morphology predicts remission from major depression following internet-based cognitive behavior therapy

**Key words:** major depressive disorder, cognitive behavior therapy, internet, anterior cingulate cortex, biomarker

**Background:** Function and morphology of the rostral and subgenual anterior cingulate cortex (ACC) have been shown to predict symptom improvement following pharmacological and cognitive behavioral therapy for depression. To our knowledge, no study has yet investigated neuroimaging predictors of outcome following internet-based CBT (iCBT). In this study, we examined whether greater baseline thickness and volume of the rostral and subgenual ACC predict subsequent clinical remission in adult MDD patients receiving iCBT as part of a clinical trial.

**Methods:** In a parallel-group RCT, adult MDD participants (18-45 years) were randomized to a ten-week period of iCBT (n=37) or to a monitored attention control (n=40). At baseline, participants were interviewed using the Structured Clinical Interview for DSM-IV and the Hamilton Rating Scale for Depression (HRSD) and underwent magnetic resonance imaging at 3T. After the intervention phase, patients received a post-treatment HRSD interview, administered by a rater blind to treatment group. Using Freesurfer, we derived cortical thickness and volume measurements for the rostral ACC (gyrus and sulcus) and subgenual ACC (subcallosal cortex). Repeated measures analyses of covariance (ANCOVA) compared thickness and volume of rostral and subgenual ACC between treatment remitters (post-treatment HDRS ≤ 7) and non-remitters, using hemisphere as a within-subject factor, and covarying for average cortical thickness or intracranial volume as appropriate.

**Results:** Sixteen participants who received iCBT were classified as remitters and 11 as non-remitters at the post-treatment visit. In the ANCOVA comparing baseline rostral ACC thickness in remitters and non-remitters, the main effect of remission was statistically significant (F(1,24)=5.20, p=.03), and the interaction of remission by hemisphere was not significant, reflecting greater left and right rostral ACC thickness in remitters. In the ANCOVA of rostral ACC volumes, the interaction of remission by hemisphere was statistically significant (F(1,24)=7.30, p=.01), reflecting larger volumes of the right rostral ACC in remitters. Subgenual ACC thickness and volume did not differ significantly between remitters and non-remitters.

**Discussion:** MRI measurements of rostral ACC anatomy may serve as predictive biomarkers of clinical remission to iCBT for depression. Internet-based and face-to-face CBT should rely on similar neural mechanisms due to their shared therapeutic content, and despite differences in treatment delivery. These findings await replication with independent and larger samples.

**Topic areas:**
Depression
Patients with Parkinson’s disease (PD) present with motor symptoms characterized by tremor, bradykinesia, rigidity and postural instability. There are approximately 1.5 million diagnosed cases of this chronic progressive disorder in the U.S. At the onset of symptoms and diagnosis ~ 70% of the midbrain DA neurons have degenerated. L-DOPA can initially restore dopaminergic (DA) levels and motor function, but with time the therapeutic window becomes increasingly narrow with L-DOPA induced dyskinesia as a common side effect. Although deep-brain-stimulation (DBS) also can alleviate motor symptoms, such interventions ultimately lead to repeat procedures, limitations for patients in receiving other medical procedures and high medical costs. The concept of cell replacement therapy has shown benefit in clinical studies using cell preparations derived from fetal ventral midbrain. However, fetal cell transplantations are not scalable for a larger patient population and require immunosuppression. Induced pluripotent stem cells (iPSCs) can be generated from affected PD patients, differentiated into midbrain dopaminergic cells using xeno-free procedures, and frozen-thawed for use in autologous transplantations. The proof-of-concept in non-human primates has previously been shown by us (Hallett et al. Cell Stem Cell. 2015 Mar 5;16(3):269-74). In recent pre-clinical efforts, we have differentiated episomal xeno-free iPSCs, derived from human PBMCs, into midbrain DA neurons. The cell-preparations have been frozen and thawed with reliable reproducibility. Stability, cell marker characteristics and functionality of the frozen-thawed cells and such preparations are now tested in vitro and in rodent models in vivo.
Expressive Suppression in the Treatment of OCD

Emotion regulation has received increased attention in the etiology and maintenance of anxiety disorders. Much of the extant literature suggests that expressive suppression, efforts to control the behavioral response of an emotion to inhibit its impact (e.g. “white-knuckling” during exposure), is a maladaptive emotion regulation strategy associated with increased depression, anxiety, and poorer quality of life. Maladaptive strategies characterize individuals with anxiety disorders and are associated with poorer outcomes. Based on the paradoxical effect of thought suppression in OCD, expressive suppression may play a similar role in the maintenance of OCD. Identifying and targeting maladaptive emotion regulation strategies may prove beneficial in OCD treatment; however, this literature appears lacking. This study is aimed at elucidating the role of expressive suppression in the treatment of unacceptable thoughts in OCD. Participants (57% male, mean age = 30 years) included 265 patients with a primary diagnosis of OCD receiving treatment at an intensive/residential treatment facility for OCD. Participants completed measures assessing OCD symptom severity of unacceptable thoughts using the Dimensional Obsessive-Compulsive Scale-Unacceptable Thoughts Subscale (DOCS-UT) and emotion regulation strategies (Emotion Regulation Questionnaire) at admission and discharge. Suppression scores were positively correlated with DOCS-UT scores at admission ($r=.194$, $p<.01$). Higher suppression at admission was associated with reduction of DOCS-UT across treatment ($\beta=.147$, $t(236)=2.317$, $p=.02$). Suppression scores decreased significantly after treatment ($t(235)=2.44$, $p=.015$). Linear regression revealed that decreased suppression was associated with a reduction in DOCS-UT severity ($\beta=.207$, $t(235)=3.36$, $p<.01$) when controlling for admission symptom severity and negative affect. Reductions in expressive suppression were found to be linked to treatment response for unacceptable thoughts. This suggests that interventions targeting emotion regulation in addition to traditional OCD treatment may enhance treatment outcome. Future studies should look at this effect, the relationship between expressive suppression and other symptom domains, and the role of negative affect in treatment.

Topic areas:
Anxiety
OCD
Kappa opioid receptors (KOR) are expressed in brain areas implicated in motivation, emotion, and learning. Although selective KOR agonists share the antinociceptive effects of opiates, they tend to produce aversive- and stress-like effects in humans and laboratory animals. In contrast, selective KOR antagonists have antidepressant-like and anxiolytic-like effects, and can block drug-seeking behaviors in rodent models of addiction. These types of findings have stimulated interest in the therapeutic potential of KOR antagonists. However, prototypical KOR antagonists such as JDTic and norBNI have exceptionally long durations of action, complicating their use in clinical trials. Here we present initial pharmacological and behavioral data on a novel KOR antagonist, CYM 52220, synthesized at The Scripps Research Institute. CYM 52220 has sub-nanomolar potency at KORs, 200-1500-fold selectivity for KORs versus mu and delta opioid receptors, no human Ether-à-go-go-Related Gene (hERG) or cytochrome P450 (CYP) liabilities, oral bioavailability and favorable pharmacokinetics, and favorable distribution to brain (>4:1 brain-plasma ratio). Using the Tail Flick Assay (TFA), we performed dose-effect and time course experiments to quantify the ability of oral administration of CYM 52220 to block the antinociceptive effects of the KOR agonist U50,488 (30 mg/kg, IP). For comparison, we also tested the KOR antagonists JDTic and LY2456302, which have long and short durations of action, respectively. Consistent with previous reports, oral administration of JDTic (20 mg/kg; PO) blocked U50,488-induced increases in tail flick latency in the TFA for at least 24 hrs whereas the KOR antagonist effects of LY2456302 (0.9 mg/kg; PO) in the TFA were only observable for 1 hr after oral administration. CYM 52220 (0.0 – 30 mg/kg; PO) dose-dependently blocked U50,488-induced increases in tail flick latency when administered 2-hr prior to testing. An AD80 dose of CYM 52220 (6.0 mg/kg; PO) attenuated the analgesic effects of U50,488 for more than 4 hrs. In conclusion, CYM 52220 is a novel, potent, selective, and orally active KOR antagonist with a relatively short duration of action that may have therapeutic potential.
McLean Research Day 2017

Original Research - Clinical

Poster # 97
Time: 1:00-1:50pm

Presenting Author: Genesis Vergara, Clinical Research Assistant II

Co-Authors: Erika C. Esposito, Nina M. Lutz, Sarah Hope Lincoln, Jeremy G. Stewart, Joseph Gold, Randy P. Auerbach

Title: The Effect of Peer Victimization on Adolescent Non-Suicidal and Suicidal Behaviors

Key words: Adolescence, Suicide, Non-Suicidal self-injury, Peer victimization

Background: Non-suicidal self-injury (NSSI)—the deliberate harm to one’s own bodily tissue without the intention of death—and suicidal behaviors commonly co-occur in psychiatric adolescent inpatients (Nock, 2010; Stewart et al., 2017). While prior research has demonstrated that peer victimization contributes to NSSI and suicidality (van Geel et al., 2015), it remains unclear whether peer victimization severity contributes to the co-occurrence of NSSI and suicidality above and beyond the effects of symptom severity.

Method: The present study included inpatient adolescents (n = 379) aged 13-18 years (M = 15.50, SD = 1.39). Participants were separated into three groups: (1) adolescents with no past year NSSI, no past year suicide ideation, and no lifetime suicide attempts (psychiatric controls; n = 63); (2) adolescents reporting past year NSSI, past year suicidal ideation, and no lifetime suicide attempts (NSSI; n = 167); and (3) adolescents reporting past year NSSI, past year suicidal ideation, and a lifetime history of suicide attempts (NSSI+SA; n = 149). During the assessment, adolescents were administered a clinical interview assessing lifetime NSSI and suicidality, and additionally, they completed self-report measures regarding peer victimization and depression severity.

Results: A one-way ANOVA comparing group differences in peer victimization revealed a significant effect [F(2, 363) = 12.00, p < .001]. Subsequent post hoc analyses showed pairwise differences among the three groups, such that psychiatric controls reported significantly less peer victimization than NSSI adolescents (p < .05) and NSSI+SA youth (p < .001). Interestingly, NSSI+SA youth also reported significantly more peer victimization relative to NSSI adolescents (p < .01). Importantly, these effects persisted, when controlling for depressive symptom severity [F(2, 362) = 4.66, p = .01].

Conclusion: Peer victimization plays a pernicious role in contributing to NSSI and suicidality in youth, and thus, underscores the importance of addressing peer victimization in the context of prevention and intervention programs for youth.

Topic areas:
Child/Adolescent
Depression
McLean Research Day 2017

Original Research - Clinical

Poster # 98
Time: 1:50-2:45pm

Presenting Author: Matthew Palastro, Senior Research Assistant

Co-Authors: Sydney Gallo, Kevin P. Hill, M.D., Staci A. Gruber, Ph.D., Garrett M. Fitzmaurice, Sc.D., Shelly F. Greenfield, M.D., M.P.H., Scott E. Lukas, Ph.D., Roger D. Weiss, M.D.

Title: Nabilone for Cannabis Dependence

Key words: Marijuana, Dependence, Cannabis, Nabilone, Pharmacotherapy

Background: Marijuana is, by far, the most commonly-used illicit drug in the United States. Despite this fact, there are no FDA-approved medications for those who are addicted to marijuana. We aimed to assess the safety, feasibility, and preliminary efficacy of nabilone, a cannabinoid agonist, to treat cannabis dependence.

Methods: 18 cannabis-dependent adults were randomized to receive either 2 mg/day of nabilone (n=10) or placebo (n=8) for 10 weeks in addition to medication management. 12 participants, 6 in each group, completed treatment. Cannabis use outcomes were assessed via self-report and twice-weekly urine cannabinoid tests; secondary outcomes included cannabis craving and anxiety.

Results: In general, participants in both groups reported reduced cannabis use by self-report over the course of the study, although these reductions were not statistically discernible. Moreover, there was no difference in cannabis use between the nabilone group and the placebo group as measured by self-report. In addition, while participants in the nabilone group’s creatinine-adjusted cannabinoid levels declined during the study, there was no difference in creatinine-adjusted cannabinoid levels between the nabilone group and the placebo group. There was a significant reduction in compulsivity and emotionality associated with craving within the nabilone group while this difference was not found in the placebo group.

Discussion and Conclusions: Nabilone pharmacotherapy was safe and well-tolerated in participants with cannabis dependence. Nabilone was not more efficacious than placebo in reducing cannabis use.

Scientific Significance: There remains a dire need for additional pharmacotherapy trials for cannabis dependence, and nabilone remains a promising candidate for such trials, perhaps utilizing a higher maximum dose.

Topic areas:
Addiction
Presenting Author: Nicole Visaggio, RN


Title: Benefits of transfer chair vs. 4 point leather or Velcro restraints vs. locked door seclusion during psychiatric emergencies in the inpatient hospital setting

Key words: restraint, seclusion, staff injuries, patient injuries, restraint chair

The use of seclusion and restraint in inpatient psychiatric care has been the subject of ethical debate for decades, prompting the movement toward reduction of the practices. Much has been written about the risks inherent to seclusion and restraint, including negative physical and psychological effects on both patients and staff (Kontio, et al., 2010). Seclusion and restraint in psychiatric inpatient care may be employed when all other forms of de-escalation have been utilized without success. Historically, restraint has included physical holds and four-point mechanical restraint while seclusion is defined as isolation in a locked quiet room. The aim of this retrospective study is to evaluate three methods of seclusion and restraint: transfer chair, four point and locked door seclusion. Variables to compare will include diagnosis, duration of episode, medication and route of administration during episode and the rate of staff and patient injuries during episodes. Age and gender of patients will also be evaluated.

Topic areas:
Outcomes/Quality
While many psychiatric disorders are characterized by impulsive behavior, impulsivity itself is a broad construct with many different facets. One specific dimension of impulsivity, impulsive responses to emotion (also called urgency), has increasingly been identified as a robust correlate of numerous forms of psychopathology (Berg et al., 2015; Johnson et al., 2013). Impulsive responses to positive or negative emotions can easily be assessed using brief self-report measures, and scores on these measures have been directly linked to deficits in cognitive control (e.g., Gay et al., 2008) and to serotonergic polymorphisms (Carver et al., 2014). However, little is known about how emotion-relevant impulsivity responds to treatment. In the present study, we tested whether impulsive responses to positive and negative emotions would decrease in response to treatment in a naturalistic, transdiagnostic cohort: specifically, individuals seeking treatment at the McLean Hospital Behavioral Health Partial Hospital Program (BHP). We also tested the hypothesis that higher levels of emotion-relevant impulsivity at discharge would correlate with higher residual symptom levels. 384 patients seeking treatment at the McLean BHP completed the Negative Urgency and Positive Urgency scales of the short form of the UPPS-P scale (Whiteside & Lynam, 2001; Cyders et al., 2014). This scale assesses trait-like impulsive responses to negative and positive emotions and was administered during participants’ second day in treatment as well as at discharge. As predicted, participants’ average scores on the negative urgency measure decreased during treatment, t(383) = 11.16, p < .001, Cohen’s dz = 0.57; positive urgency decreased as well, t(382) = 7.07, p < .001, Cohen’s dz = 0.36. Despite this improvement, higher scores on the negative urgency measure in particular were correlated with worse clinical outcomes at discharge, including a higher level of depression symptoms (CES-D, r = 0.41, p < .001); and on the BASIS-24 measure, higher levels of self-harm, r = .18, p < .001, psychosis, r = .14, p = .01, and substance abuse, r = .24, p < .001. These findings suggest that impulsive responses to emotion are responsive to treatment in a partial hospital setting, with a medium-sized decrease in negative urgency observed during treatment and a smaller reduction in positive urgency. However, higher levels of impulsive responses to negative emotions at discharge were associated with worse outcomes in several domains, indicating that additional treatments may be necessary for individuals who struggle with this form of impulsivity.

**Topic areas:**
Depression
Original Research - Pre-Clinical

Presenting Author: Gordana Vitaliano, Assistant Professor of Psychiatry

Co-Authors: Christopher W. Adam, Jay McLaughlin, Marc J. Kaufman, Franco Vitaliano

Title: Clathrin Nanoparticles Efficiently Deliver BDNF to the Hippocampus, Reverse BDNF Deficits and Improve Cell Survival and Proliferation in a GT-tg Mouse Model of HIV

Key words: Neurotechnology, BDNF delivery, Clathrin nanoparticles, HIV associated neurocognitive disorder, Gt-tg mouse model

Background: Advances in treatment of HIV-associated neurocognitive disorder (HAND) and other neurodegenerative disorders have been made by administering brain derived neurotrophic factor (BDNF) directly to the CNS, or by using drugs that can increase BDNF indirectly. BDNF promotes neuroregeneration and restores brain functions. However, BDNF cannot easily cross an intact blood brain barrier (BBB) and diffuse within the brain. The goal of this effort is to produce novel BDNF-nanoparticles that can bypass the BBB intranasally, target tropomyosin receptor kinase B (TrkB) receptor rich brain regions, and reverse neurotoxic effects of HIV transactivator of transcription (tat) protein in a mouse model relevant to HAND.

Methods: One BDNF molecule was conjugated to a clathrin heavy chain via polyethylene glycol (PEG). Nanoparticle (NP) size and uniformity were determined by electron microscopy and SDS-PAGE. GT-tg bigenic mice (tat+) were treated daily at 9 AM over 7 days with doxycycline (dox, 100 mg/kg/d i.p.) to express neurotoxic tat protein. Control animals (tat-) received only saline. BDNF-nanoparticles (0.3 mg/kg of BDNF with 2.4 mg/kg of clathrin), BDNF alone, clathrin alone, or saline (40 µl) was delivered intranasally at 2 PM, after daily dox/saline administration. For immunohistochemical studies, animals also received bromodeoxyuridine (BrdU 50 mg/kg, every 12 h i.p.) on the 1st and 2nd day of dox/saline administration. Animals were sacrificed at 7 PM on the 7th day of dox/saline administration. Cell proliferation was determined with a Ki67 antibody and survival of newborn cells with a BrdU antibody. For Western Blot (WB) analyses, an additional group of animals were sacrificed at 7 PM on the 4th day of dox/saline administration. BDNF concentrations and signaling were analyzed in the hippocampal tissues.

Results: Microscopic and WB analyses of hippocampal regions confirmed delivery of BDNF-NPs. BDNF-NPs significantly improved cell survival and proliferation in GT-tg mouse hippocampus. BrdU+ cell densities (ANOVA, F(2,10)=21.79, p=0.0002) and Ki67+ cell densities (F(2,10)=12.35, p<0.002) doubled in the granule cell layer of dentate gyrus in tat+ animals that received BDNF-NPs, compared to tat+ and tat- animals that did not receive nanoparticles. Furthermore, BDNF-NPs reversed BDNF deficits in tat+ animals by significantly increasing hippocampal levels of mature-BDNF (F(4,17)=5, p<0.007) and pro-BDNF (F(4,17)=4.4, p<0.01). Mature-BDNF levels were significantly higher in tat+ animals that received NPs, compared to tat+ animals that received saline, or clathrin, or BDNF without clathrin, or tat- control animals. Finally, BDNF-NPs activated the Akt signaling pathway by significantly increasing hippocampal levels of pAKT (F(4,13)=5, p<0.01) and Akt (F(4,18)=6.5, p<0.002) in GT-tg mice that received nanoparticles.

Discussion: Our results demonstrate that clathrin-nanoparticles enabled BDNF to effectively bypass a BBB intranasally, and double mature-BDNF levels in the hippocampus. BDNF-NPs significantly enhanced hippocampal cell proliferation and survival and reversed neurodegenerative effects of tat protein in a mouse model of HAND. Hence, clathrin provides a highly efficient nanoplatform for delivery of BDNF to the CNS. This noninvasive nanotechnology may be able to enhance neuronal plasticity and restore brain functions more quickly and completely than existing treatment methods, while using much lower therapeutic drug doses and with fewer side effects.

Topic areas: Alzheimer's/Dementia, Pharmacology
McLean Research Day 2017

Original Research - Pre-Clinical

Poster # 102
Time: 1:50-2:45pm

Presenting Author: Erica Porter, Research Assistant 1

Co-Authors: Erica N. Porter, Jack Bergman, Brian D. Kangas

Title: Effects of Self-Administered Oxycodone on Discrimination Learning and Reversal in Nonhuman Primates

Key words: Oxycodone, Self-administration, Cognition, Touchscreen

Over the past decade, prescription opioid abuse has become a major public health concern. Despite increased prevalence, however, the effects of chronic opioid abuse on cognition-related behavior remains poorly understood. Previous studies in our laboratory have shown that self-administration of other abused drugs can have adverse effects on cognitive behavior. Therefore, the present studies employed similar techniques to examine the effects of daily intravenous self-administered oxycodone. Touchscreen-based repeated acquisition and discrimination reversal tasks were designed to assay basic features relevant to learning and cognitive flexibility, respectively. Four squirrel monkeys were initially trained to self-administer oxycodone. A wide range of doses was evaluated in each subject over 1, 2, and 3-hour sessions until stable intake was observed. A peak dose of 0.1 mg/kg/inj during 3-hr sessions yielded maximum daily intake and was used for subsequent conditions. Following 30 self-administration sessions, subjects were then introduced to the touchscreen tasks. Subjects were placed in a touchscreen chamber immediately following oxycodone self-administration and learned to discriminate between two novel stimuli (acquisition) for a palatable food reward. Once discrimination acquisition was mastered, subjects then re-learned the discrimination under conditions where the consequences were switched (reversal). Dose-response functions revealed a relatively linear increase in oxycodone intake as a function of dose. In addition, extending session durations increased daily intake at all doses examined. Stable levels of oxycodone intake using the peak dose of 0.1 mg/kg/inj were maintained over extended periods of self-administration (>100 sessions). Results from touchscreen sessions indicated dramatic deleterious effects on learning and reversal in some subjects; however, in other subjects less profound effects were observed. Future studies will investigate the effects of abrupt discontinuation of opioid self-administration (withdrawal) on discrimination learning and reversal.

Topic areas:
Addiction
Pharmacology
Presenting Author: Sarah Vogel, Clinical Research Assistant II

Co-Authors: Randy Auerbach, PhD, ABPP, Jeremy Stewart, PhD, Daniel Dillon, PhD, Laura Germine, PhD

Title: Mobile Assessment of Cognitive Control in Depression and Aging

Key words: cognitive control, technology, depression, aging

Understanding the mechanisms of cognitive control is of vital importance and interest to the scientific community, specifically the ways in which cognitive control relates to psychopathology and age-related change. However, current methods of measuring cognitive control are limited to assessment in a laboratory or clinic setting, thus limiting sample size and population generalizability. The primary goals of the current study were (1) to develop and validate a Flanker interference task for mobile/web administration in large samples, and (2) to characterize dimensional variations in cognitive control related to depression and aging. We collected data from 1,694 visitors to TestMyBrain.org who completed a Flanker interference task on either a laptop/desktop or mobile device. Through a series of iterative modifications, we optimized the accessibility, engagement, and psychometric characteristics of the task to create a brief, reliable version of the Flanker for self-administration across a range of devices. Our final version of the test showed poorer accuracy and slower reaction times for flanker incongruent trials as compared with congruent (p < 0.0001 for both accuracy and RT). A subset of participants (n = 912) also completed a modified version of the Beck Depression Inventory (BDI-II). Flanker interference was significantly associated with age, anhedonia, and affective depression symptoms, but with distinct effects for depression symptoms versus older age. Age was most strongly associated with reaction time differences, with older participants exhibiting greater reaction time slowing due to flanker interference (controlling for depression and gender: B= 0.016, p<0.0001). This result held even after controlling for speed-accuracy trade-offs. BDI-II depression symptoms, on the other hand (specifically anhedonia and affective symptoms), were associated with interference effects on accuracy. High depression severity was associated with greater interference effects on performance accuracy but not reaction time (β = 0.08, p < 0.01), accounting for age and gender. Our findings suggest that mobile assessment methods can sensitively and reliably detect differences associated with both age and psychopathology, in population-based samples. Using a non-clinical, population-based sample we were able to identify significant differences in these domains, suggesting a broad application for these measures in studying and understanding cognitive control in mental health.

Topic areas:
Depression
Title: The Impact of Trauma and PTSD Symptoms in Clients with OCD: Dimensional Variations

Key words: OCD, PTSD, Treatment

Introduction: Current research indicates that many individuals suffering from Obsessive Compulsive Disorder (OCD) may also present with a history of trauma (HT; Shavitt et al., 2010). Previous research has shown that traumatic life events are related to an overall increase in symptom severity of OCD (Cromer et al., 2007). However, there is limited research addressing the impact of trauma symptoms on the individual domains of OCD symptoms. This exploratory study aims to examine the relationships between trauma symptomology and the severity of specific OCD dimensions which include, concerns about contamination, responsibility for harm, intrusive thoughts and concerns about symmetry, completeness, and the need for things to be “just right.”

Methods: Data were collected from 222 participants (57% male, 43% female, average age=31) enrolled in intensive/residential treatment (IRT) for OCD and related disorders. Participants completed the Yale Brown Obsessive Compulsive Scale (YBOCS), the PTSD Checklist-6 (PCL-6), and the Dimensional Obsessive-Compulsive Scale (DOCS) upon admission and discharge from the program. The sample was split into high and low trauma symptom groups based on the recommended cut-off of ≥14 as high trauma symptom endorsement.

Results: In line with previous research, clients’ PCL-6 scores were significantly associated with overall OCD symptom severity (r=.302, p=.000) at admission. More specifically, PCL-6 admission scores significantly correlated with DOCS2, DOCS3, and DOCS4 subscales at admission, however only DOCS3 and DOCS4 correlations remained significant at discharge. A one-way ANOVA found those in the high trauma symptom group demonstrated significantly greater DOCS2 (F(2, 217) = 5.57, p = .004) and DOCS3 (F(2, 217) = 11.5, p = .000) scores at admission. At discharge, significant differences between the groups were found for YBOCS total score (F(2, 192) = 3.492, p = .032) and scores on each DOCS subscale, however, amount of change across treatment was not significantly different.

Discussion: In line with previous findings, severity of PTSD symptoms was associated with greater OCD severity. Further, these findings suggest the relationship between trauma and OCD symptoms may vary across OCD symptom dimension. Further, clients endorsing greater trauma symptom severity at admission had significantly higher OCD severity at discharge across all four dimensions. Overall, this may suggest an initial link between the presence of trauma symptoms and increased severity of harm-based OCD symptoms and unacceptable/intrusive thoughts. Interestingly, those with high trauma symptom demonstrated greater discharge severity but there was no difference in overall amount of change, suggesting this group may have a more severe clinical presentation overall. Further research should evaluate if the course treatment response varies between these groups.

Topic areas:
OCD
PTSD
Presenting Author: Victoria Votaw, Clinical Research Assistant

Co-Authors: Roger D. Weiss, Margaret L. Griffin, Sterling L. Karakula, Olivera J. Bogunovic, R. Kathryn McHugh

Title: Anxiety sensitivity and benzodiazepine misuse among adults with opioid use disorder

Key words: Opioid use disorder, Benzodiazepines, Anxiety sensitivity, Gender differences

Introduction: Among those with opioid use disorder (OUD), benzodiazepine misuse is common and is associated with poor treatment outcomes and mortality. Identifying factors associated with benzodiazepine misuse in this population is needed in order to inform prevention and treatment efforts to reduce benzodiazepine misuse. Anxiety is associated with benzodiazepine misuse among those with opioid use, and the desire to relieve anxiety is a commonly reported motive for benzodiazepine misuse. Those with high anxiety sensitivity—the fear of anxiety symptoms and sensations—might be particularly vulnerable to benzodiazepine misuse given the association between anxiety sensitivity and the use of substances to cope. The primary aim of the present study was to examine the association between past-month benzodiazepine misuse and anxiety sensitivity among adults with OUD. Given prior evidence that women are more likely to use substances to cope with negative affect, a secondary aim was to determine if the association between benzodiazepine misuse and anxiety sensitivity was stronger in women compared to men.

Methods: Participants were adults diagnosed with OUD (N = 257; 27.2% female) receiving inpatient detoxification treatment. Participants completed a battery of self-report measures; the Anxiety Sensitivity Index-3 (ASI-3), the Overall Anxiety Severity and Impairment Scale (OASIS), and the Brief Addiction Monitor (BAM) were included in the present analyses. Analysis of covariance (ANCOVA) was used to examine the association between benzodiazepine misuse and anxiety sensitivity (ASI-3 score). This analysis controlled for age, gender, and anxiety symptoms (OASIS score), and included the gender by anxiety sensitivity interaction term to determine if gender moderated the association.

Results: Overall, 55.3% of the sample reported past-month benzodiazepine misuse, and the mean ASI-3 score was 23.6 (SD = 15.8), suggesting a high level of anxiety sensitivity. Results of the ANCOVA model indicated that benzodiazepine misuse was significantly associated with anxiety sensitivity (F[1, 251] = 3.91, p = .049, ηp2 = .02). There were also main effects of gender (p = .004) and anxiety symptoms (p < .001). The interaction between gender and benzodiazepine misuse was also significant (F[1, 251] = 9.37, p = .002, ηp2 = .04), indicating that gender moderated this association. Specifically, benzodiazepine misuse was associated with anxiety sensitivity in women, but not in men.

Conclusion: Findings from this cross-sectional analysis indicated an association between benzodiazepine misuse and anxiety sensitivity among individuals with OUD, particularly among women. This finding is consistent with literature suggesting that women are more likely than men to use substances to cope with negative affect. Future studies examining whether coping motives mediate the relationship between benzodiazepine misuse and anxiety sensitivity will help to clarify this gender difference. Interventions targeting anxiety sensitivity might be a promising approach for mitigating benzodiazepine misuse among those with OUD.

Topic areas:
Addiction
Gender Differences
McLean Research Day 2017

Original Research - Clinical
Poster # 106
Time: 1:50-2:45pm

Presenting Author: SriRamya Potluri, Research Assistant and CRC


Title: The Role of Guilt in Obsessional Belief Domains and in the Treatment of Obsessive-Compulsive Disorder (OCD)

Key words: OCD, Guilt, Obsessional Belief Domains, Treatment Outcome

Extant research indicates that many with OCD experience excessive guilt, which is associated with increased OCD symptom severity (Shapiro & Stewart, 2011). Furthermore, research suggests that dysfunctional obsessive beliefs in the domains of over-responsibility/overestimation of threat (RT), perfectionism/intolerance of uncertainty (PC), and importance of thoughts/need to control thoughts (ICT; Obsessive-Compulsive Cognitions Working Group, 2005) play a significant role in development/maintenance of OCD symptoms. There is limited research addressing the relationship between guilt and these domains or the impact of guilt on OCD treatment outcome, with previous studies utilizing non-clinical samples or those with mild/moderate severity. This study aims to examine the relationship between guilt and treatment outcome; understand the association between guilt and obsessional beliefs; and analyze how this relationship changes following treatment. Forty patients receiving intensive/residential treatment (IRT) for severe OCD completed the Interpersonal Guilt Questionnaire (omnipotent/survivor guilt), Obsessional Belief Questionnaire-44, and the Yale-Brown Obsessive-Compulsive Scale, at admission/discharge. Linear regression analyses indicated omnipotent guilt was significantly associated with overall symptom severity ($\beta=.441$, $t(32)=2.417$, $p=.022$) at admission. Further, omnipotent guilt significantly predicted symptom reduction ($\beta=.601$, $t(18)=2.129$, $p=.049$). These associations were not replicated for survivor guilt. At admission, omnipotent guilt was associated with the RT ($\beta=.564$, $t(34)=3.921$, $p=.000$) and PC ($\beta=.380$, $t(34)=2.360$, $p=.024$) subscales. At discharge, guilt was only associated with the RT subscale ($\beta=.521$, $t(19)=2.588$, $p=.019$). Guilt was not significantly associated with the ICT subscale. Findings suggest that the relationship between guilt and OCD severity may vary based on type of guilt. Study highlights the important role that guilt plays in treatment outcome as well as its relationship to the RT and PC belief domains. Interestingly, over the course of treatment, the association between guilt and perfectionism diminishes, whereas the relationship between guilt and responsibility remains significant, suggesting guilt as a potential treatment target for those with elevated RT beliefs.

Topic areas:
OCD
Background: Motivation deficits are evident in depression and likely impact treatment outcomes. However, it is unclear how different aspects of motivation or readiness for treatment change over time and impact treatment outcomes above and beyond baseline symptom severity. Additionally, previous studies have identified sex differences in depression in that females have demonstrated higher rates of major depressive disorder (MDD) than males (e.g., Bebbington, 1996). It is important to understand the effect of sex on readiness for treatment, and to assess which factors (sex, depression, or motivation) best predict treatment outcomes. To our knowledge, no studies have examined this issue in a partial hospital setting, which provides a unique opportunity to study changes in motivation and symptoms in a brief, intensive treatment environment.

Methods: Participants (N=145) with a diagnosis of major depressive disorder were recruited from a CBT-based behavioral health partial hospitalization program (BHP). Participants completed daily self-report ratings of depression on the Patient Health Questionnaire (PHQ-9) and readiness for treatment assessing 1) importance of treatment, 2) confidence in one’s ability to engage in treatment, and 3) motivation to engage in treatment at the BHP. We defined treatment response as a subjective rating on the Clinical Global Impressions Scale-Self-Report (CGI) and depression scores at discharge.

Results: Depression significantly improved over time, and both motivation for treatment and confidence improved over time at trend level (p=.051 and .055). Women showed greater treatment readiness than men with respect to motivation and confidence in the ability to engage in treatment but not in importance. However, there were no sex differences in baseline depression level. Motivation and confidence (not importance) predicted global clinical improvement and depressive symptoms at discharge beyond baseline depressive symptoms and sex.

Conclusions: Readiness for treatment can predict treatment outcomes beyond baseline symptoms. Though sex differences emerged in motivation and confidence, sex did not appear to predict outcomes. Understanding the role that different aspects of readiness for treatment holds for treatment outcomes of patients suffering from depression can guide strategies to maximize treatment response. Future research should further examine the factors that can modulate motivation for treatment.

Topic areas:
Depression
Gender Differences
Presenting Author: Adam Reid, Ph.D Post Doctoral Fellow

Co-Authors: Lisa Coyne, Ph.D., Rebecca Michel, B.S., Maria Fraire, Ph.D.

Title: A preliminary investigation of valued living during residential exposure therapy for youth with obsessive-compulsive disorder

Key words: Obsessive-compulsive disorder, Values, Exposure and Response Prevention, Residential Treatment, Treatment Outcome

Background: Approximately one-third of youth with obsessive-compulsive disorder (OCD) do not respond to Exposure and Response Prevention (ERP; e.g., Pediatric OCD Treatment Study, 2004). Poor outcomes may be due to avoidance of important life activities or simply failing to see exposure itself as a valued activity. In other words, valued living may be a broad marker of response to ERP that can be easily measured in a clinical setting. Indeed, engagement in valued living in adults has been linked with less anxiety severity (Wetterneck et al., 2013) and improved treatment response (Michelson et al. 2011). This study sought to collect pilot data supporting valued living as a clinically relevant marker of change during ERP for youth with OCD.

Methods: Data were collected from 44 youth their families receiving residential ERP treatment. The sample had an average age of 15 (SD = 1.75) and presented with clinically severe OCD (M = 29.58, SD = 5.61), as measured at intake by the clinician-rated Children’s Yale Brown Obsessive Compulsive Scale (CYBOCS). The child completed a self-report CYBOCS weekly and at discharge to provide a measure of outcome. Valued living was assessed using the five items of the Progress subscale of the Valuing Questionnaire (VQ; Smout et al., 2014) and was collected at intake, weekly, and discharge.

Results: Youth experienced, on average, a 21% reduction in obsessive-compulsive symptoms (SD = 32%). Hierarchical regression indicated that, after controlling for age and obsessive-compulsive severity at intake, higher valued living at intake, b = 0.40, t = 3.03, p < .01, and increases in valued living during treatment, b = -0.28, t = -1.79, p = .08, both were at least marginally associated with a reduction in OCD (r² = 19%).

Conclusion: This novel study supports that valued living is an important indicator of response to ERP for youth with OCD and aligns with previous research on the clinical relevance of valued living (Levin et al., 2012). These findings imply that framing exposure work in a valued context may improve ERP outcomes, although future research should seek to better understand how valued living impacts ERP response.

Topic areas:
Child/Adolescent
OCD
Presenting Author: Jonathan Wolff, Clinical Research Assistant

Co-Authors: Lauren A.M. Lebois, Lauren K. O’Connor, Nina F. Lewis-Schroeder, Sherry R. Winternitz, Kerry J. Ressler, Milissa L. Kaufman

Title: Childhood Abuse Predicts Complex Dissociative Symptoms in Adult Women with Post-Traumatic Stress Disorder: Assessment Implications

Key words: PTSD, Childhood Maltreatment, Dissociation

Increased interest in dissociative symptoms such as depersonalization and derealization has led to the designation of a dissociative subtype of PTSD in the DSM-5. Clinically, individuals with PTSD may report a broader range of dissociative symptomatology than accounted for by this subtype. Our goal was to investigate this issue empirically in a cross-sectional sample of adult women with PTSD (CAPS-5) and histories of childhood abuse, and healthy controls (N = 62). We completed linear regression analyses with the Childhood Trauma Questionnaire (CTQ) total score and the Multidimensional Inventory of Dissociation (MID) depersonalization, derealization, and mean pathological dissociation scales. The CTQ total score significantly predicted adulthood depersonalization (R2 = .35, F(1, 60) = 32.61, p < .001, b = .54, t(60) = 5.71, p < .001), derealization (R2 = .21, F(1, 60) = 15.84, p < .001, b = .41, t(60) = 3.98, p < .001), and mean MID scores (R2 = .42, F(1, 60) = 42.71, p < .001, b = .52, t(60) = 6.54, p < .001). These results demonstrate that childhood abuse predicts a broad range of complex dissociative symptoms in adulthood, and highlight the importance of comprehensive assessment for dissociation in PTSD research and treatment.

Topic areas:
Dissociative Disorders
PTSD
Women
McLean Research Day 2017

Program Description

Poster # 110
Time: 1:50-2:45pm

Presenting Author: Maya Rieselbach, Research Coordinator, BA

Co-Authors: Elena Stein, BA; Julia Cohen-Gilbert, PhD; Dana Sarvey, MD; Jessica Feinberg, LICSW; Chad McWhinnie, PhD; Marisa Silveri, PhD

Title: Evidence of Significant Symptom Change during Short Term Residential Treatment of Dually Diagnosed Adolescents

Key words: adolescent, treatment, substance abuse, dual diagnosis, symptom change

Background: Adolescence is a developmental time period characterized by rapid changes in the brain, placing teens at high risk for initiation and escalation of substance use, as well as manifestation of psychiatric conditions. Not surprisingly, the majority of adolescents seeking substance use treatment have co-occurring psychiatric disorders. Such comorbidity is associated with poorer medical and psychosocial outcomes than those diagnosed with one disorder alone. Though research supports use of an integrated treatment approach for dual-diagnosis populations, treatment services for adolescents often focus on either substance use or psychiatric health. In order to enhance dual-diagnosis treatment approaches, the efficacy of such programs needs to be established.

Methods: The current study examined 442 patients (ages 13-19, mean age = 17.0 ± 1.14 years) enrolled in a two-week residential treatment program for dually diagnosed adolescents. Within 48 hours of intake and within 24 hours of discharge, participants completed a battery of clinical assessments and self-report measures including the Center for Epidemiologic Studies Depression Scale (CESD), Multidimensional Anxiety Scale for Children (MASC), and Difficulties in Emotion Regulation Scale (DERS).

Results: Among this adolescent sample, 328 (76%) met criteria for a substance use disorder (SUD), including cannabis (79%), alcohol (51%), hallucinogen (16%), opioid (15%), and benzodiazepine (12%). Psychiatric diagnoses included Anxiety Disorders (80%), MDD (69%), ADHD (41%), Conduct Disorder/ODD (36%), PTSD (17%), and Bipolar Disorder (13%). CESD depression, MASC anxiety and DERS emotion regulation scores were all significantly lower at discharge compared to baseline, demonstrating evidence for reduced symptom severity after treatment (p<.001). There was significant evidence of sex differences for these measures, with females exhibiting higher CESD, MASC and DERS scores at both assessment time points compared to males (p<.001). While there was no significant assessment time x sex interaction observed for anxiety, females showed a greater magnitude of improvement compared to males for depression (p<.01) and emotion regulation (p<.01). Age was significantly correlated with CESD (p<.001) and DERS (p<.01) scores, where older individuals showed greater symptom reduction.

Conclusion: The results of this study demonstrate multiple outcome measures indicative of treatment success in a short-term, dual-diagnosis adolescent residential treatment program. Furthermore, these results suggest some treatment outcomes are influenced by multiple factors such as sex, age, and duration of treatment. To improve quality of treatment, it is important to identify populations that do not experience symptom reduction to the same degree as others. Further research is necessary to establish whether these changes are sustained over time.

Topic areas:
Addiction
Anxiety
Child/Adolescent
Depression
Gender Differences
Precipitated and spontaneous withdrawal from cannabinoids, particularly synthetic cannabinoids, has been documented but is not well understood. Here, we compared precipitated cannabinoid withdrawal following acute injection of CB1 antagonists to CB1-agonist treated mice, and spontaneous cannabinoid withdrawal, via the cessation of daily CB1 agonist administration. Behavioral and physiological measures were evaluated in CD1 mice implanted inter-abdominally with emitters that provide continual monitoring of locomotor activity and core temperature in freely moving animals via a telemetry system. Data were recorded every fifteen minutes for a three hour period, beginning either at the time of antagonist injection or 4-24 hours after the cessation of chronic cannabinoid administration, and beginning at different times relative to the diurnal cycle. The effects of 0.1-10.0 mg/kg rimonabant, a CB1 antagonist with putative inverse agonist properties, and 0.1-10.0 mg/kg AM4113, a neutral CB1 antagonist, were evaluated in CB-naive or CB-experienced animals. To evaluate cannabinoid withdrawal, mice were made cannabinoid-dependent by daily injection, for 5 or 60 days, with 0.03-0.1 mg/kg AM2389, a full CB1 agonist. Injections of low rimonabant doses (0.1-0.3 mg/kg) decreased locomotor activity compared to saline, whereas higher doses increased locomotor activity. Single injections of AM4113 dose-dependently increased locomotor activity. These results were consistent across CB-naive and CB-experienced animals, and were not significantly influenced by light cycle or habituation to the test environment. The cessation of AM2389 administration also produced increases in locomotor activity, with the greatest increase resulting from the cessation of a 5-day regimen of low-dose (0.03 mg/kg) twice daily injections. Neither the administration of CB1 antagonists nor the cessation of CB1 agonist administration produced changes in body temperature. These data demonstrate behavioral similarities between acute injection of cannabinoid antagonists and spontaneous cannabinoid withdrawal, but do not offer evidence of precipitated withdrawal.
A growing body of research has explored the neurodevelopmental effects of maternal immune challenge during gestational and perinatal periods. Previous research has demonstrated that treating mice with immunoreactive agents during sensitive developmental time points in pregnancy yields offspring with a behavioral phenotype reflecting the core features of autism spectrum disorder (ASD). This work is complemented by observations that individuals with ASD exhibit heightened expression of proinflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α). Collectively, these associations present a compelling argument for the interplay of the innate immune response and neurodevelopmental dysfunction characteristic of this disorder. However, considerably fewer efforts have probed the potential role of the adaptive immune response in the etiology of ASD. This relative void exists despite epidemiological associations between autoimmune disease, which is a persistent malfunction of the adaptive immune response, and autism. Toll-like receptor 7 (TLR7), a Toll-like receptor family subtype, plays a critical role in the innate immune response to viral antigens and has been repeatedly implicated in the pathogenesis of systemic autoimmune diseases. Additionally, TLR7 exhibits a unique, developmentally regulated expression pattern within the brain, suggesting its potential role in neurodevelopment. Thus, TLR7 signaling may represent a possible common mechanism relating autoimmune disease and ASD pathogenesis. Pregnant dams were administered subcutaneous injections of imiquimod, a selective TLR7 agonist, or vehicle on gestational days 12.5, 14.5, and 16.5. The offspring were subjected to an array of behavioral assays related to the core phenotypic features of ASD at distinct developmental time points. Pup ultrasonic vocalization testing assessed disparities in mouse pup communication in response to maternal isolation, open-field testing assessed exploratory behavior in a novel environment, social interaction testing assessed propensity for social approach in the open field, and self-grooming testing observed the occurrence and duration of a repetitive behavior. The results presented suggest that the induction of TLR7 signaling in mouse dams during critical periods of fetal development produces an ASD-like behavioral phenotype in offspring. These findings provide additional support for the existence of an immune-mediated subtype of ASD.

**Topic areas:**
- Anxiety
- Child/Adolescent
- Pharmacology
Title: Can Body Mass Index Predict Response to Behavioral Health Partial Hospitalization Treatment?

Key words: weight, depression, anxiety, integration, treatment

Numerous studies have established an association between weight and mental health. Such associations have often been attributed to obesity stigma, which in turn are related to poor mental health outcomes, including depression and anxiety disorders. Previous research has generally confirmed the negative consequences of obesity on mental health outcomes, including increased risk of death by suicide. Additionally, previous work has revealed the negative consequences of mental health issues on weight – including becoming overweight or obese.

The present study examined the potential for body mass index (BMI) to predict treatment response in a sample of adults at the Behavioral Health Partial Program at McLean Hospital. Given previously established associations between physical and mental health, this population is likely to respond to treatment differentially, based on BMI. A sample of 444 patients (53.2% female) was analyzed to determine whether individuals responded to mental health treatment differentially, based on BMI. Mean age of the overall sample was 33.4 (SD = 12.86; range = 18 - 67). BMI at admission ranged from 17 to 50 kg/m², (M = 26.68, SD = 6.06). Of the 392 participants for whom BMI data was available, 43.9% were in the "normal/healthy" BMI category (BMI range 18.5-24.9), 29.3% were in the "overweight" category (BMI range 25-29.9), 24.2% were in the "obese" category (BMI < 30), and 2.6% were in the "underweight" category (BMI > 18.5). Variables were further recorded to represent dichotomous BMI variables: "normal" (43.9%) versus "not normal" BMI (56.1%; underweight, overweight, obese). Participants completed self-report measures, including those assessing symptoms and behaviors (e.g., Behavioral and Symptom Identification Scale, BASIS). Symptoms and behaviors evaluated included depression, interpersonal functioning, self-harm, emotional lability, psychosis, substance abuse, and total symptoms/behaviors. Numerous associations between baseline BMI category and behaviors/symptoms upon admission were revealed. Chi square tests revealed a significant association between baseline BMI and baseline emotional lability, X² (78) = 123.05, p = .001, as well as baseline relationship functioning, X² (217) = 280.85, p = .002. A relationship was observed between baseline BMI and BASIS total, X² (339) = 467.93, p < .001. However, relationships between baseline BMI and psychosis, self-harm, and substance abuse were not significant. Several relationships between baseline BMI and behaviors/symptoms upon discharge were observed. First, chi-square tests revealed a significant association between baseline BMI and depression functioning, X² (209) = 270.88, p = .003, as well as with emotional lability, X²(57) = 75.48, p = .05, relationships [X²(155) = 196.29, p = .01], self-harm [X²(15) = 27.69, p = .02, substance abuse [X²(41) = 66.93, p = .01], and total symptoms/behaviors [X²(285) = 391.76, p < .001]. However, no relationships were observed between baseline BMI and symptoms/behaviors consistent with psychosis. The present findings underscore the importance of tailoring treatment for each patient, particularly during clinical team management group assignment. These results may also be used to inform prioritization of program therapy treatment goals, given limited amount of time in treatment. Future research may examine relationships between waist circumference and/or blood pressure and symptoms/behaviors at admission and discharge.

Topic areas:
Anxiety
Depression
Assessment of Complex Dissociative Phenomenology in Women with Post Traumatic Stress Disorder: Investigating the Issue of Cross-Measure Validity

Trauma-spectrum and dissociative disorders are receiving growing clinical and research attention. The latest revision of the Diagnostic and Statistical Manual (DSM-5) includes the option to specify when dissociative symptoms co-exist with diagnosis of Post-Traumatic Stress Disorder (PTSD). This change draws valuable attention to dissociative symptomatology; however, cross-measure diagnostic validity requires further investigation.

Forty-six treatment-seeking women with self-reported histories of childhood abuse completed diagnostic assessments including the Clinician Administered PTSD Scale (CAPS-5), Structured Clinical Interview for DSM-IV—Dissociative Disorders, Revised (SCID-D), and Multidimensional Inventory of Dissociation (MID). All 46 women met criteria for PTSD on the CAPS-5. Results for 35 participants showed consistency across assessment tools such that 7 met criteria for PTSD only, 5 met criteria for the dissociative subtype of PTSD only, and 23 met criteria for the dissociative subtype of PTSD and a dissociative disorder on both the SCID-D and MID. Results for the remaining 11 participants were inconsistent across assessments; 3 met criteria for a dissociative disorder on the SCID-D or MID but did not meet criteria for the dissociative subtype of PTSD and 8 had discrepant results across assessments. Findings underscore the need for nuanced assessment of complex dissociative phenomenology in PTSD.

Topic areas:
- Dissociative Disorders
- PTSD
- Women
McLean Research Day 2017

Original Research - Clinical
Poster # 115
Time: 1:00-1:50pm

Presenting Author: Mary C. Zanarini, Professor of Psychology

Co-Authors: Christina M. Temes, Ph.D., Laura R. Magni, Ph.D., Garrett M. Fitzmaurice, Sc.D., Marianne Goodman, M.D.

Title: Prevalence Rates of Borderline Symptoms Reported by Adolescents with BPD, Psychiatrically Healthy Adolescents, and Adults with BPD

Key words: borderline personality disorder, adolescence

Objective: The validity of borderline personality disorder (BPD) in children and adolescents has not been studied in a rigorous manner reflecting the criteria of Robins and Guze first detailed in 1970. Methods: Three groups of subjects were studied: 104 adolescent inpatients meeting DIB-R and DSM criteria for BPD, 60 psychiatrically healthy adolescents, and 290 adult inpatients meeting DIB-R and DSM criteria for BPD. Results: Adolescents with BPD had significantly higher prevalence rates of 22 of the 24 symptoms studied than psychiatrically healthy adolescents. Only rates of serious treatment regressions and countertransference problems failed to reach the Bonferroni corrected level of 0.002. Adolescents and adults with BPD had only four symptomatic differences that reached this level of significance, with adolescents with BPD reporting significantly lower levels of quasi-psychotic thought, dependency/masochism, devaluation/manipulation/sadism, and countertransference problems than adults with BPD. Conclusions: Taken together, the results of this study suggest that adolescents report BPD as severe as that reported by adults. They also suggest that BPD in adolescents is not a tumultuous phase of normal adolescence.

Topic areas:
Borderline Personality Disorder
Child/Adolescent
McLean Research Day 2017

Presenting Author: Michael Rohan, Physicist, Lecturer

Co-Authors: Rinah T. Yamamoto, PhD, Kyoko Ohashi PhD, Yunjie Tong PhD, Lia M Hocke PhD, Blaise deB Frederick PhD, Bruce M. Cohen MD PhD

Title: NIRS observation of changes in brain activity following Low Field Magnetic Stimulation

Key words: NIRS, Stimulation, therapy, electromagnetic, Depression

Introduction

Low Field Magnetic Stimulation (LFMS) is a novel electromagnetic treatment for depression. We propose that LFMS acts on an immediate depressed state rather than on deficits specific to particular diagnoses, and that physiologic effects from the fields of LFMS may be present for all subjects but will only be associated with change in mood in subjects that have active mood dysregulation.

Methods

Nine healthy controls were recruited to participate in this randomized, sham controlled, single blinded study. Subjects received either active or sham LFMS on two separate occasions within two weeks. Subjects were fitted with a 12 optode cap providing 9 channels of data in bilateral pre-frontal regions. An additional infrared plethysmograph was placed on the left forefinger to record the pulse for use in the removal of physiologic confounds. Data was then acquired in the resting state for 5 minutes, during LFMS (active or sham) for 20 minutes, and in the resting state for 5 additional minutes in a continuous experiment.

Standard artefact detection and timeseries analysis was performed to detect post-pre change in absolute deoxy- and oxy-hemoglobin levels for all channels as a global measure of change. Repeated measures ANOVA was used, within the FSL software package, to provide a group result.

Results

We observed a significant decrease in global deoxy-hemoglobin concentration (-0.44 +/- 0.25 µM, p<0.04) and a corresponding, trending, increase in oxy-hemoglobin concentration (+1.08 +/- 0.75 µM, p<0.8) associated with LFMS.

Discussion

The electric fields that LFMS induces have a global cortical distribution. Our hypothesis is that this global stimulation results in regional responses that are translated into change in mood. These observations are consistent with this.

Topic areas:

Depression
Imaging
McLean Research Day 2017

Original Research - Clinical

Poster # 117
Time: 1:00-1:50pm

Presenting Author: Maya Zegel, Clinical Research Assistant, B.A.

Co-Authors: Diego A. Pizzagalli, Ph.D., Amy C. Janes, Ph.D.

Title: Nicotine improves symptoms of depression for non-smokers with Major Depressive Disorder

Key words: nicotine, depression, anxiety, mood

Individuals with major depressive disorder (MDD) are twice as likely to smoke tobacco compared to the general population, suggesting a strong link between MDD and nicotine dependence. The link between these disorders is vague; whereas some research suggests nicotine exacerbates MDD, other suggests that nicotine ameliorates depressive symptoms such as reward dysfunction and anxiety. One limitation is that the majority of prior work focuses on individuals with MDD who also smoke, making it difficult to determine how nicotine impacts MDD without also considering the consequences of smoking. To address this limitation, we evaluated the impact of nicotine (a 2mg or 0mg lozenge) on mood and anxiety in non-smoking individuals with (n = 13) and without MDD (n = 11). All participants tested negative for alcohol and illicit drug use and were medication-free at the time of the study. Individuals with MDD had significantly higher baseline depression scores than healthy controls (p < 0.001), as measured by the Hamilton Depression Scale (HAM-D). Specifically, the HAM-D indicated that individuals in the MDD group were moderately depressed, having an average score of 23.46 ± 7.76, while healthy controls were not depressed (1.82 ± 2.18). Anxiety was evaluated by the State-Trait Anxiety Inventory, whereas mood was assessed by the Positive and Negative Affect Schedule (PANAS). Nicotine or placebo was administered in a double-blind, randomized, counter-balanced design. At baseline, individuals with MDD had significantly greater state and trait anxiety scores (p < 0.001) and lower positive mood (p < 0.001) than age- and sex-matched healthy controls. Within the MDD group, a 2mg dose of nicotine reduced state anxiety (p < 0.001) and enhanced positive mood (p < 0.05). Nicotine had no impact on healthy controls, which may be due to a floor effect of anxiety and a ceiling effect of positive mood at baseline. This finding confirms the hypothesis that nicotine ameliorates depressive symptoms in drug-naïve individuals with MDD and suggests that nicotinic agents may be useful in treating certain aspects of MDD. This work also suggests a mechanism through which those with MDD may be drawn to smoke and has implications for treating these co-occurring disorders.

Topic areas:
Addiction
Anxiety
Depression
Imaging
Presenting Author: Ashleigh Rutherford, Clinical Research Assistant II, B.A.

Co-Authors: Alexis E. Whitton, Michael T. Treadway, Manon L. Ironside, J. Eric Jensen, Amy Farabaugh, Thilo Deckersbach, Dost Öngür & Diego A. Pizzagalli

Title: A multi-modal assessment of (hypo)manic and anhedonic symptomology across mood disorders

Key words: Depression, Bipolar, Anhedonia, Hypomania, Mood Disorders

Background: Of the 5.7 million American adults diagnosed with bipolar disorder (BP), an estimated 60% of these cases were initially misdiagnosed as unipolar major depression (MDD). Following an RDoC-based approach, the current study aims to capture important differences in the biological bases of distinct symptom profiles that may be shared but also unique in bipolar versus unipolar depressive disorders, focusing on symptoms of anhedonia (inability to experience pleasure) and (hypo)mania (characterized by an excessive tendency to seek reward). Within the RDoC Positive Valence Systems matrix, we used the construct of reward learning to parse the neurobiological differences that contribute to these unique symptom dimensions.

Method: Across three units of analysis, we evaluated relationships between behavioral and neural indices of reward learning, and anhedonia versus (hypo)mania. First, we assessed the ability to modulate behavior based on positive reinforcement in a probabilistic reward task (PRT). Second, we measured feedback-related potential (FRP) amplitude in response to reward feedback. Third, we measured levels of glutamate (Glu)—a neurotransmitter integral in reward learning—within the anterior cingulate cortex (ACC) using magnetic resonance spectroscopy. To date, 92 depressed subjects (25 with bipolar disorders), and 26 healthy controls have been recruited.

Results: On a self-report measure of anticipatory and consummatory pleasure, both those with unipolar and bipolar mood disorders showed reductions in anticipatory pleasure compared to controls (ts>4.46, ps<.001). However, only individuals with unipolar mood disorders also showed deficits on consummatory pleasure (t=2.83, p=.008), suggesting that consummatory hedonic responding may be preserved in individuals with a history of (hypo)mania. Although there was no relationship between FRP amplitude and either anhedonic or (hypo)manic symptoms, ACC Glu positively correlated with severity of (hypo)mania (r=.38, p=.013).

Conclusion: The results highlight important differences between unipolar and bipolar mood disorders on measures of anticipatory vs. consummatory anhedonia, and point to a key role of glutamate in the pathophysiology of mood symptoms. These findings support the need to closely examine associations between neural activity and symptomology in order to correctly diagnose and predict mood disorders.

Topic areas:
Bipolar
Depression
Imaging
McLean Research Day 2017

Original Research - Clinical

Poster # 119
Time: 1:00-1:50pm

Presenting Author: Ying Cao, Psychiatrist in Charge, Clinical Instructor

Co-Authors: Rodriguez-Villa, Fernando, M.D.

Title: Improving Identification of L-Methylfolate Deficiency in Treatment Refractory Patients via Genetic Testing

Key words: Treatment refractory depression, Personalized and precision medicine, Psychopharmacogenetic testing, MTHFR, L-methylfolate

MTHFR is a gene that encodes the enzyme that converts synthetic folic acid and dietary folate into their active form, L-methylfolate, which is critical in neurotransmitter synthesis; heterozygous and homozygous C667T variants have 45% and 70% reduction in activity, respectively. Several studies have demonstrated L-methylfolate as an effective augmentation strategy with SSRI/SNRI. In a case series, MTHFR testing was done in 23 inpatients on the Short Term Unit North of Mclean Hospital in 2016. Of the 23 patients, selected based on treatment-refractory status and a constellation of inflammation related biomarkers and family and personal medical and psychiatric histories, 20 were MTHFR carriers--including 3 homozygous C667T; 3 homozygous A1298T; 6 heterozygous for both C667T and A1398T; and 4 heterozygous for C667T only and 4 heterozygous for A1298C only. Further, 22 of these 23 patients had serum folate levels drawn and all 22 had levels that were well above the cutoff for folate deficiency. Without genetic testing, none of these patients would “warrant” L-methylfolate supplementation that may lead to clinically significant improvement. Utility of L-methylfolate supplement needs to be further studied but genetic testing, as opposed to traditional serum testing, may offer better identification of patients who may benefit from L-methylfolate supplementation.

Topic areas:

Anxiety
Bipolar
Depression
Psychotic disorders
Individuals who endorse at least some of the criteria for Borderline Personality Disorder (BPD) are known to engage in biased trait appraisal, for example rating faces as less trustworthy than control groups do (Nicol et al., 2013; Fertuck et al., 2013; Miano et al., 2013). Despite the centrality of affective instability to BPD, no research has been done investigating how affective arousal might influence trust appraisal for individuals with borderline traits. 79 participants were recruited from the community. They were divided into a borderline group (3 or more borderline criteria endorsed on the SNAP-2) and a control group (2 or fewer borderline criteria endorsed). Participants completed an affective priming task in which IAPS pictures of negative, positive, and neutral valence were presented before a series of faces. They rated the trustworthiness of each face. We predicted that individuals with borderline features would make lower appraisals of trustworthiness overall, and would be influenced by the negative primes to a greater extent than the control group. An independent samples t-test confirmed that the borderline group made significantly lower appraisals of trustworthiness regardless of priming condition (t(75) = -2.71, p = .008, R2 = .089). There were significant main effects of priming condition (F(1.24, 93.06) = 24.74, p < .001, partial η2 = .248) and group (F(1, 75) = 7.36, p = .008, partial η2 = .089)) as well as a significant Prime x Group interaction (F(1.24, 93.06) = 4.64, p = .026, partial η2 = .058)). As predicted, negative but not positive primes showed exaggerated influence on trustworthiness ratings for the borderline group. We also examined whether rejection sensitivity mediated the influence of negative emotional primes on trustworthiness appraisals. Rejection sensitivity did not account for a significant portion of the variance in negative difference scores (β = -.051, p = .657). Finally, we examined the influence of childhood trauma on trustworthiness appraisal using a series of moderation analyses. Results showed that a model including the interaction term of group and trauma (one subscale of CTQ at a time) did not show a significant F change from models including CTQ emotional abuse (ΔR2 = .023, ΔF(1, 73) = 1.89, p = .173) or CTQ emotional neglect (ΔR2 = .008, ΔF(1, 73) = .619, p = .434). These findings replicate past work showing biased trustworthiness appraisal in individuals with subclinical BPD and extend prior work to show that that this bias may be enhanced in the context of negative affective information. However, rejection sensitivity was not related to trustworthiness appraisals or to priming effects, and childhood trauma neither predicted biased trustworthiness appraisals nor moderated the relation of borderline features and biased trustworthiness ratings.

**Topic areas:**
Borderline Personality Disorder
Special Thanks to the McLean Research Day Planning Committee 2017

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