MIND BRAIN RESEARCH DAY 2017

TUESDAY, MARCH 28, 2017 • 10:30 am - 3:00 pm

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POSTER ABSTRACTS
Background: Treatment with repetitive transcranial magnetic stimulation (TMS) can modulate pathological functional connectivity in patients with major depressive disorder (MDD). Posttraumatic stress disorder (PTSD) is often comorbid with MDD, and TMS can alleviate symptoms of PTSD. We hypothesized that neuroimaging predictors of treatment response and treatment-associated changes in connectivity would be relevant to both disorders, and that clinically meaningful changes would be associated with uncoupling of the default mode and salience networks (DMN, SN).

Methods: Resting state functional connectivity (RSFC) was acquired on participants, before (N=33) and after (n=25) 5Hz TMS therapy to left dorsolateral prefrontal cortex (DLPFC). Analyses used a priori network-based seeds relevant to TMS, MDD or PTSD: the subgenual anterior cingulate cortex (sgACC), DLPFC, hippocampus, and basolateral amygdala; to develop imaging predictors of response and to compare clinically relevant changes in connectivity after TMS. Findings were corrected using cluster-based false discovery rate, plus leave-one-out cross-validation. Imaging results were explored using data-driven multivoxel pattern activation (MVPA).

Results: sgACC to DMN connectivity significantly predicted clinical improvements, as did amygdala to ventromedial prefrontal cortex connectivity. After TMS there was significantly reduced RSFC between the sgACC and DMN, DLPFC, and insula, alongside reduced connectivity between the hippocampus and multiple SN regions. MVPA analyses confirmed seed-based results.

Conclusions: These results are consistent with prior observations of reduced DMN connectivity with TMS in MDD, and demonstrate that TMS uncouples hippocampal connectivity from PTSD-relevant salience regions. These represent network-based biomarkers relevant to commonly comorbid disorders treatable with TMS.
A POTENTIAL RETINAL BIOMARKER OF CEREBRAL AMYLOID ANGIOPATHY

Jessica Alber, PhD; Brian Silver, MD; Brian R. Ott, MD; Peter J. Snyder, PhD

Background: Cerebral amyloid angiopathy (CAA) is caused by the accumulation of amyloid deposits within the walls of the cerebral vasculature, and the clinical diagnosis of CAA is based on visual MRI reading using a four-point descriptive scale (Boston criteria). One prior study suggests that CAA patients show retinal abnormalities that reflect disruption of the cerebral vasculature. The aim of this study was to further examine potential retinal biomarkers of CAA.

Methods: 9 patients (ages 65-77 years) with probable CAA (Boston criteria) and 9 matched (age, sex, education) healthy controls (HC) completed MRI, neuropsychological testing and retinal optical coherence tomography (OCT; Optovue, Inc.). The number and total area of retinal micro-hemorrhages (dot, blot, and flame micro-hemorrhages; blood exudates) were compared to both Fazekas ratings for cerebral white matter hyperintensities (WMH) and cognitive performance, for both the CAA and HC groups.

Results: CAA patients had a significantly higher number (p<.05, d = 1.01) and area (p<.05, d = 1.04) of retinal micro-hemorrhages than the HC group. This effect was moderated by blood pressure, as the CAA group had a significantly higher diastolic (d = .85) and systolic (d = 1.44) blood pressure than the HC group. There was a significant relationship between the number of retinal micro-hemorrhages and Fazekas ratings for WMH in the CAA patients (ρ=.853, p<.01), and this trended towards significance when examining the area of retinal micro-hemorrhages (ρ=.615, p=.078). Finally, there was a relationship between area (ρ=-.695, p<.05) and number (ρ=-.573, p=.107) of retinal micro-hemorrhages and performance on measures of episodic memory in the CAA group.

Conclusions: There were significantly more retinal micro-hemorrhages in a group of CAA patients than a group of healthy controls, and this relationship was moderated by blood pressure. The strong association between retinal micro-hemorrhages and cerebral WMH parallels literature indicating a progressive increase in cerebral WMH with lobar hemorrhages in CAA (Chen et al., 2006). The relationship between retinal micro-hemorrhages, cerebral WMH, and cognitive performance warrants further exploration in larger samples using longitudinal design, and retinal micro-hemorrhages merit further exploration as a potential biomarker of CAA.
THE TRAJECTORY OF SCREEN TIME FROM ADOLESCENCE TO EMERGING ADULTHOOD

Marissa Alert, MS; Roger C. McIntosh, PhD; Maria M. Llabre, PhD; Patrice G. Saab, PhD

Objective: US adolescents spend up to 8 hours daily in screen time. Efforts to reduce sedentary time have often focused on identifying its correlates. However, little is known about the trajectory of adolescents’ screen time or factors that predict it. This study examined change in screen time from age 13 to 23 and its predictors in a representative US sample.

Method: Adolescents (N=3,705; 46.3% boys) from the National Longitudinal Study of Adolescent to Adult Health’s public-use data self-reported their screen time (hours/week watching TV and videos, and playing video/computer games) in 1994, 1996, 2001, and 2008. Piecewise latent growth models within a cohort-sequential design modelled screen time from ages 13-18 and 19-23 years. Predictors of change for each piece were gender, parental education and limits on screen time, household income, perception of neighborhood safety, race/ethnicity, body mass index, physical activity (PA), and employment status.

Results: Adolescents spent an average of 24.99 hours/week in screen time at age 13 and more than 14 hours/week until age 23. Screen time decreased 1.27 hours per week per year from age 13 to 18, then increased .39 hours per week per year from age 19 to 23 (ps<.001). From 13 to 18, decrease in screen time was associated with feeling safe in one’s neighborhood (b=2.70, p=.01), having parental limits on screen time (b=1.22, p=.02), and being Asian American (vs. white; b=2.27, p=.02). From 19 to 23, African Americans (b=-1.13, p<.001) and Asian Americans (b=.67, p=.04) had a lower increase compared to whites. More bouts of PA were also associated with lower increase in screen time (b=-.04, p=.03) during emerging adulthood. Participants who were only in school (b=.43, p=.01) or neither in school nor working (b=.91, p<.001) had a greater increase in screen time than those who were only working.

Conclusion: Interestingly, screen time increased after the age of 18, a point when many transitions, such as the entry into college, often occur. However, given the high levels of screen time maintained from age 13 to 23, effective means of curbing screen time during these developmental periods are needed. Furthermore, since the factors associated with change in screen time from ages 13-18 and 19-23 differed, this may be important to consider when developing sedentary behavior interventions.
FEASIBILITY OF LOW-FIELD SYNCHRONIZED TRANSCRANIAL MAGNETIC STIMULATION (sTMS) FOR TREATMENT OF BIPOLAR DEPRESSION

Jorge Almeida; Swearingen, H; Tirrell, E; Gobin, A; Carpenter, LL

Background: Repetitive Transcranial Magnetic Stimulation (rTMS) is an effective treatment for Major Depressive Disorder (MDD) and is based upon delivery of focal high-energy pulses of electromagnetic stimulation. However, rTMS is not approved for the treatment of depression in Bipolar Disorder because of the risk of switch to mania with such high energy stimulation. Recently, a device that delivers low-energy magnetic brain stimulation using sinusoidal-waveform showed promising treatment effects. We aim to examine preliminary feasibility, efficacy, safety, and tolerability of low-field magnetic stimulation synchronized to a participant’s intrinsic alpha frequency (IAF) (synchronized TMS, or sTMS) for treatment of depression in BD.

Methods: Subjects with bipolar disorder type 1 in a depressive episode with a baseline Montgomery-Asberg Depression Scale (MADRS) ≥ 20, a Young Mania Rating Scale ≤ 12 and taking a mood stabilizer entered the study. The subjects participated in a six-week open label treatment trial (trial registration: NCT02839798) of a device that used three rotating neodymium magnets to deliver sTMS treatment. IAF was determined from a single-channel EEG prior to first treatment. Per protocol (PP) analysis was based on MADRS scores and intent to treat (ITT) analysis was based on Inventory of Depressive Symptomatology self-rated version (IDS-SR).

Results: Preliminary results of this ongoing trial compromised 4 subjects. Two subjects completed the trial per protocol, one discontinued the trial within the last week due to perceived non-response, and one was discontinued from the trial by the investigators due worsening of symptoms. Percent change in IDSSR scores (from baseline to last available observation) were improvements of 25%, 35.9% and 16%; and worsening of 14.75%. Adverse events possible related to sTMS treatment to date include: increased anxiety, and irritability, distractibility and lower attention span, suicidal thoughts, and headache.

Conclusions: Although preliminary, these results suggest that sTMS may be feasible but its efficacy as a potential adjunct treatment in bipolar depression still needs to be further evaluated.
Background: Psychogenic Non-Epileptic Seizures (PNES), while gaining recognition, are frequently diagnosed without adequate evaluation. Making a diagnosis of PNES without appropriate workup can lead to mismanagement of other serious and potentially reversible conditions.

Case History: We describe an 18 year old female admitted to a freestanding psychiatric hospital inpatient unit for roughly 1 month of failure to thrive, anxiety, catatonia, and attacks of shaking initially concerning for PNES in the wake of numerous psychosocial stressors. The patient was repeatedly transferred to a medical emergency department for seizure evaluation, however workup was limited based on reported suspicion of PNES. On the third such occasion a brain MRI demonstrated sequelae of epileptic seizure and she was transferred to a tertiary care center Neuro ICU for status epilepticus confirmed by EEG. Her seizures were adequately treated and Anti-NMDA receptor encephalitis was confirmed with positive CSF antibodies. Treatment included IVIG, methylprednisolone, and a full course of rituximab. After a 2 month medical hospitalization, she had nearly returned to baseline and was discharged home.

Conclusions: Patients with PNES are most frequently diagnosed with conversion or somatoform disorder and only one case report of association with Anti-NMDA Receptor Encephalitis appears in the literature. Anti-NMDA Receptor Encephalitis is rare and presents with an array of neuropsychiatric symptoms making early diagnosis difficult thus delaying treatment and prolonging recovery. Early diagnosis of PNES without appropriate workup may influence subsequent providers’ care and cause delay in accurate diagnoses of such conditions and thus affect prognosis and recovery.
ELUCIDATING THE SYNERGISTIC EFFECTS OF BMP SIGNALING AND THE ACTIVATION OF FOXO TRANSCRIPTION FACTORS IN GLIOBLASTOMA

Amanda Audesse, BS; Nelli S. Lakis, MD, MSc; Douglas Anthony, MD, PhD; Alexander Brodsky, PhD; Ashley E. Webb, PhD

Aging is the greatest risk factor for most cancers, including glioblastoma multiforme (GBM). GBM’s poor patient outcomes may be attributed to ineffective elimination of stem-like cells present within the tumor. Our preliminary data from both clinical and molecular approaches suggest that the stem cell regulator FOXO3 and the quiescence-promoting BMP signaling pathway may act synergistically to promote cell cycle exit of GBM tumor-initiating cells. BMP treatment of glioma cells leads to increased FOXO3 levels, while ablation of FOXO3 through CRISPR increases cell cycle entry. Immunohistochemical analyses of multiple tumor-initiating markers including SOX2, Nestin and CD133 on a cohort of Grade IV GBMs show an inverse relationship between the intensity and extent of the tumor-initiating markers and FOXO3a. Further analyses of nuclear and/or cytoplasmic localization of FOXO3a is still under investigation. Elucidation of the molecular mechanisms at the nexus of these pathways may allow further manipulation of the stem cells from a reversible quiescent-like state to a permanent cell cycle arrest in order to reduce their tumorigenicity and improve patient survival.
GABAergic synapses are crucial regulators of the excitability of VTA dopaminergic neurons. Our previous work has shown that these synapses undergo nitric-oxide dependent long-term potentiation (LTPGABA) that is sensitive to both drugs of abuse and stress (Polter and Kauer, EJN, 2014). It remains unknown, however, whether this phenomenon is specific to certain circuits within the complex structure of the VTA. GABAergic synapses in the VTA arise from both local neurons and from long-range projections from areas such as the rostromedial tegmental nucleus (RMTg). Furthermore, dopaminergic neurons within the VTA are heterogeneous, with distinct populations projecting to the NAc and the prefrontal cortex. While this region has been highly studied, plasticity and cell-type specific properties of its inhibitory circuitry are still not well understood. Given the importance of VTA function in stress-linked disorders such as substance abuse and depression, a better understanding of plasticity within inhibitory subcircuits of the VTA and how they are modulated by stress may reveal circuit-level mechanisms underlying such diseases.

Here, we use viral-mediated expression of channelrhodopsin to optically isolate GABAergic synapses in the VTA from cells originating either from the RMTg or locally from within the VTA. With the isolated synapses we tested both basic synaptic properties and the circuit specificity of LTPGABA induced by the nitric oxide donor, SNAP. Both synapse types were found not to significantly co-release glycine or glutamate, having primarily DNQX and strychnine insensitive post-synaptic currents. The two synapse types differed with respect to short-term plasticity, with paired pulse ratios that suggested that VTA to VTA synapses have a higher release probability than RMTg to VTA synapses. In terms of LTPGABA, we found that VTA synapses reliably expressed LTP but only onto putative DAergic cells (Ih+). Non-dopaminergic (Ih-) neurons on average did not display LTPGABA, though a small percentage of those did significantly potentiate. These data suggest that local GABA neurons are capable of exhibiting LTPGABA on most cells in the VTA but that local inputs onto certain subtypes of Ih-neurons may not express LTPGABA. In contrast, inhibitory synapses arising from the RMTg do not express LTP in either Ih+ or Ih- cells. Taken together, our studies indicate that subcircuits within the VTA differ in their expression of LTP at inhibitory synapses, allowing differential modulation of these inputs by experience.
THE INFLUENCE OF EARLY LIFE STRESS AND PTSD ON FUNCTIONAL NETWORK ORGANIZATION: A NOVEL APPLICATION OF CONVERGENCE ANALYSIS

Jennifer Barredo, PhD, Linda L. Carpenter MD, Mascha van ’t Wout-Frank PhD, Emily Aiken MA, Causey Dunlap BA, Benjamin D. Greenberg MD, PhD, and Noah S. Philip MD

Background: Childhood trauma and posttraumatic stress disorder (PTSD) are associated with neural network disruption, but the impact of childhood trauma and PTSD on systems-level network organization is not well-characterized. Here we use convergence, a novel measure of functional network overlap, to examine the influence of childhood trauma and PTSD on neural organization.

Methods: Resting state MRI networks were defined in 92 participants using independent component analyses (ICA) in discovery (PTSD=31, controls=31) and replication datasets (PTSD=15, controls=15). Pearson’s correlations assessed spatial similarity between discovery and replication datasets, and between datasets and atlas networks from healthy individuals. Convergence, the voxelwise sum of ICA networks, was calculated. Subject-level statistics were entered into general linear models evaluating the impact of trauma severity (Childhood Trauma Questionnaire total; CTQ) and PTSD diagnosis.

Results: Spatial similarity between discovery and replication datasets, and between discovery and atlas networks was R2=0.57 and 0.31, respectively. Convergence between memory/salience and visual networks was influenced by CTQ (p=0.007), and there was a PTSDxCTQ interaction on affective and attention network convergence (p=0.005). In the interaction, in PTSD patients CTQ severity was associated with greater convergence, whereas the opposite was observed in controls.

Conclusions: Segregation of threat-detection systems in healthy trauma-exposed controls suggests resilience to pathological interference, a potential source of network disruption in PTSD. Greater network overlap between threat processing, and memory and/or affective systems in individuals with PTSD corroborates prior PTSD literature. Weak concordance between study and atlas networks cautions the use of atlases based on healthy individuals for psychiatric populations.
DISSOCIATING CIRCADIAN AND HOMEOSTATIC CONTRIBUTIONS TO PAIRED-ASSOCIATES LEARNING IN YOUNGER AND OLDER ADOLESCENTS USING 28-HOUR FORCED DESYNCHRONY

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Introduction: Learning is affected by sleep; less understood is the role of circadian timing. In adolescence, where learning is at a premium, marked shifts occur in both sleep and circadian biology. Understanding the roles these two systems play in learning across adolescence is important for both scientific and policy reasons. To this end, we used a forced desynchrony protocol in which independent and interacting effects of sleep and circadian rhythms can be separated to examine the issue. In humans, the circadian pacemaker typically synchronizes, or entrains, to the natural 24-hour light-dark cycle, and endogenous circadian phase and homeostatic load (time awake since an individual’s last sleep period) are coupled. In our forced desynchrony protocol the day is artificially extended to 28-hours, each cycle beginning 4 hours later than the cycle preceding it. This protocol allows for the participant’s subjective day to be decoupled from their intrinsic circadian timing. Thus independent effects of circadian rhythms and time awake upon cognitive processes can be easily measured.

Methods: Learning was measured in 18 younger (11F; 9.6-13.4 [11.9±1.0] years) and 18 older (8F; 13.5-15.9 [14.4±0.67] years) adolescents who completed 12 cycles of forced desynchrony with 16.33 hours awake and 11.66 hours sleeping in each cycle to decouple sleep-wake timing from circadian rhythms. Every 2-hours during waking, participants learned 6 randomly presented word pairs and were asked to recall one word of each pair after a 10-minute delay. Memory was scored for successful recall (i.e., hits) and mismatched items (i.e., false alarms). Accuracy, indicating robustness of recall, was calculated as the difference of hit and false alarm rates. Accuracy scores were z-scored within-participant and tagged for endogenous circadian phase (0°=dim light melatonin onset; 60° bins) and homeostatic load (hours awake; 3.5 hour bins). Accuracy scores were submitted to mixed-effects models assessing independent and interacting effects of circadian phase, homeostatic load, and age group.

Results: Independent of circadian phase, memory accuracy deteriorated with longer time awake (F(4,2566.01) = 15.57, p<.001); no independent (F(5,2569.69) = 0.85, p = .51) nor interacting (F(20,2568.96) = 1.00, p=.47) circadian effects were observed. No main-effect of age was observed, yet a significant interaction of age and time awake (F(4,2566.01) = 2.49, p=.041) indicated older adolescents had an attenuated decay in the middle hours (~9 hours awake) of the waking day.

Conclusion: These data indicate that effects of time awake on learning in adolescents can be separated from circadian influences. Younger adolescents were more susceptible to the impact of homeostatic load than older adolescents. These data underscore the importance of considering developmental changes in sleep and circadian rhythms in policy and educational settings.

Support (If Any): These data were supported by R01MH52415, R01MH01358, R01MH076969, T32MH019927, K01MH109854.
THE ASSOCIATION BETWEEN WHITE MATTER COHERENCE AND PTSD BEFORE AND AFTER REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION

John Bellone, PhD; Melissa Edwards, MA; Stephen Correia, PhD, ABPP-CN; Jennifer Barredo, PhD; Linda L Carpenter, MD; Noah S Philip, MD

Introduction & Objectives: Prior research indicates that posttraumatic stress disorder (PTSD) is associated with changes in white matter coherence. However, it is unclear how this relationship affects treatment response in cortical stimulation paradigms, such as repetitive transcranial magnetic stimulation (rTMS). Our objective was to examine the association between white matter coherence (pre-treatment only) and PTSD symptoms in patients with co-morbid PTSD and Major Depressive Disorder before and after a course of rTMS.

Participants & Methods: Participants (n = 12 Veterans and 10 non-Veterans; mean age = 53) underwent pre-treatment MRI with diffusion tensor imaging (DTI) and completed a self-report measure of PTSD symptomatology (PTSD Checklist for DSM-5; PCL-5) pre- and post-rTMS. This was an unblinded study involving up to 40 rTMS sessions delivered at 5 Hz over the left prefrontal cortex. We computed baseline fractional anisotropy (FA; a DTI measure of white matter coherence) in several pathways: the corpus callosum (fornix, genu, and splenium), right and left corticospinal tract, superior longitudinal fasciculus, uncinate fasciculus, and cingulum. We then correlated these values with pre- and post-treatment PTSD symptoms and percent symptom change. Three participants were lost to follow-up and were excluded from the post-treatment analyses.

Results: Lower white matter coherence (i.e., lower FA) in the genu of the corpus callosum was associated with worse pre-treatment PTSD symptoms (higher total PCL-5 score; \( r = -0.692, p < 0.001 \)). More specifically, lower genu FA was associated with higher PCL-5 subscales of intrusion/re-experiencing (\( r = -0.464, p < 0.05 \)), avoidance (\( r = -0.497, p < 0.05 \)), negative alterations in mood or cognitions (\( r = -0.589, p < 0.01 \)), and arousal (\( r = -0.594, p < 0.01 \)). Avoidance symptoms were also associated with lower FA in the fornix (\( r = -0.494, p < 0.05 \)) and higher FA in the left corticospinal tract (\( r = 0.429, p < 0.05 \)). After rTMS, the relationship between lower genu FA and more re-experiencing symptoms remained significant (\( r = -0.557, p < 0.05 \)) and trended toward significance with total PCL-5 score (\( r = -0.444, p = 0.057 \)). Elevations in re-experiencing, avoidance, and arousal symptoms showed correlations with higher FA in the corticospinal tracts (\( r \) ranged from \( 0.470-0.519, p < 0.05 \)). Greater percent total symptom change trended toward significant correlation with lower FA in the right uncinate fasciculus (\( r = -0.446, p = 0.056 \)).

Conclusions: This exploratory study found associations between white matter coherence and PTSD symptomatology mostly in fronto-limbic and callosal pathways at baseline. We observed fewer fronto-limbic associations at post-treatment but an association with the corticospinal tract, a major sensorimotor projection pathway. The implications of these findings for rTMS treatment of PTSD require further examination.
DO RISK FACTORS FOR BIPOLAR DISORDER IMPACT OUTCOMES FOLLOWING TRANSCRANIAL MAGNETIC STIMULATION (TMS) THERAPY FOR DEPRESSION?


INTRODUCTION: Depressed individuals with a bipolar disorder diagnosis are currently considered inappropriate candidates for treatment with standard “on-label” Transcranial Magnetic Stimulation (TMS) because the evidence base for efficacy and safety was derived largely from clinical trials that included only patients with unipolar major depressive disorder (MDD). Features of bipolarity exist along a spectrum, and the clinical history of some MDD patients referred for TMS therapy suggest a bipolar diathesis even when threshold diagnostic criteria for a bipolar affective disorder are not met. The Mood Disorders Questionnaire (MDQ) is a three-part, self-report questionnaire used by the TMS clinic at Butler Hospital to screen for bipolar disorder. To address the question of whether bipolar diathesis is relevant to TMS therapy outcomes, we identified a subset of MDD patients treated in the TMS clinic who endorsed one or more bipolar symptoms and/or reported a family history positive for bipolar disorder on the MDQ.

METHODS: Retrospective chart review data were gathered for n=105 consecutively treated TMS patients who completed the MDQ at screening. Data included serial assessment of depression symptom severity with two standardized scales (routinely done at baseline and after every 5 treatments during TMS). Outcomes in TMS patients with heightened bipolar “risk” (n=52) were compared to TMS patients (n=53) without bipolar risk factors. Last-observation carried forward values were used to determine 50% “response” status, and published threshold scores defined “remission” status.

RESULTS: No significant differences were seen between the two groups on clinical or demographic variables including age, gender, use of concurrent medications, and number of TMS treatments received. The two groups did not differ on baseline IDSSR or PHQ9 scores; mean pre-treatment IDSSR for both groups was 47. Response rates did not significantly differ for the two groups (bipolar diathesis 46% vs nonrisk group 54% using IDSSR; 49.2% vs 50.8% using PHQ9). Significantly lower remission rate characterized the bipolar diathesis group outcomes using IDSSR (13.5% versus 30.2%; p=.04) but not when using PHQ9 criteria (23.5% vs. 27.5%).

CONCLUSION: There is no substantive difference in TMS outcomes for MDD patients who have bipolar risk factors compared to those who do not, suggesting that the presence of these symptoms and family history should not raise concern when considering patients for TMS therapy.
MRI ASSESSMENT OF BRAIN IRON CONTENT IN METHAMPHETAMINE USERS

Yosef Berlow, MD; William Hoffman, MD, PhD; William Rooney, PhD

Introduction: Methamphetamine (MA) abuse produces long term changes to the dopamine system that likely contribute to the psychiatric and cognitive symptoms that are seen in MA users. Emerging evidence from preclinical studies suggests that brain iron accumulation plays a role in MA toxicity, both as a biomarker of damage and a potential source of oxidative stress; however, this relationship has not yet been characterized in human MA users. The goal of this study was to utilize in vivo magnetic resonance imaging (MRI) techniques to measure brain iron levels in human subjects with a history of MA dependence and determine if these measurements represent functionally significant biomarkers of MA toxicity. Iron is paramagnetic, and its presence increases the transverse relaxation rate constant (R2) of nearby water protons causing a loss of signal intensity on T2-weighted images. Measuring this effect using quantitative MRI techniques allows for in vivo investigation of the effects of MA on the distribution of brain iron.

Methods: MRI datasets were acquired from 27 currently abstinent MA users and 27 aged matched healthy control subjects. Series used in this study included a high-resolution, T1-weighted MPRAGE, T2-weighted TRSE, Turbo Spin Echo TSE) sequences acquired with three different echo times and a 3D proton density (PD) sequence. R2 (≡1/T2) maps were calculated at each voxel using a monoexponential decay function. Maps of the fractional macromolecular (fM) content were created by normalizing PD images intensities to the peak intensity values of voxels within the cerebrospinal fluid. Parametric maps of the distribution of iron content were then calculated using a relaxometry model incorporating the combined effects of fM and iron content. These parametric iron maps were registered to a common brain space. The effect of MA on regional iron distribution was assessed using both region of interest analysis and voxelwise linear models. Additional analyses were also conducted using the R2 and fM maps, as well as T2-weighted signal intensity measurements.

Results: Using quantitative relaxometry measures that are specific for iron, this study was unable to detect any differences in regional iron content in former MA users when compared to aged-matched healthy control subjects. These measures yielded values for iron and fM that were in substantial agreement with literature values. These measures also detected strong age associated increases in iron content within basal ganglia regions consistent with previous reports providing a positive control for these methods. While no group differences in iron accumulation were found, the MA group had significantly reduced fM values in the thalamus, suggesting increased tissue water content in this region.

Discussion: Contrary to the proposed hypothesis, this study found no evidence of altered iron accumulation in abstinent MA users, suggesting that iron accumulation is not a useful biomarker of MA toxicity. This finding is in marked contrast to a study in nonhuman primates which demonstrated an MA induced increase in iron accumulation that was similar to the effects of advanced aging. The discrepancy between these findings is likely due to interspecies differences in brain iron accumulation.
The Pupillary light reflex (PLR) is a motor reflex controlled by the parasympathetic division of the autonomic nervous system. While pupillary constriction is reflexive, it can be influenced by cognitive factors (Noga, Moyal, & Henik, 2015). The objective of the study was to assess group differences between participants with Autism Spectrum Disorder (ASD) and Typically Developing (TD) individuals in their PLR response at baseline, and in response to a cognitive task with and without social content. ASD participants (N = 12) with average IQ scores were recruited from the Rhode Island Consortium for Autism Research & Treatment (RICART). TD participants (N = 8) were recruited via outreach to local colleges. Groups were matched on IQ and chronological age. Participants ranged from 18-25 years of age. Participant’s PLR was measured for three trials across baseline, social and nonsocial conditions with a Compact Integrated Pupillograph CIP (AMTech, Weinham, Germany). Experimental protocol was carried out in a room with ambient light measured at the CIP to be 1.50 +/- 0.50 LUX. PLR was assessed in 3 conditions: baseline, social and nonsocial cognitive load. There were 3 runs per condition. During nonsocial conditions participants listened to verbal stimuli consisting of randomly generated numbers prior to the PLR test. They were asked to listen and remember how many odd or even numbers were spoken and then report that after each PLR. During the social conditions participants listened to sounds selected from the International Affective Digitized Sounds (IADS) (Bradley & Lang, 1999). They were asked to remember how many positive or negative sounds were presented and report that number after each PLR run. PLR was averaged across three trials in each condition. A repeated measures ANOVA was conducted comparing the effects of group on PLR during baseline, social, and nonsocial conditions. Results revealed a significant effect of condition on response latency (F(2,17)=28.06, p<.001). Paired sample t-tests revealed a significantly delayed PLR (longer latency) for baseline (M = 264.62, SD = 24.88) vs. nonsocial (M = 250.03, SD = 20.07) conditions (t(19) = 5.62, p<.0001) and for baseline vs. social (M = 244.93, SD = 25.00) conditions (t(19)= 7.10, p < .0001), but not between social and nonsocial conditions (t(19) = 1.58, p = .13). Main effects of group and the interaction between group and condition did not reach significance within the model. Differences between baseline and cognitive conditions indicate that top-down cognitive processing may affect the latency of the PLR. This is consistent with research showing alteration of the PLR by executive functions (Noga, et al., 2015). Baseline and group differences were not detected possibly due to sample size, but evidence has been reported for altered PLR in individuals with ASD (Fa, Mile, Takahashi, & Yao, 2009). Continued data collection will allow for a more sufficiently powered test of overall group differences in PLR and potential differential impact of cognitive load on PLR in individuals with ASD.
REPRODUCTIVE COERCION AND SEXUAL CONSENT AMONG HIGH SCHOOL YOUTH

Bogen, Katherine, BA; Oesterle, D.W., BS; Krahe, P., B.A; & Orchowski, L.M., PhD

Reproductive coercion (RC), defined as threats or acts of violence against a partner’s reproductive health or decision making, is a significant public health challenge. RC is associated with higher rates of unintended pregnancy, increased risk for STI/HIV, and often co-occurs with other forms of intimate partner violence (Alexander et al., 2016; Miller et al., 2010). Research documents high rates of RC (13.5%-16%) of RC among high school girls (Kazmerski et al, 2015; Northridge et al, 2016).

Recent publications of the Centers for Disease Control and Prevention call for researchers and program developers to examine how sexual assault prevention programs might address cross-cutting behavioral health outcomes. It is feasible that sexual assault prevention programs which empower participants to understand sexual consent in their relationships may foster sexual agency, and thereby decrease rates of RC. Towards the goal of exploring intersecting targets within sexual assault and STI/HIV intervention, the present study sought to investigate the relationship between condom use, likelihood to garner sexual consent, and likelihood to perpetrate or receive RC among 10th grade Rhode Island high school students. We posited that perpetrators of RC would be less likely to garner consent with a sexual partner or use a condom at their last experience of sexual intercourse, and that recipients of RC in the past year would be less likely to garner consent in sexual relationships and less likely to use a condom at their last sexual intercourse.

Data were gleaned from a larger examination of sexual assault prevention among 10th grade students in Rhode Island (N = 2204), among 21 schools (38% public, 52% charter, 10% private). Students who were sexually active were included in these analyses, resulting in a sample of 451 students (46.9% Male, 29% Female, 2.2% Transgender). Participants reported their sexual orientation as 82.2% straight/heterosexual, 10.8% bisexual, 2.0% gay/lesbian, and 1.5% queer. According to school-wide data 46% of students identified as a racial or ethnic minority.

Participants completed measures of condom use (Youth Risk Behavior Survey, 2015), use and receipt of reproductive coercion (Miller et al., 2011; Cook-Craig et al., 2014), and likelihood to discuss consent with a partner (McMahon et al, 2010; White House Task Force, 2014). Condom use was operationalized as use of a condom at most recent experience of sexual intercourse. Four items were summed to create an index of the extent to which the student actively sought consent during a sexual situation (Cronbach’s alpha = .88). Four items (two assessing RC victimization, two assessing RC perpetration) were utilized to identify past year RC perpetration and victimization (Cronbach’s alpha = .81 and .76, respectively). Only students that had vaginal or anal sex (N = 331) were included in analyses.

Data revealed that 18% of the sample experienced RC (15% of sexually active boys, 28% of sexually active girls), and 5% perpetrated RC (3.5% boys, 5.5% girls) in the past year. A series of t-tests suggested that perpetrators of RC (M = 14.75, SD = 5.96) were less likely to garner consent compared to non-perpetrators of RC (M = 10.28, SD = 7.82), t (18.28) = 2.38, p < .05. Likelihood to seek consent did not differ as a function of prior experience of RC. Data trended towards a difference in likelihood to garner consent between students who reported condom use at their last sexual encounter (M = 15.27, SD = 5.54) compared to those who did not (M = 13.90, SD = 6.33); t (271) = -1.83, p = .07

Increased likelihood to seek consent from a partner may protect against RC perpetration. Interventions aimed at RC reduction should therefore target potential perpetrators by highlighting the importance of consent and consent-seeking behaviors. These findings help to bolster arguments against victim blame by placing the responsibility for preventing sexual violence on perpetrators.
ADDITIVE GENOMEWIDE EFFECTS OF OPIOID DEPENDENCE: EVIDENCE FOR GENETIC CORRELATION WITH CHILDHOOD TRAUMA

Leslie Brick, PhD; Lauren Micalizzi, PhD; Marisa E Marraccini, PhD; Valerie S Knopik, PhD; Rohan HC Palmer, PhD

Introduction: The unprecedented increases in morbidity and mortality associated with the opioid epidemic are indicative of the worst drug epidemic in US history. Previous research has demonstrated a moderate genetic correlation (rG=.49) between interpersonal trauma and generalized vulnerability to drug dependence. The current study aims to expand on this work and investigate whether common genetic markers implicated in childhood trauma are also implicated specifically in opioid dependence (OD).

Methods: Sample. Genome-wide data (N=6,487) was drawn from several larger studies obtained through the National Center for Biotechnology Information Database of Genotypes and Phenotypes, including: The Comorbidity and Trauma Study, Heroin Dependence in Western Australia, the OZ-ALC Study, and ongoing genetic studies of substance dependence at Yale.

Genotyping and imputation. Genotyping was conducted using the IlluminaHuman610 Quad v1, Illumina Human660W Quad v1, and HumanCNV370 Quad v3. The 1000 Genomes Reference Panel was used to identify 5,218 individuals of European descent and autosomal data was imputed using Minimac3. A total of 1,381,076 single nucleotide polymorphisms (SNPs) that passed quality control (imputation r2>.5, call rate >99%, minor allele frequency >1%, Hardy-Weinberg p>0.0001, sample missingness >90%) across N=3,886 unrelated individuals of European American ancestry were used for subsequent analyses.

Measures. DSM-IV OD was assessed using the Semi-Structured Assessment of Drug Dependence and Alcoholism. Based on previous work, childhood trauma was parameterized as a second order factor comprising of the three subscales: physical abuse, sexual abuse, and parental partner abuse.

Statistical Analysis. Case/control genomic-relatedness-matrix restricted maximum likelihood (GREML) estimation was used to determine the proportion of variance in OD or childhood trauma attributed to additive genetic variance. Bivariate models were used to determine the genetic correlation (rG-SNP) across the phenotypes. Analyses controlled for sex, age, and other drug dependence. Parameter estimates for OD were adjusted using a transformation to a liability scale based on prevalence of OD in the population.

Results: The analytic sample consisted of adults aged 18-78 (M=40, SD=11) and was 59% male and 41% female. Approximately half of the sample (48%, n=1870) represented controls and half represented OD cases (52%, n=2024). Results of a logistic regression of OD on relevant covariates of phenotypic data revealed that OD participants were 12 times more likely to report other drug dependence and 2 times more likely to report experiencing childhood trauma, χ2(4)=378, p<.0001.

GREML indicated moderate additive genetic influences on OD, h2SNP-OD=.45 (SE=.04, p<.001), that are partially shared with additive genetic effects on childhood trauma, h2SNP-Trauma=.44 (SE=.024, p=.0269); rG-SNP(OD-Trauma)=.48 (SE=.15, p<.001). The heritability of OD for males and females was similar (h2SNP-Males=.47, SE=.06, p<.001; h2SNP-Females=.33, SE=.08, p<.001) and highly correlated, rG-SNP(Males-Females)=.87 (SE=.16, p<.001).

Discussion: Findings from this study suggest that a moderate portion of the additive genetic effects on trauma is shared with the additive genetic effects on OD. Further, the high rG-SNP across males and females for OD indicates that largely the same polymorphisms contribute to heritability across each sex, despite findings from previous literature suggesting different magnitudes of genetic effect across sex. Although this study was cross sectional in design, findings highlight the possibility that some commonly occurring SNPs influence both the general tendency towards OD and the experience of childhood trauma. Future research should strive to identify which markers implicated in childhood trauma are also implicated in OD. Potential reasons for this overlap are discussed.
Court-involved youths are at particular risk for HIV and other STIs due to high rates of engagement in risky sexual behaviors (Teplin et al., 2003). Parental involvement during adolescence can significantly reduce adolescent sexual risk behaviors (Hutchinson et al., 2003). For court-involved youths, parental involvement may be compromised by parent mental health problems (Tarantino et al., under review) and family functioning—factors that weaken parenting practices shown to be effective in reducing adolescent sexual risk (Elkington et al., 2015). However, the pathways are not clearly defined through which such factors diminish parental involvement and, subsequently, parenting practices. Studying these pathways is vital to strengthening parenting practices that reduce youth HIV/STI risk, especially within families of court-involved youths (Elkington et al., 2015). This study examined associations among parent mental health symptoms, family functioning, and parenting practices within families of court-involved youths. Baseline data were collected from 168 parent-adolescent dyads participating in a longitudinal randomized control trial examining the impact of mental health treatment among court-involved youths. Parent mental health was measured using parents’ Global Severity Index score on the Symptom Checklist-90-Revised. Family functioning was measured via parents’ General Family Functioning score on the Family Assessment Device. Parents completed the Parental Monitoring Questionnaire evaluating their impressions of their youth’s disclosure of information to them (PMQ Disclosure), their solicitation of information from their youth (PMQ Solicitation), and control over their youth’s behaviors (PMQ Control). Parents also completed the Parent Child Sexual Communication (SC) questionnaire evaluating communication with their youth about sex (SC Total), how helpful (SC Helpful) and how comfortable (SC Comfort) they felt when talking about sex with their youth, and the content discussed (SC Number of Topics). Bivariate analyses revealed that greater parent mental health symptoms were significantly related to greater family dysfunction ($r = .26, p < .01$), but not with any parenting practices. Greater family dysfunction was significantly associated with less parent-child sex communication (SC Total: $r = -.16, p < .05$), parents perceiving discussions about sex with their youth as less helpful (SC Helpful: $r = -.35, p < .01$), and parents’ having less favorable impressions of being able to solicit information from their youth (PMQ Solicitation: $r = .24, p < .01$) and their youth’s disclosure of information to them (PMQ Disclosure: $r = .42, p < .01$). Based upon these associations, exploratory multiple regression analyses, using the SPSS 24 PROCESS macro, were conducted to identify pathways illustrating the influence of parent mental health and family functioning on parenting practices. Parent mental health symptoms and parenting practices demonstrated significant, indirect associations, through family functioning, for the following outcomes: parent-child sex communication [SC Total: $\beta = -0.69, CI(-1.45, -0.19), \kappa^2 = 0.08$], parents perceiving sex conversations as more helpful [SC Helpful: $\beta = -1.23, CI(-3.63, -0.11), \kappa^2 = 0.14$], and parents having more favorable impressions of soliciting information from their youth [PMQ Solicitation: $\beta = 0.65, CI(0.22, 1.30), \kappa^2 = 0.07$], and their youth’s disclosure information to them [PMQ Disclosure: $\beta = 1.06, CI(0.53, 1.80), \kappa^2 = 0.11$]. Contrary to extensive research, parent mental health symptoms were only directly associated with family functioning and not parenting practices. However, significant, indirect associations emerged between parent mental health and parenting practices through family functioning. Study findings are important to the juvenile justice system in developing family-based HIV/STI interventions that promote parent mental health and family functioning so as to strengthen parenting practices necessary for reducing youth sexual risk.
CHANGE IN DEPRESSIVE SYMPTOMS BEFORE AND AFTER THE 2016 UNITED STATES ELECTION IN A WOMEN’S PRIMARY CARE CLINIC

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Background: The 2016 United States election campaign was characterized by several major themes that were particularly salient to women’s mental health. No studies have examined change in mood symptoms following past elections, and no studies have examined mood changes among women following the 2016 US election. Past research has examined rates of suicide following US elections and found a decrease in rates, particularly in states that supported the losing candidate.

Objective: In this study, we examined if symptoms of depression and anxiety changed following the 2016 election among women who presented to a primary care practice compared to symptoms in a non-election year.

Methods: 1212 female primary care patients who attended a new patient or annual physical between October and November 2015 and 2016 were included in analyses. All women completed self-report measures of depression and anxiety at the time of their primary care visit. A retrospective chart review was conducted to extract information on women’s symptoms of depression and anxiety, as well as age and insurance type.

Results: After adjusting for insurance type, we found that symptoms of depression were significantly elevated following the 2016 election (F=11.59, p=.037), whereas depression symptoms did not change in a non-election year (F=1.06, p=.48). Change in anxiety following the 2016 US election did not reach statistical significance (F=4.50, p=.12).

Conclusion: Findings from this study provide insight into changes in mental health among female primary care patients following the 2016 US election. Results have implications for elevated behavioral health needs in primary care offices following political events or environmental stressors. Behavioral health services that are integrated into primary care offices may be particularly valuable in managing elevations in mood symptoms and preventing mood disorders among primary care patients.
COGFLEX: A TRANSLATIONAL INTERVENTION FOR PEDIATRIC BIPOLAR DISORDER

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BACKGROUND: Bipolar disorder (BD) has been recognized as one of the most detrimental psychiatric illnesses affecting both children and adults despite our best treatments. In recent years, affective neuroscience research has progressively focused on understanding the neural mechanisms involved in BD with the hopes of improving its diagnosis and treatment. These efforts have elucidated the relationship between pediatric BD and impairment of the neural mechanisms mediating cognitive flexibility, defined as the ability to adapt one’s thinking to changing reward contingencies. During an R21 pilot study, we showed that an 8-week computer-assisted cognitive remediation intervention (referred to as COGFLEX) targeted the neural mechanisms underlying cognitive flexibility and reversal learning in our population of youth with BD. We now present preliminary analyses of the R33 double-blind randomized controlled trial (RCT) phase comparing skill building (SB) and non-skill building (NSB) versions of the COGFLEX intervention on fronto-temporal circuitry in BD youth.

METHOD: This study was IRB-approved at Bradley Hospital and Brown University. Youth ages 7-17 years diagnosed with BD (n=21) were randomly assigned to either the SB or NSB version of the COGFLEX game. The stimulus/reward relationships for the NSB version of COGFLEX remained 100/0 (i.e., stimuli were either all 100% correct [0% punished] or 0% correct [100% punished]). In contrast, the SB version of COGFLEX made increasing use of probabilistic feedback to increase task difficulty (i.e., progression through levels of 100/0, 90/10, 80/20, 70/30, and 60/40 stimulus/reward relationships). Participants played the game twice a week for 8 weeks for 30-40 minutes each session. Participants also completed a 3Tesla event-related fMRI scan with a probabilistic response reversal (PRR) task before and after the 8-week trial to assess if COGFLEX affected neural activation in prefrontal cortex (PFC) striatal-amygda1a regions implicated in reversal learning.

RESULTS: FMRI data analysis using AFNI software showed a significant group (SB, NSB) X time (pre- vs. post-COGFLEX) X PRR phase (acquisition, reversal) interaction. Decomposing this interaction via extracted neural activation using IBM SPSS Statistics showed this was driven, in part, by significant group differences in post-COGFLEX neural activation. There was significantly less activation in the post-central gyrus, the superior temporal gyrus, and the paracentral lobule of the SB vs. NSB group following COGFLEX. Additional analyses revealed that in both the inferior parietal lobule and the superior temporal gyrus, significant differences in neural activation between the SB and NSB group seemingly reversed from pre- to post-COGFLEX. Specifically, the SB group showed greater activation in these regions pre-COGFLEX, but less activation in these regions post-COGFLEX when compared to the NSB group.

CONCLUSIONS: The preliminary analysis of our R33 RCT phase suggests that the SB version of COGFLEX results in greater decrease (normalization) of neural activity than the NSB version. Further work to enroll and study the full planned sample (20 additional participants) based on pre-study power calculations is necessary to fully interpret this data. Such work is important in determining if the SB version of COGFLEX is the active ingredient of neural change that might be harnessed as a potential brain mechanism-based treatment that could reduce the symptoms and restore cognitive function in pediatric BD.
A MODERATOR MODEL OF ALCOHOL USE AND DATING AGGRESSION IN EMERGING ADULTHOOD

Charlene Collibee, MA, Wyndol Furman, PhD

Dating aggression is a significant and serious public health problem, with its prevention now a priority in the United States (White, 2009). A growing body of research has found associations between alcohol use and dating aggression in adolescence and emerging adulthood (Rothman, Reyes, Johnson, & LaValley, 2011). However, alcohol use does not always result in dating aggression (Schumacher et al., 2003) and aggression can occur in the absence of alcohol (Foran & O’Leary, 2008). A theoretical moderator model posits that the associations between alcohol use and dating aggression varies depending on both background (e.g., individual psychopathology) and situational (e.g., relationship characteristics) risk factors (Leonard, 1993; Leonard & Senchak, 1996; Riggs & O’Leary, 1989). Specifically, alcohol use is thought to be more strongly associated with dating aggression in the context of more individual psychopathology and as well as more relationship risk. No study to date has fully tested these expectations in emerging adulthood. Further, the current literature on alcohol use and dating aggression has been limited by a reliance on cross-sectional designs, and very little work has longitudinally examined these processes within a specific relationship. This study addressed current gaps in the literature by empirically examining a theoretical moderator model between alcohol use and dating aggression involvement (i.e., psychological, physical, and sexual victimization and perpetration), using an intensive longitudinal design.

Six waves of community based data were collected from 120 participants (60 females) ages 18-25, within a romantic relationship. Electronic data collection occurred once a month, and spanned six months. Participants were screened for prior dating aggression involvement either in their current relationship or a past relationship in order to recruit a higher risk sample. The measures used to assess relevant variables were: verbal, physical, and sexual dating aggression involvement (CTS2), alcohol use (AUDIT, SMAST, DDQ, NIAAA binge drinking), relationship risk factors (NRI, QMI, MJS, RMBM), and individual psychopathology (BDI-II, TSC-40, ASR).

Hypotheses regarding a moderator model were assessed using a series of multilevel models (MLMs) to examine how the links between alcohol use and dating aggression varied by the degree of both individual psychopathology as well as relationship risk. Main effects emerged such that alcohol use, individual psychopathology, and relationship risk were all associated with greater risk for dating aggression involvement. Consistent with a moderator model, interactions emerged between alcohol use and relationship risk for both psychological and physical dating aggression involvement. Specifically, the associations between alcohol use and dating aggression involvement were stronger in the context of more relationship risk. No interactions emerged between alcohol use and individual psychopathology for any form of dating aggression involvement.

The findings are consistent with a moderator model of alcohol use and dating aggression involvement, but only for relationship risk. Findings indicate that the intersection of alcohol use and relationship risk may be especially relevant during this developmental period. Discussion will address potential processes underlying a moderator model of relationship risk and alcohol use. Additionally, the discussion will further consider the potential malleability of both alcohol use and relationship risk as well as implications for intervention and prevention development.
THE ROLE OF AFFECT MANAGEMENT FOR HIV RISK REDUCTION AMONG YOUTH IN ALTERNATIVE SCHOOLS

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Objective. Adolescents in alternative schools for behavioral and emotional problems have an earlier sexual onset and higher rates of sexual risk than their peers. They also often have difficulty managing strong emotions, which can impair sexual decision-making. Human immunodeficiency virus (HIV) prevention programs for these adolescents may be most effective if skills for coping with strong emotions during sexual situations are included.

Method. This paper reports the 6-month outcomes of a three-arm randomized controlled trial comparing a HIV prevention intervention with Affect Management (AM), to a standard, skills-based HIV prevention intervention (SB), and a general health promotion intervention (HP). HP was similar to a general health class, and SB was based on previous effective HIV prevention programs used with community adolescents, while AM included affect management skills in addition to effective HIV prevention skills. Youth (n=377) in two U.S. cities were ages 13 to 19 and attending alternative schools for behavioral and emotional problems.

Results. Multiple logistic regression analyses, adjusted for the baseline scores, age and gender, found adolescents in AM were significantly less likely to report being sexually active at follow-up (80% vs. 91%, AOR=0.28, CI=0.08-0.96) and more consistently using condoms than those in HP at follow-up (62%, vs. 39%, AOR=3.42, CI=1.10-10.63).

Conclusions. Affect management techniques tested in this project, focused on sexual situations, are similar to those that are used in Dialectical Behavioral Therapy (DBT) and in clinical practice. These data suggest that these techniques might decrease risk behaviors and improve the health of adolescents with emotional/behavioral problems.
Previous studies have documented a relationship between embodiment (the perception of localized body-ownership in space) and contemplative practices such as mindfulness meditation. One common behavioral assessment of embodiment includes the rubber hand illusion (RHI), a somatic-perception illusion in which individuals attribute a sense of ownership to a rubber hand. The experimenter induces the illusion by stroking both the participant’s real hand, which is hidden from view, and the rubber hand synchronously. Interestingly, interoceptive awareness seems to be related to this illusion. In this study, we administered the RHI to experienced meditators (N=15) and healthy controls (N=15) and used the Multidimensional Assessment of Interoceptive Awareness (MAIA) to examine differences in embodiment and affective orientation toward bodily sensations between these two groups. We found that meditators reported less intense feelings of owning the rubber hand compared to non-meditators, but there was no significant difference between groups with respect to feelings of disowning the real hand. Further analysis showed that while a general feeling of trusting one’s body correlated with non-meditators’ experiences of disowning their real hand, the ability to not become distracted from unpleasant bodily sensations correlated with meditators’ experiences of disowning their real hand. These results suggest that unique affective dimensions of embodiment and interoception may be related to meditation training.
Over half of Americans receive mental healthcare through their primary care physician. There is a particular need to find innovative ways to disseminate key principles of empirically supported psychotherapy in this setting. Patients treated for major depression in primary care often receive antidepressant medication alone. These patients may not achieve a full response with medication alone, and often want or would benefit from psychotherapy. Narrative communication, or storytelling, refers to people with lived experience talking about their struggles and successful ways of coping, and may offer an alternative way to disseminate effective behavior change principles. In the current study, 12 individuals with a history of depression were filmed by a local film production studio to create a self-help video series. Two psychologists “hosted” the series and related the coping strategies described by the participants to key principles of Acceptance and Commitment Therapy (ACT), an empirically-supported type of cognitive-behavioral therapy that is efficacious for treating depression. The video intervention, titled LifeStories, was divided into four episodes accompanied by a workbook which focused on various ACT concepts, including values, acceptance, and mindfulness. After producing the video series, 11 individuals diagnosed with major depression were recruited from the community who were not receiving treatment from a mental health specialist. These individuals completed clinical interviews and assessments of psychiatric symptoms for 8 weeks total. During the first 4 weeks of the study (baseline), participants received no intervention. For the second 4 weeks of the study, participants viewed 1 episode of the LifeStories intervention each week and provided feedback. The sample was 73% female and 18% Hispanic or Latino, with a mean age of 49.8 and mean education level of 14.8 years. Participants rated video acceptability highly, with a mean of 4.57 on a 1-5 scale, with a “1” being “not at all” acceptable and a 5 being “very much” acceptable. In addition, participants gave the video series a mean rating of 3.74 for “transportation” (how engaged they were while watching the videos), with a “1” being “not at all” engaging and a “5” being “very much” engaging. Qualitative interviews with participants also revealed overwhelmingly positive feedback, with many participants commenting on how authentic the videos seemed. In terms of clinical improvement, depression symptom severity (as assessed by the Quick Inventory of Depression Symptomatology-Clinician Rating or QIDS-C) did not change significantly between weeks 1 and 4 of baseline assessment ($t = 2.06, p = 0.07$, Cohen’s $d = 0.54$). However, after participants received the LifeStories intervention from weeks 4-8, QIDS scores were reduced significantly at week 8 when compared to week 4 ($t = 4.18, p = 0.002$, Cohen’s $d = 1.76$). The next step is to conduct a pilot randomized controlled trial of the new LifeStories intervention compared to an attention control video condition.
ELUCIDATION OF TRANSCRIPTIONAL NETWORKS THAT PRESERVE ADULT NEURAL STEM CELLS

Shleshma Dhakal, Abigail Brown, Megan Gura, Trenton Woodham and Ashley Webb (PhD)

Adult neural stem cells (NSCs) are the source of new neurons in the adult mammalian brain, and are a promising source of regenerative therapies. The brain contains both actively dividing stem cells and very slowly dividing NSCs, termed quiescent NSCs. These quiescent NSCs are the source of proliferative NSCs, are actively maintained, and have the potential to be reactivated and form new neurons in response to external stimuli. While the quiescent NSCs are ultimately the critical reserve population of NSCs, the precise mechanisms by which these cells are maintained and how they are activated remain unknown. Our goal is to determine how quiescent NSCs are directly regulated at the transcriptional level. Our published and preliminary data implicate the longevity-associated transcription factor FOXO3 as a key regulator of quiescent stem cells in the adult. FOXO3 is a central regulator of both aging and stem cells, and mice lacking FOXO3 have an age-related depletion of NSCs. Using ChIP-seq, we identified neural stem cell-specific FOXO3 targets, and found that they include important regulators of cellular homeostasis during aging, including proteostasis and metabolic targets. Using functional assays overexpressing or ablating FOXO factors in NSCs, we found that FOXO3 is a direct regulator of autophagy in these cells, indicating that FOXO3-mediated cellular quality control is a key mechanism for maintaining a healthy pool of NSCs in the adult brain. Together, these experiments provide new insight into how the conserved pro-longevity FOXO transcription factors function in NSCs to regulate cellular homeostasis and longevity.
5 Hz REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION FOR POSTTRAUMATIC STRESS DISORDER COMORBID WITH MAJOR DEPRESSIVE DISORDER

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Background: Standard clinical repetitive transcranial magnetic stimulation (rTMS) for major depressive disorder (MDD) uses 10Hz stimulation to the left dorsolateral prefrontal cortex, yet little is known about the benefits of rTMS for diagnostically complicated patients. Posttraumatic stress disorder (PTSD) is commonly comorbid with MDD, and while rTMS can alleviate PTSD symptoms, ideal parameters remain unclear. We conducted an unblinded study of 5Hz rTMS for comorbid PTSD+MDD and hypothesized stimulation would reduce symptoms of both disorders.

Methods: Participants (N=40) were outpatients with comorbid PTSD+MDD, with at least moderate symptoms despite >6 weeks of stable treatment. 5Hz rTMS included up to 40 daily sessions followed by a 5-session taper. PTSD and MDD symptoms were measured using the PTSD Checklist (PCL-5) and Inventory of Depressive Symptomatology, Self-Report (IDS-SR), respectively. Baseline-to-endpoint changes were characterized using paired-sample t-tests, with Pearson correlations evaluating the relationship between PTSD and MDD changes.

Results: The intention-to-treat population (i.e., consented and completed >1 session) included 35 participants. Stimulation significantly reduced PTSD symptoms from baseline (52.2±13.1) to endpoint (34.0±21.6; p<.001). Twenty-three (65.7%) achieved meaningful clinical response, and 17 (48.6%) dropped below threshold criteria. MDD symptoms decreased from baseline (47.8±11.9) to endpoint (30.9±18.9; p<.001). Fifteen (42.9%) participants demonstrated clinical response and 12 (34.3%) remitted. Changes in PTSD and MDD were highly correlated (r=.91, p<.001).

Conclusion: Significant and clinically meaningful reductions in both MDD and PTSD symptoms were observed following stimulation. The efficacy of 5Hz rTMS for both symptom domains indicates a need for future controlled studies in this comorbid population.
LIFE SATISFACTION AMONG YOUNG AFRICAN AMERICAN ADULTS ATTENDING A PUBLICLY-FUNDED HEALTH CLINIC

Eugene Dunne, MA, Theresa E. Senn, Ph.D., Kate B. Carey, Ph.D., Michael P. Carey, Ph.D.

Introduction: Prior research has found life satisfaction to be associated with health behaviors. For individuals living in socioeconomically disadvantaged urban neighborhoods, however, additional factors are likely to influence life satisfaction, including environmental, psychological, and behavioral health factors. Furthermore, lower SES is associated with higher rates of substance use and mental health challenges. Due to suboptimal health insurance and the high cost of health care, many individuals in urban communities seek health care at publicly funded clinics. The present study explores whether health and environmental factors are associated with self-reported life satisfaction among a younger adult sample of African American patients at an urban sexual health clinic.

Method: The present study is a secondary analysis of 307 African American younger adult patients (Mage = 26.6, SDage = 6.6, 53% male) attending an urban sexual health clinic who participated in a randomized controlled trial (RCT) related to sexual risk reduction. The original RCT was approved by an institutional review board and included 973 participants who were randomized to complete one of two baseline questionnaires: a sexual risk survey or a general health survey. The current sample includes younger African American adults, aged 18 to 44, who completed the general health baseline questionnaire, including the following measures: Medical Outcomes Sleep Scale (MOS), Patient Health Questionnaire-4 (PHQ-4), Drug Abuse Screening Test (DAST), City Stress Inventory, Short Inventory of Problems-2R (SIP-2R), and the Satisfaction with Life Scale. Correlation analyses assessed the bivariate associations among demographic and health-related factors and life satisfaction. Variables with significant bivariate associations were included in a backward elimination linear regression model to determine best fitting model.

Results: Bivariate analyses indicated significant positive associations between life satisfaction and social support (r = .22, p < .001) and frequency of “feeling rested” upon waking (r = .13, p = .019). Conversely, life satisfaction was negatively associated with age (r = -.18, p = .001), sleep problems (r = -.18, p = .001), alcohol-related problems (r = -.13, p = .028), drug use problems (r = -.15, p = .010), city stress (r = -.16, p = .006), anxiety (r = -.32, p < .001), and depression (r = -.28, p < .001). Life satisfaction was not associated with gender or education. Variables with a statistically significant association with life satisfaction were entered into a backward linear regression model with p > .10 as the elimination criteria. Backward elimination resulted in the following variables remaining as significantly related to life satisfaction: age (b = -2.40, p = .017), anxiety (b = -5.32, p < .001), and social support (b = 2.89, p = .004). Feeling rested upon waking also remained in the best fitting model, although this association did not achieve statistical significance (p = .096). Overall, social support, anxiety, age, and waking feeling rested accounted for 15% of the variance in life satisfaction (R^2 = 0.15).

Discussion: The results suggests that African American adults who are younger, less anxious, and report adequate social support are more likely to report satisfaction with life. Restful sleep also appears to be related to life satisfaction, though further investigation is needed. These findings add to the current literature aimed at examining health and social factors impacting the well-being of African Americans living in low-income, urban communities. Publicly-funded clinics may serve as ideal locations to deliver brief, targeted interventions aimed at improving social and mental health factors for individuals of low-socioeconomic status.

Support: The research trial was funded by the National Institute of Mental Health (R01-MH068171; Primary Investigator: Michael P. Carey).
ASSOCIATION BETWEEN NETWORK CONNECTIVITY OF SELECT BRAIN
REGIONS AND COGNITIVE ABILITIES BASED ON DETERMINISTIC SINGLE
TENSOR AND MULTI-FIBER DIFFUSION MR TRACTOGRAPHY

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David H. Laidlaw, PHD, Paul Malloy, PHD, Stephen Salloway, MD, & Sean Deoni, PHD

Background: Diffusion-tensor imaging (DTI) tractography models white matter tracts. Multiple
fiber approaches (e.g., ball-and-sticks) can track fiber trajectory in regions of high fiber crossing
more efficiently than single-fiber methods. Alzheimer’s disease (AD) impacts cortical structural
connectivity due to changes in white matter integrity. AD impacts the precuneus, entorhinal
cortex (EC), and caudal anterior cingulate (CAC). We sought to examine the association between
these brain regions and memory and executive function based on graph theory with a comparison
of metrics derived from single-fiber and multi-fiber tractography.

Methods: Graph theory metric of node degree was derived for precuneus, EC, and CAC
bilaterally (LH, RH) in 42 participants (controls n=13; cognitively impaired n=29) using
deterministic and probabilistic tractography. Analyses were run separately by tractography
method. Linear regression models were conducted with ROI entered as the independent variables
and neuropsychological tests as dependent variables controlling for age and education.
Neuropsychological measures (raw and z-scores) were Trail Making Test B (TMTB) and

Results: Single tensor network: HVLT FR correlated significantly with degree in one ROI: LH
EC (all p<0.020). There were no significant correlations between degree and TMTB in any ROI.
Multi-fiber network: HVLT FR correlated significantly with three ROI: LH EC, LH precuneus,
and RH CAC (all p<0.03). TMTB correlated significantly with LH precuneus (p=0.042).

Conclusion: Multi-fiber tractography may provide a more robust substrate than single tensor for
identifying associations between cognitive function and graph theory-derived network
connectivity in brain regions sensitive to AD.
COPING STRATEGIES, PTSD SYMPTOMS, AND LIFE SATISFACTION: A WORKING MODEL

Jordan Edwards, PhD, Michael Furlong, Ph.D., Nancy Collins, Ph.D., Erin Dowdy, Ph.D., and Amy Cameron, Ph.D.

The present research focused on understanding the roles of coping strategy (avoidant, problem solving, and support seeking) and trauma history in predicting Posttraumatic Stress Disorder (PTSD) symptoms and life satisfaction. Exposure to traumatic events is common in the general population, and lifetime prevalence rates for PTSD are relatively high and are estimated at 8.7% among adults in the United States. Although the psychological impact of highly stressful events can be considerable, the development of PTSD profoundly affects the individual’s overall quality of life.

Structural equation modeling (SEM) was used to investigate the relation between coping strategy, trauma history, PTSD symptoms, and life satisfaction. To decrease measurement error, latent variables were created for PTSD symptoms and life satisfaction. Both the main effects and interactions associated with coping strategy and trauma history were investigated. Three separate SEM models were constructed to investigate avoidant, problem solving, and support seeking coping strategies, which have been shown to be temporally stable traits.

To investigate the hypothesized model in a non-clinical sample, completed data from 326 participants were analyzed. Two separate subsamples were targeted and included community members and college students. Community members were approached at a large shopping center and college students were approached on campus. All participants received an incentive, which included gift certificates, cash, or course credit immediately after completion of the research assessments.

Bivariate analyses failed to support two separate subsamples in terms of demographics, coping strategies, or trauma history; therefore, one combined sample was used for analyses. The demographics of the combined sample were much more similar to the demographics associated with college students than community members.

Overall, 80.1% of participants reported at least one exposure to a wide variety of traumatic events. Hypotheses regarding coping strategies in this sample, which was largely comprised of college students, were not supported. Both problem solving and support seeking coping strategies failed to significantly predict PTSD symptoms. Even more surprising was that in this sample avoidant coping actually predicted a decrease in PTSD symptoms. Results indicated that participants who experienced high levels of traumatic events benefited from a greater reduction in PTSD symptoms compared to those who had experienced low levels of traumatic events.

In all three coping strategies, an increased trauma history predicted a significant increase in PTSD symptoms, and an increase in PTSD symptoms predicted an even greater decrease in life satisfaction. In addition, an increase in trauma history actually predicted a small increase in life satisfaction when not mediated by PTSD symptoms. This indicated that in this sample exposure to traumatic events slightly increased life satisfaction when individuals did not experience adverse effects associated with the exposure. Also unexpected was the finding that avoidant coping predicted a slight increase in life satisfaction while support seeking predicted a slight decrease in life satisfaction.
SUSTAINED ATTENTION IN FOCUSED ATTENTION VERSUS OPEN MONITORING MEDITATION - BEHAVIORAL AND NEUROPHYSIOLOGICAL CHANGES

Kristina Eichel, Gloria Essien, Brendan Cullen, Alec Rogers, Dr. Willoughby Britton

Mindfulness consists of two components, attention regulation and emotional acceptance, which are reflected in the contemplative techniques: Focused Attention (FA), training to hold the focus on a certain object while de-selecting irrelevant stimuli, and Open Monitoring (OM), a moment-to-moment awareness of ongoing experience with no de-selection. Both are integrated parts of mindfulness-based interventions such as Mindfulness-Based Cognitive Therapy. Because these practices are usually offered in an integrated package, the practice-specific effects and their individual contribution to wellbeing have been difficult to determine. However, the creation of separate FA and OM modules allows for the separate effects to be assessed.

The aim of the current study (N=104) was to assess the cognitive, affective and behavioral consequences and neural correlates of each practice separately. The Sustained Attention to Response Task (SART) involves a Go/No-Go task with rare occasions of “no-go” (i.e. not pressing the key) that measures the ability to self-sustain processing of stimuli that otherwise lead to habituation and distraction to other stimuli.

The talk will focus on the consequences on error processing and its neurophysiological correlates, the error negativity (Ne/ERN) and error positivity (Pe) as event-related potentials after an erroneous response. Ne/ERN can be seen as error detection process, whereas the Pe either reflects error awareness and/or affective processing. Dismantling mindfulness in FA and OM can reveal insight into error processing, which then can be dismantled in error awareness and error acceptance, and vice versa.

Other changes of neural and behavioral correlates of sustained attention will also be presented.
DEMAND INELASTICITY AND HIGHER DEMAND INTENSITY ON THE ALCOHOL PURCHASE TASK IS ASSOCIATED WITH GREATER REDUCTION IN DRINKING IN PATIENTS WITH ALCOHOL USE DISORDER

Sarah Eltinge (Undergraduate), Kim Goodyear (PhD), Dave Chavanne (PhD), Paul Wallace (BS), Victoria Long (BS), Robert Swift (MD), Lorenzo Leggio (PhD) and Carolina Haass-Koffler (PhD)

Background: Preclinical and clinical research supports a behavioral economic conceptualization of alcohol use disorder (AUD). The Alcohol Purchase Task (APT) is a behavioral economic measure of an individual’s demand for alcohol and the elasticity (i.e. price sensitivity) of that demand. Several measures may be calculated from the APT: intensity (demand when the price of alcohol is $0), breakpoint (price at which demand is $0), Pmax (the maximum amount a person will spend on alcohol), Omax (the amount of alcohol a person will drink at price Pmax), and demand elasticity (an overall measure of price sensitivity). Each dimension of demand provides insight into some aspect of an individual’s drinking behavior; if such characterizations predict treatment efficacy, they could potentially be used to tailor treatment regimens to individual patients. In a randomized controlled trial (RCT) using doxazosin, an α1 receptor antagonist, we discovered two independent moderators, family history density of alcoholism (FHDA) and blood pressure (BP) that reduced drinks per week (DPW) and heavy drinking days (HDD) in alcohol-dependent (AD) patients. In this study, we explore the hypothesis that baseline scores on the APT moderate the effect of doxazosin as another potentially valuable moderator of alcohol consumption.

Methods: This was a double-blind placebo-controlled RCT testing doxazosin up to 16 mg/day in AD treatment-seeking patients (N = 41). Demand elasticity, intensity, breakpoint, Omax, and Pmax were calculated from the APT, and linear mixed models were used to determine the significance of these metrics in predicting DPW and HDD. Chi-squared analyses were calculated to compare FHDA and BP to the APT.

Results: The interaction of elasticity and intensity of demand at baseline was a significant moderator of the effect of doxazosin on DPW and HDD (p’s < 0.05). Among patients with both elastic and inelastic demand, doxazosin reduced DPW and HDD more in people with higher intensities of demand. However, the reduction was overall greater among patients with inelastic demand than among those with elastic demand (p’s < 0.05). There was no effect for breakpoint, Omax, or Pmax (p > 0.05). Chi-squared tests comparing elasticity, BP, and FHDA indicated the independence of these three mediators (p > 0.05).

Conclusion: These results indicate that a behavioral economic measure of alcohol demand may have utility in characterizing the plasticity of alcohol consumption in AD patients. Previously, we identified a biological marker, BP, and a genetic indicator, FHDA, that may serve the same function. In contrast to these mediators, the APT provides an indication of an individual’s actual drinking behavior and thus is the most closely linked to alcohol consumption; therefore, it is unsurprising that baseline demand elasticity and intensity on the APT are moderators of the effect of doxazosin on alcohol consumption. Furthermore, these results indicate that doxazosin treatment was the most beneficial among patients with inelastic demand and high demand intensity, i.e. those who report that they will consume a high volume of alcohol at any price point and are thus likely to be the most severely addicted. Thus, these preliminary results indicate that doxazosin stands to benefit the most severely addicted patients, which is especially promising given the few treatment options currently available for these patients. In conclusion, the APT characterizes an individual’s drinking behavior in a way that is both easily assessable and clinically relevant and thus holds great promise for use in tailoring treatment regimens for AUD.
**CHRONOBIOLOGICAL DESYNCHRONY AND MENSTRUAL CYCLE LENGTH: PRELIMINARY FINDINGS IN FIRST-YEAR COLLEGE WOMEN**

*Ashley Ernst, BA, Kobi Axelrod, Katie M. Sharkey, PhD., Mary A. Carskadon, PhD., Eliza Van Reen, PhD*

Introduction: The suprachiasmatic nucleus (SCN) of the hypothalamus is the mammalian circadian pacemaker, also referred to as the master biological clock. Measures of the circadian timing system are correlated with morningness/eveningness preference in humans (circadian phase preference). The Horne-Östberg Morningness Eveningness Questionnaire (MEQ) is used as a behavioral marker of circadian phase preference (Horne & Östberg, 1976). A mismatch between the internal circadian system, as indexed by MEQ, and behavior results in circadian desynchrony, which has been implicated in the higher occurrence of certain medical problems, such as cardiovascular disease, gastrointestinal illness, cancer, and female fertility problems. Menstrual cycle lengths shorter than 25 days or longer than 35 days are more likely to be infertile (absence of ovulation). We examined whether 1) sleep patterns and 2) the congruence between circadian phase preference and sleep patterns are associated with menstrual cycle length in first-year university students.

Methods: Women (n=206, mean age=18.6; SD=0.5 y) completed on-line sleep diaries for 9 weeks. Each diary included sleep times and menstrual bleeding (yes/no). Menstrual cycle length (MCL) was the interval from the first day of menstrual bleeding to the next first day of menstrual bleeding. No women included in this sample reported taking oral contraceptives at any time during the 9 weeks. Sleep pattern variables derived for each woman across each menstrual cycle included: mean and standard deviation of reported bedtime (BT), wake time (WT), and total sleep time (TST). Circadian phase preference was determined from the MEQ, completed in week 9 using five standard categories. A sleep timing vs. circadian phase preference “mismatch” score was calculated using the absolute difference between WT categories based on quintile split and MEQ categories (possible scores ranged from 0-4).

Linear mixed-effect models were used to examine 1) the effects of sleep patterns (i.e., mean and standard deviation of WT, BT, TST) on MCL (278 cycles) and 2) the effects of phase preference vs. WT mismatch on MCL in a subset of 188 women (256 cycles). Each woman contributed between 1-3 menstrual cycles.

Results: No significant associations were observed between sleep patterns and menstrual cycle length; however, a trend was seen for WT (beta=.5, SE=.48, p=.09) and BT (beta=.75, SE=.45, p=.1), in both of which later timing was associated with shorter MCL. Overall, average MCL was 27 days (SD=7.1). A significant association between greater mismatch and shorter menstrual cycle length was found (beta=-1.4, SE=.57, p=.02).

Conclusion: Sleep patterns alone were not significantly associated with menstrual cycle length; however, shorter menstrual cycle length was associated with a poor match between circadian phase preference and wake timing. These findings support previous literature that identified extreme circadian mismatch and fertility problems in flight attendants and shift workers. The finding that a circadian phase preference and sleep timing mismatch was observed young women on their self-selected schedule is novel.

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THE EFFECTS OF DAILY POSITIVE EMOTION ON SELF-REGULATION AND MINDFULNESS

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Introduction: Self-regulation is the ability to control behaviors and reactions in various situations, such as resisting temptations, persisting on hard tasks, or regulating emotions (Baumeister, Bratslavsky, Muraven, & Tice, 1999). Empirical research supports the Strength Model of Self-Control, which posits that self-regulation works like a muscle by getting “tired” with exertion, resulting in ego depletion (Baumeister, Vohs, & Tice, 2007). Studies have shown that positive emotions replenish self-regulation resources following ego depletion (Tice, Baumeister, Shmueli, & Muraven, 2007), but almost all studies have been conducted in single laboratory sessions. We proposed that daily positive emotion, induced through positive text messages, would build positive resources like resiliency over a one-week period, resulting in reduced depletion from self-regulation tasks in comparison to participants without the positive intervention.

Methods: Fifty-four undergraduate students (83% female) from a liberal arts college were recruited through Introduction to Psychology courses and Facebook. Participants completed a baseline assessment including the Stroop task (Stroop, 1935) and the Mindfulness Attention Awareness Scale (Brown & Ryan, 2003). They were then randomized to either the positive affect intervention (positive text messages) or the control condition (neutral text messages) and received 3 text messages per day for a week. Following the intervention, participants returned to the lab to complete a serial subtraction anxiety induction (Kirschbaum, Pirke, & Hellhammer, 1993) followed by the Stroop task (Stroop, 1935) to measure ego depletion. In addition, mindfulness was re-assessed (Brown & Ryan, 2003).

Results: Analyses revealed that participants in the positive text-message condition made significantly fewer errors (M= 2.59, SD= 2.90) on the Stroop task than the controls (M= 3.96, SD= 4.68) after the week of intervention (F (1, 51)= 5.01, p= 0.03), suggesting that those with the positive intervention experienced less ego-depletion following self-regulatory tasks. We expected that the positive intervention would also increase mindfulness in participants, but the data did not support that hypothesis (F (1, 51)= 0.00, p= 0.98, ns). Rather, participants with high baseline mindfulness (M= 1.12, SD= 1.36) showed an interesting effect in which they did not experience as much ego depletion as participants with low mindfulness (M= 2.52, SD= 2.69; t (1, 51)= 2.23, p= 0.03).

Conclusion: Findings from this study supported our hypothesis that daily positive emotions build positive resources like resiliency over time. Future interventions can build on this idea that self-control and resiliency can be strengthened. Our analyses also suggest that dispositional mindfulness may serve as a buffer to ego depletion, highlighting mindfulness as an important variable for future intervention research. Although limited by the small size and nature of the sample (ie., college undergraduates), a strength of the study was that the intervention was conducted outside of the laboratory using experience-sampling methodology, thus providing ecological validity for future mobile interventions.
HIPPOCAMPAL MITOCHONDRIAL GENE EXPRESSION CHANGES WITH DEVELOPMENT AND EARLY LIFE STRESS

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Background: Early life stress (ELS) impacts over 3.4 million American children and increases psychiatric disorder risk. In mice, ELS accelerates maturation of select brain regions, leads to precocious fear learning, and elevates anxiety and depressive-like behaviors, suggesting ELS-associated changes in the timing of brain development may impact psychopathology risk. Mitochondria play a vital role in neuronal differentiation and maturation; however, no studies have examined normative or ELS effects on mitochondrial gene expression in the brain over early development. We hypothesize that ELS will alter the developmental profile of mitochondrial gene expression, and that these effects will be associated with increased risk for negative developmental outcomes.

Methods: For ELS, C57BL/6N mice were reared with restricted access to bedding from p4-p11. Timepoints prior to (p4), immediately after ELS (p12), and across development (p16, p21, p28, p38, p50) were examined. Hippocampal samples (n=3-6/timepoint) from ≥2 different litters were isolated and cDNA synthesized; mitochondrial oxidative genes (NADH:ubiquinone oxidoreductase subunits 1-6; cytochrome b; cytochrome c oxidase I-III; ATP synthase 6 and 8) were run in multiplex with 18S as standard. Expression was calculated based on individual plate standard curves; developmental and between-group differences were examined using two-way ANOVA.

Results: Expression of each of the mitochondrial genes increased with development (p’s<.0001). Across development, ELS significantly reduced expression of several mitochondrial genes (p’s≤.05). There was also a statistical trend for an age by ELS interaction for several genes (p’s≤0.1). Data collection is ongoing and results from additional genes and with increased numbers of animals will be presented.

Conclusions: This is the first study examining mitochondrial gene expression during murine brain development. These results suggest that ELS may alter ontogeny of mitochondrial gene expression in the hippocampus, with implications for understanding ELS effects on brain and behavioral development.
EXAMINING ASSOCIATIONS BETWEEN FAMILY CONFLICT, EMOTION DYSREGULATION, AND IMPULSIVE BEHAVIORS IN ADOLESCENTS AT HIGH RISK FOR SUICIDAL BEHAVIORS

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Interpersonal problems are among the most significant risk factors precipitating self-injurious and other risky behaviors in adolescents. Family conflict specifically may be directly or indirectly related to such impulsive behaviors through poor attempts to regulate emotions. Parent and adolescent reports offer different perspectives on relationship dynamics, and could provide a more comprehensive understanding of these pathways. In this study, we aim to investigate the association between parent and adolescent reports on family functioning with emotion dysregulation and impulsive behaviors characteristic of borderline personality disorder.

Participants between the ages of 13 and 18 years old and at least one legal guardian were enrolled in an 18-week adaptation of Dialectical Behavior Therapy for adolescents (DBT-A). Adolescents were determined to be appropriate candidates for the DBT-A program if they presented with a history of suicidality, NSSI, and/or other self-destructive behaviors. Prior to initiating treatment, adolescents and their parents completed a battery of baseline questionnaires measuring a range of affective symptoms and psychosocial features, including the Borderline Symptom List-Supplement (BSL-S), Difficulties in Emotion Regulation Scale (DERS), and Parent-Adolescent Relationship Questionnaire (PARQ). The PARQ is a multidimensional measure designed to assess global distress, communication patterns, problem solving skills, maladaptive beliefs, and family structural problems. The BSL-S is a clustered index of impulsive behaviors and examines the frequency of deliberate self-harm, suicide attempts, binging, purging, substance use, hostile outbursts, and sexual promiscuity over the past week. Data collection is ongoing, thus sample sizes varied depending on which variables were being explored and ranged from N=10 to N=61.

Results indicate that adolescent self-report of emotional dysregulation is significantly related to impulsive and risky behaviors prior to treatment enrollment. A linear regression analysis was conducted to examine main effects and discriminate which dimensions from the DERS uniquely predicted impulsivity. The model accounted for 30% of the overall variance explaining risky behaviors (F(6, 53)=3.85, p=.003), and dimensions of emotional awareness (B=-.56, SE=.17, p=.001) and behavioral control when distressed (B=.39, SE=.18, p<.05) demonstrated specific associations. Higher frequency of impulsive behaviors was associated with parent perceptions of effective problem solving skills (r=-.56, p<.05), but no other dimensions of family conflict. Parent and adolescent reports on family functioning were significantly correlated with adolescent’s emotional dysregulation across several domains, particularly with emotional awareness.

Findings from the present study are preliminary, yet consistent with an extensive literature on emotional and interpersonal risk factors for suicide, deliberate self-injury, and other harmful behaviors. Collectively, these findings show promise for future analyses on causal pathways exploring whether familial problems and risky behaviors are linked through nonadaptive methods of regulating emotions.
GABA, the primary inhibitory neurotransmitter in the brain, affects neuronal excitation to influence learning and memory. Based upon pharmacological manipulations, GABAA receptors have been implicated in fear and anxiety responses, with regionally selective effects. While GABAA antagonists in the basal lateral amygdala increase fear learning, the same manipulation in the central amygdaloid nucleus yields decreased fear expression. Here, we use a mouse model to assess the effects of loss of the Gabrg2 gamma2L receptor (B6:129-Gabrg2tm1Geh/J) on fear learning and anxiety. In recent years, mutations in the Gabrg2 gamma2 subunit of the GABAA receptor have been linked with body dysmorphic disorder, epilepsy (including Dravet syndrome), generalized seizures, and febrile seizures, all disorders with high co-morbid risk for anxiety. To determine the role of the Gabrg-2 gamma2L receptor on fear learning and anxiety, wildtype and knockout mice were tested on a contextual and fear conditioning paradigm and several standard tasks to assess anxiety-like behavior. Gabrg-2 gamma2L knockout mice exhibited decreased fear learning and impaired contextual recall compared with wildtype animals. These effects were sex dependent, with males showing more profound effects than females. In these same mice, we observed no effect of gene deletion on basal anxiety-like behavior. These findings suggest that common human variants in the GABAA receptor may impinge upon basic fear associated learning, and may provide insight into the neurobiological basis of risk for anxiety-related pathology.
DEPRESSIVE SYMPTOMS AND MORTALITY IN HEART FAILURE: THE ROLE OF MEDICATION NON-ADHERENCE

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Introduction
Approximately 20% of individuals with heart failure (HF) experience depression or depressive symptoms. Depression is detrimental to prognosis in HF, roughly doubling all-cause mortality risk. However, the mechanisms underlying this relationship are not fully known. Medication non-adherence may contribute, as depressed patients are less likely to adhere to medication regimens.

Purpose
The present study evaluated the role of medication non-adherence in the relationship between depressive symptoms and mortality risk in adults with HF.

Method
Participants were 303 HF patients in a longitudinal, observational study of self-care behaviors. Participants completed 21 days of medication monitoring using an electronic pillbox. Medication adherence was treated as a continuous variable. Depression was defined as Patient Health Questionnaires scores ≥ 5. Mortality data were obtained from the Centers for Disease Control and Prevention’s National Death Index. Cox proportional hazards regression was used to assess the relationship between depressive symptoms and mortality, with and without adjustment for demographic and medical covariates, and medication non-adherence.

Results
After adjustment for covariates, depression was associated with increased all-cause (HR: 2.07; 95% CI: 1.02-4.17), but not cardiovascular, mortality risk. When medication non-adherence was added to the model, non-adherence (HR: 1.01; 95% CI: 1.002 – 1.02), but not depression, was associated with increased mortality risk.

Conclusion
Medication non-adherence appears to contribute to increased risk of all-cause mortality conferred by depressive symptoms in HF. Depression and medication adherence represent modifiable risk factors for poor prognosis. Future research is needed to understand whether interventions that concomitantly target these factors can improve outcomes.
INITIAL FEASIBILITY, ACCEPTABILITY AND USER EXPERIENCE OF A MULTI-DRUG POD-IVR: A MIXED METHODS STUDY

Melissa L Getz, Kate M Guthrie, Sara E Vargas, Rochelle K Rosen, Lauren N Dawson, Melissa Guillen, Kelley A Smith, Marc M Baum, Kathleen L Vincent

Background: Delivering efficacious HIV/STI prevention drugs for optimal effectiveness relies on user adherence. A dapivirine intravaginal ring (IVR) showed significant reductions in HIV incidence among adherent users. Sustained-release drug delivery devices such as IVRs are now considered an important path forward to address long-term adherence in HIV/STI and multipurpose prevention.

Methods: In a pre-phase-1 trial, we explored initial feasibility and willingness-to-use (WTU) a novel pod-IVR, capable of delivering multiple prevention drugs in a single ring. 6 women used single- and dual-drug rings, each for 7 days (clinical safety reported elsewhere). IVR-specific user sensory perception and experience surveys and face-to-face in-depth interviews were completed following each 7-day IVR use period, thus each woman served as her own control.

Results: We enrolled 2 Hispanic (H), 2 non-H White, 2 Black female participants (Ppt). Mean age 28y; 32.9 mean BMI; 3 with history of STI, 4 HIV tested in the last year. The pod-IVR was inserted and removed with relative ease by all. Continuous use in all but 1 use period: 1 Ppt removed/reinserted ring (1x for ~5'). 6 of 6 willing to recommend: 4 of 6 would probably/definitely use pod-IVR to prevent HIV (2 perceived no HIV risk). Probable use decreased with longer residency (7, 28, 90, 180-day). 6 of 6 would use if by prescription; 4 would use if available OTC. Qualitative data added detail to characterizing the use experience, and supported feasibility of the pod-IVR platform, with little product awareness during sustained daily use. Data also suggest promise for the pod-IVR in multipurpose prevention contexts.

Conclusions: We evaluated a pod-IVR for feasibility and WTU in the context of escalated dosing, illustrating that the pod-IVR platform itself is well-tolerated, even when the number of filled pods and active drug(s) increases. Further study is needed to assess the pod-IVR with additional drugs (study ongoing), in longer use contexts, and during sexual activity.
A PILOT STUDY OF FACEANXIETY: A COGNITIVE BIAS MODIFICATION TREATMENT FOR ANXIETY DISORDERS IN PRIMARY CARE

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The majority of Americans with anxiety disorders do not receive appropriate care. Pharmacotherapy is often not initiated or maintained due to patient preference for non-pharmacological approaches. It is unlikely there will ever be enough CBT therapists to meet population needs. Thus, there is a great need for low-intensity, scalable, non-pharmacological treatments. Primary care is the ideal setting with which to link low-intensity anxiety treatment, as this is where most anxious patients first present for care. Also, primary care linkage allows for primary care provider (PCP) monitoring and provision of more intensive treatments as needed. We will present data from an open trial of a new primary care linked Cognitive Bias Modification (CBM) treatment called FaceAnxiety. FaceAnxiety is an 8-session, transdiagnostic and personalized CBM treatment with weekly symptom monitoring by FaceAnxiety Specialists. Each session involved two tasks: a dot probe task to target attention bias and a word-sentence association paradigm to target interpretation bias. In the 14 patients enrolled, 11 completed all 8 sessions. In completers, as measured by the Hamilton Anxiety Rating Scale (HARS), anxiety symptoms were significantly reduced from pre (M = 22.0; moderate illness severity) to post (M = 15.5; minimal symptoms) intervention (t(10) = 3.80, p = .003) with a large effect size (d = .87). Further, post-intervention, seven of the eleven participants (64%) had HARS scores that fell below the clinical cut-point (<18). Qualitative exit interviews revealed high acceptability and generalization to patients’ daily lives. We will describe the development process and personalization algorithm and present data from cognitive bias assessments and qualitative exit interviews. This line of work will hopefully lead to the incorporation into primary care of readily scalable, translational, effective, non-pharmacological mental health treatment for patients with anxiety disorders.
SMOKING CESSATION TREATMENT RESPONSE AND BRAIN REACTIVITY ON A DELAYED REWARD DISCOUNTING TASK

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Significance: Smoking treatment may be improved by clarifying the determinants of treatment success. It has been demonstrated behaviorally that higher levels of delayed reward discounting (DRD; i.e., proportionate preference for smaller immediate rewards over larger delayed rewards) are associated with relapse. Neural activity during functional magnetic resonance imaging (fMRI) paradigms represents promising translational biomarkers for predicting clinical outcomes. The primary goal of this study was to identify the underlying neural indices of impulsive decision making that predict smoking cessation treatment response.

Methods: We measured behavioral and brain response during an fMRI DRD paradigm in smokers prior to an eight-week best-practices smoking cessation intervention. The analyses were conducted on 42 subjects (M cigarettes daily = 22.3; FTND = 4.9). Subjects were divided into relapse (N = 24) and no relapse (N = 18) groups. Smoking cessation relapse was operationalized as smoking at least one cigarette per day for seven days, treatment dropout, or an exhaled carbon monoxide > 10 parts per million.

For each delay interval, choices that were +/- two in each direction of the indifference point were classified as hard choices, and all other choices were classified as easy choices (control choices were included as a baseline). Following preprocessing of fMRI data, omnibus one-way three-level (easy, hard, and control) within-subject analyses of variance were conducted at the whole-group level, with significant effects followed-up with pairwise t-tests to identify specific patterns. Then between-group differences were explored for regions that were selectively most active during hard and easy choices.

Results: At the behavioral level, the no-relapse group exhibited a significantly higher area under the curve, reflecting less impulsivity (p = .02). The dorsolateral prefrontal cortex (DLPFC) exhibited significantly more activation for hard choices and was significantly more active for the no-relapse group during hard and easy trials. Regions more active during easy trials (and more active in the no-relapse group in general) included precuneus, middle temporal gyrus/superior temporal gyrus, superior temporal gyrus, middle temporal gyrus, and uvula/tuber.

Conclusions: The most notable finding is that the DLPFC is recruited for difficult decision making and is more active in successful quitters. This indicates that the DLPFC is related to adaptive decision making and positive outcomes in smoking cessation treatment.
THE NIMH DBS FOR OCD CONTROLLED TRIAL: ONE-YEAR OUTCOMES

Benjamin Greenberg, MD, PhD, Steven Rasmussen MD, Nicole McLaughlin PhD, for the DBS for OCD Collaborative Group

Introduction: Deep brain stimulation (DBS) has regulatory approvals in the EU and the US for treatment-intractable obsessive-compulsive disorder (OCD), but only limited controlled data are available.

Methods: This collaborative multicenter controlled trial, conducted across eight U.S. centers, tested the effects of ventral capsule/ventral striatum (VC/VS) DBS in 27 rigorously selected patients suffering from otherwise intractable OCD. The trial used a delayed-start, sham-controlled design. Yale-Brown OCD severity scores at presurgical baseline averaged above a score of 33, indicating an extremely ill sample. The Medtronic model 3387 brain lead used has four independently programmable electrode contacts, each 1.5mm long, spanning 10.5mm overall. It was chosen, in part, because this device can access ventral prefrontal-subcortical connections traveling in the VC/VS which are implicated in OCD. The lead was attached to an implantable neurostimulator (INActiva PC) for the masked study phase, which was replaced by a rechargeable Active RC INS (Medtronic, Inc) to minimize the need for battery replacement surgeries during chronic stimulation after controlled data were collected. During the sham-controlled DBS optimization phase and subsequent stimulation adjustments, specific electrode contacts along the length of the model 3387 lead were chosen based on acute and ongoing clinical effects.

Results: The specific DBS contacts producing therapeutic effects spanned the entire dorsal-ventral distribution of the 3387 lead (10.5mm). Effects on YBOCS OCD severity, global functioning, and on secondary measures of nonspecific anxiety and of depression were similar to those seen to date in open-label trials. This invasive and intensive treatment was generally well-tolerated.

Discussion: One year outcomes suggest there is lasting benefit from DBS at the VC/VS surgical target for intractable OCD. The fact that the empirically chosen electrode locations differed across patients suggests that the specific locations of pathways involved in therapeutic effects may vary across individuals.
INCORPORATION OF EARLY END-USER FEEDBACK INTO THE ITERATIVE DESIGN OF FIBER-BASED MICROBICIDES: CONSIDERING ADHERENCE FROM INCEPTION

Melissa Guillen, Kate M Guthrie, Sara E Vargas, Melissa Guillen, Rochelle K Rosen, Arielle Steger, Melissa L Getz, Kelley A Smith, Kim A Woodrow

Background: On-demand and sustained-release topical STI/HIV prevention and multipurpose prevention products remain priorities in sexual/reproductive health (SRH). Recently, an intravaginal ring (IVR) significantly reduced HIV incidence among adherent users. But clinical trial history of poor overall adherence continues to highlight the importance of designing products users can adhere to. Optimizing topical products for greatest effectiveness could have significant public health impacts.

Methods: Adaptive iterative design methods were used to optimize both drug delivery and potential use of drug-eluting fiber forms, beginning with on-demand, vaginally-inserted dissolving fiber formulations. Following initial fiber design, women completed user evaluation focus groups to consider fabric geometry and dissolution parameters.

Results: 39 women participated in 3 pairs of iterative focus groups. In each, prototypes were presented, in random order and discussed in detail. In the first pair (N=14) 5 geometries and textures were considered: square, circle, rectangle, tube, and capped tube. The next pair further considered the same geometries, along with dosing regimen (daily v weekly). In the final 2 groups, 3 prototypes were considered: 2 circles (one quick-dissolving, one slow) and the capped tube, which had emerged as the lead geometry. Discussion focused on impact of dissolution time on application (digital v applicator), geometry, and texture. Importance of geometry, dosing, dissolution, and application options were weighted by participants. The capped tube (digital insertion) and quick-dissolving circle (applicator insertion) emerged as priority forms.

Conclusions: Conducting open-ended user-centered design iteration led to unanticipated outcomes, yet identified formulation parameters that could be further designed and evaluated. Knowing property thresholds and use parameters users consider imperative to consistent use aided subsequent iterations and led to progress in both formulation and overall product design.
Low executive working memory capacity (eWMC) is associated with alcohol use disorders (AUDs) and poor self-regulation. The importance of eWMC to adaptive functioning has led to a recent influx of studies attempting to improve eWMC using various training methods. However, numerous studies raise questions about just how effective working memory (WM) training is, for whom WM training may work, and the associated long-term transfer of WM training to improvements in core eWMC and related symptoms. Studies of the efficacy of WM training have been hampered by a lack of appropriate control groups, questionable training methods or programs, and narrow outcome measures. A previously successful rigorous and adaptive WM training protocol was used (Harrison, 2013), which utilizes two adaptive complex dual-span WM tasks for active training (AT) and two Visual Search (VS) tasks for control training. We also included comprehensive baseline and follow-up assessments of eWMC (3 near and 3 moderate transfer measures). Subjects were recruited for two groups: those with AUDs, (n=46) or those without an AUD or other Substance Use Disorder (Controls, n=44). Participants (N=90; 45 men; 45 women, M age=22.5 years) were randomly assigned to either AT (n=48) or VS (n=42). Linear mixed effects models were used to examine training task improvement, transfer effects, and predictors of training improvement and transfer.

Analysis revealed main effects of session (B=0.167, p<0.001), indicating improvement on training tasks as session increased; and condition (B=0.58, p<0.001), suggesting those in VS improved more than those in the AT. This model also revealed session by group interaction (B=0.0146, p<0.01), suggesting controls improved more across training sessions compared to AUDs. There was evidence for significant transfer among two near transfer measures at initial follow-up (Bs= 3.10-7.19, p<0.05). At follow-up 2 (one month), only one measure of near transfer remained significant. There was no evidence of transfer for any of the three moderate transfer measures.

Additionally, group status (B= 1.72, p<.001) predicted adherence, in that AUDs had a higher likelihood of dropping from the study. Additionally, baseline IQ predicted training improvement on both AT tasks (B= .10, p<.05; B= .14, p<.001), but neither of the VS tasks. Importantly, baseline WM predicted transfer on two near transfer tasks (Bs = .19-.21, ps < .001-.05); and two moderate transfer tasks (Bs= .10 -.21, ps< .05-.01) and baseline IQ (WASI) predicted transfer on all three near transfer measures (Bs=.31 -.36, ps< .01 - 05) and two moderate transfer measures (Bs= .30-.37, ps< .01 -.001). Final training session (15) performance (on both AT tasks, but not VS tasks) predicted transfer effects for all six near and moderate transfer tasks (Bs=0.91 to 2.48, ps <.001-.05). Results indicate that participants who performed at higher levels on the AT tasks showed significant evidence of transfer.

Results suggest that those with AUDs are able to improve on WM training programs, and show significant transfer to other similar measures of eWMC. However, AUDs were also less likely to complete the training protocol. Additionally, more improvement on the AT tasks themselves predicted transfer effects, suggesting those who show more improvement on training are more likely to show improved eWMC overall. Importantly, baseline intelligence (before initiation of the training protocol) predicted both improvement on the AT tasks and transfer on the majority of transfer measures suggesting those with higher intelligence were more likely to benefit from WM training. This and future studies provide direct translation to the development of cognitive interventions for treating AUDs and related externalizing psychopathology.

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Previous studies have demonstrated that performing an action toward an object can impact the visual perceptual processing of that object. For instance, the congruence between hand movements and visual stimuli improves visual discrimination performance. In our recent work, to examine how easiness of action influences perceptual sensitivity, we asked participants to perform an orientation change detection task using a titled Gabor patch, while preparing a point-to-grasp movement towards it. We observed that when they grasp a right-titled patch with their dominant right hand, which was easier than grasping a left-titled one, orientation discrimination was better. Here, we examined whether orientation discrimination sensitivity could be further enhanced with training of grasping precision. To address this question, we compared the orientation discrimination sensitivity before and after an action training session, in which participants were required to grasp various titled objects. We found that the magnitude of grasping accuracy improvement in the action training session was positively correlated with the improvement of the orientation discrimination. The effect, however, was not observed with perceptual training in the absence of action. In conclusion, we suggest that the easiness of action as well as training of action precision can influence the sensitivity of perceptual discrimination.
SMARTPLAYROOM: SEMI-AUTOMATED BEHAVIORAL ANALYSIS IN NATURALISTIC ENVIRONMENT

Pankaj Gupta, Elena Tenenbaum, Stephen Sheinkopf, Thomas Serre & Dima Amso

Child development is a pressing scientific frontier in modern society. The scientific community has benefitted from the use of computer-based tasks to study development at the process level - attention, memory, learning. However, these approaches offer a limited snapshot into naturalistic cognitive function in developing populations. At the same time, the robust quantification of complex naturalistic behaviors imposes a major bottleneck and controversies in behavioral studies have arisen because of the inherent biases and challenges associated with the manual coding of behavior.

We have recently designed a quantitative digital data collection space called the SmartPlayroom. The space is equipped with mobile eye tracking, wireless heart-rate and galvanic skin response sensors, audio and video recording, and depth sensor technologies. This room looks like any playroom in a home or school but is designed to naturally collect data in real time and simultaneously on all aspects of children’s behavior including movement kinematics, language, eye movements, and social interaction while a child plays and explores with or without instruction, walks or crawls, and interacts with a caregiver.

Here we provide preliminary evidence of the feasibility and utility of the SmartPlayroom in naturalistic data collection relevant to visual attention. Amso et al (2014b) examined the development of bottom-up visual attention in 2-5 year-old typically-developing (TD) and children with autism spectrum disorders (ASDs). Our data showed that children with ASDs used bottom-up attention more than TD children. However, we didn’t find differences in use of visual processing channels among groups, even as Amso et al (2014a) found that developmental change in visual feature channels may guide attention to salience. It may be that 2D displays do not capture the full range of visual complexity in naturalistic viewing, particularly as relevant to motion and depth. Thus, we repeated this experiment in the SmartPlayroom in (N = 8) TD children 2-5 years and age-matched children with ASDs (N = 8). Children played freely while they wore the portable eye tracker. We generated gaze distribution maps per participant and used the Saliency Toolbox to compute color, intensity, orientation and motion maps. Relevant to this proposal, we are finding striking differences in analytic power as a function of the 2D versus naturalistic methodologies. Computerized 2D static scene tasks are constrained by how much time a child will sit in front of a computer. Thus, children in the Amso et al (2014ab) study saw 12 images. In the SmartPlayroom, children were happy to play for several minutes and we were able to compute saliency and feature maps per frame, resulting in a total of 20,000 frames per child for analysis. Measurement reliability is dramatically magnified. Moreover, ecological and construct validity are substantially improved over our 2D work with the inclusion of motion and flicker channels in the SmartPlayroom data collection. Preliminary data indicate that children with ASDs are more likely than TD to distribute gaze based on scene salience and additionally are more likely to orient to scene locations rich in color, orientation, and motion during free play in the SmartPlayroom.
CHARACTERIZATION OF TASK-EVOKED PUPILLARY RESPONSES REFLECTING LC-NA ACTIVITY - POTENTIAL INDICES FOR COGNITIVE RESERVE

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Cognitive reserve is an abstract concept proposed to account for the disconnection between the severity of clinical symptoms and underlying brain pathology in neurodegenerative disorders such as Alzheimer’s disease (AD) (Stern, 2002). That is, individual differences in the ability to tolerate Alzheimer-related neuropathological changes are thought to be attributable to differences in cognitive reserve, although the neural mechanisms mediating cognitive reserve have not been fully characterized. The locus coeruleus (LC), a brainstem nucleus that is the primary source of noradrenaline in the forebrain, has been proposed to be one of the underlying processes of cognitive reserve during normal aging and AD (Robertson, 2013). Neuronal density in LC, for example, has been found to correlate with rate of cognitive decline in post-mortem examination (Wilson et al. 2013). The ability to obtain objective neural markers of cognitive reserve in conjunction with neuroimaging biomarkers of pathological burden (e.g., beta amyloid load) may allow clinicians to more accurately identify individuals at risk for developing Alzheimer’s disease during their preclinical stage.

Previous studies have demonstrated that pupil dilation can serve as an indirect measure of locus coeruleus-noradrenergic (LC-NA) activity, suggesting that pupil dilation can potentially serve as a marker of cognitive reserve. The aim of the present study is to develop a set of canonical tasks that elicit LC-mediated pupillary responses across several cognitive domains. In particular, the current study aims to establish a set of pupillary and behavioral parameters reflecting LC-NA function in young adults that can then be applied to aging populations.

Participants completed three cognitive tasks (phasic alerting, flanker interference, and recognition memory) that have previously been shown to elicit robust pupillary responses. Pupil dilation was continuously measured throughout the duration of each task. Behavioral performance in each task was as expected: For the phasic alerting task, response time (RT) was significantly faster for visual targets proceeded by an auditory cue than by no cue. For the flanker interference task, RT for congruent trials was faster than for incongruent trials. For the recognition memory task, old/new discrimination accuracy was above chance and below ceiling performance.

Regression analyses indicated that baseline and trial pupil sizes independently predicted RT across all tasks, suggesting independent contributions of both tonic and phasic arousal components mediated by LC-NA functioning. For the phasic alerting and flanker interference tasks, auditory cued targets and incongruent trials elicited larger pupillary responses than the no cue targets and congruent trials, respectively, but pupillary response magnitude did not predict behavioral RT alerting or congruency effects between subjects in either task. This lack of correlation between the behavioral and pupillary responses could be due to ceiling performance and robust cognitive resources in the young adults. In the recognition memory task, the old words elicited a larger pupillary response than the new words and correlated with behavioral accuracy, suggesting an LC-mediated memory retrieval enhancement. Time-on-task effects were found for baseline and trial pupil sizes but not for behavioral RT, suggesting that additional cognitive processes are recruited throughout the task to reduce cognitive effort mediated by LC-NA but maintain behavioral performance in this young adult group. Collectively, the regression coefficients derived from these tasks may provide a comprehensive profile of LC-NA activity that can be used to operationally characterize cognitive reserve within the context of aging, and that can in turn be used to more accurate identify elderly individuals at risk for cognitive decline.
THE POWER OF TURNING THE OTHER CHEEK: THE UTILITY OF NON-PUNITIVE RESPONSES TO FAIRNESS VIOLATIONS

Joseph Heffner, BS; Oriel FeldmanHall, PhD

Background: Decades of research in behavioral economics and experimental psychology demonstrates that humans strongly desire punishment when deciding how to restore justice, even when punishment is costly. In contrast, past work from our lab reveals that retributive punishment is no longer preferred when non-punitive options are available (FeldmanHall, O., Sokol-Hessner, P., Van Bavel, J., & Phelps, E., 2014). Non-punitive options include taking care of the victim’s needs (e.g. monetary endowment) rather than emphasizing punishing the perpetrator (e.g. monetary reductions). One possible interpretation of these findings is that highly retributive punishment is not a proportional response to fairness transgressions. The purpose of this study is to investigate whether reduced punishment and reduced compensation are valued as forms of justice restoration.

Given the structure of western legal systems, where victims are not tasked with deciding punishment sentences, we further explored whether decisions to restore justice are moderated by the decider’s perspective. We posited that victims would punish more than non-vested third parties, since research indicates that sanctions by second parties directly harmed are much stronger than third-party sanctions.

Methods: We recruited 98 subjects to play the Justice Game. In this economic game, Player A has the first move and can propose a division of a monetary pie with Player B (Player A: $1 – x, Player B: x). Player B can then reapportion the money by choosing between two options; (1) reduced punishment: a ‘just deserts’ motive where the perpetrator deserves punishment for the wrong committed – so that Player A is punished some amount while Player B is compensated; (2) reduced compensation: a non-punitive motive where the victim deserves recompense – so that Player B is compensated some amount while Player A is unaffected. We utilized a pairwise comparison design that allowed us to directly contrast each choice type with its ‘maximum’ counterpart; reduced punishment choices are always juxtaposed against full compensation while reduced compensation choices are always juxtaposed against full punishment. This allowed us to determine when participants switch between compensation and punishment as a function of their monetary payoff. Participants were asked to make decisions both for themselves, and for another – where their monetary payout was not affected by their decisions.

Results & discussion: When maximum compensation is available, participants’ choices are insensitive to partial punishment levels, regardless of role or level of fairness infraction. In contrast, preference for reduced compensation revealed an interaction between role and fairness infraction such that participants endorsed maximum punishment as the offer became increasingly unfair. This effect was strongest when deciding for oneself compared to making decisions for another.

Despite past research showing that people value punishment, these results provide evidence that even small amounts of punishment are not valued—even when free. This suggests that people only value retributive justice in the absence of any other means of restoring justice. If, however, people value the highest paying outcome, then they should be indifferent toward varying amounts of compensation. That there is very little value for punishment even when punishment reaps the highest reward, suggests that a high value is placed on restorative justice. Together, these results provide further evidence that the utility of punishment may be limited and that other prosocial options for justice restoration dominate when responding to fairness violations.
IMPROVING HEARING HEALTH AWARENESS IN HEALTHCARE AND SUPPORTING VETERANS WITH HEARING LOSS

Adriana Hyams, PhD; Daniel Jones, PhD; Jennifer Lambert, PhD

Introduction: Hearing loss affects 80% of older adults in the general population, and 60% of OEF/OIF/OND Veterans have hearing loss or tinnitus. Hearing loss is the #1 service connected disability at the VA and the fastest growing. Research shows hearing loss is associated with poorer quality of life (i.e., social, emotional, physical, cognitive, and occupational health). Despite these associations, hearing loss is often overlooked by interdisciplinary healthcare professionals, and Veterans are unlikely to seek help for hearing loss when needed. Research shows assistive listening devices (e.g., hearing aids) are associated with improved quality of life, but only 2% of Veterans get hearing aids even though they are free at VA. If healthcare professionals are educated about the importance of hearing health, they may promote better quality of life in their patients.

Methods: Brief in-services were presented to interdisciplinary mental health and primary care teams at the Providence VAMC. Attendees (N = 116) were educated about hearing loss' and hearing aids' association with quality of life among Veterans. They were provided with education about the limitations of hearing aids and the success of audiological rehab at optimizing hearing aids’ functioning. They were encouraged to refer to the Audiology Clinic if Veterans are suspected of hearing loss and if they struggle with their hearing aids. Professionals were given a double-sided handout with highlights from the in-service, tips to identify hearing loss, strategies for communication, and tips to optimize hearing aids. Attendees completed a pre-test and post-test to evaluate learning and the likelihood they would use the handout and refer to the Audiology Clinic. Data analysis included paired samples t-tests and means/standard deviations. A hearing loss support group was also created with the goal of improving quality of life in Veterans with hearing loss.

Results: A paired samples t-test compared how often attendees thought they should consider hearing loss in case conceptualizations at pre and post-test. There was a statistically significant increase before (M = 3.02, SD = 1.00) and after (M = 3.98, SD = .93) the presentation, t(93) = -8.96, p < .0005 (two-tailed). Cohen’s d (.99) indicated a large effect size. Specifically, the average person thought they should consider hearing loss sometimes at pre-test, which increased to often at post-test. Attendees were also asked how much difficulty they thought Veterans have psychosocially and functionally due to hearing loss. There was a statistically significant increase in the amount of impairment attendees believed Veterans had due to hearing loss before (M = 17.93, SD = 5.27) and after (M = 20.29, SD = 5.01) the in-service, t(86) = -5.18, p < .0005. Cohen’s d (.46) indicated a moderate effect size.

Anecdotally, professionals appear more likely to educate Veterans with hearing loss and refer them to the Audiology Clinic or a hearing loss support group. Veterans have reported that this group was much needed, and they have consistently attended the weekly group, stating that it helps to know there are others with similar problems and to receive tips for hearing aid use from their peers. There has been such demand for the group that two sections have been created.

Conclusion: Providing education to interdisciplinary healthcare professionals can successfully increase awareness about the importance of hearing health in patient conceptualizations. Professionals are open to increasing their competence and to help patients get the hearing healthcare they need. Veterans have praised the added attention to their hearing health in the form of the support group. Thus, hearing health can be improved with the help of healthcare professionals, which bodes well for improving quality of life.
Non-suicidal self-injury (NSSI) involves direct, deliberate destruction of body tissue in the absence of suicidal intent (Favazza, 1987, 2011). The implicit identification hypothesis suggests that NSSI is maintained through identification with NSSI as an effective means of achieving particular outcomes (e.g., affect regulation; Nock, 2009). Preliminary research suggests that implicit NSSI identity is concurrently related to NSSI behavior (Nock & Banaji, 2007) and that the development of an explicit NSSI identity may influence continued NSSI (Breen et al., 2013). However, relatively little is known, quantitatively or qualitatively, about the role of NSSI identity on NSSI behavior. The current study uses a mixed methods approach to examine both implicit and explicit identification with NSSI. We examined implicit associations with NSSI using the Self-Injury Implicit Association Task – Identity Version (SI-IAT; Nock & Banaji, 2007), and explored explicit identification with NSSI through an investigator-generated qualitative interview. Participants include 143 adults in a psychiatric partial hospitalization program.

Quantitative analyses indicated significant differences on SI-IAT performance at Time 1, $t(125) = -4.86, p < .001$, and Time 2, $t(109) = -2.22, p = .03$, by NSSI status. Among those with NSSI history, SI-IAT performance was consistent between Time 1 and 2, $t(59) = -1.06, p = .29$. However, significant differences emerged between Time 1 and 2 SI-IAT performance for participants with no NSSI history, $t(54) = -2.70, p = .01$. SI-IAT performance was not correlated with self-reported depression for either group (all ps > .11). Preliminary quantitative results suggest that the SI-IAT – Identity version appears to validly capture stable, persistent identification with NSSI among those with NSSI history, and differentiate between groups based on NSSI status.

Among the six participants with quantitative and qualitative data, NSSI methods included cutting ($n = 5$), scratching ($n = 3$), biting ($n = 1$), and embedding ($n = 1$). One participant had a distant history of NSSI; the remaining participants had engaged in past month ($n = 4$) or past week ($n = 1$) NSSI. Preliminary qualitative data suggests that participants have well developed personal NSSI narratives involving NSSI functions (e.g., affect regulation, anti-suicide) and preceding emotions (e.g., loneliness, sadness). Notably, four participants described explicit identification with NSSI, using NSSI-specific labels to describe themselves (e.g., “cutter”). These identity labels were associated with stigma ($n = 1$), shame ($n = 2$), and embarrassment ($n = 1$) and were not perceived as positive aspects of the self. Together, qualitative analyses suggest explicit identification with NSSI is prevalent and ego-dystonic.

Preliminary data suggest that individuals with a history of NSSI maintain stable implicit identities with NSSI, regardless of having negative attitudes towards explicit identification with NSSI. Elucidation of the shared and unique effects of implicit and explicit identity on NSSI behavior has the potential to inform empirically supported intervention efforts targeting intra-individual characteristics for NSSI. Data analysis is ongoing and will involve additional mixed methods analyses to integrate quantitative and qualitative results (Creswell, 2013).
A transdiagnostic view of mental illness seeks to understand the psychological constructs which are common to, and underlie, conditions whose behavioral topography appears to differ; concurrent approaches to treatment seek to treat these different conditions with single interventions that target those underlying processes. Transdiagnostic interventions possess advantages particularly in avoiding assessment or treatment planning demands and fulfilling a role as low-intensity interventions in group or guided self-help modalities. The present investigation examined the effects of a novel cognitive-behavioral transdiagnostic group didactic intervention, targeted at improving general psychological functioning, in a sample of undergraduate students. The sample (N = 181) included individuals both above and below a published clinical cutoff score indicating poor psychological functioning. After pre-assessment, participants were randomized either to receive a transdiagnostic intervention, consisting of five weekly group meetings of 60–90 minute duration, or a waitlist control condition. A subset of the randomized sample (n = 82) successfully completed post-intervention assessments and were available for analysis. Analyses show that participants who received an adequate dose (defined as three attended sessions) of the intervention improved significantly on a measure of psychological functioning when compared to controls, t(77) = 3.41, p < .001. Additionally, participants differed by group in improvements on two transdiagnostic variables. Intervention participants reported significant decreases compared to controls in depressive rumination, t(69) = 1.97, p = .042 and reported significant decreases compared to controls in intolerance of uncertainty, a variable linked to anxiety disorders, t(69) = 2.28, p = .025. However, pre-post differences in self-reported anxiety and depression symptomatology were not different between intervention and control groups. Findings provided preliminary evidence of the utility of this brief intervention for improving functioning. Of note, findings were suggestive of transdiagnostic treatment effects, which may improve psychological functioning without addressing specific psychiatric symptoms. Presently, the intervention protocol is being modified for use with a Veteran population.
PARENTAL DISCLOSURE OF CHILD EXPOSURE TO DOMESTIC VIOLENCE: EFFECTS OF SOCIODEMOGRAPHIC FACTORS OVER TIME

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Childhood exposure to domestic violence is associated with a range of negative outcomes, even when children are not directly involved in the violence between caregivers (MacMillan & Wathen, 2014; McTavish et al., 2016; Teicher & Samson, 2016). Identifying violence and providing services for families can improve outcomes for all members, but minimization is common (MacDonald et al., 2016; MacMillian & Wathen, 2014). Parents’ tendency to minimize children’s exposure can be related to their personal history of abuse, as well as contextual factors such as poverty and housing instability (Evans et al., 2016; Velonis et al., 2015). Research is somewhat limited with regard to other potentially influential factors and how they change over time. The present study examines sociodemographic characteristics that may be associated with parental disclosure of child exposure to violence in a sample impoverished families at two time points.

Participants were 82 parents and their children, ages 3 – 5 (Mage = 50.72 months), recruited from a child maltreatment clinic and the local child welfare agency. All children had substantiated cases of moderate to severe domestic violence exposure in the six months prior to baseline per record review using the System for Coding Subtype and Severity of Maltreatment in Child Protective Records (Barnett et al., 1993). Children were racially/ethnically diverse (39% white, non-Hispanic, 39% Hispanic, 10% black, and 11% other) females (55%) and males (45%). Caregivers were mostly mothers (95%), had no more than a high school degree (61%), and were unemployed (60%). Nearly all families qualified for public assistance (85%). At baseline and six month follow up, parents completed measures of demographics, economic pressure (Conger et al., 1994), and a clinical interview to assess child trauma exposure, including domestic violence (Scheeringa & Haslett, 2010). Parents were considered to have “disclosed” their child’s exposure to violence if they endorsed this item on the clinical interview. Relations between sociodemographic factors (parental employment, relationship status, and economic pressure) and disclosure of violence were examined using t-tests and chi-square tests.

Despite all children having documented histories of exposure to violence, 51% and 57% of parents disclosed this exposure on the interview at baseline and follow up. Results indicated that sociodemographic related to parental disclosure. At baseline and follow-up, parents who disclosed were more likely to be single ($\chi^2 = 4.64, p < .05; \chi^2 = 5.51, p < .05$). In families with two parents in the home, caregivers were less likely to disclose compared to single parent households at baseline ($\chi^2 = 11.91, p < .01$) and follow up ($\chi^2 = 10.40, p < .01$). At baseline, caregivers whose children maintained contact with fathers were marginally less likely to disclose compared to those whose children did not have contact ($\chi^2 = 3.90, p < .10$); however, at follow-up this relation did not hold. At follow-up, but not baseline, employed parents were more likely to disclose violence ($\chi^2 = 6.19, p < .05$). Lastly, perceived economic pressure at baseline was not related to baseline disclosure, but parents who reported higher levels of perceived economic pressure at follow-up were more likely to disclose domestic violence at follow-up ($t = -3.77, p <.001$).

Results show parents who perceived more economic pressure and parents who were employed were more likely to disclose violence at home as more time passed from the exposure. These seemingly contradictory findings underscore the importance of nuanced examination of sociodemographic risk factors. In addition, caregivers living with a partner or in a relationship may be less likely to discuss violence. Clinicians should keep these factors in mind when assessing domestic violence with clients and work with them to feel safe disclosing.
Background: Autism spectrum disorder (ASD) is recognized as one of the most impairing and common psychiatric conditions, affecting as many as 1 in every 68 children today with data from the Centers for Disease Control showing that the incidence of ASD has increased roughly 123% from 2002 to 2010 in the United States. Greater understanding of the brain and behavior mechanisms of ASD is essential to improve the diagnosis and treatment of ASD. Towards this end, prior research suggests that ASD may involve an imbalance between excitatory glutamate (GLU) and inhibitory gamma-aminobutyric acid (GABA) neurotransmission of a circuit mediating social information processing, including the bilateral posterior superior temporal sulcus (pSTS), inferior frontal gyrus (IFG), and primary motor cortex (M1). To test this hypothesis, we present a preliminary analysis of a Brown CNS Function COBRE Pilot project focused on determining (a) resting state functional connectivity (RSFC) alterations in this social information processing circuit among ASD vs. typically-developing control (TDC) youths without psychopathology, and (b) if RSFC alterations can predict response to paired pulse transcranial magnetic stimulation (ppTMS) of the primary motor cortex as a probe of this circuit.

Method: Adolescents, ages 15 to 18, were enrolled in an IRB-approved study at Bradley Hospital and Brown University after informed parental consent and child assent. Two groups of participants were enrolled: (1) youths with ASD (n=10) and (2) TDC (n=10). All participants underwent 3 Tesla MRI scanning, including a high resolution T1-weighted MPRAGE anatomical image and a seven minute RSFC fMRI sequence. RSFC analyses used a priori seeds in the pSTS, IFG, and M1 to conduct connectivity analyses. Additionally, all participants underwent a ppTMS session performed with the Magstim Bistim to optimally measure cortical excitation and inhibition over the primary left motor cortex. A conditioning magnetic stimulus was consecutively followed by a test magnetic stimulus separated by a predetermined inter-pulse interval of 3 ms to evaluate short interval intracortical inhibition (SICI) and an inter-pulse interval of 100 ms to evaluate long interval intracortical inhibition (LICI).

Results: We found significant between-group differences in RSFC in two of the proposed nodes of the social information circuit between ASD and TDC youths. Specifically, we found ASD youths had significantly decreased RSFC between the bilateral IFG and the bilateral precentral gyri [F=3.22, p=0.005]. ASD youths also had decreased connectivity both cross-hemispherically between the bilateral IFG and within the IFG compared to TDC youths [F=3.22, p=0.005]. Interestingly, ASD youths had increased RSFC between the bilateral M1 and the left IFG [F=3.22, p=0.005]. Additionally, we explored correlations between RSFC extracted from the proposed nodes to ppTMS responses at the inter-pulse intervals of 3 and 100 ms.

Conclusion: This study is the first to unify neuroimaging with neurostimulation across the proposed nodes of the social information processing circuit in order to advance what is known about the neural underpinnings of ASD. Our preliminary analyses suggest that youths with ASD have less RSFC between the implicated nodes of the IFG and M1. These network functional connectivity deficits and E/I imbalances may have a primary role in the pathophysiology and shared behavioral phenotype of ASD. Our study highlights the need for developmental neuroimaging studies to continue to explore the link of E/I imbalances in circuits to structural, functional, and RSFC alterations, and to behavioral markers integral to ASD.
MACHINE LEARNING ALGORITHM FOR AUTOMATIC DETECTION OF CT-IDENTIFIABLE HYPERDENSE LESIONS ASSOCIATED WITH TRAUMATIC BRAIN INJURY

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Background:
Traumatic brain injury (TBI) is a major cause of death and disability in the United States. Time to treatment is often related to patient outcome. The performance of fast and accurate cerebral imaging is an important component of patient care. Current methods of detecting and quantifying intracranial pathology are time-consuming, in that they require careful review of the 2D/3D images by a radiologist. Additional time is allotted for image protocoling, acquisition, and processing. These steps occur in series, adding time to the process of identifying and treating brain injury - a condition where time to treatment is critical.

Overview:
Using machine learning and computer vision, we demonstrate a technique to rapidly and automatically detect CT-identifiable lesions. To identify important image features that can distinguish TBI lesions, we use the scale invariant feature transform (SIFT) and deep convolutional neural networks (CNN). Our learning algorithm is a linear support vector machine (SVM). The technique was validated using 409 CT scans of the brain, acquired via the Progesterone Treatment, Experimental Clinical Trial (PROTECTIII) study considering patients with moderate to severe TBI. CT data are annotated by a central radiologist and include patients with positive and negative scans. Additionally, the largest lesion on each positive scan was manually segmented. We reserved 80% of the data for training the SVM and 20% for testing. Preliminary results are promising with prediction accuracies as high as 92.55% (sensitivity = 91.15%, specificity = 93.45%), indicating the potential usefulness of this technique in clinical scenarios.

Methodology:
Given CT slices from all the training cases with positive (lesion) and negative (no lesion) ground truth annotations, our goal is to predict whether a new slice contains a lesion. Further, using the slice predictions, we want to predict whether a new case (i.e. a whole CT volume) contains a lesion in it. We divide our method description into two stages: feature extraction and machine learning algorithm, as explained below.

Feature extraction:
Feature extraction is one of the key components in computer vision. We implemented two different types of image features: SIFT and CNN. SIFT is a feature descriptor that first extracts key points in the CT slices that are local extrema of the difference of Gaussian filter response across different scales. Then local SIFT descriptors are computed from all the key points on each CT slice. K = 200 dimensional histogram is our final representation for each CT slice. We use the vlfeat library for all feature computations. A CNN is a multi-level artificial neural network with alternating convolutional and pooling filters in its different levels. We used the AlexNet, which is a network with 5 convolutional layers and 3 fully connected layers. We used the network weights pre-trained on the ImageNet data set.

Machine learning algorithm:
Our machine learning algorithm is a linear SVM. We used the liblinear library [3] for all computations. We classified our testing data (slices from the testing cases) as positive (lesion) or negative (no lesion) and computed our prediction accuracy by comparing them with the ground truth slice annotations. Furthermore, we use a simple neighborhood voting rule to decide if a slice prediction is to be retained. To transition from slice based prediction to case based prediction, we predict the whole case as positive if its CT scan has at least 6 mm of lesion.

Conclusions:
We present a machine learning approach for identifying presence of hyperdense lesion in CT data, both in individual slices and entire cases, and demonstrated high accuracy, specificity, and selectivity. To our knowledge, this study is the first successful use of a data set of this size for automatic detection of lesions due to TBI. We find that SIFT performed better than the CNN features.
NEIGHBORHOOD SAFETY AND INTERNALIZING BEHAVIOR PROBLEMS AMONG PRESCHOOLERS LIVING IN POVERTY: THE ROLE OF FAMILY VIOLENCE

Samantha Klaver, B.A., Stephanie H. Parade, Ph.D., Ronald Seifer, Ph. D., Audrey R. Tyrka, M.D. Ph.D.

Community violence and neighborhood safety can have harmful effects on children. Past research has demonstrated that exposure to community violence is a risk factor for externalizing behavior problems among children (Lynch & Cicchetti, 1998). Research on the effect of exposure to community violence on internalizing behavior problems is less consistent, with some studies demonstrating that exposure to community violence is a risk factor for internalizing problems (Lynch & Cicchetti, 1998), and others demonstrating no links between community violence and internalizing behaviors (Singer, Anglin, Song, & Lung hofer, 1995). These inconsistencies in the literature suggest that family factors, such as violence within the home, may buffer or exacerbate links between community violence and child behavior outcomes. The current study examined links between neighborhood safety and internalizing behavior problems in preschool-aged children from impoverished families, and considered the possibility that domestic violence exposure and childhood maltreatment moderates the effects of neighborhood safety on child behavior problems.

The participants in the study included 180 preschoolers (85 male, 95 female) living in poverty. Children ranged in age from 3 to 5 years and were racially and ethnically diverse. 91% of families qualified for public assistance. Review of child protection records and semi-structured interviews in the home were used to assess child exposure to early adversity including exposure to domestic violence and other forms of childhood maltreatment. One hundred and five children had substantiated cases of moderate-severe childhood maltreatment, and 85 were exposed to domestic violence. Parents reported on their perceptions of neighborhood safety using an adapted version of the Neighborhood Quality Scale (Kim et al., 2008), as well as child internalizing behavior problems using the Child Behavior Checklist (CBCL; Achenback & Rescorla, 2000).

Multiple regression analyses demonstrated that there was no significant main effect of neighborhood safety on internalizing behavior problems. However, there was a significant interaction of neighborhood safety and domestic violence exposure in the prediction of internalizing behaviors (B = -2.27, SE = .94, p = .018). Examination of simple slopes revealed that neighborhood safety was negatively associated with internalizing behavior problems among children who were exposed to domestic violence (B = -1.67, SE = .68, p = .016), but not among children who had no domestic violence exposure (B = .29, SE = .66, p = .67). In contrast, child maltreatment status did not moderate effects of neighborhood safety on internalizing behavior problems.

The findings indicate that living in an unsafe neighborhood is a risk factor for internalizing behavior problems among preschoolers, but only in the context of domestic violence exposure. Interventions for children who are living in unsafe neighborhoods may be most effective when also addressing family violence. Interestingly, child maltreatment status did not moderate the effect of neighborhood safety, perhaps because maltreatment may have occurred outside the home, by a perpetrator outside the family. Additional applied implications and directions for future research will be discussed.
PRINCIPLES TO PRACTICE: A PILOT PROGRAM IN PRECLINICAL MEDICAL ETHICS EDUCATION

Jonathan Kole, Ella Sorscher, Alexa Kansberg

INTRODUCTION
National accreditation leaders in medical school and postgraduate education drafted the Romanell Report in 2015 to review the current state of medical ethics education. Despite an agreed need for learner competency in professional ethics, they found no consensus methods to deliver this education. Our project was developed as an attempt to answer their call for new pedagogical approaches. Specifically, we endeavored to trial structured case-driven curricula in preclinical medical students and evaluate student experience and learning.

METHODS
We followed 26 first and second year medical students: fifteen choosing to enroll in a Medical Ethics elective and eleven enrolling in a non-ethics elective, allowing the curricula to be assessed in a prospective case-control design. The course consisted of eight two-hour sessions, followed by anonymous surveys after each session to assess student reaction. To gauge learner knowledge acquisition and behavior change, all 26 students were assessed before and after the course with two timed open response case analyses. A rubric was created by two Master level ethicists and each exam was blindly graded by two independent evaluators to ensure reliability and concordance. Any disagreement in grading went to multiple grader review.

RESULTS
Learners consistently reacted positively to the course material presented, with 88% of students reporting being satisfied to very satisfied overall with the course sessions and 91% of students rating the case studies as relevant or very relevant to their careers. Pre and post course assessments were collected on 12 ethics course students and 9 non-ethics students (four did not complete both tests, one excluded for referring to textbook during pre-test). Among study group, mean score improved 5.2 points from pre to post test, a statistically significant (p=0.0027) 52% elevation in score. The control group mean change was a 0.33 point decline between pre and post test.

CONCLUSIONS
This pilot program serves as a model curricula to provide case-based medical ethics education for preclinical students. Our course received consistently positive student reviews. Even with a small sample of students, learners demonstrated significant improvement in ethical reasoning beyond standard medical education. In this way, our curriculum demonstrates capacity for enhancing learner knowledge acquisition and behavioral change. Future directions include reflective improvement of course material, enhancing and validating assessment tools, and evaluating extension of the program to new teachers and more students.
TRANSCRANIAL DIRECT CURRENT STIMULATION-AUGMENTATION OF VIRTUAL REALITY EXPOSURE FOR PTSD: PRELIMINARY RESULTS

Victoria Larson, BS; Mascha van ’t Wout-Frank, PhD; Noah S. Philip, MD; Benjamin D. Greenberg, MD PhD

Background: Exposure-based therapy for posttraumatic stress disorder (PTSD) uses tenets of extinction learning to reduce anxiety and stress-based symptoms. Meta-analyses indicate exposure is efficacious, yet patients with combat-related trauma continue to exhibit residual symptoms. Both animal and human studies implicate the ventromedial prefrontal cortex (vmPFC) in extinction-related processes. Non-invasive brain stimulation protocols designed to increase endogenous vmPFC activity using may enhance such processes, thus improving clinical outcomes. We tested effects of transcranial direct current stimulation (tDCS) targeting vmPFC during presentation of a standardized virtual reality (VR) warzone environment. We predicted that anodal tDCS, compared to sham, would result in a sharper decrease in psychophysiological arousal and reduce self-reported symptoms in Veterans with PTSD.

Methods: Eight male Veterans with warzone-related PTSD completed six standardized, warzone (Iraq/Afghanistan) VR exposure sessions while receiving 25 minutes of 2 mA tDCS or sham stimulation with the anode over AF3 and cathode over PO8, informed by current modeling. Four Veterans received active tDCS, and four Veterans received sham. Skin conductance responsivity (SCR) was the primary outcome measure, evaluated during each VR session. A secondary outcome measure was the change in self-report PTSD symptom severity, pre-post all VR sessions and a one month follow-up.

Results: Preliminary data analyses found a significant effect of repeated VR session exposures on SCR across the active and sham groups (p<0.001). While there was no significant overall effect of tDCS (p=0.73), there was an interaction between number of sessions and tDCS (p<0.0001). This suggests that SCR to repeated presentation of VR combat events diminished more quickly when paired with tDCS versus sham. We further observed a clinically meaningful reduction in PCL5-rated PTSD symptom severity (pre: 46.50 ± 13.5; immediate post: 32.67 ± 15.4; one-month follow-up: 29.33 ± 14.91; p=0.02). All participants reported tDCS was tolerable. As a group, they did not accurately guess which treatment they received (p=0.49).

Conclusions: These preliminary results provide technical feasibility of combining tDCS with trauma relevant, exposure-based protocols. Although this data should be approached with caution given the small number of participants, it is suggestive of our approach to improve psychophysiological habituation and PTSD symptoms. Ultimately, the results of this research will inform a larger study on the efficacy of tDCS to improve current therapeutic interventions for Veterans with PTSD.
BETA RHYTHMS CAN SUPPRESS TACTILE DETECTION THROUGH SOMATIC GABA_B CURRENTS IN SUPERFICIAL PYRAMIDAL CELLS

Robert Law PhD, Hyeyoung Shin, Shane Lee PhD, Christopher Moore PhD, Stephanie Jones PhD

It is presently unknown how prestimulus beta-band (15-29Hz) activity in primary somatosensory cortex (SI) decreases tactile detectability. We provide the first theoretical account for this phenomenon following a thorough reanalysis of previously collected data using powerful modern tools. Building from recent work showing beta can emerge from simultaneous layer-specific inputs to cortex (Sherman, et al 2016), we used a detailed biophysical model to study beta’s impact on filtering tactile evoked responses in the SI circuit. We determine a particularly simple mechanism capable of linking beta to tactile detection: recruitment of interneuron populations acting on superficial pyramidal somata through GABA_B currents.

Our modeling examines two general scenarios. In the first, prestimulus beta spills over into the poststimulus period, directly modulating SI’s response to sensory input. In the second, beta in the prestimulus period acts indirectly by causing long-timescale activity in SI that itself interferes with detection. Simulations of both cases reveal a final common pathway: somatic GABA_B currents that silence transcortical messaging from LII/III principal cells for several hundred milliseconds. Aside from this shared endpoint, the two mechanisms yield dramatically different patterns of activity, producing telltale differentiating features in model sensory evoked responses.

We confirm the presence of these features in human recordings using source localized MEG data from a threshold level detection task (Jones, et al 2007), ascertaining significant case differences (low vs. high beta; detection vs. non detection) with sensitive but high-powered nonparametric tests. We also confirm high-frequency spectral predictions from the model in mouse LFP, where time-frequency evidence favors the latter, indirect mechanism. We conclude our study by examining known interneuron populations with the necessary properties for causing the GABA_B currents in our model, finding that neurogliaform cells, a relatively understudied but clinically relevant class, are particularly suited for mediating beta’s perceptual effect.
MATERIAL EXPOSURE TO BACTERIAL INFECTIONS DURING PREGNANCY AND RISK FOR SCHIZOPHRENIA AND OTHER PSYCHOSES AMONG ADULT OFFSPRING

Young A (Heather) Lee, BA; Jill Goldstein, Ph.D.; Larry Seidman, Ph.D.; Ming Tsuang, M.D., Ph.D., D.Sc.; Stephen Buka, Sc.D.

We investigated maternal exposure to bacterial infections during pregnancy in relation to the development of schizophrenia and other psychoses in adult offspring. The sample included 116 offspring with psychotic disorders in adulthood and 15,305 unaffected offspring from the Boston and Providence cohorts of the Collaborative Perinatal Project, a socioeconomically diverse pregnancy cohort conducted between 1959 and 1974. The obstetric histories of pregnant women were recorded by trained, non-physician personnel through semi-structured interviews starting at the first prenatal visit. These were subsequently integrated with complete hospital record review by obstetricians for finer categorization of specific types (e.g., viral, bacterial) and gestational timing of known or presumed infectious conditions. Offspring with possible psychoses were initially identified through personal interviews and/or record linkage with psychiatric treatment facilities. To yield confirmed diagnoses of psychoses, these identified individuals were re-contacted and interviewed by trained diagnosticians using the Structured Clinical Interview for DSM-IV (SCID). We found that individuals who were exposed to any infection in utero were at greater risk for psychotic illness in later life than unexposed individuals (OR=1.74, 95% confidence limits (CLs): 1.09, 2.77, p=0.02). The effect was greatest for infections that occurred in the second trimester of pregnancy; individuals who were exposed to any infection in the second trimester were at much greater risk for developing psychoses than unexposed individuals (OR=2.14, 95% CLs: 1.16, 3.96, p=0.02). Unlike viral infections, non-viral infections during pregnancy were associated with a significant increase in the risk of psychoses in later life. Specifically, bacterial infections predicted significantly elevated risk for psychoses in adult offspring (OR: 3.00, 95% CLs: 1.48, 6.07, p=0.002). Similar patterns of the second-trimester effect were observed for bacterial infections. Individuals who were exposed to bacterial infections in the second trimester were at significantly higher risk for psychoses than those who were unexposed to any prenatal bacterial infections (OR=5.31, 95% CLs: 2.25, 12.52, p=0.005). These results are consistent with previous investigations reporting maternal infections during pregnancy as a potential risk factor for psychoses among adult offspring. Furthermore, they suggest a novel finding that exposure to bacterial infections—especially in the second trimester—is associated with an elevated risk for psychotic disorders in adulthood. Larger samples, causal mediation analyses, and animal models should help elucidate whether bacterial infections lead to structural and functional abnormalities in the fetal brain, thereby increasing the subsequent risk of schizophrenia and other psychoses.
Background: The Butler Alzheimer's Prevention Registry was developed by the Butler Hospital Memory and Aging Program to stimulate participation in clinical trials on Alzheimer's disease (AD) and other memory disorders within Rhode Island and Southern New England region. This is an interim report on registrant characteristics and trial screen outcome.

Methods: We invited adults aged 55 to 85 with normal memory or mild memory loss to join the registry. Consented individuals completed a screening interview by telephone or through an online survey. Eligibility for referral to specific research trials was based on medical history and availability.

Results: Over a period of 10 months, 341 people consented and completed screening, of which 186 met eligibility to be referred to a prevention trial screen and 33 required clinical memory evaluation. The most effective recruitment strategy was earned media (58.1%), followed by referrals from other national registries (16.4%), family and friends (10.4%), clinicians (10.1%), and community events (4.9%). Registrants had a mean age of 68.7 (SD 7.9) and 16.1 mean years of education (SD 2.6); 69.1% were female, and 97% were Caucasian. 79.2% reported a family history of memory loss or dementia, most frequently referring to their parent. 46.1% had subjective cognitive complaints, but only 38.6% expressed concerns and 32% observed a decline in their cognition over the past year. Memory difficulties (80.9%) were the most common first symptom, followed by word-finding difficulties (15.1%). To date, 30 individuals have been enrolled in a clinical trial (9 treatment, 21 observational), 50 are in trial screening, and 93 are invited to cognitive testing and genotyping for further characterization.

Conclusions: The registry serves as an effective strategy to prescreen individuals and facilitate recruitment into research trials, with earned media being the most productive source of recruitment. However, thus far the respondents are predominantly Caucasian, college-educated participants. Other targeted recruitment strategies are needed to increase ethnic minority representation. The registry provides a platform for cohort studies and dementia risk analysis. Further risk assessment including genotyping and cognitive screen will be included in the next phase of the project to further characterize risk profiles in preclinical and symptomatic AD.
WHERE IS YOUR (MIND)FULNESS? IT MATTERS FOR SLEEP

Lipsky, Jonah; Acero, Pamela, BS; Cho, Lianne; Kriedler, Patrick, MSc; Britton, Willoughy, PhD

Background: Past research on meditation and sleep has produced conflicting results indicating both sleep-enhancing and arousing effects of mindfulness. This discrepancy may be due to the divergent effects of different meditation practices. The present study compares the differential effects of focused attention (FA) meditation and open-monitoring (OM) meditation on sleep.

Methods: Twenty-one individuals with mild-to-severe depression on antidepressant medication were randomized into an 8-week meditation course on either FA or OM meditation. Sleep Efficiency (SE) was measured with portable EEG devices (Z-Machines) on multiple nights before and after treatment.

Results: A significant group by time interaction indicated an increase in SE for FA practitioners and a decrease in SE for OM practitioners (F(2,22) = 6.2, p = .02, d = 1.14). Increases in mindful awareness were associated with worse sleep in OM practitioners (r = -0.60) but with improved sleep in the FA group (r = .43). In other words, directing attention towards thoughts and emotions (OM) increased insomnia, whereas focusing the attention away from thoughts and emotions towards a neutral object such as the breath (FA) was associated with improved sleep.

Discussion: Despite both mediation practices being called mindfulness, the results suggest they may have opposite effects on sleep. Thus, for treating insomnia, the object of mindful attention matters.
SAFETY, TOLERABILITY AND PHARMACOKINETICS OF THE MGLUR5 NEGATIVE ALLOSTERIC MODULATOR GET73 FOLLOWING SINGLE AND REPEATED DOSES IN HEALTHY VOLUNTEERS

Victoria M. Long, BA, Carolina L. Haass-Koﬄer, Pharm.D., Kimberly Goodyear, PhD, Antonella Loche, PhD, Roberto Cacciaglia, PhD, Robert M. Swift, MD, PhD, Lorenzo Leggio, MD, PhD

Background and Purpose: Preclinical work suggests that the metabotropic glutamate receptor subtype 5 (mGlu5) may represent a novel target to treat neuropsychiatric disorders, especially alcohol use disorder and obesity. The goal of this first-in-man study was to evaluate the safety, tolerability and pharmacokinetics of GET73, a novel mGluR5 negative allosteric modulator.

Experimental Approach: This was a double-blind, placebo-controlled study conducted in healthy male volunteers in two phases: Part 1 and Part 2. GET73 was administered as single ascending doses (n=48; Part 1) or multiple ascending doses (n=32; Part 2). Primary endpoints were the incidence of adverse events (AEs) among drug conditions and drug tolerability. The secondary endpoints were the pharmacokinetic (PK) parameters of GET73 and its major metabolite MET2.

Key Results: Single GET73 doses of up to 600-mg and repeated ascending doses of up to 450-mg twice/day were safe and well-tolerated. All AEs in the study were mild or moderate in severity. Total GET73 exposure increased with each increased GET73 dose. A dose-related increase in mean maximum plasma drug concentration was observed after repeated dosing. Maximum plasma drug concentrations occurred between 0.5–2.05 hours after administration in all groups for both single and repeated doses. The PK parameters of the main metabolite of GET73, MET2 were consistent with those of the parent drug.

Conclusions and implications: This first-in-human study indicates that GET73, as single or multiple ascending doses, is safe and well-tolerated when administered to healthy male volunteers.
A PHASE 1 RANDOMIZED CROSS-OVER DRUG-ALCOHOL INTERACTION STUDY WITH THE MGLUR5 NEGATIVE ALLOSTERIC MODULATOR GET73 IN HEALTHY MALE VOLUNTEERS

Victoria M. Long, BA, Carolina L. Haass-Koffler, Pharm.D., Kimberly Goodyear, PhD, Antonella Loche, PhD, Roberto Cacciaglia, PhD, Robert M. Swift, MD, PhD, Lorenzo Leggio, MD, PhD

Aim: Preliminary preclinical work suggests that GET73, a novel metabotropic glutamate receptor subtype 5 (mGluR5) negative allosteric modulator, may represent a novel pharmacological treatment for alcohol use disorder (AUD). A Phase 1 first-in-man study indicated the safety, tolerability and pharmacokinetic (PK) profile of GET73 in healthy male volunteers. The goal of the study was to assess the bioavailability of GET73 and of its major metabolite MET2 when co-administered with alcohol and evaluate the safety of this drug-alcohol interaction.

Methods: This was an open-label, randomized, crossover study in healthy male volunteers (n =12). A 2 X 2 design was employed to compare the effect of 300-mg GET73 administered as single dose (Part 1) and then trice a day (Part 2) with and without alcohol.

Results: The relative bioavailability of 300-mg of GET73 administered with alcohol (compared to the dosing in absence of alcohol) was 150% in the single dose and 112% in the trice a day dose. There were no significant differences in relative bioavailability between administering GET73 at either doses in the presence or absence of alcohol. The MET2 AUC∞ ratio was 0.844 in the single dose and 0.958 in the trice a day dose. When alcohol was co-administered, there was a reduction in metabolic conversion of GET73 to MET2 following both single and trice a day GET3 administration. GET73 was well tolerated at any dose, both in the presence and absence of alcohol, with no notable difference in the incidence of adverse events (AEs).

Conclusions: Alcohol does not affect the bioavailability of GET73 and its metabolite MET2 in healthy male volunteers. GET73 and MET2 exhibited, independent from the co-administration or not of alcohol, little evidence of accumulation. Overall, the incidence of AEs was low, no dose-related incidence in AEs nor difference in the presence or absence of alcohol co-administration were observed.
A common conclusion regarding the efficacy of different kinds of psychotherapies for depression is that all therapies are likely to be equally efficacious because they all rely on the relationship or working alliance between the patient and the therapist. These conclusions are premature because depressive disorders are highly heterogeneous and this heterogeneity is rarely taken into account in treatment studies. The first study explored differential treatment outcomes in the context of a randomized trial (N = 622) that reported no differences between a high-intensity treatment regime starting with cognitive-behavioral therapy (CBT), a lower-intensity stepped care condition starting with a brief therapy (BT), and treatment as usual (TAU). A closer examination of the data revealed that the treatments were equally efficacious at the 18-21 month follow-up for most of the sample. However, CBT (60%) was superior to BT (44%) and TAU (39%) in the subset of clients who were expected to have a poorer prognosis. The second study explored the variability of the effects of the working alliance, a psychotherapy construct traditionally associated with nonspecific or common psychotherapy effects. In a sample of clients receiving CBT for depression (N = 60), for clients with less recurrent depression the alliance was a stronger predictor of outcomes than is generally reported in the research literature (r = 0.52). By contrast, for clients with more recurrent depression, the alliance did not predict outcomes (r = -0.02). In the third study, these findings were replicated in the CBT condition of a randomized controlled trial (RCT; N = 241). However, the findings did not generalize to the short-term psychoanalytic supportive psychotherapy (SPSP) condition in the RCT, suggesting that this pattern may be specific to CBT. Taken together, the findings suggest that the efficacy of evidence-based psychotherapies and the effects of different psychotherapy processes are limited to specific, potentially identifiable, subsets of clients.
A NEURAL TISSUE ENGINEERING APPROACH TO EXTRACELLULAR MATRIX-DERIVED HYDROGELS

Matthew Luminais, Elisabeth Evans, Diane Hoffman-Kim PhD

Background: Several neurological pathologies may benefit from cell transplant therapy; however, enhanced CNS regeneration from successful cell therapy relies on the ability of the transplanted cells to adhere, survive, and migrate into the targeted lesion site. Given the low viability and poor positional targeting of existing cell transplant methods, there is a need to develop biomaterials, which when co-delivered with grafted cells, improve cell survival and retention at the delivery site. Towards this end, one regenerative biomaterial strategy is to use decellularized donor tissues to generate biomaterials that retain biochemical and physical cues from healthy extracellular matrix (ECM). Additionally, recent literature has shown that decellularized donor tissue ECM can be fabricated into hydrogels to retain native biochemical matrix signatures. Although decellularization and hydrogel fabrication methods have been reported for whole brains, it is unknown whether these methods can be applied to engineered neural microtissues. A tailorable tissue engineering platform allows for greater control over the final material characteristics, which are affected by cell type and culture conditions. Here, our goal was to generate three-dimensional matrices from engineered microtissues and test the feasibility of processing them into hydrogels.

Methods: Three different types of spheroid microtissues were generated through a self-assembly method using the following cell sources: adult rat cortical cells enriched for neurons, rat adult hippocampal neural stem cells, A7 and Neu7 cell lines, which are permissive and inhibitory astrocytic cell lines originally derived from rat optic nerve tissue. We evaluated three existing decellularization protocols, including two developed for brain tissue and one previously used with tissue-engineered constructs, on 6-week old microtissues. In parallel, the decellularized hippocampal neural stem cell tissues were digested in a pepsin-hydrochloric acid solution and adjusted to physiological pH, salt concentration, and temperature to initiate polymerization.

Results: All decellularization protocols evaluated were effective at removing cellular debris from the neural microtissues, however the protocol previously used for tissue-engineered constructs best preserved the structural integrity of the ECM. Within each microtissue type, the patterning of laminin revealed distinct architectures, varying in topography and porosity. The decellularized rat adult hippocampal neural stem cell microtissues were successfully fabricated into hydrogels that were stable over many days and capable of supporting proliferation when re-seeded with neural stem cells.

Conclusions: Here, we show that acellular matrices can be derived from engineered neural microtissues and that these matrices can be processed into stable hydrogels. As a proof of concept, we have demonstrated through the culture and subsequent decellularization of three different example microtissues, representative of various cerebral cortex niches, that matrix architecture can be engineered through the inclusion of specific neural cell populations. The ability to fabricate these decellularized matrices into hydrogels provides an important proof of concept, and future studies will investigate cell proliferation, migration, and differentiation in response to these materials.
PROPERTIES OF RETINOGENICULATE SYNAPSES OF INTRINSICALLY PHOTOSENSITIVE RETINAL GANGLION CELLS

Ryan Maloney PhD, Scott Cruickshank PhD, David Berson PhD

Intrinsically Photosensitive Retinal Ganglion Cells (ipRGCs) provide absolute luminance signals to the dorsal lateral geniculate nucleus (dLGN), but how the dLGN integrates this input is unclear. To explore the relevant synaptic networks, we assessed the effects of selective activation of ipRGC afferents on postsynaptic thalamocortical cells (TCs) in the dLGN.

We made patch-clamp recordings from postsynaptic thalamocortical cells (TCs) in dLGN slices while selectively stimulating ipRGC axons optogenetically. Channelrhodopsin2 was selectively expressed in ipRGCs by injecting a Cre-dependent virus into the eyes of heterozygous melanopsin-Cre mice (Opn4cre/+). The virus was an AAV2 carrying a flexed construct coding for mCherry-Channel Rhodopsin fusion protein, driven by the EF1 alpha promoter. Virus was injected neonatally (P7-10) and retinas harvested 4-6 weeks later for recording (age P40-P50). In live coronal slices of the dLGN (300 µm thick), TCs were targeted visually based on proximity to fluorescent mCherry-labeled ipRGC terminals. For each cell, we measured the response to trains of optical ipRGC-activating stimuli both in current clamp and voltage clamp. We varied the clamp potential of the recorded cell (Vhold) to differentiate between excitation and inhibition.

All cells targeted based on nearby expression of mCherry-labeled ipRGCS terminals exhibited both excitatory and inhibitory currents in response to optic activation of local ipRGC axons. The size of these currents varied dramatically. Excitatory currents ranged from 12 to 14,000 pA (measured at Vhold _75mV) and inhibitory currents ranged from 90pA to 1500 pA (Vhold _35mV). Additionally, a small subset of synapses exhibited prolonged post-stimulus responses, lasting up to 30 seconds after stimulation of the ipRGC afferents.

Our results show that the synaptic connection between ipRGCs and TCs of the dLGN is highly variable, suggesting that ipRGCs may play a diverse role in the circuitry of the dLGN. Some of this diversity may be linked to the diversity of ipRGCs, several subtypes of which are thought to innervate the dLGN. This conclusion differs from the conventional view of the dLGN as a simple relay of RGC responses, suggesting instead that TC responses show a functional diversity beyond that of their RGC input. Our results also open the possibility that a subset of RGC input may more broadly modulate the activity in the dLGN.
OBSESSIVE-COMPULSIVE SYMPTOMS PREDICT POSTTRAUMATIC GROWTH: A LONGITUDINAL STUDY

Daria Mamon, PsyD, Zahava Solomon, Ph.D., Sharon Dekel, Ph.D

Although posttraumatic growth (PTG) has received growing attention, the relationship between PTG and distress remains unclear. This longitudinal study examines the relationship between posttraumatic obsessive-compulsive (OC) symptoms and PTG. Israeli veterans were followed over 17 years using self-report questionnaires of OC symptoms, posttraumatic stress disorder (PTSD) and PTG. Hierarchical regression analyses demonstrated that OC symptoms predicted PTG, even when initial PTG levels and PTSD symptoms were controlled for in the combatants group. These preliminary findings suggest that OC symptoms may play an important role in facilitating psychological growth. Future research is warranted to explore the mechanisms responsible for this relationship.
Background: Suicide is the third leading cause of death among adolescents living in the United States (Nock et al., 2013). In order to ensure safety, many adolescents expressing suicidal thoughts and/or behaviors are admitted to inpatient care. Importantly, adolescent suicidal thoughts and behaviors cut across diagnostic categories.

Objective: The present study examines adolescents hospitalized for suicidal thoughts/behavior who have been admitted to Bradley Hospital inpatient unit. By analyzing the descriptive data of these adolescents being treated for suicidal thoughts and behaviors, this poster aims to describe diagnostic and demographic information among adolescents hospitalized for suicidal thoughts and behaviors.

Method: Participants (N= 58) were recruited from a larger study (R01MH105379; Biomarkers, social, and affective predictors of suicidal thoughts and behaviors in adolescents;PI: Nugent) that explores the interactions of social environment and (epi)genetics, and how these factors influence post-discharge course for adolescents hospitalized for suicidal thoughts and behaviors. Diagnoses were determined using The Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS), a semi-structured interview. Demographics of the participants were collected using self-report questionnaires.

Results: Demographic information sample from this sample revealed that 77.6% were biologically female. 8.62% of these adolescents reported that they identify with a gender that is different than the biological sex they were assigned at birth. Consistent with hospital demographics, the majority of participants were Caucasian (72.4%), with 12.1% reporting more than one race and 8.6% endorsing African American/Black race. In regards to ethnicity, 13.79% identified as Hispanic/Latino. Consistent with recruitment criteria, participants ages were roughly evenly distributed in age from 13-17 (M=15.2, SD=1.6). Consistent with past research, a majority of participants met criteria for a depressive disorder: 67% met criteria for Major Depressive Disorder (MDD), 46.5% past major depressive episode, 5.2% MDD with psychotic features, and 39.6% Persistent Depressive Disorder (Dysthymia). Diagnosis with an anxiety disorder was also prevalent: 6.8% Panic Disorder, 20.6% Social Anxiety Disorder, 36% Generalized Anxiety Disorder and 10.34% Oppositional Defiant Disorder. Less common diagnoses included: 5% ADHD (Predominantly Hyperactive-Impulsive type) and 4 participants did not meet any diagnostic criteria. All other diagnoses were reported at less than 5% of the sample.

Conclusions: These findings highlight the demographic and diagnostic background information of adolescents hospitalized for suicidal thoughts and behaviors at Bradley Hospital. Overall, these findings are consistent with the literature regarding diagnoses commonly observed among individuals hospitalized for suicidal thoughts and behaviors, particularly related to the prevalence of depressive disorders. Notably, a number of adolescents reported that they identify with a gender that is different than the biological sex they were assigned at birth. Though few studies have explored risk for suicidal thoughts and behaviors in gender minority youth, Grossman and D’Augelli (2007) found that 25% of transgender youth in their sample reported suicide attempts. Limitations of this work include a small sample size, cross-sectional description, and reliance on self report and interview methods. The larger project, when completed, will permit a longitudinal multi-method examination of this and other research goals.
THE FIVE ITEM BRIEF ASSESSMENT OF FAMILY FUNCTIONING SCALE (BAFFS): AN ULTRABRIEF MEASURE OF FAMILY FUNCTIONING

Abigail Mansfield, PhD; Gabor Keitner, MD

The purpose of the present study is to present the Brief Assessment of Family Functioning Scale (BAFFS), a five item measure of general family functioning. It is designed to be used to assess family relationships when brevity is especially important. The BAFFS was derived from the 12 item General Functioning Scale of the Family Assessment Device (GF FAD). The GF FAD was subjected to principal components analysis, and five of the items loading .70 or higher on a one factor solution were selected to create the BAFFS. These five items correlated highly with the 12 item General Functioning scale and the mean of the 60 item FAD in a large sample. They also correlated highly with an established measure of couple satisfaction, the DAS-4 in a clinical help-seeking sample. The BAFFS demonstrated construct validity with an interview based rating of family functioning. In summary, the BAFFS provides busy practitioners with an ultra-brief measure of perceived family functioning that can be used at each visit and to track change over time.
SUBJECTIVE COGNITIVE DECLINE IN MEMBERS OF THE RHODE ISLAND ALZHEIMER PREVENTION REGISTRY

Seth Margolis, Ph.D., Geoffrey Tremont, Ph.D., Charles Denby, B.A.,
Benjamin Heller & Brian Ott, M.D.

Background: Recent research suggests that subjective cognitive decline (SCD) may be a harbinger of mild cognitive impairment (MCI) and Alzheimer’s disease (AD). However, its prognostic significance remains unclear. To date, no studies have examined independent predictors of SCD in individuals concerned about incipient dementia enrolled in an AD prevention registry. This cross-sectional study characterized prevalence of SCD, APOE status, baseline cognitive screening performance and aspects of family and personal health history in the Rhode Island Alzheimer Prevention Registry. We also assessed which factors independently predicted SCD.

Methods: Participants were 100 registry members with undisclosed APOE test results (78% female, 97% Caucasian, mean age=64±7.5 years, mean education=16±2.5 years). Multivariate linear regression predicted SCD (0=no memory decline, 1=decline without concern, 2=decline with concern) based on APOE status (ε4+ or not), reported AD family history, baseline Minnesota Cognitive Acuity Screen (MCAS) performance, and personal histories of mild psychiatric conditions (e.g., depression, anxiety) and neurological events without persisting cognitive sequelae (e.g., migraine, concussion, TIA).

Results: Most participants reported AD family history (87%). APOE ε4+ status was highly prevalent (41%). Nearly a quarter of the sample reported mild psychiatric (23%) and neurological histories (22%). MCAS scores were in the non-impaired range in 84% of individuals, and in the MCI range in 16%. Of the 65% endorsing SCD, 63% expressed concern about perceived memory changes. Results of the regression analysis (R2=.14, p=.02) revealed that AD family history (β=.53, p=.04) and personal history of mild psychiatric (β=.41, p=.05) and neurological conditions (β=.48, p=.02) independently and significantly predicted SCD whereas APOE status (β=.04, p=.88) and MCAS performance (β=.00, p=.88) did not.

Conclusions: In this cross-sectional study, SCD was common among AD prevention registry members. However, SCD was not significantly associated with cognitive screening performance or APOE status. Rather, SCD varied as a function of reported AD family history, which could plausibly be mediated by health anxiety. SCD was also associated with personal history of mild psychiatric and neurological conditions, which raises the question of whether perceived declines were misattributed to such symptoms. Future research should examine these relationships longitudinally in AD prevention registries and other healthy aging cohorts.
THE TIME VARYING EFFECTS OF PSYCHOSOCIAL FACTORS ON SUICIDAL IDEATION IN YOUTH FOLLOWING PSYCHIATRIC HOSPITALIZATION

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Introduction: The link between bullying experiences and suicidal thoughts and behaviors in adolescents has been well established; however, no studies have examined correlates between bullying and STB among adolescents hospitalized for STB. The current study investigated how bully experiences impact the effect of in vivo experienced affect on suicidal ideation (SI) measured via ecological momentary assessment (EMA) during the high-risk period following discharge.

Methods: The sample included 43 adolescents hospitalized for STB participating in a larger study (NIMH MH105379) examining epigenetic and social factors influencing adolescent recovery from STB. Adolescents completed clinical interviews and self-report questionnaires during hospitalization. Upon discharge from the hospital, each youth was provided with a mobile phone that signaled momentary assessments throughout their days for a total of three weeks. Participants responded to approximately five EMA assessments each day. Assessment times varied according to predefined individual schedules (e.g., time of release from school, work responsibilities, therapy, etc.).

The Adolescent Peer Relations Instrument (APRI), a self-report questionnaire measuring school bullying experiences prior to hospitalization, was collected during hospitalization. EMA sampling was used to measure in vivo self-report of positive (e.g. happy, confident, excited) and negative (e.g. hopeless, sad, worried, and lonely) affect and SI. Items measuring positive and negative affect were taken from the Positive and Negative Affect Scale (PANAS).

In order to measure the influence of bullying experiences on temporal changes in negative affect following hospitalization we used a Time-Varying Effect Model (TVEM). TVEM is a nonparametric regression based approach that models coefficients as functions of time through spline smoothing. This approach enables researchers to estimate dynamic, nonlinear relationships in intensively measured longitudinal data. In each model, SI was modeled as the outcome with a logistic distribution and positive/negative affect variables were entered in separate models as a time varying predictor. To determine the influence of bullying on this relationship, pre-hospitalization bullying victim experience was entered as a time-invariant covariate in each model.

Results: The analytic sample included 43 participants (67.4% female, 14% Hispanic or Latino) aged 13-19 (Mean = 16, SD = 1.65). A total of 1,992 momentary assessments of hopelessness, sadness, worry, loneliness, happiness, excitement, confidence, and suicidal ideation were completed, yielding an average of 46.13 assessments per participant (SD = 30.44, min = 3, max = 105). Results suggest that for individuals reporting average levels of positive or negative affect, the odds of reporting SI was less likely (odds ratio < 0.25 for days 1-21, with slight increases around day 5 and day 20). Models that included the negative affect variables (hopelessness, sadness, worry, and loneliness) resulted in steadily increasing odds of engaging in SI while models that included positive affect variables (happiness, excitement, and confident) resulted in steadily decreasing odds of engaging in SI. Bullying experiences prior to hospitalization were not significantly related to SI in any of the models.

Discussion: Although bullying experiences were not significant predictors of SI among adolescents during the three weeks post-hospitalization for STB, increases in negative affect was associated with significant odds of engaging in SI while increases in positive affect resulted in lower odds of engaging in SI. Importantly, these models also point to potentially periods of time when the relationship between emotional affect and SI are strongest. This information can guide future intervention research to help identify key variables within critical periods of time to aid adolescents during the transition and recovery from hospitalization.
Tsc1 DELETION IN THE DEVELOPING THALAMUS SYNCHRONIZES ACTIVITY IN RELAY NEURONS VIA ECTOPIC ELECTRICAL SYNAPSES

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Tuberous Sclerosis (TSC) is a developmental genetic disorder caused by mutations in Tsc1 and/or Tsc2. Neurological signs in TSC patients include epilepsy and autism, but the cellular mechanisms underpinning TSC are poorly understood. One brain region implicated in the pathology of some TSC patients is the thalamus. The laboratory previously generated a mouse model in which Tsc1 was selectively deleted in ~70% of relay neurons on E12.5 (Normand et al., Neuron, 78:895, 2013). This deletion led to enlarged relay neurons with abnormal intrinsic excitability, and anomalous circuitry and synchrony in the thalamus; the deletion was also sufficient to cause aberrant repetitive grooming and seizures. One way to enhance neuronal synchrony is to interconnect cells with electrical synapses, which are comprised of neuronal gap junctions: intercellular channels that provide conductive pathways from one cell to another. The laboratory previously showed that electrical synapses are present in VB relay neurons early in development, but are entirely abolished by the second postnatal week in wild-type mice (Lee et al., J. Physiol, 588:2403, 2010). Surprisingly, we found sparse but strong electrical synapses between Tsc1Δ/Δ relay neurons in slices of the ventrobasal (VB) nucleus of the thalamus (Tsc1Δ/Δ mice: ~8% of cell pairs, Tsc1+/+ mice: 0% of pairs; ages P20-P24). Electrically coupled Tsc1Δ/Δ relay neurons had synchronized subthreshold and spiking activity. Additionally, inhibitory inputs from the thalamic reticular nucleus to one thalamic relay neuron could, via electrical synapses, delay the activity of an adjacent neuron and briefly synchronize the activity of the cell pair afterwards. We also addressed whether Tsc1 deletion in relay neurons alters chemical synapses. Relay cells with Tsc1 deletions had a lower frequency of miniature excitatory postsynaptic currents, although the kinetics of these events were unaltered. Additionally, TRN inputs to Tsc1Δ/Δ relay neurons had slightly altered kinetics but unaffected short-term dynamics. Interestingly, Tsc1Δ/Δ relay neurons received more frequent feedback inhibition than control relay neurons.

To summarize, prenatal Tsc1 deletions led to the induction of ectopic electrical synapses among mature relay neurons, as well as to changes in intrathalamic chemical synapses. These synaptic changes may enhance synchrony among relay neurons and the cortex they project to, and contribute to repetitive grooming and seizures.
Objective: This study aimed to characterize parenting behaviors in mothers of adolescent daughters at risk for developing Borderline Personality Disorder, with risk defined by the daughter’s engagement in repetitive nonsuicidal self-injury (NSSI), and to test hypothesized examine associations between parenting behaviors and adolescent psychopathology.

Method: Participants were dyads of mothers and their 14-18-year-old daughters (n = 51); of the daughters, 24 (47%) had a history of NSSI and 27 (53%) had no NSSI and no psychopathology. Dyads completed questionnaires related to perceived maternal validation and invalidation and participated in face-to-face interactions, which were later rated for parenting behaviors. Results: The two groups did not significantly differ on parenting. For the sample as a whole, parenting behaviors were associated with indices of adolescent psychopathology, more consistently so for adolescent reports relative to maternal reports or observational ratings of parenting behaviors. Adolescents’ reports of high maternal invalidation in combination with low validation were associated with their higher levels of adolescent psychopathology regardless of NSSI.

Conclusions: We failed to find support for the hypothesized parenting deficits in mothers of adolescent females engaging in NSSI. Adolescents’ perceptions of their mothers engaging in a combination of higher invalidation and lower invalidation were associated with higher levels of adolescent psychopathology regardless of NSSI.
3D ILLUSTRATION TO QUANTIFY VOLUME OF SUBDURAL AND EPIDURAL HEMATOMAS

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Introduction:
Traumatic brain injury (TBI) is a major cause of death and disability in the US. Recent advances in 3D illustration (3DI) can precisely quantify intracranial pathology on computed tomography (CT). The current standard of measurement, ABC/2, demonstrates variability in precision with bleed phenotype. The aims of this project are to assess the accuracy of an automated 3DI process and compare this to the standard ABC/2 scale.

Methods:
Baseline CT scans collected during the ProTECTIII multicenter clinical trial (n=881) were retrospectively reviewed by a central neuroradiologist. Cases of subdural and epidural hematoma were identified (n=260). The radiologist calculated ABC/2 score using OsiriX (Mac) and RadiAnt (PC) workstations. In a blinded fashion, research assistants concurrently generated 3DI using the following methods: DICOM data were resampled to 1.5 mm thickness slices and symmetrized using medical image analysis software (Aquarius TeraRecon Inc, 2012). Lesions were then compiled into single volumetric regions of interest (3D Slicer v4.5, 2015). Hemorrhages were divided into two groups for analysis: Group 1. volume of hemorrhage was <50 cm3 (n=195) and Group 2. volume of hemorrhage ≥50 cm3, n=65). Agreement was assessed via Bland-Altman analysis. This study was IRB approved.

Results:
There is a significant difference between the results of the 3DI and ABC/2 methods. In Group 1., the estimated relative bias between the two measurements (after transformation) is 0.17 (SD 1.16; p-value 0.044; 95% CI 0.005, 0.333). In Group 2, the relative bias is -0.712, SD 1.22, p-value <0.0001, 95% CI (-1.013, -0.410).

Conclusion:
The 3DI method calculates detailed surface area measurements in large and small volume hemorrhages, while the ABC/2 method averages cross-sectional area. ABC/2 estimates vary by bleed phenotype and offer less topographical precision than 3DI. This is particularly true in extra-axial hemorrhages, which are frequently crescent-shaped and irregular. The 3DI method produces a more detailed measurement of brain hemorrhage than ABC/2, data important to patient treatment and prognostication.
DEVELOPMENTAL CONSEQUENCES OF MATERNAL SMOKING DURING PREGNANCY ON OFFSPRING AUDITORY MEMORY: A SIBLING COMPARISON STUDY

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Children exposed to maternal smoking during pregnancy (SDP) in utero tend to perform more poorly on tests of memory with auditory demands relative to their nonexposed counterparts (Fried, Watkinson, & Gray, 2003), but SDP does not occur independent of other familial risk factors. Prenatal exposure to SDP is correlated with parental and contextual factors that could act as more proximal risk factors for poorer child outcomes (Knopik, 2009). Therefore, in addition to environmental risk, mothers who smoke during pregnancy may also be more likely to confer genetic risk for poorer functioning to their offspring. As such, poor and inconsistent control for covariates, notably heritability, preclude concluding causal effects of SDP on child auditory memory. To our knowledge, there are no genetically-informed studies of auditory memory in children exposed to SDP. Existing studies that are not genetically-informed find associations between SDP and auditory memory to be attenuated, but still significant, after controlling for measured confounds (e.g., maternal education). It remains unknown if the link withstands rigorous control for general, unmeasured familial (genetic and environmental) confounds.

Data were drawn from the Missouri Mothers and Their Children study (Knopik et al., 2015). Families were identified based on birth record report (obtained from the Missouri Department of Health and Senior Services Bureau of Health Informatics) that mothers changed smoking behavior between any two pregnancies. Diagnostic interviews were completed with 173 families (344 pregnancies). Assessments occurred when children were 7-16 years old (Child 1 [older sibling] average age=13.02, 54% male; Child 2 [younger sibling] average age=10.22, 51% male). Maternal report of SDP was obtained using a modified version of the Missouri Assessment of Genetics Interview for Children—Parent on Child (Todd et al., 2003). Parent and child auditory memory were assessed with the Digit Span subtest of the Wechsler Adult Intelligence Scale (WAIS; Wechsler, 1991) and Wechsler Intelligence Scale for Children—IV (WISC; Wechsler, 2005), respectively. This task requires participants to repeat sequences of numbers spoken aloud by an interviewer both verbatim (assesses short-term auditory memory) and in reverse order (assesses auditory working memory).

The sibling comparison approach involved fitting a series of hierarchical linear models to assess within- and between-family association between SDP and auditory memory while accounting for non-independence of the data. Thus, it controls for genetic and familial influences that siblings share, enabling us to explore if SDP has a direct effect on child auditory memory. 72% of the variance in child auditory memory was attributable to within-family differences, whereas 28% was attributable to between-family differences, indicating that the variability in auditory memory was primarily a function of differences between siblings rather than differences across families. Further, the casual effect of SDP on auditory memory was fully attenuated when familial confounds (i.e., maternal report of her marital status, age, and education at the birth of each child, qualification for food stamps [yes/no] at the time of delivery [collected from the birth record], maternal auditory memory, and child age], sex, second-hand smoke exposure during pregnancy [by the father]) were considered, indicating that familial factors act as more proximal risk factors for poorer child auditory memory than SDP.

These findings: 1) suggest that these proximal environments may serve as effective targets of interventions seeking to improve children’s auditory memory in families with nicotine dependent mothers; and 2) underscore the need for genetically-informed studies of the effects of SDP on child outcomes. This should not diminish concern regarding SDP, but instead, advance knowledge of what factors are and are not potential causes of auditory memory problems.
INCREASED PRESENCE OF FAMILIAL PSYCHIATRIC AND NEURODEVELOPMENTAL DISORDERS IN GROUPS WITH UNCLEAR OR NEGATIVE AUTISM SPECTRUM DISORDER DIAGNOSIS IN A STATE-WIDE AUTISM REGISTRY

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Background: Family history is important to consider in patients with Autism Spectrum Disorder (ASD) as literature has shown increased presence of familial psychiatric disorders compared to the general population. Psychiatric comorbidity is also high in ASD and associated with functional impairment and increased diagnostic challenges (Leyfner et al. 2006; Molloy et al. 2011). Disorders that are especially prevalent in these families include depression, bipolar, and anxiety disorders (Cohen & Tsiouris, 2006; Micali et al., 2004).

Objective: To investigate differences in family psychiatric and neurodevelopmental history in individuals referred to an ASD research registry grouped by level of diagnostic confirmation and confidence.

Methods: Participants were the first 1,000 individuals enrolled in a state-wide autism registry (Male = 780; Mage = 13.6 years, SD = 9.6). Referrals were based on existing diagnosis or concern for ASD. Participants were categorized into three groups: (1) ASD (N = 533): having a community diagnosis of ASD confirmed by the ADOS-2; (2) ASD-unclear (N = 318): having an inconsistency between community diagnosis and ADOS-2 result; and (3) non-ASD (N = 101): having a negative ADOS and no community diagnosis. Family history was obtained by interview. Analyses examined group differences of individual disorders as well as composite scores of total number of neurodevelopmental and psychiatric disorders.

Results: Using one-way ANOVA and Tukey post-hoc tests, controlling for false-discovery rate, there was increased presence of multiple psychiatric and neurodevelopmental disorders in non-ASD and ASD-unclear groups as compared to ASD group. The overall number of psychiatric disorders in first-degree relatives was significantly higher in ASD-unclear (M = 2.15, SD = 2.05, F ((2, 862) = 14.0, p < .001) and non-ASD (M = 2.42, SD = 2.35, p < .001) as compared to ASD (M = 1.56, SD = 1.66). The non-ASD group reported more neurodevelopmental disorders in first-degree relatives (M = 1.62, SD = 1.70, p = .013) than the ASD group (M = 1.11, SD = 1.48). Follow-up analysis showed that probands in ASD-unclear (M= 2.3, SD = 1.7) and non-ASD groups (M= 2.5, SD = 1.7) had increased psychiatric comorbidities as compared to ASD group (mean = 1.58, SD = 1.5, F (3,546) = 16.1, p < .001). There was a significant positive correlation between number of psychiatric diagnoses in the proband and number of psychiatric disorders in first-degree relatives (r = .28, N = 550, p <.001). A linear regression was performed controlling for biologic sex and age (R2 = 0.13, F (3, 546) = 25.92, β = .27, t = 6.8, p < .001), that confirmed a statistically significant association between number of first-degree family diagnoses and number of proband comorbidities.

Conclusions: Individuals in the ASD group had less family members affected with neurodevelopmental or psychiatric disorders and less psychiatric comorbidities as compared to ASD-unclear and non-ASD groups. This finding supports that registry referrals of ASD-unclear and non-ASD individuals are in part due to more complicated psychiatric presentation, and demonstrates the need for clinical tools that can aid in differentiating these groups.
Individual differences in dopaminergic tone underlie tendencies to learn from reward versus punishment. These effects are well documented in Parkinson’s patients, who vacillate between low and high tonic dopaminergic states as a function of medication. Yet very few studies have investigated the influence of higher-level cognitive states known to affect downstream dopaminergic learning in Parkinson’s patients. A dopamine-dependent cognitive influence over learning would provide a candidate mechanism for declining cognitive integrity and motivation in Parkinson’s patients. In this report we tested the influence of two high-level cognitive states (cost of conflict and value of volition) that have recently been shown to cause predictable learning biases in healthy young adults as a function of dopamine receptor subtype and dopaminergic challenge. It was hypothesized that Parkinson’s patients OFF medication would have an enhanced cost of conflict and a decreased value of volition, and that these effects would be remediated or reversed ON medication. Participants included N=28 Parkinson’s disease patients who were each tested ON and OFF dopaminergic medication and 28 age- and sex-matched controls. The expected cost of conflict effect was observed in Parkinson’s patients OFF versus ON medication, but only in those that were more recently diagnosed (<5 years). We found an unexpected effect in the value of volition task: medication compromised the ability to learn from difficult a-volitional (instructed) choices. This novel finding was also enhanced in recently diagnosed patients. The difference in learning biases ON vs. OFF medication between these two tasks was strongly correlated, bolstering the idea that they tapped into a common underlying imbalance in dopaminergic tone that is particularly variable in earlier stage Parkinsonism. The finding that these decision biases are specific to earlier but not later stage disease may offer a chance for future studies to quantify phenotypic expressions of idiosyncratic disease progression.
IMPROVEMENTS IN INTERNALIZING SYMPTOMS IN A CHILD PARTIAL HOSPITAL SETTING: PARENT AND CHILD PERSPECTIVES

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Objectives: The purpose of the current study is to provide preliminary evidence for the effectiveness of a child partial hospital program in treating internalizing symptomatology (i.e., anxiety, depression, emotional problems) for children aged 7 to 12 years with a range of psychiatric, social, and behavioral difficulties.

Methods: The sample group consists of archival clinical data from 203 consecutive admissions to a partial hospitalization program in the Northeast. Children attend the program for 6 hours per day Mondays through Fridays. Interventions include cognitive behavioral, behavioral, and family systems approaches. The majority of youth in our sample group were male (68 percent), with a mean age of 10 years. The racial composition of the sample group was 81 percent white, 11 percent Hispanic/Latino, 7 percent African American, 3 percent American Indian, 3 percent mixed race, and 6 percent other. The average length of stay is 23.5 days. For the current study, clinical outcomes research was implemented into admission and discharge procedures. Survey data were collected via a data capture system, RedCap, through self-reporting by an iPad system, e-mail, or paper copy. Parents completed the emotional problems subscale of the Strengths and Difficulties Questionnaire (SDQ), and children completed the Children’s Depression Inventory (CDI) and the Screen for Child Anxiety and Related Disorder (SCARED).

Results: One-way, repeated-measures ANOVAs indicated that parents reported significant improvements in emotional problems (F1,111 = 16.62, P < 0.001). Child reports suggested significant decreases in depression total score (F1,160 = 6.55, P < 0.05), interpersonal problems (F1,161 = 6.89, P < 0.01), ineffectiveness (F1,160 = 7.55, P < 0.01), anxiety total score (F1,165 = 3.86, P = 0.05), and social anxiety (F1,165 = 8.76, P < 0.01).

Conclusions: Results demonstrate preliminary evidence that children and families participating in a child partial hospital program report significant improvements in child internalizing symptoms upon discharge, particularly in areas related to overall anxiety, depressive symptoms, and social problems. Thus, this study yields support for embedding an assessment of clinical outcomes in a treatment service, as well as for efficacy of treatment for internalizing problems from both child and parent perspectives.
PATHWAYS TO HARM: SEXUAL IDENTITY AS A MODERATOR OF THE ASSOCIATION BETWEEN ALCOHOL USE AND NEGATIVE CONSEQUENCES

Alyssa Norris, M.A. & David K. Marcus, Ph.D.

Although lesbian, bisexual, and questioning individuals are more likely to experience negative consequences from alcohol use than heterosexual individuals, they also tend to use alcohol in greater amounts. Researchers have not examined whether substance use is associated with more harmful outcomes controlling for level of use. Using the American College Health Associations’ National College Health Assessment (N = 43,252), the present study examined whether sexual identity moderated the relationship between frequency of alcohol use and alcohol-related negative consequences. Consistent with existing literature, lesbian and bisexual women were more likely to use alcohol than heterosexual women, although the pattern of alcohol use was more variable for men. Sexual identity moderated the pathway from alcohol use frequency to alcohol-related harm. Individuals who were unsure of their sexual identity had consistently stronger associations between use and harm compared to their heterosexual peers. A lesbian identity appeared to protect students from harm.
MISPERCEPTIONS OF SEXUAL VIOLENCE IN THE CLASSROOM: EXPLORING THE ROLE OF TECHNOLOGY TO TARGET DESCRIPTIVE AND INJUNCTIVE SOCIAL NORMS

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Sexual assault is a significant public health problem; occurring along a continuum of severity ranging from unwanted sexual touching to completed rape, with serious consequences to victims and society. According to data from the National Incident-Based Reporting System, adolescents have the highest rates of sexual assault compared to any other age group. Further, 46.7% of adolescent females in grades 7 through 12 reported some form of sexual victimization on the Sexual Experiences Survey, with 12.7% of the assaults involving alcohol.

The Social Norms Approach (SNA), is a promising, theory and evidence-based methodology for sexual violence among adolescents. Programs utilizing the SNA have been successful for in diverse settings, including programs targeting hazardous drinking, tobacco use, and other health behaviors. Recent research indicates that the SNA is a promising approach for the prevention of sexual assault in a number of preliminary studies. More specifically, SNA predicts that an intervention which aims to correct misperceptions by exposing actual norms will lead people to reduce problem behaviors or increase participation in healthy behaviors. This approach distinguishes two types of norms; descriptive norms which typically refer to the perception of others’ behavior, and injunctive norms involve perceptions of which behaviors are typically approved or disapproved.

The present study is an exploratory study seeking to pilot technology-based social norms exercises revealing both descriptive and injunctive norms as part of a sexual assault prevention program for high school youth. The present research seeks to answer several questions: a.) the extent to which students misperceive descriptive and injunctive norms; 2.) the extent to which students misperceive normative beliefs, attitudes, and behaviors of peers of the same gender. Additionally, researchers hypothesized that demonstrating these normative exercises via an innovative, technology-based method would increase student engagement.

Data is gleaned from 52 administrations of Session 1 (14 questions); 41 administrations of Session 2 (2 questions); 37 administrations of Session 3A (2 questions specific to boys); and 5 administrations of Session 3B (2 questions specific to girls). As part of a sexual assault prevention program administered to Rhode Island high school students, subjects participated in a four-season workshop. Through the use of iClickers, an anonymous, technology-based data collection tool, participants answered eighteen questions related to normative perceptive of sexual violence. Questions assessed multiple domains of normative perceptions, including injunctive norms, descriptive norms, and actual behavior.

Among the social norms questions students responded to, findings indicate that there are greater discrepancies between actual norms and descriptive norms. Furthermore, students were found to have greater misperceptions of questions about their same-gender peer group when compared to generalizable questions. Findings also highlight the gradual decrease in the gap of misperceptions between actual and perceived norms among subsequent sessions.

These findings greatly inform development and design of sexual violence prevention programs utilizing environmental approaches such as at the social norms approach. Of particular relevance, these data reveal that there is a greater misperception of descriptive norms, which has numerous implications on the sequence of presenting programmatic content. Additionally, future research may consider exploring the extent to which injunctive norms predict attitudes and behaviors related to sexual violence. Additional findings from this study are discussed in regards to their implications for sexual violence prevention program development, design, and evaluation.
ASSOCIATIONS BETWEEN MENTAL CONTAMINATION, DISGUST, AND OCD SYMPTOMS IN THE CONTEXT OF TRAUMA

Rachel Ojserkis, MA; Dean McKay, PhD

Background: Mental contamination (MC), the sensation of internal dirtiness in the absence of a physical contaminant, has been associated with OCD (Coughtrey, Shafran, Knibbs, & Rachman, 2012) and PTSD symptoms (Badour, Feldner, Blumenthal, & Bujarski, 2013). Though preliminary work has examined the role of disgust within this high-order construct in community samples (Travis & Fergus), PTSD (Badour, Ojserkis, McKay, & Feldner, 2014), and OCD (Melli et al., 2014), the unique influences of disgust and MC on OCD symptoms occurring in the context of trauma remain unclear. Thus, this study examined associations between MC, disgust constructs, and OCD symptom severity in trauma-exposed individuals.

Method: Undergraduates endorsing lifetime traumatic experiences (N = 250) completed online questionnaires measuring MC (Vancouver Obsessional Compulsive Inventory-Mental Contamination Scale), disgust propensity and sensitivity (Disgust Propensity and Sensitivity Scale-Revised), OCD and PTSD symptom severity (Obsessive-Compulsive Inventory-Revised; PTSD Checklist for DSM-5), and negative affect (Positive and Negative Affect Schedule).

Results: Participants were 71.2% female, 76.0% White, and 20.38 years old on average (SD = 2.79). Linear regressions examined the impact of MC versus disgust propensity and sensitivity on OCD symptom severity, controlling for gender, negative affect, and PTSD symptoms. MC was a significant predictor of OCD symptoms above and beyond disgust propensity and sensitivity (model: Adjusted R-squared = .54, F(6,241) = 49.68, MSE = 75.00, p < .001; MC: R-squared change = .13, β = .49, p < .001). These findings extended to a subsample (n = 49) demonstrating PTSD caseness on the PCL-5 (R-squared change = .13, β = .61, p = .001). Additionally, disgust sensitivity moderated the association between disgust propensity and MC, such that higher levels of disgust sensitivity strengthened the association between disgust propensity and MC, controlling for gender, negative affect, PTSD, and OCD symptoms (model: R-squared = .60, F(7,240) = 50.94, MSE = 82.78, p < .001; interaction: b = .04, SE b = .01, p = .004).

Conclusions: Results suggest that disgust constructs interact to predict MC, and that MC is a stronger predictor of OCD symptoms than disgust constructs, amongst trauma-exposed individuals. Clinical implications, limitations, and future directions will be discussed.
TARGETING BODY IMAGE AMONG ADULT WOMEN ATTEMPTING WEIGHT LOSS

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Body dissatisfaction (BD) is prevalent among overweight and obese adults. Because negative body image is a risk factor for maladaptive eating and exercise behaviors, it may be a barrier to weight loss. This study targeted BD among overweight and obese women by evaluating effects of a randomized intervention on eating and exercise behavior, quality of life (QOL), and weight loss.

Overweight and obese women (n=44; 71% white; 7.9±7.6 years; BMI: 30.5± 2.9) were recruited and screened for BD and a desire to lose weight. Participants were randomized to one of two, 4-week, treatment conditions: a usual care (UC) group (n=21) engaged in daily tracking of diet and activity level; or an intervention (INT) group (n=23) engaged in daily tracking with four weekly, one-hour Body Project group meetings. The Body Project is a widely studied intervention designed to target BD among adolescent females. At baseline and program completion, height/weight were measured and participants completed self-report questionnaires of body image, eating and exercise, and QOL. Analysis of variance (ANOVA) was utilized for analyses. Results indicated time main effects for BMI (F(1, 33)=8.00, p=.01), BD (F(1, 33)=14.93, p<.001), and QOL: mental (F(1, 33)=7.05, p=0.01), physical (F (1, 32)=5.19, p=0.03) and weight-related (F(1, 33)=17.33, p<.001). In both groups, BMI and BD decreased and quality of life improved. Neither group reported change in thin ideal internalization, body appreciation, eating- and exercise-related variables, or negative affect. Post-hoc repeated measures ANOVAs among individuals who endorsed elevated BD (n=26) revealed significant time by group interactions for body appreciation, thin ideal internalization, and BMI. Improvements in all outcomes were observed only in the INT group.

The results suggest that BD can be targeted successfully among adult women attempting weight loss, but not all individuals may benefit from body image treatment. Among women with elevated BD, the Body Project intervention generated beneficial results and could be useful in treating select participants in behavioral weight management.
MODELING CHANGE IN CHILD INTERNALIZING AND METHYLATION OF GLUCOCORTICOID RECEPTOR GENE NR3C1: THE ROLE OF CHILD MALTREATMENT

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BACKGROUND: A growing body of literature supports the hypothesis that exposure to childhood maltreatment is associated with methylation of the glucocorticoid receptor (GR) gene, NR3C1, which is a key regulator of the hypothalamic-pituitary-adrenal axis. Further, emerging evidence suggests that methylation of NR3C1 in preschoolers is, in turn, associated with internalizing problems. Yet, prior work has been exclusively cross-sectional, greatly constraining our understanding of epigenetic processes over time. In the current study we utilized repeated assessments of children’s internalizing problems and methylation of NR3C1 to understand (1) how child maltreatment contributes to change in NR3C1 methylation over time and (2) how methylation of NR3C1 contributes to change in internalizing problems, or vice versa, over time.

METHOD: Participants were 262 preschoolers (53.8% female), including 50% with child welfare documentation of moderate-severe maltreatment in the past six months. Preschoolers were 3-5 years-old, and racially and ethnically diverse (44% Hispanic, 30% White Non-Hispanic, 13% Black, 13% other races). Nearly all children were living in poverty (91%). Review of child protection records was used to assess child maltreatment. Caregiver report on the CBCL was used to assess child internalizing problems at baseline and again at a 6-month follow-up. Methylation of exons 1D and 1F of NR3C1 was measured from saliva samples via sodium bisulfite pyrosequencing at both time points. To assess changes in internalizing behaviors and NR3C1 methylation, we utilized simultaneous latent change score (LCS) models. Of relevance to our main research questions, the flexibility of LCS allows for a simultaneous analysis of the predictors of individual differences in the initial level of and subsequent changes in children's methylation and internalizing problems. Separate models were estimated for change in exons 1D and 1F.

RESULTS: Results indicate that methylation of exons 1D and 1F of NR3C1 decreases over time (both p < .01). Findings from the conditional LCS models are depicted in Figures 1 and 2 for exons 1D and 1F, respectively. Results across models suggest that (a) higher baseline levels of NR3C1 exons 1D and 1F methylation were associated with higher baseline levels of internalizing problems; (b) higher baseline levels of internalizing problems predicted decreases in methylation of NR3C1 at exon 1D, but not 1F, over time; (c) higher baseline methylation levels of NR3C1 at exons 1D and 1F predicted increases in internalizing problems over time; (d) child maltreatment was positively associated with baseline levels of internalizing problems and NR3C1 exons 1D and 1F methylation; and (f) child maltreatment predicted decreases in methylation of NR3C1 at exons 1D and 1F, but not internalizing problems, over time.

CONCLUSIONS: Findings from the current study shed light on a dynamic process of NR3C1 methylation that is sensitive to childhood maltreatment. Further, results show that methylation of NR3C1 is a predictor of changes in internalizing problems, as well as some support for the reverse. The current study is the first to demonstrate change in methylation of NR3C1 over time and the first to examine predictors of this change.
BROWN’S NIMH-FUNDED R25 GRANT TO SUPPORT PSYCHIATRY RESIDENT RESEARCH TRAINING: OVERVIEW AND 2016-2017 UPDATE

Katharine Phillips, MD, Audrey R. Tyrka, MD, PhD, Noah S. Philip, MD, Sara E. Vargas, PhD

In 2013, Brown University’s Department of Psychiatry and Human Behavior was awarded an R25 grant from the National Institute of Mental Health to support research training of our psychiatry residents. This grant has substantially increased opportunities for our residents to conduct high-quality, cutting-edge research to prepare them for successful careers as physician-scientists in psychiatry and neuroscience. The R25 provides residents with intensive research training at a critical point in their careers, with the goal of increasing the number and preparedness of psychiatrists who conduct innovative research in translational, basic, or clinical areas.

The R25 combines an intensive longitudinal mentored research experience with an individualized research-focused didactic curriculum and career development activities. Residents have 10% protected time for research in their first and second years, 33% protected time in the third year, and 80% protected time in the fourth year. R25 activities are integrated with Brown’s four-year residency program so that R25 residents meet all ACMGE and American Board of Psychiatry and Neurology requirements.

R25 residents are mentored by outstanding faculty who are conducting innovative research and are carefully matched with residents’ specific research interests. This poster highlights the key components of the R25 program and provides an update on the R25 residents’ research projects and accomplishments.

R25 residents have been very productive in terms of publications and presentations, have received support to attend and present their findings at national conferences, and have received numerous travel, poster, and other research awards.

In summary, our NIMH-funded R25 grant has substantially enhanced our residents’ research training experience by capitalizing on the support provided by the grant, high-caliber research mentorship, and strong institutional support at Brown. Institutional prioritization of psychiatry and brain science, our department’s cross-disciplinary collaborations, and our faculty’s productivity and longstanding commitment to research mentoring are ensuring that our residents have an exceptional research training experience.
GENDER DIFFERENCES IN FACTORS OF BURDEN AND DEPRESSION AMONG DEMENTIA CAREGIVERS

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Objective: Previous literature has examined burden and depression predominately as unitary constructs in relation to dementia caregiving. Little has been done concerning gender differences in the specific factors of burden and depression in dementia caregivers. The current study examined whether empirically validated dimensions of caregiver burden, as measured by the Zarit Burden Interview (ZBI), and depression, as measured by the Center for Epidemiologic Studies Depression Scale (CESD) differed by gender for dementia caregivers.

Participants and Methods: The sample consisted of 211 community-residing dementia caregivers (mean age= 62.8; 77% female) who reported some degree of distress and were enrolled in a longitudinal intervention study. Dementia severity was mild-moderate. Baseline levels of burden were assessed using the ZBI, and baseline levels of depression were assessed using the CESD.

Results: Confirmatory factor analysis ($\chi^2$(2) $p < .001$) revealed 3 facets of burden: impact of caregiving on caregivers’ lives, guilt, and frustration/embarrassment, and 4 facets of depression: depressed affect, somatic and retarded activity, positive affect, and interpersonal feelings. Overall burden ($p<.001$) and the impact of caregiving on caregivers’ life ($p<.001$) factor were significantly higher in females than in males. Additionally, overall levels of depression ($p=.018$) and both the depressed affect ($p=.005$) and positive affect ($p=.012$) factors were significantly higher in females. There were no significant gender differences with care recipient’s dementia severity at baseline.

Conclusions: Findings suggest that distressed male and female dementia caregivers experience burden and depression differently. Results from this study could potentially be used to identify gender-specific interventions related to different subtypes of burden and depression to optimize quality of life for dementia caregivers.
NOCICEPTIVE INPUTS TO TRIGEMINAL NUCLEUS CAUDALIS NEURONS; IMPLICATIONS FOR MIGRAINE

Bruno Pradier, D. Kim, HB Shin, D. Lipscombe, J.A. Kauer

Migraine is a disabling and episodic brain disorder with high prevalence and complex pathophysiology. Animal models suggest that sensitization of the trigeminal pathway plays a major role in the pathology of migraine, yet little is known about long-term changes in trigeminal afferents or their synapses in the brainstem trigeminal nucleus pars caudalis (TNC). We used mice expressing channelrhodopsin-YFP in TRPV1 lineage neurons (generated from TRPV1-Cre (B6.129-Trpv1tm1(cre)Bbm/J)) to investigate different forms of synaptic plasticity at nociceptive primary afferents projecting onto second order relay neurons within the TNC. We found with immuno-labeling that these afferents mostly colocalize with CGRP-containing C- and Aδ-fibers, thereby indicating that light stimulation would only activate a specific subset of primary afferents predominantly designated to the transmission of nociception. Light stimulation at the slice edge (473 nm, 0.4 - 1 msec) evoked excitatory postsynaptic currents (EPSCs) and often polysynaptic activity in neurons in laminae I-II in acutely prepared transverse TNC slices. Using low-frequency stimulation with light (LFS, 1 Hz) we robustly induced long-term depression of light-evoked EPSCs (n = 6, 58% ± 13%, p < 0.05). Similar effects were observed on light-evoked EPSCs by bath applying PACAP, a neuropeptide that induces migraine in humans and sensitizes the trigeminal pathway in mice (n = 5, 66% ± 8% at 10 - 20 min after washout, p < 0.05). We hypothesize that reduced excitatory input onto inhibitory neurons could disinhibit projecting neurons, thereby yielding an increased net output to connected brain regions. In contrast to LFS using light, after application of electric high-frequency stimulation (HFS) EPSCs either potentiated (n = 5 out of 14, Δ > 20% 20 min post stimulation) or depressed (n = 7 out of 14, Δ < 20% 20 min post stimulation), while the overall average remained unaffected (101% ± 14%). The variability in these responses may reflect the heterogeneity of the neuronal population and might differ in GABAergic vs glutamatergic postsynaptic cells. Our data demonstrate various forms of persistent synaptic plasticity, which might be relevant to migraine that depend on the type and frequency of stimulation.
TREATMENT OUTCOMES FOR FAMILIES PARTICIPATING IN PARTIAL HOSPITAL PROGRAM: IMPROVEMENTS IN CHILD MENTAL HEALTH AND PARENTING FUNCTIONING

Teresa Preddy, Katharine E. Musella, Stephanie H. Parade, Anne S. Walters, & Jeffrey I. Hunt

Objective: The purpose of the current study is to provide evidence for the effectiveness of a multidisciplinary child partial hospital program (CPHP) in the treatment of emotional and behavioral symptoms for children with serious mental illness. This study also evaluates whether a CPHP is effective in improving parenting behaviors.

Methods: The sample includes 203 consecutive admissions to a CPHP in the Northeast. Children aged 7-12 with severe psychiatric, social, and behavioral difficulties attend the program 5 days per week for 6 hours per day. Treatment is provided by a multidisciplinary team and interventions include cognitive behavioral, behavioral, and family systems approaches. During the admission, children participate in group, milieu, occupational, family, and art therapies. Children also receive psychiatric services. The majority of the youth in the sample were male (68%) and white (81%) with a mean age of 10. The average length of stay was 23.5 days. For the current study, clinical outcomes research was implemented into admission and discharge procedures. Survey data was collected via a data capture system, RedCap, through self-reporting by an Ipad system, email, or paper copy. Parents completed the Clinical Global Impression Scale (CGI; Guy, 1976) and the Family Assessment Questionnaire (FAQ; Stormshak & Dishion, 2009). Children completed the Behavior Assessment System for Children- Second Edition (BASC-2; Reynolds & Kamphaus, 2004).

Results: One-way repeated measures ANOVAs indicated that parents reported significant improvements in child severity of illness from admission to discharge, F(1, 97)=90.69, p<.001. Parent reports also suggested significant improvements in child Emotional Problems, Conduct Problems, and Hyperactivity ps<.001. Child reports suggested improvements in Emotional Symptoms, Attitude to School, Attitude to Teachers, Atypicality, Social Stress, Anxiety, and Depression, ps<.05.

Additionally, parents reported improvements in use of positive parenting behaviors including Parenting Warmth, Use of Incentives, Proactive Parenting, and Limit Setting ps<.01.

Conclusions: The current study demonstrates evidence that children and their families report significant improvements in child mental health functioning upon discharge from a CPHP. Further, parents report significant improvements in parenting strategies over the course of admission. Accordingly, this study yields support for the efficacy of partial hospitalization treatment for children with severe mental illness and their families.
EVALUATING MODELS OF NEUROPSYCHIATRIC ILLNESS USING VOLUMETRIC ANALYSIS OF MOUSE BRAIN MRI

Brandon Pruett, MD, Eric M Morrow, PhD, MD

With the advent of more and more genetic mouse models of neuropsychiatric conditions, it becomes important to verify the validity of these models by ensuring that they replicate key features of the illnesses they are modeling such as expected changes in brain region volumes. These models are also extremely useful in that given their relative homogeneity and increased simplicity it becomes possible to ascertain perhaps more subtle brain regional changes than could be easily measured in a heterogeneous human population with a given illness. In addition, modeling brain changes over the lifespan is more accessible in animal models than in rare genetic disorders in human. In this regard, small animal imaging, in particular magnetic resonance imaging (MRI), could be an extremely useful technique. However, methods for volumetric analysis of rodent MRI is somewhat limited especially compared to those that exist for Human MRI analysis. As an initial experiment, we collected post-mortem MRI of adult male wild-type C57BL/6J mice. These mice were first perfused with 4% paraformaldehyde using a standard perfusion protocol modified in that it included an enhancing agent (1mM gadolinium) in the paraformaldehyde solution. Following perfusion, hair, skin, and ears were removed but the skull was left intact and soaked in a solution of phosphate buffered saline (PBS) containing 0.05% sodium azide and 1 mM gadolinium. Samples were later imaged at the Small Animal Imaging Lab (SAIL) facility at Brigham and Women’s Hospital on a 7.0T Bruker BioSpec® USR using a T2-weighted sequence. As a proof of concept, we measured the volume of several brain regions including the corpus callosum and striatum using the segmentation feature of the freely available software 3D Slicer 4.6. This process, while somewhat time intensive, was able to yield volumes for these regions that were reasonably similar between the wild-type mice indicating limited variability across experiments in initial studies. These methods are sufficiently promising to support a subsequent pilot study involving small animal MRI volumetric analysis in mice with mutations in genes implicated in rare genetic disorders involving neuropsychiatric disorders such as autism or neurodegenerative disorders.
THE EFFECTS OF ADVERSE CHILDHOOD EXPERIENCES ON MATERNAL HEALTH IN THE PRENATAL PERIOD

Kantoniony Rabemananjara, BA, Rebecca Newland, PhD, Ronald Seifer, PhD, Blythe Berger, ScD, Kristine Campagna, MEd, Ann Barone, Stephanie Parade, PhD

Adverse childhood experiences (ACES, e.g. abuse, neglect, witnessing domestic violence) are strongly linked to physical and mental health problems across the lifespan (Dube, Felitti, Dong, Giles, & Anda, 2003; Bellis, Lowey, Leckenby, Hughes, & Harrison, 2014). Individuals raised in poverty are more likely to experience multiple adverse events during childhood (Child Trends, 2013), placing them at risk for health disparities. Although there is emerging evidence on the impact of ACES for maternal health in the prenatal period (Leeners et al., 2014), less is known about how childhood and current stressors differentially affect maternal health during pregnancy or about the ways in which socio-economic (SES) factors might alter or exacerbate the impact of ACES on maternal health. The current study examines the effects of childhood and current stressors and whether SES factors moderate the impact of ACES on maternal health.

Data were drawn from an ongoing study of ACES and maternal-child health. The current report includes 102 low-income pregnant women over the age of 18. Women were recruited during their pregnancy from Women, Infants, and Children clinics and a large birthing hospital. 70% were unemployed, 69% had less than or equivalent to a high school education, and all received public assistance. The majority of women identified their race as White (44%), Black (16%), or “Other” (28%). 42% identified themselves as Hispanic. The Adverse Childhood Experiences Questionnaire (Felitti et al., 1998) was used to measure maternal ACES in childhood. The measure of current stressors experienced during pregnancy was adapted from the ACES measure and with other life stress measures. Maternal health in pregnancy was measured using a self-report questionnaire in which participants endorsed current medical problems. Correlational analyses show a significant association between ACES score and current health conditions ($r = .359$, $p < .01$). The correlation between current stressors and current health conditions was also significant ($r = .247$, $p < .05$). A partial correlation was analyzed to determine the association between ACES and current health conditions when partialling out the effects of current stressors. Results indicated that ACES were related to current health conditions, over and above the effect of current stressors ($r = .295$, $p < .05$). Finally, we conducted a generalized linear model (GLM) to examine a combination of SES factors during pregnancy (unemployment, education, and marital status) as a potential moderator. Results demonstrated that the interaction of ACES and SES in the prediction of maternal health was not significant.

Results suggest that women who have experienced a greater number of adverse childhood experiences have poorer health during pregnancy. Indeed, childhood stress appears to impact the health of pregnant women, even when controlling for the effect of current stressors during pregnancy, regardless of socio-economic status. Maternal health in pregnancy has the potential to impact both maternal and infant health and development. Thus, results demonstrate the importance of identification, prevention, and treatment of adverse childhood experiences, as the longstanding risks of ACES on maternal health continue into the prenatal period.
MEASURING SENSORY EXPERIENCES ELICITED BY PRODUCT PROPERTIES DURING RECEPTIVE ANAL SEX: IMPLICATIONS FOR PREVENTION DESIGN AND MARKETING

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Background: To curb the spread of HIV, semisolid prevention products for both vaginal and rectal use are being evaluated. Adherence to these products continues to be a challenge. The sensory experiences elicited by product properties and volumes how the product feels on a sensory level and impacts the sexual experience and willingness to use can be measured and used to inform design and to target potential user populations.

Methods: We adapted previously validated vaginal user sensory perception and experience (USPE) scales to receptive anal sex (RAS) and tested preliminary psychometrics. In one study, males and females (N=15) evaluated 10 mL doses of 3 formulations with distinct semisolid properties (e.g., viscosity, smoothness) during RAS. Separately, N=8 males evaluated HEC gel at different volumes (3.5mL; 10mL). Each completed web-based USPE surveys for each product experience.

Results: Psychometric properties of USPE scales measuring sensations during insertion and RAS (e.g., awareness, lubricity, messiness) ranged from good to excellent for both item loadings and internal consistency. Effect size differences between formulations in the combined sample (N=23) were generally in the small-medium range. Effect size differences between formulations were greater between sexes, indicating potentially distinct sensory experiences. In general, females reported higher averaged scale item scores than males. The majority of differences occurred in sexual activity scales (e.g., Lubricity (p< .001), Application Product Awareness (p=.035), Pleasure (p=.002)).

Conclusions: Users differentiate between sensory experiences elicited by formulation properties and volume. USPE scales may allow identification of relevant sensory experiences that predict product choice and use. This is particularly true given differences in sensory experiences between male and female users during RAS, as these distinctions may have implications for prevention product design by sex. Full psychometric validation is required.
A QUALITATIVE INVESTIGATION OF OBESITY AND BODY DISSATISFACTION AMONG WOMEN WITH POSTPARTUM DEPRESSION

Jennifer Ramirez, MA; Cynthia L. Battle, PhD

Background: Overweight and obese women experience significantly higher rates of depression during pregnancy and postpartum, in comparison to normal-weight women (Molyneaux, Poston, Ashurt-Williams, & Howard, 2014). Understanding the co-morbidity of obesity and depression during the perinatal period is important in promoting optimal health for women and their children. Increasing evidence suggests that a woman’s subjective sense of body dissatisfaction may be a critical factor in the association between postpartum depression and obesity, however a recent review highlights significant limitations in this literature (Downs, DiNallo, & Kirner, 2008; Han, Brewis, & Wutich, 2016; Silveira, Ertel, Dole & Chasan-Taber, 2015). In addition, although a number of prior investigations have examined body dissatisfaction during the perinatal period, the measures used in these studies have been designed for non-perinatal samples and may therefore fail to capture unique aspects of women’s experience that relate to bodily changes during the perinatal transition (Silveira et al., 2015).

Objectives: This study aims to explore women’s experiences regarding the association between overweight/obesity, body dissatisfaction, and depression in a sample of clinically-depressed postpartum women. We will investigate specific elements of body dissatisfaction relevant to perinatal bodily changes, and how these concerns may be associated to women’s distress. Finally, we will seek input from perinatal women regarding their perceptions of the most widely-used body satisfaction measure, the Body Attitudes Questionnaire (BAQ; Ben-Tovim & Walker, 1991), and discuss ways in which the measure may be modified to better capture the specific concerns of perinatal women.

Methods: Fifteen women will be recruited from the Women & Infants Day Hospital or Outpatient Behavioral Health service. In-person qualitative interviews will be conducted and participants will complete a brief battery of surveys. Surveys will include a demographics questionnaire, a physical health behaviors/concerns questionnaire, and the BAQ (Ben-Tovim & Walker, 1991). Medical records will be reviewed for documentation of past and current psychiatric diagnoses, medical conditions, and medications. Interviews will be audio recorded and transcribed. To date, several women have been recruited for the study. Data collection will be completed by June, 2017.

Results: At study completion, descriptive statistics will be calculated to determine the prevalence of demographic characteristics. Items on the BAQ will be summed to determine total and subscale body dissatisfaction scores, then descriptive statistics will be calculated to describe levels of body dissatisfaction experienced in this sample. Transcripts of the qualitative interviews will be analyzed using thematic content analysis (Hsieh & Shannon, 2005) in order to provide a more in-depth understanding of the connections between women’s mood symptom and weight concerns during the perinatal period.

Conclusions: This study will elucidate the nature of women’s concerns about weight and body issues during the perinatal period, informing future quantitative research. It will also contribute to the body of research promoting the importance of integrated psychiatric and medical care among perinatal women.
CANNABIS USE AND ATTENUATED POSITIVE PSYCHOTIC SYMPTOMS: A MULTIPLE MEDIATION MODEL

Lauren Reeves, MA, Thomas M. Olino, Ph.D., Lauren M. Ellman, Ph.D.

Cannabis use has been associated with various psychosis outcomes, including psychotic disorders, the clinical high risk period of psychosis, and subthreshold measures of psychotic symptoms in non-clinical samples, such as attenuated positive psychotic symptoms (APPS). The present study examined whether individual- and contextual-level factors account for the relationship between cannabis use and psychosis. Specifically, we hypothesized that the relationship between cannabis and psychosis would be mediated by social functioning; negative, depression, anxiety, and aggression symptoms; context of cannabis use; and motivations for cannabis use. Nine hundred and forty-five young adults ages 18-35 years (M = 20.1 years, 24.4% male) completed a battery of self-report questionnaires. Psychosis outcomes included a dimensional measure of APPS and a dichotomous measure indicating potential higher/lower risk for psychosis, based on number of distressing symptoms endorsed (i.e., D-APPS status). A multiple mediation framework was used, and significance of mediators was evaluated through estimating the significance of indirect effects using bootstrapped confidence intervals. Increases in negative and aggression symptoms mediated the relationship between higher cannabis use and increases in APPS. Negative and aggression symptoms, context of cannabis use, and using cannabis to cope with unpleasant affect mediated the relationship between cannabis use and high-D-APPS status. Results indicate that individual and contextual-level characteristics may contribute to the relationship between cannabis use and psychosis.
NEUROPSYCHIATRIC SYMPTOMS AND AWARENESS OF COGNITIVE DEFICITS IN MILD COGNITIVE IMPAIRMENT

Gretchen Reynolds & Geoffrey Tremont

Objective. Reduced awareness of cognitive deficits is prevalent in dementia, but less commonly studied in mild cognitive impairment (MCI). Neuropsychiatric symptoms are common in MCI and may predict conversion to dementia. The relation between these symptoms in MCI is not well understood, as extant research has reported mixed findings. This study examined the relation between caregiver-rated awareness and neuropsychiatric symptoms in MCI, given that these symptoms may be comorbid and may predict future disease course.

Participants and Methods. Participants were 26 adults with MCI (11 men, 15 women; mean age=73.96; mean MMSE=26.73) and their caregivers. Caregivers rated their significant other on the Neuropsychiatric Inventory, and on a scale of awareness of cognitive problems (Likert scale 1-5, with higher ratings indicative of poorer awareness).

Results. Reduced awareness was reported among 42.3% of MCI participants. Independent samples t-tests revealed that MCI participants who endorsed difficulty with anxiety (p=.003), impulsivity (p=.049), sleep (p=.027), and appetite (p=.019), showed reduced awareness of cognitive problems, relative to participants who denied these neuropsychiatric symptoms. There were no between-group differences in awareness among participants with and without other neuropsychiatric symptoms (delusions, hallucinations, agitation, depression, mania, apathy, irritability, repetitive behaviors).

Conclusions. Poorer awareness of cognitive deficits in MCI is associated with anxiety and impulsivity, as well as with sleep and appetite concerns. These findings suggest that awareness of deficits and specific neuropsychiatric symptoms in MCI may share underlying neural correlates, e.g., frontal-subcortical dysfunction. Future research should continue to examine neuropsychiatric symptoms and awareness of cognitive deficits in MCI in order to elucidate potential mechanisms and inform treatment.
MULTIPLE CO-MORBID CONDITIONS, SLEEP, AND ACADEMIC PERFORMANCE IN URBAN CHILDREN WITH ASTHMA

Katharine Reynolds, MA, Julie Boergers, Ph.D., Sheryl J. Kopel, M.Sc. & Daphne Koinis-Mitchell, Ph.D.

Background. Asthma morbidity is highly prevalent in urban minority children. Multilevel factors on the individual (e.g., asthma medication adherence), family/cultural (e.g., family poverty), and socio-contextual (e.g., allergy triggers) levels can increase risk for poor asthma outcomes. Allergic Rhinitis (AR), Sleep Disordered Breathing (SDB), and obesity are common comorbid conditions highly prevalent in urban minority children with asthma. As prior work has demonstrated associations between asthma, sleep and academic problems in children, the present study aimed to examine the unique and combined associations of common co-morbid conditions including AR, overweight/obesity, and SDB, on sleep and academic performance of urban minority children with persistent asthma. Additionally, we examined the associations between a Cumulative Risk Index (CRI), representing the number and severity of co-morbid conditions, and sleep and academic outcomes. The moderating role of CRI on the association between asthma-related lung function and sleep and academic outcomes was also assessed.

Method. Urban children (n = 249) between 7-9 years of age (M = 8.29, SD = .88; 47% male) with persistent asthma from African American, Latino and non-Latino white backgrounds participated. Asthma and AR were assessed using guidelines-based approaches. Overweight/obesity was assessed using body mass index (BMI) and SDB risk was assessed via parent report. Sleep quality and duration were assessed daily via 4-weeks of actigraphy. Asthma-related lung function was assessed daily using home based spirometry (AM2). A CRI score of asthma related co-morbidities was computed as the number of co-morbidities each child met clinical criteria for (range=0-3).

Results. Co-morbid conditions in our sample were prevalent (AR, 85.1%; overweight/obese, 39.4%; SDB 43.8%). African Americans had the highest proportion of children who qualified for the most co-morbidities (20.5% for 3), followed by Latino children (18.1% for 3). Higher SBD risk was associated with more school absences both in the entire sample and in the Latino group. A higher CRI score was associated with shorter sleep duration and more absences. A higher CRI score also significantly moderated the association between asthma-related lung function and sleep efficiency; specifically, for children with one co-morbid condition, better lung function was associated with better sleep efficiency.

Conclusion. To our knowledge, this is the first study to examine a cumulative risk index of co-morbid medical conditions and its association with sleep and academic outcomes within a sample of carefully evaluated children with asthma and AR. The rates of individual co-morbid conditions and multiple co-morbid conditions (CRI) were highly prevalent in the current sample, and these rates were seen at larger proportions within ethnic minority groups. Greater frequency of co-morbid conditions was associated with worse sleep and academic outcomes (i.e., sleep efficiency and absences). Additionally, SBD risk was associated with more school absences both across the entire sample and within the Latino group. Together, findings demonstrate increased risk for poorer sleep and more frequent school absences among urban minority children with asthma who also had more co-morbid conditions. Further, for children in our sample who had one co-morbid condition, better lung function was associated with better sleep quality. Clinically, the current study highlights the importance of considering co-morbid conditions that may exacerbate asthma and affect children’s sleep and daytime functioning during assessment and treatment of asthma and/or sleep. As managing asthma and additional co-morbid conditions in the context of urban stressors may be challenging, prioritizing the level of risk associated with each co-morbid condition is an important steps for providers to take when treating urban children with persistent asthma.
A PID MODEL OF FEEDBACK-CONTROLLED DECISION-MAKING IN DYNAMIC ENVIRONMENTS

Harrison Ritz (BSc, MSc), Matt Nassar (PhD), Michael J. Frank (PhD), Amitai Shenhav (PhD)

People need to make decisions in environments that are noisy and non-stationary, relying on feedback control systems to adapt their behavior. An under-studied approach for modeling these cognitive control processes comes from the engineering field of Control Theory, which provide general principles for regulating dynamical systems. As one of the most popular model of industrial process control, the proportional-integral-derivative (PID) controller holds particular promise given that its response properties mirror those observed in behavioral and neurological measures of human decision-making. The PID controller combines simple estimates of errors in the past, present, and expected future, allowing for robust regulation with neurologically-plausible computations. In the current set of experiments, we tested whether aspects of human decision-making can be well-described by the PID algorithm.

Across two datasets, we found that the PID controller was an accurate model of participants decisions in noisy, changing environments. First, in a re-analysis of a change-point detection experiment by McGuire and colleagues (1), we found that the PID model accurately predicted participants choices, and provided a better fit than the standard delta-rule model. Based on these findings, we developed a drifting change-point task that was better suited to detect PID-like adjustments. This modified task again provided strong evidence in favor of our model. We found that participants qualitatively resembled the optimal PID gains, despite the reversal of these parameters across task.

These experiments provide preliminary evidence that human decision-making in dynamic environments resembles PID control. While further research is needed to differentiate PID control from models of optimal control, and to test the domain-generality of this model, this work demonstrates that the PID control model has the potential to characterize core algorithmic properties of cognitive control.
SOCIAL AVOIDANCE AS A PREDICTOR OF PSYCHOSOCIAL FUNCTIONING IN BODY DYSMORPHIC DISORDER: A PROSPECTIVE LONGITUDINAL ANALYSIS


Body dysmorphic disorder (BDD) is a common and severe disorder that consists of distressing or impairing preoccupation with nonexistent or slight defects in one’s physical appearance (e.g., a “huge” nose, or “disfigured” skin). Individuals with BDD often have high levels of social anxiety and avoidance, which often occurs as a symptom of BDD but may also occur independent of BDD-related social anxiety. In turn, social avoidance is associated with poor global social functioning in BDD. However, no prior studies have explored the degree to which social avoidance predicts change over time in domains of social functioning such as the quality of relationships with family members and friends or participation in recreational activities. The present study aimed to fill this gap by prospectively examining relationships between social avoidance and various domains of social functioning in BDD.

Individuals with a lifetime history of BDD (N=197) completed measures of social avoidance and psychosocial functioning. Severity of social anxiety in general (i.e., due to BDD or any other source) was rated with the Social Phobia Inventory (SPIN). Participants were interviewed with the Duke Brief Social Phobia Scale (BSPS) to assess social anxiety independent of BDD. These measures of social anxiety, as well as measures of psychosocial functioning, including the LIFE-RIFT, were completed at study intake. Psychosocial functioning was subsequently evaluated with the same measures at 1-year, 2-year, 3-year, and 4-year follow-up assessments.

Mixed model analyses examined the degree to which baseline social avoidance predicted changes in psychosocial functioning over time. Results showed that higher baseline levels of social anxiety independent of BDD concerns on the BSPS predicted poorer relationships over time with participants’ mothers (p = .017), fathers (p = .017), siblings (p = .001), children (p = .014), spouses (p = .031), and friends (p = .027) as well as worsening global social adjustment (p = .011), declining psychological functioning (p = .031), and poorer social and occupational functioning (p = .014). Social anxiety due to BDD or any other source, as assessed by the SPIN at study intake, predicted declining quality of recreational activities (p = .007) and worsening psychological functioning (p = .020).

Collectively, these results suggest that social avoidance, especially avoidance over and above body image concerns, may be a potent contributing factor to declines over time in social functioning for individuals with BDD.
MATERNAL EDUCATION, THE QUALITY OF THE HOME ENVIRONMENT, AND INFANT SOCIAL-EMOTIONAL HEALTH


Healthy Families of America (HFA) is an evidence-based home visiting program funded by the United States Department of Health and Human Services. The program provides support to parents with young children, targeting low income families receiving public assistance, to encourage strong healthy relationships between parents and children. One aim of HFA is to promote economic self-sufficiency among families by supporting parental educational attainment, which in turn is expected to promote healthy child development. Yet the process by which maternal education promotes child development is not fully understood, particularly among families living in poverty. We examined links between maternal education and infant behavior outcomes in a sample of mothers enrolled in HFA, and considered the possibility that the quality of the home environment is mechanism underlying this association.

The sample was composed of 123 mother-infant dyads at 12 months postpartum. 70% of mothers were Hispanic, and 30% were Non-Hispanic. 38% of mothers were white, 12% Black, 22% Biracial, and 28% self-identified as “Other”. Half of mothers were single parents. 85% of mothers were unemployed, and 24% were under twenty at the time of their child’s birth. 79% of mothers had less than or equal to a high school degree, and all participated in the HFA home visiting program. Mothers completed the Brief Infant Toddler Social Emotional Assessment (Briggs-Gowan & Carter, 2006) to assess child behavior problems, and research assistants completed the Psychological Impairment Rating Scale to assess child social-emotional incompetence following an observational assessment. Additionally, the Home Observation for Measurement of the Environment (Caldwell & Bradley, 1984) was used to assess the quality of the home environment.

Results demonstrated that maternal education was associated with the quality of the home environment (F(1) = 7.10, p = .009), child internalizing behavior problems (F(1) = 7.23, p = .008), and observed child social-emotional incompetence (F(1) = 9.87, p = .002). Lower quality home environments (M = 34.22), more child internalizing problems (M = 2.91), and greater child social-emotional incompetence (M = 2.39) was observed among families of mothers with less than or equal to a high school degree, compared to those families with mothers who had attained more than a high school degree (M’s = 37.23, 1.69, 1.98, respectively). Externalizing behaviors were not associated with maternal education or the quality of the home environment.

Additionally, the quality of the home environment was negatively associated with child social-emotional incompetence (r = -.49, p < .001). Examination of indirect effects demonstrated that there was a significant effect of maternal education on social-emotional incompetence through the quality of the home environment (B = .15, SE = .06, CI = .0446 to .2822), suggesting that the quality of the home environment partially mediated the link between maternal education and child social-emotional incompetence. In contrast, the quality of the home environment was not associated with child behavior problems.

These results illustrate the importance of supporting maternal education and the quality of the home environment to enhance child social-emotional health. Implications for supporting mothers within home visiting interventions will be discussed.
A FUNCTIONAL HOMOLOGY BETWEEN ADHD AND ACUTE SLEEP DEPRIVATION: AN ALE META-ANALYSIS OF FMRI-MONITORED EXECUTIVE FUNCTION

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Introduction: Sleep disruption is a common symptom reported in those with attention deficit hyperactivity disorder (ADHD). Likewise, inattention and impulsivity as described in ADHD are markedly similar to those experienced in healthy individuals subjected to acute sleep loss. Yet no study to date has combined experimental manipulation of sleep and functional magnetic resonance imaging (fMRI) in ADHD. Understanding how the neural signatures of ADHD and sleep deprivation may converge or diverge is critical to informing both experimental studies of sleep in ADHD and potential sleep-specific interventions. Thus, we performed a novel, comparative meta-analysis of fMRI-monitored executive function between sleep deprivation and ADHD.

Methods: An initial literature search of task-based fMRI studies in the contexts of total sleep deprivation (TSD) compared to rested sleep and ADHD compared to typically developing controls (TDC) yielded 253 unique articles for TSD and 1158 unique articles for ADHD respectively. A structured review process of these articles identified 100 executive function experiments in the ADHD literature and 26 in the TSD literature that met our inclusion criteria. From these 126 articles, peak coordinates were extracted for contrasts of interest: that is, ADHD versus TDC and acute TSD versus rested conditions. For meta-comparison purposes, all coordinates were normalized to a standard Talairach atlas-space. Initial GingerALE analyses (thresholded at p < 0.005) were implemented for the ADHD and sleep deprivation literatures separately. These estimates were then forwarded to a conjunction analysis to identify brain regions mutually modulated in both ADHD and sleep deprivation, as well as regions where activity changes were significantly (p < .005; permutation-testing) different between ADHD and TSD.

Results: The ALE-conjunction analysis revealed overlapping deactivations between ADHD and sleep loss in central executive-function-regulating regions: dorsal medial cingulate cortex, precentral gyrus, left inferior parietal lobule, and left inferior frontal gyrus. ALE-contrast analyses also identified exaggerated hypoactivations in ADHD within right dorsolateral prefrontal cortex, right anterior insula, and right temporoparietal junction. No regions were hyperactivated to a greater degree in ADHD, compared to sleep loss. In contrast, sleep deprivation was associated with significantly exaggerated hyperactivation in subcortical arousal centers, namely thalamus and striatum.

Conclusion: Our meta-analysis indicates that ADHD and acute sleep deprivation may share a common neural signature: hypoactivation of executive function neuroanatomy, namely conflict/attention regions in the cingulate-frontal-parietal network. ADHD was associated with exaggerated, but not unique, patterns in the above regions, yet sleep loss exhibited unique hyper-activation in subcortical arousal centers (e.g., thalamus), echoing a potential compensatory response not present in ADHD. These data, which indicates which neuroanatomy may be shared, rather than distinct, highlight the need for greater research uniting these often disparate contexts.

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CHARACTERISTICS OF PATIENTS TREATED IN A PERINATAL PARTIAL HOSPITAL PROGRAM

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Background: The Women and Infant’s Hospital (WIH) Day Hospital is a unique clinical program designed to treat pregnant and postpartum women experiencing significant depression, anxiety or other distress. Battle et al. (2006) used chart abstraction to summarize clinical characteristics of this population, finding that the majority of patients (80.6%) had a primary diagnosis of MDD, and a substantial minority also carried a comorbid anxiety disorder diagnosis. Later, Schofield et al. (2014) found that more than half endorsed clinically elevated anxiety. Though informative, one limitation of these studies was primary reliance on retrospective chart review, rather than prospective assessments. The current, ongoing prospective investigation seeks to examine characteristics of treatment-seeking perinatal psychiatric patients using standardized assessments at multiple time points measuring depression and anxiety, functioning, childhood trauma, maternal attachment, and other factors. The current analyses represent a preliminary examination of baseline data collected on the initial sample.

Methods: Patients seen at the WIH Day Hospital complete a battery of standardized questionnaires at admission and discharge as a part of regular clinical care. Starting in 2015, patients could optionally consent to have their de-identified data added to a research database, including: the Edinburgh Perinatal Depression Scale (EPDS; Cox et al., 1987); Generalized Anxiety Disorder Scale-7, (GAD-7; Spitzer et al., 2006); Work and Social Adjustment Scale (WSAS; Mundt et al., 2002); and Adverse Child Experience Questionnaire (ACE; Felitti et al., 1998); the Maternal Attachment Scale (MAAS; Condon, 1993) and the Postpartum Bonding Questionnaire (PBQ; Brockington, et al., 2001). Demographics, maternal health history, medications, and psychiatric history are obtained via chart abstraction.

Results: To date, baseline data have been collected for 386 women. Of these, 110 (28.5%) were pregnant and 276 (71.5%) postpartum; 55.5% were Caucasian; 67.1% were in a committed relationship. 91.7% had a prior history of psychiatric treatment and 50.1% were taking one or more psychotropic medicines. Primary DSM diagnoses included unipolar depressive (60.3%), anxiety (24.9%), bipolar (12.2%), psychotic (1.0%), and other (1.6%) disorders. The sample had a mean of 20.39 on the EPDS and 15.5 of the GAD-7, confirming high depression and anxiety symptoms. 88.5% of patients reported at least one adverse childhood experience and 62.5% reported 3 or more. The mean score on the WSAS was 26.8, indicating moderately severe functioning (James et al 2002). With regard to maternal attachment and bonding, the mean MAAS score was 47.1, markedly lower than a mean of 75 found in a general sample (Condon and Corkindale,1997). On the Postnatal Bonding Scale, over a third (35.5%) reported significant impairment in maternal-infant bonding.

Conclusions: As seen in previous studies, a majority of women enrolled in a perinatal day hospital present with a diagnosis of a unipolar mood or anxiety disorders, and most have a prior psychiatric history. Most women had experienced multiple childhood traumas, difficulty with functioning, and problems bonding with the baby. These findings highlight the need to take into consideration possible trauma history and other psychosocial factors that may contribute to or result from psychiatric symptoms experienced in this population. More generally, the large number of perinatal patients who present for care at this specialized program, with significant levels of symptoms and impairment, underscores the pressing need for providers with advanced training in perinatal mental health.
PILOT ANALYSIS OF NEURAL ALTERATIONS IN PEER ACCEPTANCE AMONG YOUTH ENGAGED IN NON-SUICIDAL SELF-INJURY

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Background: Both suicide and non-suicidal self-injury (NSSI) are large public health concerns for today’s youth, with suicide the second leading cause of death (11%) for those aged 10-24 in the United States, and NSSI found in 20-40% of all children seen in the emergency department for any reason. Moreover, while NSSI involves self-harm in the absence of intent to die, NSSI increases the risk of a subsequent first-onset suicide attempt by 7-8 fold. Thus, greater understanding of the neural mechanisms underlying NSSI itself and how those mechanisms predict a first-onset suicide attempt are of significant public health concern. To address this gap in knowledge, we present a pilot analysis of neural alterations during peer acceptance and rejection among youths who engage in NSSI (without any prior suicide attempts) vs. typically-developing controls (TDCs) without any history of psychopathology. We hypothesized that NSSI youths would have significantly increased PFC-amygdala activity during peer acceptance and rejection by peers vs. TDCs.

Method: Two groups of children ages 9-17 participated in this ongoing IRB-approved study at Bradley Hospital and Brown University after informed parent consent and subject assent: (1) those who engage in NSSI without any prior suicide attempts (n=4), and (2) healthy controls without any history of psychopathology (n=6). Peer acceptance/rejection was evaluated using the Chatroom task fMRI paradigm. In chatroom, participants are told they will take turns with two other peers being scanned elsewhere connected via the web selecting who they would rather talk to about a series of common interests. FMRI and structural MRI scans were completed at Brown University’s MRI Research Facility’s Siemens Prisma 3T MRI scanner.

Results: We found significant between-group differences in activation in the left inferior frontal gyrus when participants were selected by peers [F(1,8) = 35.88, p < .001]. Post-hoc comparisons revealed that this effect was driven by increased activation for NSSI youths compared to healthy controls when selected by male peers (t = 1.17, p < .05). Activation in the left superior frontal gyrus was also significantly different between NSSI youths and healthy controls [F(1,8) = 44.68, p < .001], driven by increased activation for NSSI youths when selected by female peers (t = 4.075, p < .05).

Conclusions: Our preliminary analyses show that it is feasible to enroll and scan NSSI and TDC youths. Moreover, while preliminary given sample size, our data suggest NSSI-only youth may have frontal cortex activation alterations during peer acceptance that need to be evaluated with our full planned sample size both to determine if this does represent a core brain/behavior alteration in NSSI itself, and to determine how it relates to a subsequent first-onset suicide attempt.
PROTEIN CHARACTERIZATION OF INTRACELLULAR TARGET-SORTED, FORMALIN-FIXED NEURONAL CELL SUBPOPULATIONS

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Two commonly used, complementary strategies to study cellular heterogeneity include high-throughput, single-cell processing and enrichment/purification of targeted cell types via cell sorting. Here, we describe a novel method based on the latter approach. Specifically, we developed a fixation/intracellular target-based FACS/protein extraction method to achieve more accurate cell subpopulation protein characterization, as assessed by western blot. Using a customized protocol, protein was extracted successfully over multiple independent iterations from fixed, immunolabeled, sorted samples without compromising yield or quality. As a feasibility experiment, a subpopulation of primary, rat, neural cells exhibiting high beta-III tubulin antibody fluorescence (TUBB3) were selected for and processed. These cells showed distinct expression differences from the unsorted population for cell type-specific (phosphorylated tau) and non-specific (total tau) disease-relevant protein targets. Inherent variation of tau expression exists under both normal and pathological conditions (e.g., differences in anatomical regions, cell types and their subpopulations, etc.), and our method provides a means to study how this variation changes in specific cells with respect to disease progression or treatment. While TUBB3 expression in the brain was demonstrated as a feasible target, our platform methodology is compatible with virtually any fluorescent antibody and can be applied to study other relevant cell sources/tissues complicated by heterogeneity to establish more accurate protein profiles. Additionally, protein assessment using this technique is potentially applicable to other more quantitative assays, such as ELISA and proteomics.
Developmental theory for an internalizing pathway to alcohol use disorder (AUD) in adolescence has suggested that it is chronic internalizing symptoms in childhood and early adolescence that leads to rapid escalation in alcohol use (AU) in later adolescence and AUD in young adulthood (Hussong et al., 2012). To test this question we used a bifactor structural equation model (SEM) to split pure internalizing, pure externalizing, and co-occurring internalizing and externalizing symptoms into three separate orthogonal factors across three waves of longitudinal data. We then created hierarchical factors for pure internalizing, pure externalizing, and co-occurring symptoms, which captured the chronicity in each symptom dimension across late childhood and early adolescence (age range: 11-15). These chronicity factors were then used to predict alcohol use disorder (AUD) latent factors at W3 and W7 (age: 17-19) controlling for age, gender (55% female), early initiation of alcohol (8%), and W3 AUD when testing paths to W7 AUD in a community sample of adolescents (N = 387; 83% White). The Youth Self Report was used to measure problem behavior (Colder et al., 2013) at W1-W3, while AUD was modeled at W3 and W4 using 14 consequences of alcohol appropriate for 13-15 year olds (Windle & Windle, 1996) and 6 subscales of the Young Adult Alcohol Consequences Questionnaire as well as the MINI for AUD symptoms, respectively. Fit for the hierarchical bifactor SEM was excellent ($x^2 [440] = 527.23, p = .003$; RMSEA = .023 [90% CI = .01 - .03]; CFI = .99; SRMR = .04) and fit for the full model with AUD at W3 and W7 was good ($x^2 [1289] = 1979.45, p < .001$; RMSEA = .037 [90% CI = .03 - .04]; CFI = .94; SRMR = .06). Standardized factor loadings were high for AUD (.64 - .97); high for co-occurring internalizing and externalizing symptoms (.45 - .85); and moderate for pure internalizing (.43 - .57) and externalizing symptoms (.41 - .63). Hierarchical factor loadings were high for all 3 chronicity constructs (.78 - .89). Contrary to developmental theory, chronicity of pure internalizing symptoms in early adolescence was marginally negatively related to AUD at W3 (B = -.12) and unrelated to AUD at W7 (B = -.10). In contrast, stability in pure externalizing symptoms (B = .29) and in co-occurring symptoms (B = .28) were positively related to AUD at W3 (R2 = .24), while only pure externalizing had a positive effect on W7 AUD (B = .29; R2 = .20) above and beyond W3 AUD (B = .27). Analysis of indirect effects (ab) from the IVs to W7 AUD through W3 AUD suggested that chronic pure externalizing symptoms (ab = .07; SE = .03), chronic co-occurring symptoms (ab = .03), and early initiation of alcohol (ab = .04; SE = .02) all predicted W7 AUD through W3 AUD, while chronic pure internalizing did not (ab = -.03; SE = .02). The pattern of results is consistent with a growing body of evidence that suggests that internalizing symptoms are only related to AUD in the context of externalizing symptoms. Moreover, pure externalizing symptoms had the strongest effects on AUD.
PROFILES OF TIC SUPPRESSION IN YOUTH WITH TIC DISORDERS: THE ROLE OF REWARD AND PUNISHMENT

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Introduction: Tic suppression is the ability to inhibit a tic. Although tics are involuntary, prior research suggests that tics can be voluntarily suppressed. Factors involved in tic suppression include tic-contingent consequences, contextual factors, and individual factors such as age and co-occurring psychopathology. Whereas it is recognized that tic suppressibility differs between individuals, researchers have yet to identify tic suppression patterns within and across individuals. Identifying these patterns may help point to clinically meaningful moderators of tic suppression.

Objective: The current study explored profiles of tic suppression in youth who completed a well-established tic suppression task involving conditions of baseline, tic contingent reward, and tic contingent punishment.

Hypothesis: We predicted four profiles of tic suppression: non-responder (no change in tic frequency between baseline and both suppression conditions), reward responder (lower tic frequency in the reward condition relative to the punishment condition), punishment responder (lower tic frequency in the punishment condition relative to the reward condition), and non-preferential responder (equal decrease in tic frequencies across both suppression conditions).

Method: Tic frequency data from 13 children, ages 9-16 years (M = 11.69, SD = 2.06; Male = 84.6%), with chronic tics who participated in two completed studies were examined. Average tic frequency (tics per minute) was calculated for each condition. These conditions included a baseline condition where participants were free to tic, a reward condition where participants received a point for tic-free intervals, and a punishment condition where participants lost a point for every tic. Participants were considered a responder if tic frequency decreased by at least one tic per minute in either suppression condition. This criterion assured that varying degrees of suppression were recognized as a response. Therefore, a participant was considered a non-responder if their average tic frequency decreased by less than one tic per minute or increased in both contingency conditions. Type of responder was determined on the basis of change scores from baseline to contingency conditions. The difference between reward and punishment change scores was calculated for each participant. Additionally, difference scores across participants were averaged and a 95% confidence interval was calculated. Participants with difference scores falling outside of the 95% confidence interval were considered preferential responders. Negative scores indicated greater suppression during punishment (punishment responders) and positive scores indicated greater suppression during reward (reward responders). Participants with difference scores falling within the confidence interval were considered non-preferential responders.

Results: Consistent with our hypothesis, four profiles of tic suppression emerged. Three participants fell within the non-responder subtype. Two participants fell within the punishment responder subtype and two participants fell within the reward responder subtype. Six participants fell within the non-preferential responder subtype.

Conclusion: The majority of youth in this sample successfully suppressed their tics in the context of an environmental contingency. Most youth were equally successful at suppressing tics in the context of reward or punishment. A subset of youth with chronic tics may be resistant to environmental contingencies or suppress tics better in positively reinforcing versus punishing contexts. Limitations include floor effect and small sample size. Future research would benefit from identifying tic suppression profiles using larger sample sizes and examining predictors of group membership.
Suicidal ideation (SI) is a significant predictor of future suicide attempts and completed suicide. Peer victimization, including (direct e.g., overt) and indirect (e.g., relational and reputational), is a known risk factor for suicidal thoughts and behaviors. Similarly, trait affect may influence the experience of peer victimization, such that higher levels of negative affect and lower levels of positive affect may exacerbate the effects of peer victimization on suicidality. However, we have yet to understand whether trait negative affect and peer victimization confer unique risk or work in concert to confer risk for suicidal ideation. Thus, the current study aims to examine the comparative strength of both, negative affect and peer victimization and positive affect and peer victimization, in predicting SI, and evaluate their interactive effects on suicidality.

Undergraduate students from Temple University (N = 458) participated in an online survey about the participants' cognitions (suicidal ideation), emotions (e.g., positive and negative affect), and stressors (e.g., peer victimization). Hierarchical linear regressions indicated that peer victimization, both direct (t = 3.54, p < .001) and indirect (t = 3.60, p < .001), interacted with positive affect to predict SI, such that peer victimization significantly predicted SI among those with lower levels of positive affect (t = 4.45, p < .001; t = .72, p < .001). Additionally, indirect and direct peer victimization had a significant interaction with negative affect, such that peer victimization predicted SI more strongly among individuals with higher levels of negative affect (t = 3.29, p = .001; t = 3.24, p = .001), but not lower levels (t = -1.28, p = .20; t = .49, p = .62). These findings suggest that high levels of negative affect and low levels of positive affect might exacerbate the relationship between peer victimization and suicidal ideation. These findings are clinically relevant seeing that a clinician cannot stop the victimization of an individual. However clinical treatment can target working with an individual’s levels of negative and positive affect to reduce levels of suicidal ideation.
THE NTI-31 AS A MEASURE OF NARCISSISM

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Introduction: Social media allows for a person to portray themselves in a manner that is ideal and attractive. This public display could allow for an increase in a grandiose sense of self, by validating the self through “likes” on social media. This type of weak narcissism (Lasch, 1978) requires constant external validation, in a style could potentially create difficulties in interpersonal relationships and other aspects of functioning. The growth of this more mild form of “everyday narcissism” yields the importance of revisiting previous narcissism measures in order to examine the extent to which they effectively measure low levels of narcissistic traits. This type of mild narcissism could be cause for clinical concern as it could impact interpersonal and self-functioning at low levels just as Narcissistic Personality Disorder impacts functioning on a broader scale (American Psychiatric Association, 2013). Popular measures of narcissism, such as the widely-used NPI-16 (Ames, Rose, & Anderson, 2005) possess small ranges of scores which may make it difficult to detect subtle scores of narcissism. In addition, the NPI-16 also utilizes forced choice methodology that can discourage scorers from endorsing the obviously narcissistic trait in an attempt to appear socially desirable. The current study outlines our development of a new measure, the Narcissistic Trait Index – 31, which utilizes a Likert-scale with low face validity. All thirty-one items were created by the authors in accordance with the DSM-V definition of Narcissistic Personality Disorder (American Psychiatric Association). We assess the validity of the NPI-31 with the NPI-16 (Ames et al.). It is hypothesized that high scorers on the NPI-16 (Ames et al.) will also score high on the NTI-31.

Methods: Seventy-three undergraduate students enrolled at a liberal arts college were recruited through email (71% female; 79.5% white). During an online assessment, participants completed the NPI-16 (Ames, Rose, & Anderson, 2005) in addition to the NTI-31 in order to assess the validity of the NTI-31.

Results: Total scores on the NTI-31 ranged from 36 to 90 (M = 61.47, SD = 10.65). Total scores on the NPI-16 (Ames, Rose, & Anderson, 2005) ranged from zero to eleven (M = 3.74, SD = 2.91). A reliability analysis of the NTI-31 yielded a Cronbach’s alpha of .837. To assess the criterion validity of our measure a Pearson correlation coefficient was computed to examine the relationship between the scores on the NTI-31 and the NPI-16 (Ames et al.). The resulting correlation was significant, r (71) = .55, p < .001, r2 = .3.

Conclusion: The hypothesis that the NPI-16 (Ames, Rose, & Anderson, 2005) the NTI-31 would correlate was supported. The NTI-31 had a mean score that was more central than the NPI-16 (Ames et al., 2005), suggesting that the NTI-31 may be more successful in measuring lower levels of narcissistic traits. The reliability of the NTI-31 was higher than the reliability of the NPI-16 (Ames et al.), suggesting better internal consistency in the current measure. However, the validity of the NTI-31 was lower than that of the NPI-16 (Ames et al.). This may be the result of how the authors of the NPI-16 (Ames et al.) correlated their measure to their criterion, the NPI-40. Items from the NPI-16 (Ames et al.) were taken directly from the NPI-40. There was a high reliability coefficient because the items were the same. This does not imply the NTI-31 and the NPI-16 (Ames et al.) tap into different constructs. The evidence suggests that future use and development of the NTI-31 could produce a useful measure for detecting a range of more mild everyday narcissism in subclinical populations. Future research should address sampling and the creation of cutoff scores for clinical use.
THE EVIL OF BANALITY: WHEN CHOOSING BETWEEN THE MUNDANE FEELS LIKE CHOOSING BETWEEN THE WORST

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What kinds of choices worry us most? In our previous research we asked this question using sets of items with moderate to high value for the decision-maker. In that work, we found that choices between higher value options were most attractive, but also provoked the most anxiety. Here, across three studies, we tested whether choice anxiety would continue to decrease when considering sets of low or “zero” value items. Participants made hypothetical choices between sets of four goods (constructed based on earlier ratings of each item), and then retrospectively rated their experience of anxiety and liking for each set. Surprisingly, we found that choice anxiety is a U-shaped function of set value: high for choices between the least valuable items, lower for moderate-value sets, and high again for high-value sets. These results decouple anxiety from set liking, since liking instead decreased monotonically with decreasing set value. Moreover, when having participants separately rate the choice options on a bipolar scale (negative to positive) we found that liking for the low-value sets was actually negative, suggesting that such items might be perceived as aversive rather than simply unpreferred. In relation to this bipolar scale, anxiety corresponded to the distance of the average set value from the zero point on the scale (i.e., the magnitude of negativity or positivity associated with the overall set). Collectively, our findings are consistent with the possibility that choice anxiety scales with the motivational salience of one’s choice set, and that such sets can acquire negative value even in the range of hypothetical gains.
A CLIMATE FOR EVIDENCE-BASED PRACTICE IMPLEMENTATION IN THE PATIENT-CENTERED MEDICAL HOME

Marisa Sklar, PhD

Ongoing problems of access and quality in health care have prompted significant reform efforts in recent decades. The United States is far behind other countries in amenable mortality, being the worst of sixteen industrial nations, and also ranks poorly on access and safety. The Patient Protection and Affordable Care Act (ACA) is guiding current health care reform. Part of the ACA, the patient-centered medical home (PCMH), is seen as an important component of delivery system innovation for facilitating health care improvements. The PCMH approach is being broadly expanded in the United States and Canada and emphasizes ongoing patient-physician relationships, improved care access, and provision of comprehensive care by addressing all health care needs.

Implementing treatments and interventions with demonstrated effectiveness (i.e., evidence-based practices (EBPs)) is a critical component of achieving improved patient health and experience at a reduced cost. A climate in the PCMH that supports the use of EBPs is essential for achieving these outcomes. With the ever-increasing efforts to reform our health system through the transformation of primary care practices into PCMHs, identifying and addressing organizational factors that facilitate EBP implementation within the PCMH are crucial. Within the PCMH model of service delivery, a climate that supports EBP implementation is likely to facilitate improved patient health outcomes, though the extent to which organizational climate within the PCMH supports the implementation of EBPs is unknown.

This study used mixed-methods research to assess EBP implementation climate (i.e., the extent to which organizational members perceive that the adoption of EBPs is expected, supported, and rewarded) and attitudes about EBPs in the PCMH, and their association with PCMH transformation. This study assessed and compared differences in EBP implementation climate and attitudes about EBPs among staff and physicians in the following two primary care practices affiliated with the Memorial Hospital of Rhode Island: 1) the Family Care Center (FCC) that has transformed into a Level 3 PCMH over the past 10 years and has the highest level of recognition available for meeting nationally recognized PCMH standards, and 2) the Internal Medicine Clinic (IMC) that only recently received certification as a Level 2 PCMH during the course of this study. In addition to participating in individual interviews, participants completed a survey containing validated instruments to assess EBP implementation climate and attitudes about EBPs. Preliminary survey results follow.

Results from analysis of variance suggested differences between FCC (n = 39) and IMC (n = 21) staff and physicians with regard to attitudes toward EBPs, and implementation climate. In addition to reporting significantly more positive attitudes toward EBPs overall (x̄FCC= 3.05, x̄IMC= 2.76; F(1,59) = 4.79, p = .033), FCC staff and physicians reported significantly greater willingness to adopt EBPs if required (x̄FCC= 3.07, x̄IMC= 2.50; F(1,58) = 5.48, p = .023), and if the EBP was appealing (x̄FCC= 3.41, x̄IMC= 2.94; F(1,57) = 4.84, p = .032), compared to IMC staff and physicians. Additionally, FCC staff and physicians reported significantly greater educational support for EBPs than IMC staff and physicians (x̄FCC= 2.96, x̄IMC= 2.48; F(1,58) = 4.10, p = .048).

Understanding factors that facilitate EBP implementation within the PCMH is becoming increasingly important given plans for widespread adoption of the PCMH model. These preliminary results suggest more positive attitudes about EBPs, and greater EBP implementation climate, in practices more closely aligned with nationally recognized PCMH standards. Limitations to this study will be reviewed. Recommendations for the development and utilization of interventions tailored specifically to accelerate the sustainable implementation of EBP in the PCMH will also be presented.
STIMULI REDUNDANCY ACROSS COMMONLY USED NEUROPSYCHOLOGICAL INSTRUMENTS

Ashley Smith Watts & David C. Ahern

Objective
Repetition of stimuli across neuropsychological instruments may have an impact on assessment such as an unintentional priming effect, with potential clinical implications. For example, for a patient on the cusp of Mild and Major Cognitive Impairment, redundant stimuli could influence responses, scoring, and eventual diagnosis. Likewise, awareness of stimuli overlap may enrich qualitative interpretations of neuropsychological assessment data (e.g., providing evidence to help distinguish between dysexecutive and amnestic memory deficits). The present study examines the frequency of stimuli redundancy to illustrate potential issues.

Data Selection
We examined stimuli redundancy across two sets of frequently used instruments for memory assessment: (a) the top 10 most commonly used instruments (Rabin et al., 2005), and (b) our clinic’s standard battery. The frequency of each item was measured and proportions of shared stimuli were calculated. Our analyses also examined synonyms, categorical overlap, and presentation modality. A case example is provided for illustrative purposes.

Data Synthesis
The results confirm the presence of stimuli redundancy across tests. The range for overlap between individual instruments was 0%-7.7%. For example, Dementia Rating Scale-2 and Hopkins Verbal Learning Test had 3.3% overlap (3 overlapping items/91 total items). Our case study specifically illustrates the utility of accounting for stimuli repetition for identifying dysexecutive performance on memory tests.

Conclusions
The rate of stimuli redundancy was relatively low but present. Importantly, many of the overlapping stimuli are used for memory assessment; awareness of this issue could provide useful interpretive information to identify dysexecutive (versus amnestic) performance on memory tests.
PREDICTORS OF DAILY PATTERNS OF PHYSICAL ACTIVITY AMONG LATINA PARTICIPANTS IN A PHYSICAL ACTIVITY INTERVENTION

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Physical activity (PA) interventions based on the Transtheoretical model frequently target behavioral, cognitive, and other psychological factors to move people through a series of stages associated with adoption and maintenance of PA. This study examined long-term daily patterns of PA among adult Latinas enrolled in a 12-month PA intervention. Objective daily PA data was collected using pedometers over 12 months among 122 Spanish speaking Latinas (age M = 41.1 years, SD = 10.0; baseline BMI M = 29.5, SD = 4.3; 50.0% married; 45.1% unemployed). We fit a linear mixed effects regression model, regressing PA (i.e. total daily steps) onto demographic variables (partner and employment status), number of young children, day of week, season, baseline depression, days with pedometer, and time-varying predictors including BMI, self-efficacy, stage of change, behavioral and cognitive processes, and social support. Participants averaged 6,603 steps/day. PA was highest during weekdays and summer. PA was significantly negatively associated with days with pedometer, number of young children, and baseline depression; and positively associated with enjoyment, behavioral processes, and stage of change. Neither self-efficacy nor social support significantly predicted PA. We further examined the interaction between self-efficacy and stage of change and results suggest individuals in early stages of change demonstrated a significant negative relationship between self-efficacy and PA relative to the non-significant effects observed among those in more advanced stages of change. Progression through stages of change in this intervention was associated with increased daily PA. The significant interaction between self-efficacy and stage of change indicated that individuals in early stages of change may be more confident in their ability to increase their daily PA relative to those who have begun implementing such changes. Seasonality, weekday, and number of young children all impeded daily PA, the latter being consistent with subjects’ self-reports of barriers to engaging in PA. Results suggest that the addition of a daily activity monitors to interventions can provide some insight into how and when specific intervention approaches impact physical activity.
A TIPPING-POINT CONFORMITY EFFECT FOR JUSTICE: GROUP CHOICE SHIFTS PREFERENCES FOR PUNISHMENT

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How does group behavior influence individuals’ preferences for retributive justice? Past work characterizes fairness preferences as temporally stable (Peytsakhovich, Nowak, & Rand 2014), and demonstrates an overall preference not to punish fairness violations when non-retributive options are available (FeldmanHall et al. 2014). However, much research demonstrates the power of groups in biasing an individual’s choice (Asch 1951; Zaki, Schirmer, & Mitchell 2011). Therefore, many questions remain: does group preference for punishment influence individuals’ punitive behavior, and if so, how many punishers are necessary within the group to shift preferences towards punishment? We find that preferences for punishment are susceptible to conformity effects when fairness infractions are either minimal or severe. Furthermore, a group majority is required to shift punitive behavior to align with the group, indicating a “tipping-point” conformity effect.

40 participants completed a variant of the Justice Game, an economic task created to measure punitive and non-punitive responses to fairness infractions (FeldmanHall et al. 2014). In the Justice Game, there are two players. The first mover, Player A, is endowed with $10 and chooses how much to offer Player B. Player B then has the option to: 1) Accept Player A’s offer as-is; 2) Compensate themselves by increasing their own payout to match Player A’s payout, without punishing Player A; or 3) Reverse Player A’s offer, a highly retributive option that maximizes their own payout and minimizes Player A’s payout. Participants always played as Player B.

Subjects first completed a baseline phase of the Justice Game in the absence of information about others’ justice preferences. Subjects subsequently played another phase of the task alongside four other individuals who together responded collectively as Player B. Each of the players sharing the role of Player B could choose to accept, compensate, or reverse Player A’s offer in sequence, and could see the choices players made in real time.

Results reveal that in the absence of information about others’ preferences, subjects rarely choose punishment (9% of the time when fairness violations are minimal (40% split)), but increase their punishment rates as offers become more unfair, choosing punishment 38% of the time when fairness violations are more severe (10% split). However, after being exposed to the other player’s preferences, subjects shift their endorsement of the punitive option. When fairness violations are minimal, subjects increase their punitive behavior by 19%, demonstrating a robust conformity effect. In contrast, a counter-conformity effect is observed when fairness violations are severe, with subjects choosing to decrease their punitive behavior by 14%.

We also examined whether decisions to conform increase linearly as the number of other players desire punishment, or whether a critical mass of punishers is needed. Results indicate a “tipping-point” conformity effect such that only a majority endorsement of the punishment option increases the subject’s own punitive behavior in response to minimal fairness violations, suggesting that group preference can powerfully bias decisions of justice.
Recent expansions in the optogenetic toolbox, laminopsins, are fusion proteins of light-activated ion channels or pumps (channelrhodopsin or Leptosphaeria maculans) and Gaussia luciferase (a bioluminescent enzyme) which bypass the need for an external light source. In the presence of a corresponding luciferin, the luciferase emits cold light sufficient to open the actuator. The ability to manipulate membrane potential in excitable cells has many potential benefits for neuroscience research. For example, dopamine release is essential in processes pertaining to reward, learning, and motor control. Optogenetic studies are able to manipulate these cells on a fast time scale. However, until now we have been unable to manipulate membrane properties on a longer time scale of minutes without the use of DREADDs, which rely on endogenous signaling pathways. Here we seek to demonstrate the ability of laminopsins to alter the membrane potential and firing rate of VTA dopamine neurons and hippocampal neurons using laminopsins. We virally transduced AAV9-hSyn-LMO3 (LMO3; channelrhodopsin fused to Gaussia luciferase) into the VTA or hippocampus of C57BL/6 mice and characterized transduced cells using whole-cell patch clamp recordings in acute midbrain or coronal slices, respectively. We characterized membrane depolarization in current clamp or inward currents in voltage clamp using sodium channel antagonists to block synaptic transmission. The response to luciferin was also characterized in slices not containing the virus. Finally, a bioluminescence and light-induced currents were tested in a transgenic mouse line expressing LMO3 in VGAT positive cells using a Cre driver.
RECI PRO CAL PEER EDUCATION, YOUTH EMPOWERMENT, AND GLYCEMIC CONTROL IN ADOLESCENTS WITH TYPE 1 DIABETES

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Adolescents and young adults with diabetes have more difficulty maintaining blood glucose in range than younger children or adults. Biological (pubertal and hormonal changes), behavioral (risk taking), social (peer influence), and affective factors (increased incidence of mental health disorders) are significant contributors to heightened risk in this population. Peers are an important source of emotional support and self-esteem and this is especially important during adolescence. Enhanced self-esteem and self-efficacy have been associated with improved glycemic control leading one to evaluate how peer relationships may mediate glucose management. In a study by Heisler et al, adults in a reciprocal peer support arm showed greater decreases in hemoglobin A1C than patients in a nurse care management control group. To date, there has been little research examining the effects of reciprocal peer education and its effects on self-efficacy and glycemic control in youth with type 1 diabetes.

AYUDA, (American Youth Understanding Diabetes Abroad), is a non-profit organization that sends youth volunteers (approximately 50% of whom have type 1 diabetes) to develop and implement sustainable diabetes management programs in resource-poor settings. AYUDA’s innovative peer learning model serves as a catalyst to empower youth living in program countries to better manage their condition. Although the impact of AYUDA’s programs on glycemic control among the native youth participants has been studied, the effect that volunteering and leading the program itself has on AYUDA’s adolescent and young adult American volunteers with diabetes has not yet been examined.

This study seeks to determine the extent to which positive peer relationships and reciprocal peer education among adolescent and young adult program volunteers with type 1 diabetes can improve blood sugar control, adherence to treatment and mood. This study will sample AYUDA volunteers with type 1 diabetes to evaluate measures of empowerment, adherence, affective symptoms and blood glucose control before and after participation in an AYUDA program. First time AYUDA volunteers with type 1 diabetes will be approached via email prior to their participation in an AYUDA program, immediately after participation and again 3 months post-participation. Subjects will complete a compiled survey including the PHQ-9, a measure of depression (suicidality question removed due to anonymity), the GAD-7, a measure of anxiety, the Patient Activation Measure and the Diabetes Empowerment Scale, assessments of confidence in self-management, the Problem Areas in Diabetes Questionnaire and the Diabetes Distress Scale, evaluations of emotional distress associated with diabetes, the Blood Glucose Monitoring Questionnaire, an assessment of affective response to blood sugar testing, and the Adherence in Diabetes Questionnaire, a measure of treatment adherence. Self reported A1C values and qualitative questions asking subjects to reflect on their experience are also included. Analysis will be done using within-person changes in t-test scores to compare scores before and after the intervention and again at 3 months post intervention.

The working hypothesis is that positive peer relationships, reciprocal peer education, and character building experiences which result from volunteers participation in AYUDA programs will lead to improved mood and greater sense of empowerment and self-efficacy thus promoting greater adherence to diabetes care, and improved glycemic control (as evidence by decreased hemoglobin A1C levels), and that this effect will be lasting.
GET ACTive! EFFICACY OF A BRIEF ACCEPTANCE-BASED BEHAVIORAL INTERVENTION TO PROMOTE EXERCISE ADOPTION AND MAINTENANCE

Courtney Stevens & Angela Bryan

Purpose: Participating in regular moderate-vigorous physical activity (MVPA) has been shown to confer both prophylactic and therapeutic benefits for mental and emotional health across the lifespan. A recent longitudinal, multi-cohort study found that compared to getting no MVPA, engaging in 1-5 times the recommended minimum amount of weekly MVPA reduced risk for all-cause mortality by 31-39%. Unfortunately, half of American adults are insufficiently active and another quarter engage in no MVPA at all. Consistent with the tenets of Hedonic Theory, prior work has shown that experiencing more favorable affect (feeling more pleasure) in response to acute bouts of MVPA is positively associated with greater MVPA engagement up to a year later. Conversely, discomfort/displeasure experienced during MVPA is associated with less subsequent MVPA engagement. For these reasons, affect experienced in the context of MVPA represents a viable marker for who will and will not respond to standard MVPA promotion programs. Given the public health impact of MVPA on disease burden, novel approaches to promote MVPA persistence in the context of displeasure/negative experiential content are sorely needed.

Method: This investigation sought to demonstrate that participants may be able to learn acceptance-based skills for modifying the relationship between their inner experience (e.g., negative affect, physical discomfort, worry thoughts) and their subsequent behaviors. The central aims of this investigation were to (1) compare exercise change across time and condition, and (2) assess mechanisms of exercise behavior change over time. A sample of N = 119 insufficiently active women aged 21 – 65 were randomly assigned to 1 of the 3 conditions: (1) acceptance-based health coaching (ACT), (2) education-based health coaching (EDUC), or (3) no-health coaching control (CTRL). The study was divided into: Phase 1 Adoption (baseline visit – post intervention), and Phase 2 Maintenance (3-, 6-, and 9-months follow up). During Phase 1, all participants completed a 30-day exercise program, and ACT and EDUC participants received visit 1 and 2 workshops. All participants were contacted at 3-, 6-, and 9-months post-intervention to complete follow-up assessments.

Results: The overall trend across Phases 1 and 2 was for ACT participants to score highest on exercise outcomes. Notably, a time X condition interaction for PAR total minutes of exercise was observed such that ACT participants completed more exercise minutes in the past week at visit 2 compared to EDUC and CTRL participants, F(2,103) = 4.58, p = .012, η2 = .082. Additionally, only ACT participants completed 150-minutes of exercise per week, on average, over the course of the 30-day intervention (as recorded objectively by HR monitors). Repeated measures tests showed significant main effects of time on exercise scores through Phase 2, F(3, 201) = 22.99, p < .001, η2 = .255; but not significant main effects of condition or time X condition interactions. Regarding mechanisms of action, assignment to ACT predicted higher experiential acceptance scores at visit 2, and visit 2 experiential acceptance scores predicted exercise scores at both 3-, 6-, and 9-months follow-up as tested via mediational analyses (r’s = .415, .406, and .318, respectively).

Conclusions: These results demonstrate that a brief acceptance-based intervention can strengthen MVPA commitment and improve tolerance of aversive MVPA-related experiences. There is great potential for future work to incorporate acceptance-based intervention content when targeting MVPA adherence among populations for whom MVPA is likely to feel most aversive (e.g., weight management, chronic pain, cardiac/pulmonary rehab patient populations). Additionally, future extensions of this work should assess the optimal intervention “dose” and delivery method (e.g., face-to-face versus mHealth) for bolstering these associations across time.
ONTOGENY OF MATRIX METALLOPROTEINASES (MMP-2 AND MMP-9) IN THE CORTEX OF SHEEP

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Background: Matrix metalloproteinases (MMPs) are the family of zinc endopeptidases. They are responsible for remodeling the extracellular matrix (an important component of the blood-brain barrier) which is very crucial in brain development. MMPs are responsible for degrading the extracellular matrix proteins, regulating cell receptors and cleaving their ligand binding domain. MMPs play important roles in cell proliferation, differentiation and cell death processes during development and in adults.

Objective: To collect comprehensive data on the ontogeny of MMP-2 and MMP-9 in the cortex of male and female sheep belonging to four different gestation groups (60%, 70%, 85% and 90%), new born and adult sheep.

Design/Methods: Sheep brain samples were collected and assigned to six different groups according to their gestation and maturation stages. The different groups assigned were 60% gestation (n= 7), 70% gestation (n=6), 85% gestation (n=8), 90% gestation (n=8), New Born (n=5) and Adult (n=3). The sheep brain samples from the different groups were analyzed using the Braford Protein Assay in order to obtain the concentration of protein. After the concentrations were collected, the samples were prepared for western blotting which was used to determine the activities and levels of MMP-2 and MMP-9. Gel-Pro was used to analyze the western blot films. The films were scanned and uploaded on Gel-Pro, the bands were analyzed, and results were collected and uploaded on the MS Excel. The GP, %CV and brain pool values were calculated, then graphs were created. Statistical Analyses: Statistical analyses of the data was performed using Statistica with Kruskal-Wallis ANOVA

Results For MMP-2: From the multiple comparisons table and graph; when the 60% and 70% gestation groups were compared to the Adult group, it can be seen that there was a significant increase of MMP-2 levels. The MMP-2 levels in the 60% and 70% gestation groups were lower than the levels in the Adult group. Using the multiple comparisons table and the graph, it can be seen that there was an increase in MMP-2 levels as we look from the 60% and 70% gestation groups to the Adult group.

Results For MMP-9: The active MMP-9 levels (active GP values) were analyzed with multiple comparison p value and the p-value (0.0001) was smaller than 0.05 which concluded that the values were significant. The multiple comparisons table and graph showed that the Adult group had higher levels of MMP-9 than the 60% and 70% gestation groups. The ratio of active MMP-9 levels to the total MMP-9 levels (Active GP to Total GP values) was calculated and obtained. After analyses, the p-value (0.0002) was smaller than 0.05 which concluded that the values were significant. Using the multiple comparisons table and the graph, it can be seen that the MMP-2 levels in the 60% and 70% gestation groups were lower than the levels in the Adult group.

Conclusions: There were observations of ontogenic increases in the cerebral cortical MMP-2 and MMP-9 protein expressions during sheep development. The levels of MMP-2 and MMP-9 in the 60% and 70% gestation groups were significantly lower than the amount in the adult group. These results sparked an interest to examine the downstream or upstream effects on the MMP-2 and MMP-9 in brain injury. Although MMP-2 and MMP-9 were shown to increase as development advances, the graph shows that MMP-2 and MMP-9 suddenly decrease in the New Born group. This observation from the bar graph raises questions about the blood brain barrier activity and steroid concentration in fetus right before and after birth. There could be a correlation between cortisol levels and MMP-2 and MMP-9 levels. This correlation and relationship will be examined by in future experiments which are being carried out. The effects of steroids on the activities MMP-2 and MMP-9 will also be explored.
Clinical trials rely on robust and accurate methods to assess clinically significant improvements, and there continues to be a need to develop outcome measures sensitive enough to detect change in core symptoms and deficits related to Autism Spectrum Disorder. Presently, the Autism Diagnostic Observation Schedule (ADOS) and caregiver reports are utilized to determine change in autism symptomology over the course of a child’s treatment. However, ADOS scores are not considered sensitive to treatment change (Anagnostou et al., 2015) and caregiver reports are subject to placebo effects (Guastella et al., 2015). The Brief Observation of Social Communication Change (BOSCC) was designed to capture small changes in response to social communication treatment in individuals with Autism (Grzadzinski et al., 2016). The present analysis investigated the reliability and validity of the BOSCC as well as relationships between BOSCC scores and child characteristics.

Participants (N=16) with ASD were recruited from the Rhode Island Consortium for Autism Research and seen as part of a larger study developing biomarkers of autism symptoms. Community diagnoses of ASD were confirmed with the Autism Diagnostic Observation Schedule, 2nd Edition (ADOS-2). Participants ranged in age from 2 to 6 years (M=4.18, SD=1.02).

The BOSCC was administered according to the most recent guidelines (Lord et al, in preparation). Behaviors were coded from video recordings by two independent observers. Inter-rater reliability was assessed with intra class correlations (ICCs) for the total score as well as for individual codes. Overall inter-rater reliability was excellent (ICC=.94). ICCs on individual items ranged from .42-.98 (M = .76, SD = .18). Validity of the total score on the BOSCC was initially assessed with a correlation with the ADOS-2 Calibrated Severity Score (CSS; r = .25, p = .36). The CSS allows for comparison of severity across ADOS-2 modules corresponding to children’s language ability, but has the limitation of a relatively restricted range. Most participants (14/16) were assessed with ADOS-2 Module 1 (for those with no to minimal language) allowing for a test of the relationship with ADOS-2 score and the BOSCC total score. This correlation was significant (r = .73, p = .003). Correlations were also used to assess relationships between child characteristics and autism symptoms as measured by the BOSCC. Higher BOSCC total scores were associated with lower IQ (r = -.75, p = .001) but were not associated with chronological age (r = .10, p = .71).

The present analysis provides preliminary insight into relationships between the BOSCC and ADOS scoring algorithms while considering individual characteristics. The nonsignificant relationship between BOSCC and ADOS-2 CSS scores may have been related to a restricted range of the ADOS-2 severity score. However, the positive relationship between the BOSCC and total ADOS-2 scores for the subset of children with minimal language supports validity of the BOSCC. The significant relationship between BOSCC and IQ scores signals the need to determine if BOSCC scores measure changes in symptoms and behaviors independent of differences in intellectual functioning.
FOOD INSECURITY AND ANAPHYLAXIS RISK IN CHILDREN WITH FOOD ALLERGY

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Objective: Pediatric Food Allergy (FA) is a serious chronic condition affecting 4% to 8% of US children, and is increasing in prevalence (Gupta et al., 2010). Little is known about how FA impacts families of diverse racial/ethnic backgrounds. FA reactions can result in a variety of symptoms, ranging from skin irritation (e.g., hives) to vomiting/diarrhea, and in the most severe cases, food-induced anaphylaxis (FIA), a rapid, potentially life-threatening reaction (Sicherer, & Sampson, 2014). Food insecurity is defined as the uncertainty or inability to acquire enough food to meet the requirements of all members of a household because of financial or resource constraints (Coleman-Jensen et al., 2014). When compared to Caucasian children of the same age and gender, black and Hispanic youth diagnosed with FA are more likely to endorse low food security (Johns & Savage, 2014). Despite these findings, little is known about why families with FA experience food insecurity, regardless of differences in age, income, and education. The goal of the present study is to provide a preliminary investigation of food security, perceived FA risk, and anaphylaxis in children with FA. We expect that children of families who are food insecure will be more likely to have history of FIA due to their limited control over food selection.

Methods: Participants were 183 caregivers (50% mothers) who had a child with physician-diagnosed FA (57% male; MAge = 7.5 years, SD = 3.2 years; 67% White, 22% Black, 21% Hispanic or Latino). Caregivers completed an online survey that provided information regarding demographics, perceptions about food security, and history of child FIA. The associations between demographic characteristics (i.e., ethnicity/race, income, education) and food insecurity and were examined, with a specific focus on cultural and socioeconomic challenges. Household food security, as suggested by the National Health and Nutrition Examination Survey (NHANES), was coded using the following guidelines: Full food security: no affirmative response in any items (22%); Marginal food security: 1-2 affirmative responses (19%); Low food security: 3-7 affirmative responses (17%); Very low food security: 8-18 affirmative responses (42%). Our data was categorized into a dichotomized distribution (secure (i.e., no or marginal): N= 75, 41%; insecure (i.e., low or very low): N= 108, 59%).

Results: Chi-square tests indicated significant associations between food security status (insecure vs. secure) and parental perceived of FA-related risks. Parents who indicated food insecurity reported an increased risk for accidental ingestion ($\chi^2 (1, n = 183) = 11.99, p = .001, phi = .27; 41% vs. 17%$), severe reaction ($\chi^2 (1, n = 183) = 6.24 p = .01, phi = .20; 45% vs. 24%$), and death ($\chi^2 (1, n = 183) = 22.55, p < .001, phi = .36; 38% vs. 12%$). Food security status was also associated with child history of FIA ($\chi^2 (1, n = 183) = 5.54, p = .02, phi = .19$). No association was observed between food security and income status (i.e., above/below the federal poverty line). An independent-samples t-test was conducted to compare other demographic characteristics with food security status. No differences were observed in food security status, child ethnicity, or child age.

Conclusions: Findings from the present study highlight the high proportion of food security in families with FA. Observed differences in perceptions of FA-related risks may be a consequence of the adversity these families face in order to meet basic nutritional needs, whereas more food secure families may not have such concerns and can dedicate more time/resources to examine food items for potential FA triggers. Surprisingly, no associations were observed for food security status and child demographic characteristics/age. Future research is needed to examine FA risks and the impact food insecurity given the potential risk food insecurity may place on families.
NUMBER OF PAST-YEAR MISSED CLINIC VISITS AS AN INDICATOR OF CURRENT HEALTH FUNCTIONING AMONG YOUNG PEOPLE LIVING WITH HIV

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Adolescents and young adults (young people) living with HIV (YPLH) show disproportionately low rates of retention to HIV care when compared to other age groups. One indicator of retention is number of missed clinic visits (MCV) in the past year. Among adults, it is associated with poor antiretroviral (ART) adherence, low CD4 count, and virologic failure. Less is known about MCV among YPLH who face unique obstacles to attending their doctors’ appointments such as becoming increasingly responsible for managing their own healthcare. Moreover, few studies have explored the association between MCV and behavioral health outcomes, and examined potential demographic and social-cognitive predictors of MCV. To better understand these associations, this study examined MCV in a sample of U.S.-based YPLH clinic patients aged 12 to 24 (N = 2,215). First, we observed the effect of MCV—categorized as missing no visits, one visit, or two or more visits—on HIV care cascade outcomes while adjusting for demographic covariates. We found that compared to participants with full past-year retention, YPLH who missed two or more visits were significantly less likely to report taking ART (adjusted odds ratio [AOR] = .75, 95% confidence interval [CI] = .61, .92). Among those on ART, YPLH who missed one or two or more visits had a lower likelihood of reporting 100% past-week ART adherence (AOR = .36, CI = .28, .47 and AOR = .66, CI = .47, .92, respectively) versus YPLH who did not miss any visits. Missing two or more visits was also associated with an increased odds for poor immunological functioning (i.e., CD4 count lower than 500; AOR = 1.29, CI = 1.07, 1.56) but not viral suppression. Second, we conducted bivariate analyses to explore the association between number of MCV and behavioral health functioning. In general, more missed visits was related to worse functioning. For example, those who missed two visits vs. none had greater current psychological distress (M = 1.17, SE = .03 vs. M = .83, SE = .02; F(2) = 46.23, p < .001) and higher rates of past-year suicidal ideation (20% vs. 13%; \( \chi^2(2) = 18.78, p < .001 \)). In addition, YPLH with two or more missed visits compared to YPLH with full retention were more likely to report frequent alcohol use (24% vs. 19%; \( \chi^2(2) = 9.38, p < .01 \)), marijuana use (36% vs. 22%; \( \chi^2(2) = 42.82, p < .001 \)), and other drug use (8% vs. 4%; \( \chi^2(2) = 19.05, p < .001 \)) in the past three months. They also reported higher rates of recent unprotected anal or vaginal sex (34% vs. 28%; \( \chi^2(2) = 9.79, p < .01 \)) and unprotected sex while under the influence of alcohol or drugs (19% vs. 11%; \( \chi^2(2) = 21.30, p < .001 \)). Finally, we explored patients’ demographic factors and social-cognitive resources as predictors of MCV in a multivariate logistic regression. Higher levels of HIV treatment self-efficacy and social support but not treatment readiness or provider support were predictive of a lower likelihood of missing two or more visits. Female YPLH, older adolescents (compared to younger adolescents), YPLH identified racially as Black or of a mixed race background (compared to White YPLH), YPLH who acquired HIV behaviorally (compared to perinatally), and YPLH without a high school education were all at greater risk for MCV. In addition, housing instability had a positive association with MCV. Our results demonstrated that number of past-year MCV can potentially be indicative of multiple problematic health outcomes beyond HIV-related health functioning. Providers working with YPLH should consider screening for MCV as it may prompt the need for additional risk assessments. Given the many factors associated with MCV among YPLH, interventions to improve treatment retention would benefit from a holistic approach which addresses structural barriers to engagement (e.g., housing instability) as well as patients’ social support and behavioral health needs.
IMAGING UP STATES IN A MOUSE MODEL OF AUTISM

Brian Theyel, MD & Barry Connors, PhD

Background
Research in mice with genes known to be highly penetrant for Autism Spectrum Disorder (ASD) in humans is progressing, but the individual neurocircuit abnormalities that cause ASD remain unknown. Here, we present some preliminary data from a mouse in which one such gene, TSC1, is deleted in approximately 60-70% of thalamocortical relay cells. This mouse repetitively grooms and seizes, which are both prevalent in the human disease tuberous sclerosis and in individuals with ASD. Emerging data suggest that an imbalance in the ratio of excitation to inhibition in cortex may account for many symptoms in ASD, as well as seizures. Here, we hypothesize that, due to an expected increase in the ratio of excitation:inhibition large activations of cortex lasting around 0.5-1 second are more easily elicited when thalamocortical relay cells are stimulated in mutant animals relative to controls.

Mutants
We used flavoprotein autofluorescence imaging and field potential recordings to identify network activations resulting from electrical stimulation of the thalamus at various current intensities. The intensity required to activate cortex half the time was defined as the threshold. Mutant and wild-type control thresholds were compared with 2-sample t-tests.

Results
No significant differences in threshold were found in a comparison of thresholds of 7 mice from one group, and 4 from another (P = 0.57; Means 16.4 and 12.8, with standard deviations of 10.6 and 5.0 respectively). Going forward we will analyze the spatial spread of activation, and electrophysiological inputs to cortex.
USING KEY ITEMS FROM THE PRIME SCREEN TO IDENTIFY INDIVIDUALS AT RISK FOR PSYCHOSIS

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Accurate identification of individuals experiencing prodromal symptoms of psychosis may be critical to the initiation of early treatment, which has been shown to be associated with a host of positive outcomes including symptom improvement and the delay, and possible prevention, of psychosis onset. To facilitate identification, the self-report PRIME Screen was developed to efficiently probe attenuated positive symptoms as a first step in risk assessment. The PRIME has been shown to identify individuals with a heightened risk for psychosis by demonstrating acceptable rates of sensitivity and specificity in predicting those determined to be at clinical high risk (CHR) for psychosis based on a thorough risk interview. Despite promising findings, the predictive utility of the PRIME is limited due to the relatively high rates of individuals who screen positive, but are not determined to be at CHR. Given the common anxiety-based feeling of losing control of one’s thoughts and behaviors, and/or of being negatively perceived or targeted, the potential exists for individuals to endorse some items on the PRIME based on symptoms better explained by anxiety. This study aims to evaluate the PRIME using multiple scoring methods within a heterogeneous sample of 123 help-seeking youth (aged 12-22). Given the potential for several PRIME items to be endorsed due to anxiety symptomatology, ratings were compared across three groups: high-risk for psychosis (n = 50), low-risk with anxiety (n = 31), and low-risk without anxiety (n = 42). Results indicate that the psychosis-risk group had significantly higher ratings than the low-risk groups on eight of twelve PRIME items. Compared to the low-risk participants with anxiety, the psychosis-risk group had significantly higher ratings on six “key items”. The PRIME’s ability to predict risk status, as defined by the Structured Interview for Psychosis-risk Syndromes, was then examined; the author-recommended PRIME cutoff was compared to a full-sample optimized cut-point and a cutoff based on key item endorsement. The key item scoring approach yielded higher rates of specificity and accuracy compared to the author-recommended and sample-optimized cutoffs. Results suggest that these six key items may be particularly important for predicting psychosis-risk among help-seeking young people. Scoring considerations that increase the PRIME’s accuracy may improve the real-world application of this screener for identifying high-risk individuals in clinical settings.
INCREASED PSYCHIATRIC COMPLEXITY OF AUTISM SPECTRUM DISORDER: EXPLAINING DIAGNOSTIC INCONSISTENCIES

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Recent studies have indicated that the Autism Diagnostic Observation Schedule (ADOS) has reduced specificity in samples with a broad range of developmental and behavioral disorders (Molloy et al. 2011), and a pilot study found that “false-positive” ADOS results may be attributable to symptoms of co-morbid psychiatric conditions (Stadnick et al. 2015). However, literature has yet to appropriately quantify phenotypic characteristics of individuals with diagnostic inconsistencies in ADOS and community diagnosis.

The objective of the study is to identify whether clinical characteristics differ in individuals with discordance between community diagnosis and ADOS as compared to individuals with concordance in these same measures.

The sample was comprised of 762 individuals (ages 3 – 18; Mage = 13.27 years, SD = 9.45, 78.3% male) selected from a state-wide ASD registry. Participants entered the registry either with an existing diagnosis or due to a concern of an ASD. All participants were administered the ADOS-2 upon enrollment. Participants were grouped into four diagnostic categories depending on status of community diagnosis and ADOS-2 result: (1) Community ASD diagnosis and a positive ADOS-2 (N=533); (2) Community diagnosis and a negative ADOS-2 (N=54); (3) No community diagnosis and a positive ADOS-2 (N=109); and (4) No community diagnosis and a negative ADOS-2 (N=66). The presence of psychiatric diagnoses and the reports of current medications were obtained through caregiver-completed questionnaires. The number of different psychotropic medications were summed to create four dichotomous variables representing antidepressants, Attention-deficit/hyperactivity disorder (ADHD) medications, antipsychotics and mood stabilizers. Autism severity was measured by standardized scores available through a caregiver-completed Social Responsiveness Scale, Second Edition (SRS-2).

A series of logistic regressions of co-morbid diagnoses with age and gender as covariates revealed that the discordant subgroups were more likely to have depression ($\chi^2 = 61.47, p < .001$), anxiety ($\chi^2 = 51.93, p < .001$), ADHD ($\chi^2 = 18.70, p = .002$) and oppositional defiant disorder ($\chi^2 = 13.97, p = .016$). Chi-square analyses revealed a significant difference between diagnostic groups and the likelihood of taking antipsychotic ($p = .031$) and ADHD ($p = .020$) medication. However, these effects did not survive follow-up logistic regression analyses controlling for age and gender. Further, there was a significant difference between diagnostic groups on SRS-2 severity ($F(3,659) = 5.34; p = .001$). Participants with a positive ADOS-2 result and community diagnosis scored higher on the SRS-2 compared to those with no ASD diagnosis ($p = .003$). Results support the sensitivity of the SRS-2 to measure ASD symptom severity in a subgroup more likely to have a true positive diagnosis.

Children presenting to an ASD registry with inconsistencies between community diagnosis and ADOS-2 findings had increased rates of caregiver-reported psychiatric diagnoses and psychotropic medications as compared to those whose ADOS-2 result was concordant with community diagnosis of ASD. The results concur with prior reports of reduced specificity of the ADOS-2 in the presence of co-occurring psychiatric symptoms. These findings are both empirically and clinically relevant, confirming the need for cautious interpretation of positive ADOS-2 results in the presence of psychiatric complexity.
Understanding the brakes on circuits underlying reward seeking behavior is an integral part of addressing and treating drug addiction and other psychiatric disorders. In the mesolimbic reward circuit, dopaminergic neurons of the ventral tegmental area (VTA) are modulated by inhibitory synaptic inputs. These GABAergic inputs are comprised of several distinct subpopulations, originating locally from VTA interneurons and also from projection neurons including those from the rostromedial tegmental nucleus (RMTg). While the synaptic input from GABAergic interneurons in the VTA has been widely studied using electrical and optogenetic stimulation as well as behavioral studies, the properties and involvement of RMTg inhibitory synapses onto VTA dopamine cells are yet to be elucidated. Lying adjacent and caudal to the VTA, the RMTg is also referred to as the “tail of the VTA”. The close proximity of these two inhibitory populations raises questions about the boundary between the VTA and RMTg, and whether they in fact represent two distinct inhibitory subpopulations. In this study, Cre-driven viral expression of fluorescent reporters and channelrhodopsin was used to test whether the inhibitory populations of the VTA and RMTg are neuroanatomically and electrophysiologically distinct. Dual anterograde viral labeling of inhibitory neurons in RMTg and VTA showed no co-localization of the two populations, indicating that they are structurally distinct from one another. Differences in the timing of synaptic inputs from each region were also observed. In addition, combining retrograde tracing from the VTA with anterograde viral expression of RMTg inhibitory projections confirmed the connectivity of GABAergic efferents from the RMTg to the VTA. Collectively, our neuroanatomical and electrophysiological data indicate a distinction between the VTA and RMTg GABAergic populations, and contributes to the delineation of inhibitory inputs to VTA dopamine neurons.
GENETIC FATE MAPPING OF SPINAL COMMISSURAL NEURONS

Alastair Tulloch, PhD, Shaun Teo, Julia Schoenwald, Marc Tessier-Lavigne, PhD; Alexander Jaworski, PhD

Commissural neurons in the mouse embryonic spinal cord are a prime model system to study axon guidance. These neurons arise from multiple progenitor domains in the developing neural tube and settle in various laminae of the spinal cord. The unifying feature of these neurons is that they send axons across the ventral midline. After midline crossing, commissural axon trajectories diverge along the rostro-caudal axis, and rostrally-projecting axons ultimately innervate various supraspinal targets in the thalamus, mesencephalon, cerebellum, and medulla. Thus, commissural neurons are a highly heterogeneous population of cells with respect to their cell body position, axonal trajectory, and neurotransmitter phenotype. Although the guidance of commissural axons during development has been studied in great detail, the mature phenotype of commissural neurons has not been characterized comprehensively. This is largely due to extensive neuronal migration within the developing spinal cord and lack of a specific genetic marker to track commissural neurons.

To follow the fate of commissural neurons from the embryonic into the adult mouse spinal cord, we generated mice expressing Cre recombinase from the Robo3 locus. Robo3 is an axon guidance receptor selectively expressed by all spinal commissural neurons, where it is required for axon crossing of the ventral midline. Here, we use Robo3Cre mice in combination with a Cre-dependent reporter line to elucidate the developmental origin of commissural neurons and characterize their positions and molecular makeup in the adult spinal cord. Our studies provide insights into the development and ultimate fate of commissural neurons, and our Robo3Cre mice serve as an important genetic entry point for further analyses of commissural neuron development, connectivity, and function.
Background: The evaluation of anticipated and experienced outcomes, and the accompanying emotions, are crucial to flexible decision-making. When choosing between multiple options, receiving information about outcomes of options not chosen allows the re-evaluation of attained outcomes, and can result in feelings of regret or relief. This general ability to reason about outcomes had a different decision been made (“what might have been…”) is termed counterfactual reasoning. Thus, regret and relief can be described as counterfactual emotions based on the conscious realization that a decision made differently would have led to a better or worse outcome, respectively. Prior research has demonstrated a role of the orbitofrontal cortex (OFC) in the experience of regret and relief. The goal of this study was to investigate whether the application of inhibitory transcranial direct current stimulation (tDCS) targeting the OFC could dampen the experience of decision-induced regret and relief.

Methods: Thirty-eight participants completed 96 rounds of a previously used gambling task and were asked to rate their happiness (-50 to +50 scale) with attained monetary outcomes of a chosen gamble before and after being shown the unattained, counterfactual outcomes, i.e. what they would have received had they selected the other gamble. The difference in happiness rating before and after revealing the unattained counterfactual outcomes was taken as a measure of regret (negative shift) or relief (positive shift). During this task, 20 participants received 2 mA cathodal tDCS over EEG coordinate Fp1 for 20 minutes, intended to target the OFC, and 18 participants received sham stimulation over the same location.

Results: Linear mixed model results showed that participants who received cathodal tDCS reported both less regret and less relief than participants who received sham stimulation (p=0.004). This finding was not due to the groups differing in the gambles they selected (p=0.62), attained monetary outcomes (p=0.15), or initial happiness valuations before the counterfactual outcome was revealed (p=0.12).

Conclusions: These data demonstrate that tDCS can specifically dampen the experience of counterfactual regret and relief, without affecting emotional reactivity in general. This is consistent with literature highlighting the OFC’s vital role in forming associations between affect-based responses and abstract information about outcomes and reward value evaluation. The ability to modulate value-based cognitive processes using tDCS is of clinical relevance for neuropsychiatric disorders, such as anxiety or stress-related disorders to reduce excessive feelings of regret (or fear thereof fear of) and drug abuse to reduce overvaluation of immediate rewards.
WHAT DRIVES DRIVING: DIFFERENCES IN THE RELATIONSHIP OF VISUAL SEARCH AND SENSORY BINDING TO DRIVING PERFORMANCE BETWEEN HEALTHY AGING AND ALZHEIMER’S DISEASE

Umesh Venkatesan, MS; Elena Festa, PhD; Brian Ott, MD; William Heindel, PhD

Objective: Patients with Alzheimer’s disease (AD) demonstrate deficits in cross-cortical visual feature binding that are distinct from age-related changes in selective attention. This may have consequences for driving performance given the demands placed on multisensory integration. The current study examined the relationship of visuospatial search and sensory binding to driving in elderly controls (EC) and patients with early AD.

Participants and Methods: Patients (n=71) and EC (n=40) completed a visual search task requiring either luminance-motion (L-M) or color-motion (C-M) integration, analogs of intra- and cross-cortical binding, respectively. Standardized road test and naturalistic (video recorded) driving data were collected along with clinical screening measures commonly used in driving evaluations (e.g., Trail Making A&B, Clock Drawing).

Results: Visual search and clinical test scores were differentially related to driving behavior in each group. Both L-M and C-M visual search and Trails B were associated with standardized road test performance in EC, while C-M integration, Trails A, and Clock Drawing were associated with naturalistic driving performance in AD. Stepwise regressions indicated that Trails B and L-M measures best predicted standardized road test performance in EC, while C-M integration and Clock Drawing best predicted naturalistic driving performance in AD. Backward logistic regression analyses also indicated that C-M integration and Trails A best predicted group membership.

Conclusions: Findings suggest that while selective attention is most relevant to driving behavior in EC, multisensory integration may be most sensitive to driving in AD. This latter relationship may only emerge in naturalistic settings, which better reflect patients’ driving behavior. Measures of visual integration may offer distinct insights into driving behavior. The study findings thus have important implications for the assessment of driving competency in both healthy elders and those with early AD.
NOVEL FRAGMENT OF AMYLOID PRECURSOR PROTEIN (APP), ETA-CTF, IS SELECTIVELY DEGRADED BY CATHEPSIN L

Haizhi Wang, MD; Nianli Sang, PhD; Can Zhang, PhD; Ramesh Raghupathi, PhD; Rudolph Tanzi, PhD; Aleister Saunders, PhD

Alzheimer's disease (AD) is a progressive neurodegenerative disease characterized by the deposition of amyloid beta peptide (Abeta). Abeta is a proteolytic product of Amyloid precursor protein (APP). In this study, we investigate whether protein degradation plays a role in the processing of APP. We found that inhibiting protein degradation with ALLN induces accumulation of novel APP fragments. This effect is independent of cytotoxicity and protein synthesis. We further showed that inhibition of cathepsin, and not calpain or proteasome, mediates the accumulation of novel APP fragments. Our data suggests that APP undergoes alternative processing which generates the novel fragments; these fragments undergoes rapid clearance/degradation via cathepsin (most likely cathepsin L) under physiological conditions.
FEASIBILITY AND TOLERABILITY OF COMPUTERIZED COGNITIVE-BEHAVIORAL THERAPY COMBINED WITH BIFRONTAL TRANSCRANIAL DIRECT CURRENT STIMULATION FOR TREATMENT OF MAJOR DEPRESSION

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INTRODUCTION: Major Depressive Disorder (MDD) is a common and debilitating psychiatric disorder. Furthermore, up to 30% of patients show little or no improvement in symptoms despite adequate treatment with available therapies and medications. Therefore, there is a need to devise new and effective treatments that are readily available and easily used by patients. Cognitive behavioral therapy has been shown to be effective in the treatment of MDD and can be presented in a computerized form (eCBT), allowing for easy dissemination to patients outside of the clinic. Transcranial Direct Current Stimulation (tDCS) is a form of neurostimulation which may have antidepressant effects and has been shown to improve outcomes when used in combination with medication therapies.

METHODS: We investigated the feasibility of this treatment by randomizing adults with MDD to receive active or sham bifrontal tDCS in combination with eCBT. Subjects were asked to complete 12 GoodDaysAhead® online CBT skills training modules (target 3 per week) at the research clinic, concurrent with the blinded stimulation.

RESULTS: n=14 were enrolled and received at least one blinded treatment session; n=5 (active tDCS) and n=4 (sham tDCS) completed all study procedures. No serious adverse events were reported, despite a wide range of concomitant medications used by participants. A drop-out rate of 36% reflected lack of efficacy, dislike of the eCBT modules, and side effects of tDCS (e.g. unpleasant sensations on the scalp). The combined groups showed some mean improvement in depression scores over time, but there was no statistical difference in efficacy outcomes between active and sham groups, in part owing to small numbers. Two participants (one active and one sham) met categorical response criteria on endpoint measures and one participant (sham) met criteria for remission. Side effects were generally mild and included unpleasant sensations at the stimulation site, sleepiness, and headache. Active protocol completers reported more adverse events (29 events) than sham completers (7.6 events) but this was significant only at trend level (p=.073). However, both groups reported comparable numbers of moderate or severe adverse events (3.4 events for active completers and 3.75 events for sham completers, p=.310), predominantly relating to unpleasant scalp sensations. 67% of active participants and 40% of sham participants reported sleepiness. 55% of active participants and 20% of sham participants reported headache. However, none of these side effects were severe enough to warrant discontinuation.

CONCLUSION: Combining tDCS and eCBT in a protocol that could potentially be self-administered by patients at home appears to be generally well tolerated, even when used on top of concurrent medications.
Adolescence is a developmental period marked by significant changes in brain areas related to executive functioning (EF) (Blakemore & Choudhury, 2006). These neurodevelopmental changes often co-occur with increasing substance use, including marijuana. Chronic cannabis use, particularly when use begins in adolescence, has been associated with a substantial decline in performance on neuropsychological tests of EF (Meier et al., 2012). This has clinical implications as EF may play a role in both modulating craving for substance (Giancola & Tarter, 1999) and responding effectively to stressors (Williams et al., 2009). Although the relationship between stress and craving in aggregate has been substantiated (see Hyman & Sinha, 2009), less is known about this relationship in adolescent marijuana users, and even less about stress-induced craving in the moment. Also, no studies have directly investigated the effect of EF on the stress-craving relationship in the natural environment. We used ecological momentary assessment to (1) disaggregate the effect of momentary changes in stress from general individual stress levels on marijuana craving in adolescents and (2) evaluate the influence of EF on stress-induced craving.

Adolescent cannabis users (≥ twice weekly/month; n=85; Age: range=15-24, M=19.75, SD=2.08; 54.3% female ) were recruited from the community. Participants came to the laboratory where they completed the Boston Naming Test (Kaplan et al., 1983) and the Retrieval Fluency, Memory for Words, and Story Recall subtests of the Woodcock Johnson®-III Tests of Cognitive Abilities. The test scores were z-scored and averaged to create a composite EF score. All participants also completed a week of random assessments in the natural environment via electronic diaries. When alerted, participants responded with their current levels of stress and tension (0=not at all to 10=extremely, α=.80), if marijuana cues were present (0=cues not present, 1=cues present), and urge to smoke at the present moment (0=no urge to 10=strongest ever).

We used multilevel modeling (SAS 9.4) to assess the three-way interaction of stress, the presence of cues, and EF on urge to smoke. We modeled stress in two ways: (1) momentary stress (centered within persons) to capture moment-to-moment fluctuations in the experience of stress, and (2) average stress (centered at the grand mean) to index the between-individual proneness for stress-related feelings. The three-way interaction of EF and marijuana cues with stress were not significant; however, the two-way interactions of EF and stress were significant, both for the momentary stress influences (b = −0.22, p < .001) and average stress (b = −0.55, p = .014).

Our results suggest that, on average, higher EF protects teens with higher overall stress levels against the urge to smoke. This work also moves beyond research showing general associations by assessing stress and craving in adolescents’ daily lives. Our results show that higher EF helps to protect teens from experiencing cravings in specific situations when teens are highly stressed relative to their own general stress level. These findings suggest that interventions designed to enhance EF may be tailored specifically to reduce stress-related craving at times or situations when it matters most.
SUBJECTIVE VALUE ENCODING DURING COGNITIVE EFFORT-BASED DECISION-MAKING

Andrew Westbrook, PhD

With growing interest in the clinical and theoretical implications of phenomenal cognitive effort and cognitive motivation, new questions have emerged about regions of the brain supporting effort-based decision-making. One question concerns which regions of the brain encode dimensions of subjective value as individuals weigh the costs and benefits of expending cognitive effort. To investigate this, fMRI was used in combination with a powerful, novel behavioral economic paradigm which operationalizes cognitive effort in terms of effort-based reward discounting. The operational measure integrates information about objective reward magnitude, working memory load, and subjective sensitivity to effort costs, and is used as a parametric regressor of brain activity while participants evaluate offers to expend effort in pursuit of reward. Results support the encoding of subjective value dimensions in a canonical network of regions otherwise implicated in encoding diverse rewards varying by delay, risk, or demands for physical effort, particularly within the ventromedial prefrontal cortex, ventral striatum, anterior insula, and the anterior cingulate cortex. Dynamics in prefrontal regions, during first offer evaluation, are moreover predictive of subsequent choice, implicating them causally in decision-making. Finally, cognitive load encoding during offer evaluation reflects the encoding of load during cognitive task performance, suggesting networks by which information about subjective effort costs become integrated into valuation processes during decision-making and thus influence an individual’s propensity to expend cognitive effort.
FAMILY CONTEXTUAL STRESS, CORTISOL, AND BEHAVIOR PROBLEMS IN HIGH-RISK PRESCHOOLERS

Diana Westerberg, PhD; Stephanie Parade, PhD; Audrey Tyrka, MD, PhD; Thomas Geraciotti, MD; Brittney Josefson, BA; Emma Welch, MS; Ronald Seifer, PhD

Research and theory relates chronic stress in early childhood and physiological functioning (del Giudice et al., 2011; McEwen 1998). Cortisol is a stress hormone of the Hypothalamic Pituitary Adrenal (HPA) Axis system; a key player in stress physiology. Past studies have found relations between family contextual stressors with higher and lower basal cortisol levels in early childhood (Blair et al., 2011; Cutili et al., 2010; Zalewski et al., 2012). Furthermore, equivocal research links cortisol levels with both internalizing and externalizing behavior in young children (Brotman et al., 2007; McGinnis et al., 2016). Children growing up in poverty are at increased risk for experiencing behavior problems (Qi & Kaiser, 2003) and being exposed to numerous stressors associated with poverty. The present study aims to carefully measure numerous contextual stressors, HPA axis functioning, and behavior problems in a sample of high-risk families to better understand the relations among these factors.

Participants were 241 children (54.4% female; Mage = 51 months; 43.2% White, 15.8% Black, 23.1% biracial, and 18.0% other; 44.2% Hispanic/Latino) and their caregivers (93.4% mothers). Record review was used to recruit families with a maltreated child from the local child welfare agency and an emergency maltreatment assessment (n = 100). Families without an indicated case of maltreatment within the past six months were recruited from a pediatric medical clinic and childcare centers (n = 69). Over half of caregivers were at least high school graduates (40.9%, High School; 39.1%, > High School), in single parent households (52.3%), and unemployed (56.0%). Family mean annual income was $22,181.

Children’s saliva was sampled 5 minutes after waking (Mtime= 8:15am), in the afternoon (Mtime= 2:18pm), and before bed (Mtime= 8:41pm) on 3 days by caregivers, who completed saliva collection training. Cortisol levels assayed from valid samples were averaged across days yielding composite morning, afternoon, and evening levels (Bruce et al., 2009). Caregivers completed demographic questionnaires, the CBCL (Achenbach & Rescorla, 2000), the Diagnostic Infant and Preschool Assessment (Scheeringa & Haslett, 2010), and semi-structured contextual stress interview at baseline and 6 month follow-up. Diurnal levels and sampling times were used to calculate diurnal output (area under the curve; AUC). Morning cortisol and AUC were log transformed due to skewness (Zalewski et al., 2016). Correlations examined relations among study variables. Regression analyses tested relations between maltreatment status, contextual stress, cortisol measures, and their interactions, as they related to internalizing, externalizing, and mood symptoms at baseline and follow up, using Bonferroni corrections for multiple comparisons.

Mean morning, afternoon, and evening cortisol levels were .40, .23, and .20 μg/dL, respectively. Internalizing behavior at follow up and morning cortisol were significantly, positively related even when controlling for maltreatment status and contextual stress. Regression analysis showed a significant three-way interaction predicting mood symptoms at follow up. For children with a maltreatment history, high stress more strongly related to mood symptoms when children also had high morning cortisol, whereas this relationship was weaker when children had low morning cortisol. In contrast, among children without a maltreatment history, lifetime stress and mood symptoms were more strongly related for children with low morning cortisol compared to those with high morning cortisol.

Overall, results showed unique patterns of association between cortisol measures and behavior at baseline and follow up. Results suggest relations between cortisol and internalizing behavior are most robust for morning cortisol levels compared to diurnal output. Results and implications for literature and future research will be discussed.
MECHANISMS OF ATTENTION INVOLVED IN MULTIPLE TARGET VISUAL SEARCH

James Wilmott, BA & Joo-Hyun Song

Previous work investigating how spatial attention operates during visual search has used a single unique feature target (oddball task) while manipulating the number of distractors to model real world search. Use of this paradigm has shown the spatial scope of attention is adjusted in a task dependent manner; detection tasks require use of distributed attention while shape discrimination tasks require focused attention (Bravo and Nakayama 1992). As single target search only represents a subset of actual search tasks, it remains unclear how attention functions in more complex search arrays with multiple targets. We extend the traditional oddball task by manipulating the number of targets and distractors to characterize how spatial attention functions in more complex search tasks. Subjects alternatively performed a discrimination and detection task for one or two targets while fixating at a central location. Targets were defined by color and could randomly appear at a subset of six locations around an imaginary circle. Reaction time (RT) increased with the number of targets in the discrimination task but did not change with number of targets for detection; this pattern held across different distances between targets. These results indicate that when there are multiple targets in a search array there is a cost associated with using a focused scope of attention but not when using distributed attention. Additionally, we found RT in two target trials was quicker when a target fell within each hemifield in relation to when they were in the same hemifield. We interpret this result as evidence for feature pop-out local to each hemifield. This finding indicates there may be separate attentional resources for visual search within each hemisphere, complementing similar findings in multiple object tracking tasks (Alvarez et al. 2012).
Objective: To develop a skills-based program “Skills to Enhance Positivity (STEP)” to enhance positive affectivity (PA) and the practice of PA skills for adolescents and to assess feasibility and acceptability in delivering STEP to adolescents admitted to an inpatient psychiatric unit due to suicide risk. The objective of STEP is to decrease suicidal behavior via increased PA. Modeled on the Broaden and Build theory of emotion, we purport that increased PA leads to improvements in problem solving, social support, and reasons for living. We hypothesize PA will directly and indirectly (through above mechanisms) decrease suicidal behavior. STEP focuses on 3 sets of skills: mindfulness meditation, gratitude, and savoring. There are 3 individual sessions and 1 family session delivered on the inpatient unit or shortly after discharge, followed by 1 month of daily text messaging (with optional extension to 3 months in RCT) and weekly phone calls to facilitate practice of mood monitoring and positive affect skills.

Method: Participants were hospitalized adolescents, between 14-18 years old, admitted primarily due to suicide risk. Assessments were completed at baseline, post-treatment (1M) and follow-up (4M), with final phone f/u at 6 months. We obtained assent/consent and enrolled 20 adolescents into the Open Development Trial (mage=15.9; SD=1.5), and 52 into the RCT (mage=15.6; SD=1.5). Participants were predominantly female (67%) and White (76.5%).

Results: Average session attendance 81% in Open Phase and 89% in RCT, and mean daily response rate to text messages was 72.4% days in Open Phase and 70.2% in RCT with over 50% opting for the 3 month text extension, demonstrating high feasibility for both sessions and texts. STEP was described as good or excellent by 91.7% of parents and 100% of adolescents. There were no completed suicides, and only 1 suicide attempt in the open trial. Our preliminary data from the pilot RCT phase also appear promising, with 50% less suicidal events compared to Enhanced TAU (6 vs. 13) and 50% less participants reporting suicide events (5 vs. 10). There was also support for improvement in attention to positive affect on a dot probe task (F=3.55; p=.05) and non-judging, gratitude, and satisfaction with life (in which significant within group pre-post improvements were detected in the STEP condition only).

Conclusions: The current data indicate preliminary acceptability of the STEP intervention and its efficacy in reducing suicidal behaviors, suicidal ideation, and depression. Furthermore, both adolescents and parents responded favorably to the text messaging component.
ASSESSING THE NEUROPROTECTIVE EFFECTS OF 17β-ESTRADIOL ON FEMALE THREE-DIMENSIONAL CORTICAL MICROTISSUES EXPOSED TO ISCHEMIC CONDITIONS

Samantha Zambuto, BS & Diane Hoffman-Kim, PhD

Women typically have a lower risk of stroke during midlife compared to men in the same age group; however, women’s risk dramatically increases post-menopause (Lisabeth 2012). Notably, hormone changes, including a significant decrease in estradiol levels, are associated with menopause (Lisabeth 2012). Researchers have hypothesized that these hormone changes could contribute to increased stroke risk in post-menopausal women (Lisabeth 2012). Hormone therapies have the potential to alleviate some of these risks and better protect women from neurological injuries and pathologies, as demonstrated by numerous in vitro and in vivo studies (Engler-Chiurazzi 2016). However, the detailed, cellular mechanisms of estrogens’ mode of action are still not well understood. The ultimate goal of this work is to study and characterize sex differences in response to ischemic conditions and the effects of 17β-estradiol (E2) on female, three-dimensional (3D) cortical microtissues exposed ischemic conditions. A method was developed for culturing sex-specific 3D cortical microtissues as an in vitro model of male and female brains. Bridging two-dimensional (2D) neural cell culture and in vivo brain studies, 3D neural cell culture has the potential to advance studies in complex neurodegenerative diseases and proffer a more realistic model of the central nervous system (Dingle 2015). Unlike 2D neural cultures, 3D cortical microtissues mimic the in vivo environment because they have a stiffness comparable to the brain, contain a heterogeneous mixture of cell types, including neurons, glia, and neural progenitor cells, are electrically active, produce their own extracellular matrix, and contain capillary-like networks (Dingle 2015, Boutin 2017). Sex-specific 3D cortical microtissues were exposed to oxygen-glucose deprivation using the GasPak EZ Anaerobe Container System and glucose-free cell medium for 24 hours followed by a recovery period of 24 hours in normoxia and cell growth medium. Immediately following oxygen-glucose deprivation and a 24 hour recovery period, viability was measured using a lactate dehydrogenase assay. Estrogen receptor expression was verified in 2D neural cell cultures via immunohistochemistry.
EEG SIGNAL AFTER 5-Hz TRANSCRANIAL MAGNETIC STIMULATION IN PATIENTS WITH COMORBID POSTTRAUMATIC STRESS DISORDER AND MAJOR DEPRESSION

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Background:
Repetitive transcranial magnetic stimulation (rTMS) delivered over left DLPFC is standard of care for pharmacoresistant major depression (MDD), and shows promise in commonly comorbid conditions, such as PTSD. Mechanisms of action of rTMS are not fully understood.

Methods:
We studied potential electrophysiological signatures associated with the delivery of 5 Hz rTMS in individuals with comorbid MDD and PTSD (N=20). We obtained the EEG recordings from 8 scalp electrodes before and after up to 40 daily rTMS sessions over left DLPFC, at 120% of resting motor threshold. We calculated EEG coherence between possible electrode pairings (8 recording sites, 28 electrode pairings). Coherence quantifies the statistical dependence of signal in two channels and can be used as a measure to estimate strength of association between the recorded sites. We used Support Vector Machine, a machine learning algorithm, to separate out pre and post rTMS EEG recordings based on the coherence.

Results:
The classifier performed above chance in identifying the recording session most notably when data from Alpha, Delta and Theta bands were used (Alpha: 57.9 ± 1.6%, Delta 72.0 ± 1.5%, Theta 59.2 ± 1.7%, all performances significantly above 50% with p<0.001 ). Examination of the classification algorithm revealed that rTMS reduced coherence between the L DLPFC rTMS site and sites nearby, while EEG coherence between the L DLPFC and more distant regions changed little after rTMS.

Conclusions:
rTMS treatment may be associated with changes in EEG coherence closest to the stimulation site.
A LOCALLY TRANSLATED Lck PATHWAY REGULATES HUMAN GLIOMA STEM CELL MIGRATION, TUMOR GROWTH, AND CANCER STEMNESS GENE EXPRESSION

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Migration of human glioma stem cells (hGSCs) within the brain parenchyma makes glioblastoma one of the most aggressive and lethal tumors. Studies of the cellular and molecular mechanisms underlying hGSC migration are hindered by the limitations of existing migration models. Here we developed a dorsal root ganglion axon-oligodendrocyte-hGSC co-culture to study in real time the migration and interaction of hGSCs with their microenvironment. hGSCs interact with myelinated and non-myelinated axons through the formation of pseudopodia. Isolation of pseudopodia-localized polysome-bound RNA reveals transcripts of lymphoid cell kinase (Lck), Paxillin, Crk-II and Rac1 that undergo local translation. Inhibition of Lck blocks the activation of this pathway, the formation of pseudopodia and the migration of hGSCs. In vivo intraventricular administration of a Lck inhibitor using an orthotopic xenograft mouse model results in significant inhibition of tumor growth and significant down-regulation of cancer stemness gene expression. Targeting this Lck pathway constitutes a novel treatment paradigm for human glioblastomas.
GRANGER MEDIATION ANALYSIS OF FUNCTIONAL MAGNETIC RESONANCE IMAGING TIME SERIES

Yi Zhao, MS & Xi Luo, PhD

Making inference about brain effective connectivity is of great interest in task functional magnetic resonance imaging (fMRI) experiments. In this study, we are interested in clarifying the causal mechanisms of an external stimulus on the interested outcome brain region, by considering another brain region that functions as an intermediate variable. To achieve this, causal mediation analysis under structural equation modeling framework is considered. However, attaining causal interpretations requires both the "no unmeasured confounding" and the "no interference" assumptions. These two assumptions generally do not hold in fMRI datasets. To address the existence of unmeasured confounding, a correlation between model errors is introduced; and to characterize the temporal and interregional dependency, the principle of Granger causality is implemented. In this paper, we propose a Granger Mediation Analysis framework that provides inference about both spatial and temporal causality between brain regions for multilevel fMRI time series. Simulation studies show that our method reduces the bias in estimating the causal effects compared to existing approaches. Applying the proposed method on a real fMRI dataset, our approach not only estimates the causal effects of brain pathways, but effectively captures the feedback effect of the outcome region on the mediator region.