Recent studies have shown that ensembles of single neurons in primate motor cortex exhibit low-dimensional dynamics during the preparation and execution of reach and grasp actions (Aghagolzadeh and Truccolo, 2015; Vargas-Irwin et al., 2015). Here, we examined neural dynamics in the Rhesus Macaque primary motor (leg) area during a variety of locomotion tasks (e.g. walking on a treadmill, ladder, corridor, backwards and bipedal walking). We used latent state-space models, specifically Poisson linear dynamic systems (PLDS), to infer the low-dimensional dynamics (trajectories) in ensembles of cortical neurons. Our findings are threefold: (1) Inferred low-dimensional dynamics showed similar qualitative features across different locomotion parameters: neural trajectories under variations in speed and direction tended to fall on the same “manifold.” (2) Decoding from the inferred low-dimensional trajectories generalized better across different locomotion tasks than decoding directly from the entire population of recorded neurons. PLDS-based decoding achieved a 5% increase in R2 (Kruskal-Wallis test, p<0.05). A point process filter coupled to a Wiener filter was used for PLDS-based decoding. (3) The performance of PLDS-based decoding was also more robust to small sample-size training, while decoding directly from the entire population was significantly affected by the reduction in the sample-size. Our results reveal the dynamics of coordinated activity in ensembles of motor cortical neurons during locomotion, and offer more robust decoding approaches for brain-machine interfaces aiming at restoring movement.
Oscillations in the alpha (7 – 14 Hz) and beta (15 – 29 Hz) bands observed in primary somatosensory cortex as well as in the muscles have been shown to be functionally relevant for sensory perception and modulated in an attention dependent manner (Jones et al. 2010, van Ede et al. 2011, van Ede and Maris 2013). Recent attempts have been successful in utilizing transcranial alternating current stimulation (tACS) to impose these rhythms in cortex (Feurra et al. 2011) as well as modulate corticomuscular coherence, a measure of coordination between the cortex and the muscles (Wach et al. 2013). In this study, we investigated the causal role of these oscillations in the muscles by applying tACS over somatosensory cortex during a tactile detection task while recording simultaneous electroencephalography (EEG) and electromyography (EMG). First, we helped design and create an electrophysiology system using open-ephys (open-ephys.org), an open source initiative that is both flexible and inexpensive. Using our custom built system, we were able to obtain preliminary data that suggests pre-stimulus beta oscillations in the muscles predict detected vs. non-detected trials. Although tACS at alpha band frequencies did not elicit significant effects in spectral profiles or task performance, future studies should investigate this further. These findings begin to provide preliminary evidence for a causal role of sensorimotor oscillations in gating sensory processing, even at the level of the muscles, and may have major implications for field-based clinical diagnosis and therapeutics with EMG in disorders characterized by maladaptive rhythmicity, such as Parkinson’s disorder.
REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION CORRECTS NEURAL NETWORK PATHOLOGY IN PATIENTS WITH COMORBID POSTTRAUMATIC STRESS AND MAJOR DEPRESSIVE DISORDERS

Sarah Albright, BA & Noah S. Philip, MD

Background: Repetitive transcranial magnetic stimulation (rTMS) may correct pathological resting state functional connectivity (RSFC) in major depressive disorder (MDD). MDD is often comorbid with posttraumatic stress disorder (PTSD); neuroimaging in both disorders indicates altered RSFC of the default mode network (DMN), executive control network (ECN) and salience network (SN). This is the first study to evaluate changes in RSFC, due to rTMS, in PTSD+MDD patients.

Methods: We imaged 21 participants before and after an open-label trial of 5Hz rTMS to the left DLPFC (40 daily sessions, each including 3000-4000 pulses). 5Hz was selected based on our prior report of efficacy for co-morbid PTSD+MDD. Imaging analyses used a priori network based seeds, in the subgenual anterior cingulate (sgACC), dorsolateral prefrontal cortex (DLPFC), and basolateral amygdala (BLA), as representative nodes of the DMN, ECN and SN, respectively. To quantify the relationship between changes in neuroimaging and clinical symptoms, RSFC data was correlated with changes in MDD+PTSD symptoms.

Results: Treatment with rTMS induced several changes in RSFC. When seeding the sgACC, rTMS resulted in increased RSFC with angular gyrus, and anticorrelations with the DLPFC. When seeding the DLPFC, rTMS treatment was associated with broad-based anticorrelations with various nodes of the DMN, inclusive of the posterior cingulate/precuneus and lateral parietal regions, as well as the lingual gyrus. Furthermore, rTMS was associated with a significant increase in RSFC between the BLA and ventromedial prefrontal cortex, as well as reduced RSFC with lateral parietal regions (all cluster-corrected FDR < .05). Observed changes in RSFC were generally correlated with changes in clinical symptomatology, particularly in PTSD (e.g., r = .457, p = .031 for BLA-VMPFC RSFC and PTSD symptoms).

Conclusions: This data indicates that rTMS can correct network abnormalities in a transdiagnostic sample, with findings relevant to both disorders under study. Reduced amygdala-prefrontal connectivity is thought to be a core component of the neurobiology of PTSD, and these results indicate that rTMS can strengthen these functional connections, and that connectivity results correlate with observed clinical changes. Furthermore, rTMS appears to induce anticorrelated patterns of RSFC between the DMN and SN as well as between the ECN and DMN, indicating that this non-invasive intervention can normalize neural network patterns.
BIPOLAR DISORDER FEATURES ASSOCIATED WITH SUBJECTIVE ACTIVATION IN MAJOR DEPRESSIVE DISORDER SUBJECTS TREATED WITH REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION

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Lawrence Price, MD, Linda Carpenter, MD

Background: Major depressive disorder (MDD) is highly prevalent, and is associated with a substantial loss of quality of life. Meta-analyses have shown that high frequency repetitive transcranial magnetic stimulation (rTMS) to be associated with clinically relevant antidepressant effects and with a benign tolerability profile. Although its mechanisms of action are not completely understood, it allows for discrete and safe non-invasive modulation of cortical excitability and function. Despite the antidepressant effect and benign tolerability profile, some subjects receiving rTMS treatment report subjective activation, such as insomnia, restlessness, and increased anxiety. It is not well understood if such subjective activation could be related to the high frequency of the stimuli delivered, or potential individual psychopathology related to depression in the context of bipolar disorder spectrum. The aim of this study is to investigate the relationship between clinical efficacy, and subjective activation with bipolar disorder features.

Methods: The Mood Disorder Questionnaire (MDQ) was used to characterize bipolar disorder features. The MDQ is a three-part, self-report questionnaire that screens for a lifetime history of, and a current symptoms of manic or hypomanic episodes. We investigated the first part containing 13 items that assess individual symptoms characteristic of bipolar disorder. We studied 185 individuals with Major Depressive Disorder that received at least five treatments or more TMS treatments (delivered with standard 10 Hz stimulation parameters) in our clinic between 2009 and 2015. The medical record and rTMS treatment databases were used to determine which patients showed signs of activation associated with TMS (warranting change in stimulation parameters). Bipolar diathesis, estimated by the number of positive items endorsed on the MDQ will be evaluated as a predictor of TMS-induced activation that was sustained for at least 50% of the treatment course.

Results: 106 individuals had reliable MDQ data and 58% of the sample had at least one change in stimulation parameter from 10Hz to 5Hz during the course of rTMS treatment, however, only 26% (n=28) of the individuals had sustained parameter change for at least 50% of the treatment course. On average, the sample with TMS-induced activation had 70% of the stimuli delivery at 5Hz. Interestingly, the activated subgroup had significantly higher bipolar features as measured with MDQ part one scores (Mann-Whitney U - z=2, p=0.047).

Discussion: rTMS is currently approved only for treatment of episodes of unipolar Major Depressive Disorder and not for Bipolar depression. Several studies have shown induction of hypomania with rTMS in bipolar patients and the optimal stimulation parameters are not known for bipolar depression. It is not known why some MDD patients do not tolerate standard 10 Hz rTMS therapy without developing insomnia, irritability, anxiety, or agitation. Our present findings may suggest that activation related to rTMS might be related to underling bipolar disorder psychopathology.
PROGRAM FIDELITY IN AN OPEN TRIAL OF YOUR VOICE YOUR VIEW: FACILITATOR RATINGS AND EXTERNAL RATER OBSERVATIONS

George Andoscia, BS, Peter Krahe, Kyla Teeters, Miryam Yusufov, Lindsay Orchowski, PhD

Introduction: Assessment of fidelity is necessary to ensure adherence to proposed program protocol. Poor or inconsistent adherence to theoretically planned protocol often results in a loss of program effectiveness, especially in cases such as the Your Voice Your View program, where implementation takes place at various program sites over an extended period of time. When monitored throughout intervention implementation, program fidelity can also help researchers understand the relationship between specific program components and the program’s outcomes. It is for these reasons that this study evaluates program fidelity by reviewing external rater’s observations of facilitators’ style and adherence to protocol, and the self-assessments of facilitators delivering the intervention. The sessions reviewed in this study took place during a small open trial of the Your Voice Your View program in two campuses of a Rhode Island public charter school.

Methods: Five sessions were conducted at each of the open trial school’s campuses, for a total of ten sessions. The sessions include: Session 1, Session 2, a Boys’ Session 3, a Girls’ Session 3 and Session 4. An external rater from outside of our project team evaluated each of the sessions, rating the facilitators in adherence to the script by marking “yes” or “no” across a varying number of key session topics (Session 1 - 16; Session 2 - 23; Girls’ Session 3 - 18; Boys’ Session 3 - 20; Session 4 - 21). The rater also noted delivery style using a four-point Likert scale (1=strongly disagree, 2=disagree, 3=agree, 4=strongly agree) to indicate agreement with various observable facilitator characteristics. In addition to the external ratings, program facilitators completed post-session self-assessments noting completion of the session, technical difficulties encountered, classroom management difficulties encountered, and self-ratings on adherence to the script (Likert scale - 1=Missed a Lot, 2=Missed a Little, 3=Right On, 4=Added a Little, 5=Added a Lot) and engagement as a facilitator (Likert scale - 1=strongly disagree, 2=disagree, 3=agree, 4=strongly agree).

Results: Results indicate that 90% of sessions were delivered in their entirety and technical difficulties and classroom management issues were each encountered in 30% of sessions. Adherence-to-script self-ratings from facilitators averaged out to 3.25 for Session 1, 3.0 for Session 2, 2.75 for Girls’ Session 3, 3.5 for Boys’ Session 3 and 3.3 for Session 4. Mean external ratings of session fidelity were as follows: Session 1 – 96.88%, Session 2 – 95.65%, Girls’ Session 3 – 100%, Guys’ Session 3 – 97.5% and Session 4 – 97.62%. The mean response for facilitators’ self-rating of engagement in sessions was 3.89. Finally, the external rater’s mean assessments of delivery style ranged from 3.9 to 4.0 across the five sessions.

Discussion: Findings from this review of external ratings indicate high levels of treatment fidelity in both adherence to the proposed protocol and facilitator style. Facilitator self-assessment aligns with these findings as well. Findings from this open trial have implications that have helped to guide further refinement of protocol and facilitator training, and evaluations of treatment fidelity in this program will continue to be carried out throughout program implementation.
Students with disruptive problem behaviors often require additional support than what is available in public schools given high academic demands, crowded classrooms, and low staff to student ratios.1 The least restrictive environment for these students may therefore fall to an alternative education (AE) setting that consists of smaller class sizes and higher levels of supports. The main goals of such placements are to return students to their public school district after stabilization, replace maladaptive behaviors with appropriate ones, and provide targeted remediation.2 There is great opportunity for student growth in AE settings when preventative, evidence-based techniques (e.g., positive behavior interventions and supports; PBIS) are used to foster a proactive and rewarding school culture and to teach skills for future success. One particular challenge in AE settings is that of seclusion and physical restraint (S/R), which is often perceived as necessary and used to keep students and staff safe. Research suggests this often distressing, reactive method of behavior management is not efficacious in eliminating problem behaviors, teaching/modeling appropriate, prosocial behaviors, or providing skills to manage difficult emotions. Evidence is emerging, however, to suggest that S/R incidents can be reduced and even eliminated with the use of PBIS.3 This presentation will provide an overview of the emerging literature examining PBIS in AE settings and describe the preliminary data of a pilot study that implemented PBIS within an AE setting in the Northeastern United States.

This poster aims to contribute to the growing literature by providing specific examples of benefits and barriers to PBIS implementation in behaviorally intense settings. It will also examine: (a) the process of student and staff buy-in; (b) strategies used to engage key stakeholders; (c) introducing and sustaining data-based decision making at the school-wide level; and (d) finding balance between promoting growth/development, while still supporting both student and staff needs. Measures used within the study included seclusion and restraint (S/R) data, student satisfaction surveys, the Staff Perceptions of Behavior and Discipline (SPBD)-4 survey, and permanent products (e.g., school rewards). Procedures included: meeting individually with staff and students to introduce PBIS, initiating interdisciplinary focus groups (e.g., clinicians, teachers, behavior staff) to establish consistent school wide expectations, electing a school mascot, and launching a Student School Spirit Committee. Additional methods included providing staff trainings, introducing a mindfulness program and additional social emotional learning initiatives, and promulgating the PBIS initiative with parents and community. Lastly, student strengths and staff talents were used to foster creative, interactive, and functional teaching strategies across age levels and cognitive abilities in order to make the learning environment more engaging and rewarding. Preliminary data will be presented and insights to implementation will be offered.
INTER-ALPHA INHIBITOR PROTEINS REDUCE THE QUANTITY OF MICROGLIA IN THE HIPPOCAMPUS AFTER HYPOXIC-ISCHEMIC BRAIN INJURY IN THE NEONATE

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Background: Inter-alpha inhibitor proteins (IAIPs) are immunomodulatory proteins that play a significant anti-inflammatory role in hypoxic-ischemic injury. Our study group has recently shown that administering IAIP after hypoxic-ischemia improves histopathological brain injury, reduces cortical neuronal cell death, and improves brain weight and behavioral outcomes in neonatal rats. Microglia are a glial cells that act as macrophages in the CNS and are important constituents in the neuroinflammatory response in the brain and, thus, are a potentially important therapeutic target for brain injury.

Objective: To determine the effect of IAIP treatment on microglial expression in specific brain regions of neonatal rats after HI brain damage.

Design/Methods: The Vannucci model was used to induce neonatal hypoxic-ischemic brain injury. Postnatal day 7 rats were assigned to a non-ischemic sham-control group (Sham, n=11), a right carotid ligation and hypoxia exposed (8% oxygen for 90 min) placebo-treated group (Isch-PL, n=12), or a right carotid ligation and hypoxia IAIP-treated group (Isch-IAIP, n=12). The sex of the rats was recorded. IAIP (30 mg/kg) or PL was given intraperitoneally at 0, 24 and 48 h after HI. 72 h after HI, brains were collected, sectioned, and prepared for slides. Slides were treated with Iba-1 immunofluorescent staining (selective for microglia) and DAPI staining by first deparaffinizing the brain tissue sections with graded alcohol treatment, then heating the samples in a sodium citrate buffer, and later adding primary and secondary antibodies to the brain tissue. Stereological Analyses were then performed with the StereoInvestigator 10.0, Fractionator probe to observe and quantify microglia present in the hemisphere, cortex, corpus callosum, and hippocampus.

Results: The number of Iba-1 positive microglial cells per area (number/µm²) of tissue was lower in Sham than in the Isch-PL animals in the cortex, hippocampus, and hemisphere of female and in the hippocampus and corpus callosum of male rats neonatal rats (P<0.05). IAIP treatment reduced (P<0.05) the number of positive Iba-1 of cells across all brain regions compared with the PL treated HI in the male but not female neonatal rats. IAIP treatment specifically reduced the number of positive Iba-1 of cells in the hippocampus of the males (P<0.01) neonatal rats. IAIP treatment did not significantly lower the number of microglia in any brain regions in female rats compared to Isch-PL.

Conclusions: IAIP treatment significantly reduced the number of microglia in the damaged hippocampus of male rats after HI brain injury. Our findings suggest there may be sex differences in the anti-inflammatory effects of IAIP treatment. The mechanisms for this finding remain to be determined.
THE IMPACT OF PERINATAL MATERNAL DEPRESSION AND TREATMENT ON MOTHER-INFANT INTERACTIONS AT 6 MONTHS OF AGE

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OBJECTIVE: Previous research suggests an association between maternal depression during pregnancy and impaired mother-infant attachment. The impact of postnatal remission has not been considered in the literature. This study examines the effect of successful remission of prenatal depression on mother-infant interactions using the face-to-face still face (FFSF) paradigm.

METHODS: Mother-infant dyads (n=84) from the Fetal and Infant Response to SRI Treatment (FIRST) study were examined. Psychiatric diagnoses, severity of depression and anxiety, and prenatal medication usage of mothers were assessed at trimesters 2 and 3 and 1 and 6-months post-delivery. Women were classified into 3 distinct groups: Never Depressed, Remitted Depression, and Ongoing Depression based on change in psychiatric diagnosis from prenatal to 6 months post-delivery. Blinded assessors coded mother-infant interactions during the FFSF at 6 months post-delivery for positive and negative interactions. The FFSF provides a structured set of interactions to examine infant emotional regulation in response to interactions with their mothers. This standardized paradigm examines when mothers are engaged and present to their infants versus times when they are unengaged and nonresponsive.

RESULTS: The Remitted group spent less time in negative behaviors compared to the Ongoing Depression group (p < .049) and did not differ from the Never Depressed group. Infants whose mothers had ongoing depression increased in their negative emotional displays following periods of unengagement in contrast to the remitted and never depressed groups (p< .02). Over the FFSF paradigm, mother-infant dyads in both the remitted and ongoing depression groups showed a decrease in positive mutual interactions following periods when mothers were unengaged (p < .02), suggesting emotional dysregulation in the dyad.

CONCLUSION: Findings highlight the importance of how remission of prenatal depression may mitigate the negative impact of maternal depression on infant emotional regulation.
A PILOT RANDOMIZED CONTROLLED TRIAL OF PRENATAL YOGA AS AN INTERVENTION FOR DEPRESSION DURING PREGNANCY

Cynthia Battle, PhD, Lisa Uebelacker, PhD, Kaeli Sutton, BA, Susanna R. Magee, MD, MPH, Ivan Miller, PhD

Objective: This small, randomized trial evaluated a 9-week prenatal yoga intervention vs. a 9-week health education control condition among pregnant women with depression. We examined change in depression over time as the primary outcome, and also examined other variables such as safety, instructor adherence, and mindfulness.

Methods: Following IRB approval, we recruited 20 depressed pregnant women into an RCT of a gentle prenatal yoga program (PYP) vs. a perinatal health education condition, the Mother-Baby Wellness Workshop (MBWW). All women provided informed consent and were medically cleared for participation by their prenatal care provider. Participants were randomized to PWP or MBCC and invited to attend classes once per week for 9 weeks.

Results: Mean age of participants was 28.9 years (SD = 5.8). 25% were from racial/ethnic minority groups. 90% met criteria for MDD during the current pregnancy; 10% met criteria for minor depression. The majority (75%) were not in any mental health treatment. In terms of safety, we systematically asked if participants had injuries due to participation in yoga classes or home practice. No yoga-related injuries were reported. In terms of depression, all participants reported decreases in depression symptoms on both a structured interview (Quick Inventory of Depression Symptoms; QIDS) and a self-report scale (Edinburgh Postnatal Depression Scale; EPDS). We assessed changes over time between the two groups using a general linear mixed model. Although changes were not statistically different between PYP and MBWW in this pilot study, they did favor the PYP arm for both measures of depression, with a difference between groups of 0.48 standard deviation units for the QIDS and 0.4 standard deviation units for the EPDS. We also assessed change in mindfulness at pre- and post-treatment and there was a trend (p < .10) towards differences between groups at endpoint favoring PYP. Finally, to examine fidelity, an expert prenatal yoga instructor rated > 20% of PYP classes on manual adherence using an 18-item structured checklist. Good adherence was observed, with an average adherence rating of 92%.

Conclusion: In a preliminary RCT, we found support for prenatal yoga as a safe, effective intervention to decrease symptoms of depression and increase mindfulness. Our team has recently started a larger scale RCT in order to evaluate the intervention and potential mechanisms of action.
Background: Traditional research regarding STI prevention has focused on the harmful consequences of sexual activity. This approach, however, does not acknowledge the equally consequential role that pleasure and enjoyment play in this risk. A recent movement within sexual health and STI prevention aims to promote safer sex within a viewpoint of sexual pleasure (Philpott, Knerr, & Boydell, 2006; Philpott, Knerr, & Maher, 2006). Incorporating this perspective requires an understanding of what people mean, and what factors are considered, when discussing sexual pleasure. The purpose of this study is to identify and examine the factors that influence sexual pleasure among couples taking part in a vaginal microbicide perceptibility study.

Methods: 24 monogamous HIV-/STI-negative heterosexual couples took part in a vaginal microbicide study during which the female inserted prototype vaginal products and then had vaginal sex with her male partner during three study visits. All couples completed user sensory perception and experience (USPE) questionnaires; 15 of these couples completed in-depth qualitative interviews about product experiences. This study examines the results from these qualitative interviews using thematic analysis (Guest, McQueen, & Namey, 2011) and a framework matrix (Green & Thorogood, 2013).

Results: Participants indicated that several factors influenced their notions of sexual pleasure. First, the experience of different physical sensations was found to be uniquely related to sexual pleasure within each couple. For example, some participants noted that sexual pleasure was negatively impacted by dryness, while others felt that lubrication reduced sensation and also reduced pleasure. Second, sexual pleasure was increased when the wetness produced by the product mimicked a woman’s natural lubrication from sexual arousal. Finally, many participants reported that their own pleasure was tied to their partner’s pleasure.

Conclusions: This study suggests sexual pleasure in this vaginal microbicide study was influenced by 1) participants’ own experiences, 2) their partner’s experiences, and 3) when product perceptibility factors were similar to their typical sexual experience. It is important to better understand the factors that influence how people perceive sexual pleasure to improve acceptance and uptake of STI prevention products.
MOTIVATIONAL PATHWAYS FROM ANTCEDEANTS OF ALCOHOL USE TO CONSEQUENCES: A STRUCTURAL MODEL OF USING ALCOHOL TO COPE WITH NEGATIVE AFFECT

Claire Blevins, MS & Ana Abrantes, PhD

Background: Drinking among college-aged individuals can be problematic. The motivational model of use, which examines various cognitive factors, personal characteristics, and environmental factors can provide greater understanding of what contributes toward the decision to drink in these young adults.

Objectives: The current study evaluates proposed paths from antecedents of alcohol use, motives for drinking, and subsequent outcomes of alcohol use, drawing from seminal research on the motivational model and drinking motives.

Methods: This model was tested in a sample of 303 undergraduate drinkers (77.9% female, mean age=19.8 years), and evaluated the potential impact of gender and pattern of use.

Results: Results indicate that expectancies, maladaptive coping, and negative affect personality styles are associated with coping motives for drinking, and that coping motives significantly predict problems associated with use. These results are similar for males and females, and among heavy and lighter drinkers.

Conclusion: Findings support the role of the coping motive in problematic outcomes associated with drinking and suggest that antecedents of use and drinking motives are potential targets of prevention and intervention.
RESTING STATE FUNCTIONAL CONNECTIVITY IN YOUTHS WITH PRIMARY BIPOLAR DISORDER VERSUS PRIMARY ADHD

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Background: The challenge of disentangling the symptoms of bipolar disorder (BD) and attention deficit hyperactivity disorder (ADHD) is one of many diagnostic difficulties clinicians face today. Addressing this need requires greater understanding of the brain/behavior mechanisms that are unique vs. shared in youth with primary BD vs. those with primary ADHD. In prior work, we have compared resting state functional connectivity (RSFC) in BD vs. typically-developing control (TDC) youths without psychopathology. Now, we sought to extend that work by conducting the first study comparing RSFC in larger samples of BD and TDC youths to a new sample of youths with primary ADHD.

Method: Children ages 7-17 were enrolled in an IRB-approved study at Bradley Hospital and Brown University after informed parental consent and child assent. Three groups of participants were enrolled: (1) youths with primary BD (n=25), (2) youths with primary ADHD (n=23), and (3) TDCs (n=29). All participants underwent 3 Tesla MRI scanning including a high resolution T1-weighted MPRAGE anatomical image and an 8-min RSFC fMRI sequence. RSFC analyses used a priori seeds in the dorsolateral prefrontal cortex (DLPFC), amygdala, and accumbens plus whole brain methods implemented in Configurable Pipeline for the Analysis of Connectomes (CPAC).

Results: Our analyses show that youth with primary BD have significantly and specifically decreased RSFC between the left DLPFC and the left inferior frontal gyrus and between the right DLPFC and the left insular cortex. The complementary whole-brain approaches showed that BD youths had specifically increased local network RSFC by degree centrality (DC) methods in the right superior frontal, left precentral, and right post-central gyri. Finally, voxel mirrored homotopic connectivity (VMHC) showed decreased intra-hemispheric RSFC in both BD and ADHD youths vs. TDCs in the right paracingulate and bilateral middle frontal gyri.

Conclusions: In sum, our current study supports previous structural and RSFC studies suggesting that the frontal lobe, specifically the DLPFC, has a primary role in pathophysiology of pediatric BD. Further research is needed to determine the effects of medication and mood state on RSFC in youths with BD and ADHD. This study highlights the need for developmental neuroimaging studies to promote structural, functional, and RSFC alterations integral to BD.
CADASIL AS A CAUSE OF STROKE IN THE YOUNG: A CASE REPORT

Andrew Bouley, MD & Shadi Yaghi, MD

We present a case of a thirty-one year-old man without significant vascular risk factors presenting with hemiparesis and dysarthria. MRI findings showed a small area of restricted diffusion with some enhancement, as well as extensive white matter disease with involvement of the external capsule suggestive of small vessel vasculopathy. NOTCH3 genetic testing led to the diagnosis of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). CADASIL is an autosomal dominant inherited small vessel disease of the central nervous system that causes migraines, recurrent strokes, and cognitive decline. Our patient had an atypical presentation due to the lack of personal history of migraines or a positive family history. In young patients, CADASIL can mimic acute demyelinating disease. Clinical history, MRI characteristics, CSF profile, and genetic testing can help differentiate CADASIL from multiple sclerosis.
Central nervous system vasculature is formed through a complex process of angiogenic sprouting from existing blood vessels. Multiple pathologies, such as ischemic and traumatic injuries, brain cancers, and neurodegenerative diseases, can adversely affect this vasculature. However, brain vascular development and pathology are not well characterized. Three dimensional in vitro models promote in vivo-like cell behavior, and additionally allow for significant control over study input variables. We have recently characterized the glial and neuronal network formation, mature neuronal electrical activity, and in vivo-like mechanical properties of postnatal rat cortical cells in an in vitro three-dimensional self-assembly spheroid culture (Dingle*, Boutin*, et al. Tissue Engineering C, 2015). Herein, we present the spontaneous formation of extracellular matrix tubular network structures within this cortical spheroid model. Structures contained the basement membrane proteins laminin, collagen type IV, and fibronectin, and networks grew to 2500 µm in length in spheroids of 250-300 µm diameter. Laminin immunostaining revealed tubular structures in 3 day-old spheroids, which decreased in size until they were absent in 14 and 21 day-old spheroids. Additionally, the basement membrane-like tubular structures were associated with cells positive for nestin, a stem cell marker that has also been identified in endothelial progenitors and proliferating endothelial cells. Ongoing studies are investigating the cells and mechanisms involved in the growth and breakdown of these tubular structures, with the ultimate goal of vascularizing future tissue-engineered constructs.
INVESTIGATING SHARED ADDITIVE GENETIC VARIATION FOR ALCOHOL DEPENDENCE ACROSS INDIVIDUALS OF AFRICAN AND EUROPEAN ANCESTRY

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Valerie S. Knopik PhD, Matthew C. Keller, PhD

Purpose. Molecular genetic research has supported the use of a multivariate phenotype representing alcohol dependence in studies of genetic association. One recent study found that additive genetic effects on Diagnostic and Statistical Manual of Mental Disorder version four (DSM-IV) alcohol dependence criteria overlap, describing a common pathway model that consists of a single latent variable representing alcohol dependence. Common single nucleotide polymorphisms (SNPs) explained 31% of variance in this latent factor. However, these findings were conducted using a sample of European Americans and minimal research exists to provide insight into whether this finding is consistent in a population of African descent. Using a large sample of individuals from European ancestry (EA) and African ancestry (AA), we investigated the extent to which additive genetic variance tagged by common SNPs explain variation in alcohol dependence and whether these markers are shared across the two populations.

Methods. Genome-wide data from four large databases obtained through the National Center for Biotechnology Information Database of Genotypes and Phenotypes. These include the Study of Addiction: Genetics and Environment (N=4,316), the Australian twin-family study of alcohol use disorder (N=6775), the Alcohol Dependence GWAS in European- and African Americans (N=2,909), and the Genome-Wide Association Study of Heroin Dependence (N=6486). The union of SNPs across all studies (totaling 2,050463 SNPs) were imputed within EA and AA groups and then pooled for subsequent analyses.

To prepare each data set for imputation, a number of steps were taken using the SNP & Variation Suite Software. In the first step, EA and AA individuals were identified. Quality control (call rate<0.95, minor allele frequency [MAF] > 0.10) and strand orientation checks were conducted for each data set. Each data set was combined with the 1000 Genomes (1KG) reference database to determine ancestral groups. Principal components analysis was used to identify EA and AA’s, followed by multidimensional scaling to remove outliers within the identified groups. In the second step, EA and AA individuals were extracted from the larger sample data and stricter quality control (call rate<0.95, MAF>0.01) and strand orientation checks were conducted. Finally, data sets were separated by chromosome and submitted for imputation using Minimac3 with the 1KG reference panel.

After imputation, data were pooled and 1,656,234 autosomal SNPs that survived quality control (MAF>0.01, Hardy-Weinburg equilibrium p-value<0.0001, call rate>0.99, individual missingness>0.10, imputation r2>0.5) and were common across EA’s (N=6515) and AA’s (N=2196) were retained. Confirmatory factor analysis was used to extract factor scores within each ancestral group based on common variance across all seven DSM-IV criteria for alcohol dependence. Unrelated participants with phenotypic data were included in subsequent analyses, controlling for sex, study of origin, and age. Genomic-relatedness-matrix restricted maximum likelihood estimation was used to determine the proportion of variance in the alcohol dependence factor that can be attributed to additive genetic variance within each population and a bivariate extension of this model was used to estimate the genetic correlation across the EA and AA populations.

Results. SNP-based heritability estimates for the alcohol factor was 0.21 (SE=0.05, p<0.001) for EA’s and 0.30 (SE=0.14, p=0.001) for AA’s. Bivariate analyses across AA/EA's demonstrated a large, significant genetic correlation, rG=0.76 (SE =0.45, p=0.030).

Conclusion. Results from the largest pooled genome-wide sample of alcohol dependence to date revealed similar univariate SNP-based heritability estimates for individuals of European and African ancestry. A large, significant, genetic correlation provided evidence for genetic overlap in markers for the alcohol dependence factor across these populations.
CHILDHOOD TRAUMA AND AFFECT POST DISCHARGE IN ADOLESCENTS HOSPITALIZED FOR SUICIDAL THOUGHTS AND BEHAVIORS

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Suicide is one of the leading causes of death in adolescents (Mcloughlin, Gould, & Malone, 2015) and as such, many adolescents are hospitalized for suicidal thoughts and behaviors. The period post-discharge for adolescents who have been psychiatrically hospitalized is an important transition, in which adolescents and children have high rates of rehospitalization, particularly within the first month (James et al., 2008). One such predictor of suicidal thoughts and behaviors in adolescents is a history of childhood trauma (Diekstra & Wolters, 1992; Giaconia et al., 1995). Childhood trauma has been found to be related to negative affect (Lardinois, M., Lataster, Mengelers, & Myin-Germeys, 2011; Weber et al., 2008) and more specifically, increased anger in various populations (Cecil, Viding, Barker, Guiney, & McCrory, 2014; van Vugt, Lanctôt, Paquette, Collin-Vézina, & Lemieux, 2014). The present study examined the influence of childhood trauma on adolescents’ self-directed anger following hospitalization for suicidal thoughts and behaviors. Participants were recruited from a larger study (R01MH105379 - PI: Nugent) (N=17) which examines the interaction of (epi)genetics and social context on affect during the post discharge period for adolescents who have been hospitalized for suicidal thoughts and behaviors. Ecological Momentary Assessment (EMA) sampling was used to assess endorsement of anger symptoms across a three week period post discharge. In this sample, 82.3% of adolescents identified as white, 5.9% as black or African American, and 11.8% as more than one race. Nearly 12% of adolescents identified as Hispanic or Latino and 82.3% identified as female at birth. Childhood Trauma was assessed using the Childhood Trauma Questionnaire (CTQ; Bernstein & Fink, 1998), and anger was measured using the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1998) questionnaire. One-way Analysis of Variance was used to examine whether adolescents who reported moderate to severe levels of abuse or neglect evidenced increased EMA assessed anger towards self as compared to little to non-abused/neglected participants during the first, second, or third weeks after discharge. Findings supported a trend toward increased levels of anger during the first week post-discharge in adolescents reporting moderate to severe abuse (44% of the sample; Mean = 2.25, SD = .91) as compared with adolescents reporting low abuse (Mean = 1.53, SD = .51), F (1, 15) = 4.00, p = .06. These findings point to important differences in levels of anger directed towards self during this high risk period for adolescents with a history of moderate to severe abuse. Further data collection is needed in order to permit more refined characterization of this effect, with the potential for implications for intervention targeting adolescents with higher levels of anger towards self.
LINGUISTIC PROCESSING AND SCRIPT-DRIVEN IMAGERY FOR TRAUMA EXPOSURE

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While a number of empirically-supported treatments have been developed for posttraumatic stress disorder (PTSD), these treatments are neither widely available nor universally efficacious. The current study translates a traditional PTSD assessment technique, Script-Driven Imagery, into a computerized training for elevated trauma reactivity. The imaginal-exposure based training was supplemented with Affect Labeling to determine whether linguistic inhibitory regulation augmented the effects.

Methods: Participants (n=66) were college students and community members with trauma exposure and trauma-related distress and were randomized to one of three conditions: imaginal exposure to individualized traumatic events (Exposure only), exposure plus Affect Labeling, or exposure plus an active linguistic control condition, Distract Labeling. Physiology and self-report trauma distress were measured at pre- and post-training and multilevel models were used to analyze changes over Time by Condition.

Results: The training was effective at reducing self-reported distress and physiological activation from pre- to post-training, with significant effects of Time on Heart Rate (HR) during the trauma script (z= -6.50, p<.001, Hedges’ g=.83), HR during trauma imagination (z= -6.15, p<.01, Hedges’ g=.91), startle electromyography (EMG) responding during trauma imagination (z= -3.84, p<.001, Hedges’ g=.53), self-report on the Posttraumatic Diagnostic Scale (z= -4.44, p<.001, Hedges’ g=.45), and the Impact of Events Scale (z= -3.08, p<.01, Hedges’ g=.31). There was some evidence that linguistic processing (including Affect and Distract Labeling) conferred a benefit over No Labeling. Specifically, there was a Time x Condition (Label vs. No Label) interaction on startle during trauma imagination (p<.05). Those expressing more sadness throughout experienced greater benefit (z= -2.47, p<.05), and those expressing more anger experienced less benefit (z= 2.56, p<.05). Satisfaction ratings were generally high and there were no differences by Condition in participant satisfaction (F(2,58)=.18, p=.83).

Conclusions: This study provides initial support for the acceptability and efficacy of this independently-operated computerized training for PTSD. It also demonstrates some benefit of linguistic processing in enhancing emotion regulation.
MULTI-FIBER WHITE MATTER ATLAS CONSTRUCTION WITH DIFFUSION MRI

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This work develops and evaluates computational tools for brain atlas construction with diffusion MR imaging. The complex anatomical features of brain white matter pose a challenge for image-based modeling, particularly when representing anatomical structure across many individuals. We present work to address these limitations and propose a non-parametric model-based image processing framework for constructing population atlases that accurately represent the geometric structure of complex fiber bundle anatomy. The proposed framework enables the interpolation, smoothing, and fusion of multi-fiber diffusion MR imaging data using model-based kernel regression estimation, and we use the proposed method in combination with the ball-and-sticks diffusion model, which can represent a mixture of isotropic diffusion and multiple fiber compartments in each voxel. This was evaluated with experiments using synthetic phantom datasets and an in-vivo dataset consisting of 80 human adult subjects. The synthetic data experiments show how the proposed framework can reduce errors in fiber orientation and better estimate model complexity in crossing fiber regions. The in-vivo data experiments demonstrate the creation of a population atlas using deformable tensor-based registration, and we compare the resulting multi-fiber atlas to the standard approach using the single diffusion tensor model. The results show that the multi-fiber atlas includes anatomical features not typically found in standard population atlases and highlight the limitations of single tensor modeling. In particular, we show how the proposed technique enables the reconstruction of the lateral projections of the corpus callosum, crossing fibers of the brainstem, and fronto-parietal connections of the superior longitudinal fasciculus I, II, and III. Looking forward, this method has potential applications to scientific and clinical imaging studies, as it can provide a study-specific reference for mapping anatomy across a population, and it may provide more accurate reconstructions of fiber bundles that are relevant to neurosurgery.
A META-ANALYSIS OF THE INHIBITORY EFFECT OF INTRANASAL OXYTOCIN ON AMYGDALA ACTIVATION IN HUMANS: A NEUROIMAGING PERSPECTIVE

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Background: Intranasal oxytocin administration has been shown to effect change in amygdala activation in response to a variety of stimuli using functional neuroimaging in humans. However, the results of different studies in this area appear to be mixed, with some studies showing increased amygdala activation following oxytocin administration and some showing inhibition. Although there has been research on the various conditions that influence the differential effects of oxytocin on amygdala activity, the literature lacks a comprehensive analysis of the overall effect exogenous oxytocin on the amygdala.

Method: We conducted a meta-analysis on the effect of a single administration of intranasal oxytocin on amygdala activation in studies employing functional neuroimaging methodology. The search yielded twenty-four studies that reported data on this activation relative to placebo controls (k = 24, N = 869). A random-effects model and moderator analyses were performed using the metafor package for the statistics program R.

Results: Overall, the effect of intranasal oxytocin administration on amygdala activation in the right hemisphere, compared to baseline, relative to placebo, was inhibitory (Z = -2.93, p = 0.003, Hedges g = -0.20, 95% CI [-0.07, -0.33]). This effect was not observed in the left hemisphere. This effect was not moderated by sample differences in: sex, average age, clinical diagnosis, nor the quantity of total dose administered.

Conclusion: Intranasal oxytocin administration results in a general decrease in amygdala activation compared to placebo across a variety of different stimuli in the right hemisphere. This effect was not detected in the left hemisphere, and it was not modulated by differences in study methodology, rendering the brain-to-nose pathway an unlikely explanation for the observed effect. Further human studies must be done to elucidate possible clinical and practical applications to this minimally invasive technique.
INCREASED IRRITABILITY MAY DISTINGUISH PARTICIPANTS WITH COMORBID BPD ENROLLED IN A LONGITUDINAL STUDY OF BIPOLAR DISORDER

Cintly Celis-de Hoyos, MA, Shirley Yen, PhD; Heather Hower, MSW; Lauren Weinstock, PhD; Daniel Dickstein, MD; Jeffrey Hunt, MD; Michael Strober, PhD; Boris Birmaher, MD; Martin B. Keller, MD

Compared to the general population, adults with bipolar disorder (BD) are almost three times more likely to have comorbid borderline personality disorder (BPD) (Yen et al., 2015), and may be at increased risk for experiencing poor long-term outcomes, e.g., increased suicidality, interpersonal dysfunction, worsened mood course. BD and BPD share domains of dysfunction, including increased irritability, a symptom linked to negative psychosocial (Perlis et al., 2010) and health (Caprara et al., 1985) outcomes. This study investigated whether comorbid BPD+/BD adults reported increased trait and state irritability than BPD-/BD adults. At their most recent follow-up assessment (M = 11.5 years, SD = 1.17 years), participants enrolled at one of three sites of the Course and Outcome of Bipolar Youth (COBY) study, completed self-report measures of their state (Brief Irritability Test) and trait (Affective Reactivity Index) irritability. Overall, BPD+/BD participants (n = 17) endorsed increased trait (p=.02) and state irritability (p=.01) and that their irritability caused them problems (p =.01) than BPD-/BD participants (n = 51). Further analyses will examine whether demographic or other clinical characteristics help explain differences in state or trait irritability among these groups, or whether these differences are better accounted for by having comorbid BPD.
UNDERSTANDING THE ROLE OF SOCIAL ENVIRONMENT AND EARLY SYMPTOMS OF PTSD IN ADOLESCENTS FOLLOWING PHYSICAL TRAUMA

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Introduction: Approximately 68-80% of adolescents experience a traumatic event, this percentage varying based on the sample population and definition of “traumatic event”, with 3-57% meeting diagnostic criteria for Posttraumatic Stress Disorder (PTSD). Symptoms following a traumatic event may fall under a diagnosis of Acute Stress Disorder (ASD) and/or PTSD, with a strong association between the two disorders. ASD describes acute posttraumatic symptoms occurring 2 days to 1 month after trauma, with more focus on dissociative symptoms, and PTSD describes long-term symptoms lasting more than one month following a traumatic event. Studies have shown that biomarkers of early stress, including heart rate, can be mitigated by the post-trauma social context. Studies have relied on self-reported social context, which are limited both in details and by reporter biases. Technological advancements, such as the Electronically Activated Recorder (EAR), allow more detailed characterization of the social context by recording ambient sounds and minimizing reporter bias. Our hypothesis is that adolescents who spend more time with others in non-conflictual and directly engaging social interactions following experiencing a traumatic event will evidence fewer symptoms of ASD relative to adolescents whose interactions are conflictual and disengaged.

Methods: Following IRB approval, patients between ages 13 and 17 seen at the Hasbro Children's Hospital Emergency Department with a complaint involving physical trauma were screened over 175 hours June to October 2015. Eligible participants were medically stable adolescents who required a trauma team activation, treated in a critical care room, or admitted due to injuries sustained as result of their trauma. Patients with any suicidal ideation, psychotic symptoms, or trauma involving sexual abuse were excluded. Upon discharge, recruited participants were given an EAR set to record for a duration of 30 seconds every 12 minutes and were given instructions to wear the device during the first weekend following their discharge. Participants returned 2 weeks following their discharge and completed a qualitative clinical interview as well as returned their EAR device. Participants were compensated for their participation in the study.

Results: 32 patients were screened for eligibility. Of 15 eligible patients, 8 participants were recruited and consented (7 males and 1 female). Participants that refused cited transportation constraints or lack of interest. Mean age was 15.2. A total of 453 audio recordings were obtained. Researchers screened audio files and any remarks regarding trauma or direct engagement were noted. The Clinician Administered PTSD Scale for Children and Adolescents (CAPS-CA) was administered by a staff clinical psychologist.

Conclusions: Among participants reporting greater symptoms at 2 weeks, audio files were more likely to capture conflictual interactions between the participant and their family. Family injury-related conversations with adolescents who were more symptomatic at 2-weeks were also noted to involve comments regarding money or responsibility for participant care. These results demonstrate a positive association between conflictual social interactions and symptoms of ASD that are also early symptoms of PTSD following trauma and further extend our understanding of the quality of support necessary to support adolescents following traumatic events.
TREATMENT OUTCOMES FOR YOUTH COMPLETING FULL MODEL DBT-A OR MULTI-FAMILY SKILLS TRAINING ONLY

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Background: Dialectical behavior therapy (DBT) is an evidence-based intervention for adults with Borderline Personality Disorder (BPD) presenting with chronic suicidality and/or non-suicidal self-injury (NSSI). Miller and colleagues (1997, 2007) adapted DBT for adolescents (DBT-A) by involving family members in treatment and tailoring course material to fit typical adolescent social challenges. These alterations make the extension of findings with adults untenable and research focused on the treatment outcomes of DBT-A is needed. Emerging data highlights the promise of DBT-A as an intervention for multi-problem youth. Specifically, studies of DBT-A have found decreased suicidal ideation, suicidal behavior, NSSI, BPD symptomology, and depressive symptoms, as well as improved general psychosocial functioning (Woodberry & Popenoe, 2008; Fleischhaker et al., 2011; James et al., 2008, 2011; Miller et al., 2000; Mehlum et al., 2014). Questions, however, remain about which components of DBT-A are necessary or sufficient for facilitating these positive outcomes. The current investigation is intended to examine and compare the treatment outcomes of youth completing the DBT-A multi-family skills training (MFST) only and youth completing Full Model DBT-A (i.e., MFST plus individual therapy, phone coaching, and consultation team).

Methods: All participants (N=16) were 13-18 years old and completed the Beck Depression Inventory, 2nd Edition (BDI-2; Beck et al., 1996); Beck Anxiety Inventory (Beck & Steer, 1993), Borderline Symptoms List (BSL; Bohus et al., 2007), Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004), and DBT Ways of Coping Checklist (DBT-WCCL; Neacsu et al., 2010) at pre- and post-treatment. Of these 16, n=9 completed the 18-week DBT-A MFST group only, whereas n=7 completed Full Model DBT-A.

Results: Paired-sample t-tests were conducted to compare pre- and post-treatment data for all adolescents completing DBT-A (combining multi-family skills training only and full model; n=16). Adolescents demonstrated significantly decreased depressive symptoms, decreased borderline symptoms, improved emotion regulation, and increased DBT skills use. They did not demonstrate significant changes in anxiety symptoms or dysfunctional coping. A multivariate analysis of variance (MANOVA) was then conducted to assess for potential group differences in pre/post change. Group (MFST only vs. Full Model) was the fixed factor and change scores on the BDI, BSL, DERS, and DBT WCCL (Skills Use subscale) were dependent variables. Groups, did not differ in their pre/post change on measures of depression, anxiety, borderline symptoms, emotion dysregulation, and skills use. However, treatment retention was higher among adolescents receiving the Full Model DBT-A model compared to adolescents receiving MFST only (87% vs. 71%, respectively).

Conclusions: Consistent with previous studies examining the efficacy of DBT with adults and DBT-A with youth, adolescents in both treatment groups showed positive treatment outcomes although not in all areas assessed. While the groups did not differ in their pre/post change, treatment retention was higher with Full Model DBT-A vs MFST only. A limitation of the current study was the small sample size. Future studies should compare DBT-A MFST only to Full Model DBT-A with larger samples to more thoroughly identify the active treatment components needed to facilitate particular positive outcomes. This could potentially allow providers to offer services to more teens with fewer resources (i.e., should MFST only continue to compare favorably to Full Model).
REDUCED NEURAL SIGNALING IN YOUNG ADULTS WITH BIPOLAR DISORDER DURING COGNITIVE FLEXIBILITY

Rachel Christensen, BS, Lauren I. Kasoff, BS, Erin Bojanek, BS, Kerri Kim, PhD, Jeffrey I. Hunt, MD, Shirley Yen, PhD, Heather Hower, M.S.W., Matthew Killam, BA, Martin Keller, MD, Ellen Leibenluft, MD, Daniel P. Dickstein, MD

BACKGROUND: Bipolar disorder (BD) has been recognized as one of the most detrimental psychiatric illnesses affecting both children and adults, despite our best treatments. A better understanding of the brain and behavior mechanisms of BD in children and adults is essential for improving its diagnosis and treatment. Previous research suggests that BD children have impairments in cognitive flexibility, defined as the ability to adapt one’s thinking to changing reward contingencies. Cognitive flexibility can be measured in the lab and in the MRI scanner using reversal learning paradigms, whereby participants must use trial-and-error learning to determine which of two simultaneously presented stimuli is mostly correct, and then to adapt when the stimulus/reward association is reversed (i.e., previously rewarded stimulus is now punished and vice versa). Now, we sought to deepen our understanding of this deficit, by determining if young adults with childhood-onset BD had impairments in two computational components of reversal learning – expected value signaling (EV; expected outcome) and prediction error signaling (PE; difference between predicted and received outcome).

METHOD: This study was IRB-approved at Bradley Hospital and Brown University. Participants included 3 groups of young adults (ages 18-30): (1) those with BD type I or II (BD; n=33), (2) those with BD not otherwise specified (BD-NOS; n=15), and (3) typically developing controls (TDC; n=61). All BD I, II, and NOS participants were enrolled in Brown’s site of the Course and Outcome of Bipolar Youth (COBY) study. Participants’ 3Tesla MRI scan included a high-resolution MPRAGE structural scan and an event-related fMRI scan with a probabilistic response reversal task involving four 6.5-minute runs. Deficits in reversal learning were examined via the neural activation modulated by the EV and PE of each participant.

RESULTS: We found significant differences in the EV signaling in the left fusiform gyrus [F(2,106)=9.28, p=0.000], the middle frontal gyrus [F(2,106)=7.87, p=0.001], and the left superior occipital gyrus [F(2,106)=6.07, p=0.003] between BD and TDC participants. PE signaling was also significantly different in the left fusiform gyrus [F(2,106)=5.62, p=0.005], the middle frontal gyrus [F(2,106)=4.35, p=0.015], and the left superior occipital gyrus [F(2,106)=6.16, p=0.003] between these groups. These differences were driven by a reduction in BD subjects’ EV and PE signaling during the reversal learning task when compared to that of TDC subjects.

CONCLUSIONS: This study is the first to propose computational impairments in reversal learning in young adults with BD and to identify the brain regions associated with these deficits. Our results suggesting that BD young adults show less association between EV and their choices during a reversal-learning paradigm could indicate that these individuals have increased difficulty predicting outcomes during decision making in a more generalized context. Thus, our findings may highlight the neural underpinnings of poor behavioral choices made by BD young adults in a real-life setting, such as choosing to participate in risky behaviors without mindfulness of potentially negative outcomes. Further research should examine the potential for cognitive remediation therapies that target the neural regions associated with reduced EV and PE signaling in individuals with BD.
FUNCTIONS OF NONSUICIDAL SELF-INJURY IN SEXUAL AND GENDER MINORITY YOUTH

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Background: Non-suicidal self-injury (NSSI) is defined as the intentional destruction of one’s body tissue without the intent to die for reasons not socially sanctioned. In addition to immediate physical harm, NSSI is associated with many psychiatric problems, including depression, anxiety, and increased risk for suicidal behaviors. A recent meta-analysis found that sexual and gender minorities (e.g., lesbian, gay, bisexual, and transgender; LGBT individuals were two times as likely to engage in NSSI compared to heterosexual individuals. Moreover, in a study of a community sample of LGBT youth, 47.2% of the participants had engaged in intentional cutting, a prevalence rate that is higher than most studies of NSSI. The current study expanded on the research on NSSI amongst LGBT youth by examining the prevalence and functions of NSSI in a clinical sample of LGBT youth and their heterosexual counterparts. Understanding why this population engages in NSSI may aid in tailoring interventions to address the underlying functions of their behavior.

Methods: Participants were adolescents (N = 52, 53% LGBT; aged 13-18 yrs, M: 15.6, SD 1.47) recruited from an inpatient psychiatric unit due to elevated suicide risk (e.g., recent suicide attempt, suicidal ideation, or self-injury with suicidal ideation). Structured diagnostic interviews and self-report instruments were administered to adolescents and their parents/guardians to assess demographic variables, psychiatric disorders, history of suicidal behaviors, suicidality, life satisfaction, and peer victimization. The Inventory of Statements About Self-injury (ISAS) was administered to assess 13 functions of NSSI, as well as the frequency of 12 NSSI behaviors.

Results: At admission, LGBT youth reported greater suicidality, peer-victimization, and life dissatisfaction, compared to heterosexual youth (p < .05). 100% of LGBT youth reported engaging in NSSI in their lifetime, compared to 68% of heterosexual youth (p < .05). Moreover, LGBT youth engaged in a greater variety of NSSI behaviors (M= 5.22, SD = 2.6) compared to heterosexual youth (M= 2.76, SD = 2.8; p < .05). LGBT youth were more likely than heterosexual youth to engage in cutting, severe scratching, banging, and interfering with wound healing (p < .05). Of the 13 functions of NSSI, LGBT youth endorsed affect regulation, self-punishment, self-care, anti-dissociation, and anti-suicide more than heterosexual youth (p < .05). LGBT youth also reported more exposure to abuse, compared to heterosexual youth; however, analyses based on presence of abuse revealed non-significant findings.

Conclusions: Findings suggest a greater risk profile for LGBT youth, compared to heterosexual youth, of those in an inpatient psychiatric unit. Improving affect regulation, decreasing self-punitive cognitions, and providing alternative coping mechanisms may serve as treatment goals for reducing NSSI in LGBT youth.
Brain-computer interface (BCI) technology is being developed to enhance communication and independence for individuals with locked-in syndrome (LIS). Assisted with the BrainGate2* BCI system, individuals with LIS have been able to use their intracortical neural activity to control a computer cursor. The neural activity encodes directional tuning that can be filtered for a continuous cursor signal, while an intended discrete click state may occur simultaneously. Several algorithms have been proposed for directional control but less emphasis has been placed on decoding click. Here we present a new click decoding algorithm with the goal of enhancing BCI typing performance. Our approach relies on training a LDA classifier with unique labels for directional “sub-regions”, i.e. ranges of cursor directions (e.g. 0-90 degrees, 90-180 degrees etc.).

By characterizing cursor motion more specifically, the goal is to improve the distinction of click from ongoing movement. This multi-class LDA (MCLDA) makes the final classification decision based on a maximum likelihood estimate of the click class vs. all cursor movement classes.

In a preliminary session, BrainGate participant T9 (who has tetraplegia due to ALS but is not locked-in) was instructed to imagine moving his hand to control a computer cursor and imagine closing his hand to click. To calibrate the cursor kinematic filter and click decoder, the participant was asked to use the described imagery on a radial-task in which the cursor repeatedly moved from the center of the screen to each of eight surrounding targets. Once the cursor reached the target, the participant imagined to click. The neural activity recorded during this process was labeled and used to train a MCLDA. Using the trained classifier, T9 then commanded cursor movements and click in several radial-task assessment blocks, obtaining 80% target acquisition over the entire session, with a maximum 87% accuracy and 95% precision in one block. Offline analyses demonstrated that the MCLDA outperformed the two-class LDA in each assessment block within this session.

Developing a reliable click signal is essential for effective long-term BCI use. Future sessions with the MCLDA will investigate typing performance. Furthermore, a “dynamic classifier selection” can be used to choose the best “sub-region” classifier at each incoming test point. BCIs that deliver reliable computer control could improve the quality of communication for individuals with ALS, tetraplegia, and other neurological impairments.

*CAUTION: Investigational Device. Limited by Federal Law to Investigational Use.
Cognitive reserve theory posits aspects of early life modify deleterious clinical effects of neuropathological processes. Our goal was to evaluate the role of reserve markers modifying neuropathological processes associated with postoperative delirium. The Successful Aging after Elective Surgery (SAGES) study enrolled 560 adults age ≥ 70 years scheduled for major surgery. Patients were assessed preoperatively and daily during hospitalization for delirium using the Confusion Assessment Method. We used logistic regression models to test the significance of interactions between brain and cognitive reserve markers and a pathology marker in explaining postoperative delirium. Markers of reserve included the Wechsler Test of Adult Reading (WTAR), lifetime cognitive activities scale, occupational cognitive complexity, occupational management demand, head circumference, intracranial volume, energy expenditure. Our marker of pathology was CRP level measured on postoperative day 2. Three of the 7 cognitive reserve markers including vocabulary knowledge measured by WTAR performance, lifetime cognitive activities, and educational attainment significantly (all p-values < .01) modify the relationship between pathology measured by CRP and postoperative delirium. Effects were trivial to small magnitude for educational attainment and lifetime cognitive activities, and small for WTAR score. High baseline WTAR score lowers the risk of delirium associated with CRP, but high levels of CRP overwhelm this protective effect. High preoperative vocabulary ability, a marker of premorbid cognitive functioning or crystallized cognitive ability, may attenuate risk of delirium associated with inflammatory processes. Our results provide modest evidence for the role of reserve in delirium.
BRAIN-CONTEXT INTERACTIONS IN TIC SUPPRESSION: DESCRIPTION OF A NEW METHODOLOGY INTEGRATING rTMS AND A BEHAVIORAL EXPERIMENTAL PARADIGM

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Background: Chronic tics are the most common movement disorder in children. Tics occur involuntarily but can temporarily be suppressed voluntarily. The mechanisms underlying tic suppression are poorly understood but likely involve complex interactions between biological and contextual factors. Unfortunately, integrated methods for studying brain-context interactions in tic suppression have historically been lacking. Neuromodulation offers potential for studying these interactions. The supplementary motor area (SMA) plays a key role in facilitating context-dependent motor output and is hyperactive in those with tics (Orth, 2009). Repetitive transcranial magnetic stimulation (rTMS) over SMA has been explored as a tic treatment (Wu et al., 2014); however, research has yet to focus on the role of SMA in voluntary tic suppression. Here we describe an innovative methodology integrating rTMS over SMA with an established behavioral paradigm developed to study the effects of context on tic suppression (Woods & Himle, 2004). This methodology will enable us to examine the effect of inhibitory rTMS over SMA on tic suppression in various contexts. It is hypothesized SMA inhibition will be associated with decreased tic frequencies and premonitory urges, improved voluntary tic suppression, and enhanced suppression in the presence of contingent reinforcement.

Methods: Participants are youth ages 13-18 years with chronic tics of at least moderate severity (n = 30 total). Study components include: 1) clinician-administered diagnostic interviews and parent- and child-report measures of tic and psychopathology symptoms; 2) brain MRI, involving a bilateral finger-thumb tapping task to highlight SMA, and 3) active or sham (randomized) rTMS over SMA coupled with administration of the behavioral tic suppression paradigm. During phase 3, participants first complete a tic suppression task involving three 3 min conditions (replicated twice each): free-to-tic baseline, tic suppression, and reinforced tic suppression. Participants are videotaped covertly; tic frequency and urge ratings are later recorded by coders blind to rTMS status. Second, participants undergo sham or 1hz rTMS in a single 33min train (2000 pulses) at 110% resting motor threshold with a Magstim Air-cooled or Sham 70mm figure-eight coil positioned over SMA using an MRI-guided neuronavigation platform. Finally, the tic suppression task is repeated to enable pre- to post-TMS comparisons of tic frequencies and urge ratings.

Results: Data collection is ongoing. Initial efforts suggest that this protocol is acceptable to participants and feasible to conduct. Dependent variables are tic frequency and subjective urge ratings. Since the methodology incorporates a single-subject multielement withdrawal design within a larger group design, results will be examined using both small-n analyses and inferential group statistics to compare dependent variables pre- to post-TMS.

Conclusions: Research on the mechanisms underlying tic suppression has historically focused on the separate effects of biology and context despite recognition that brain-context interactions drive symptom expression. Methodological integration of established behavioral experimental paradigms with TMS is a promising strategy for probing tic suppression neurocircuitry within different contexts.
AN IPHONE APP/GAME IMPROVES ART ADHERENCE AND INCREASES CONDOM USE

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Background: Despite the need for consistent adherence, youth and young adults living with HIV (YLWH) have suboptimal rates of adherence to antiretroviral treatment (ART). We have developed the first iPhone game to promote ART adherence among YLWH in the United States. The smartphone app/game includes content consistent with the Information-Motivation-Behavioral Skills (IMB) Model. While gaming, participants experience absorbing action-oriented adventures that increase information about their health (e.g. knowledge about ART and HIV), improve motivation (e.g. action-figures experience health benefits of adherence), and build skills (e.g. condom use). A smart pill bottle monitoring device (Wisepill) is integrated into the app/game to both measure adherence and enhance game play.

Methods: A small randomized controlled pilot study (12 week intervention and 4 week follow-up) among 36 participants on ART (Mean age 22.1, 94% African American, 72% non-heterosexual, 100% sexually active) examined the preliminary efficacy of the gaming intervention compared to a comparison group on adherence, and HIV risk behavior.

Results: The IMB adherence intervention (integrating Wisepill adherence data with the IMB informed game), was well-liked (100% “liked” or “really liked” it), and useful (91% reported that texts from the game helped them remember their medication “somewhat” or “a lot”) . Compared to subjects in the control group (n=18), participants in the IMB Gaming Intervention (n=18) showed improved adherence to ART as measured by Wisepill (57% vs. 43%, p<0.05), and more frequent condom use (54% vs. 27%, p= 0.08) at 16 weeks accounting for baseline scores.

Conclusions: An interactive, engaging, IMB-consistent, HIV-specific app/game can improve ART adherence and decrease HIV risk behaviors. The game can be played by participants on an iPhone and is appealing to YLWH.
ACTIVITY-DEPENDENT INFLUENCE OF CORTICOTHALAMIC OUTPUT ON THE EXCITABILITY AND SENSORY-EVOKED ACTIVITY OF THALAMIC NEURONS IN VIVO

Shane Crandall, PhD, Scott J. Cruikshank, PhD & Barry W. Connors, PhD

The transfer of sensory signals from periphery to cortex is a dynamic process involving reciprocal communication between the cortex and the thalamus. While cortical activity is thought to modulate the excitability of thalamocortical (TC) cells, the sign of this modulation (suppression or enhancement) often varies between studies. Because corticothalamic (CT) cells directly excite TC cells and indirectly inhibit them by exciting GABAergic neurons in the thalamic reticular nucleus (TRN), CT effects will thus depend on the interactions between monosynaptic excitation and disynaptic feed-forward inhibition. Indeed, previous in vivo work in the rodent vibrissa-to-barrel cortex system has shown that the dual nature of CT activity has a strong spatial organization (Temereanca & Simons, Neuron 2004; Li & Ebner, J. Neuroscience, 2007). Surprisingly, whether temporal dynamics of CT output in vivo can also determine the sign of impact has received less attention. Our most recent in vitro work strongly suggests such a feature exists in the CT system (Crandall et al., Neuron, 2015). For many possible reasons, however, our in vitro-based conclusions may not directly predict CT effects on sensory processing in the intact system. Here, by optogenetically controlling the CT pathway from vibrissa cortex to the ventral posterior medial nucleus of the thalamus, we explore the activity-dependent influence of CT output on the excitability and vibrissa-evoked responses of aligned thalamic neurons in intact, head-fixed mice.
SHORT-TERM SYNAPTIC DYNAMICS CAN CONTROL THE SIGN OF CORTICOTHALAMIC INFLUENCE IN THE MOUSE SOMATOSENSORY THALAMUS IN VITRO

Scott Cruikshank, PhD, Shane R. Crandall, PhD; Barry W. Connors, PhD

The neocortex makes massive excitatory projections to thalamic relay nuclei via corticothalamic (CT) cells of layer 6. The same CT neurons make collateral synapses on GABAergic cells of the TRN, permitting powerful disynaptic feedforward inhibition of thalamic nuclei. The combination of monosynaptic excitation and feedforward inhibition leads to potentially complex influences by the CT pathway. Some reports have suggested that excitation predominates, others that feedforward inhibition is dominant, and still others have indicated that the balance of excitation versus inhibition depends on topographical relationships between cortical neurons and thalamic targets (reviewed in Alitto & Usrey, Neuron, 2015).

We and others have previously noticed that synaptic dynamics in the system may play a role controlling the net sign of CT influence. CT excitatory synapses on thalamic relay cells are highly facilitating whereas the feedforward inhibition mediated by GABAergic TRN cells becomes depressed during repetitive activation (Cruikshank et al, Neuron, 2010). This has led to the prediction that transient activation of CT projections might lead mainly to suppression of relay cell excitability whereas sustained CT activity could lead to net enhancement of excitability (von Krosigk et al, Neuroscience, 1999). Here we tested this prediction, examining the effects of CT input on excitability and tonic spiking activity of thalamic relay neurons in vitro. We found that transient CT activation led to a profound suppression of relay cell excitability and spiking, whereas sustained activation (at 10 Hz) produced net enhancement.

In the course of our study we confirmed that NMDA conductances carried a high fraction of excitatory CT current when thalamic membrane potentials were held near spike threshold. This led to the possibility that the enhancement of thalamic cell excitability observed during sustained CT activity might have been caused more by positive feedback through postsynaptic NMDA conductances than by short-term synaptic facilitation of glutamate release at the CT terminals. To test whether the activity-dependent shifts in CT effects were caused by the unique properties of NMDA conductances versus short-term synaptic plasticity (i.e., facilitation of excitatory transmission or depression of inhibition) we varied each of these properties using dynamic clamp. We found that short-term synaptic plasticity played the dominant role and that the unique I/V and kinetic properties of NMDA conductances were not required for the activity-dependent switch in the sign of CT influence (Crandall et al, Neuron, 2015).
ASSESSING THE ROLE OF SOCIAL RELATIONSHIP FACTORS IN A CLINICAL TRIAL OF MINDFULNESS-BASED COGNITIVE THERAPY

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Introduction: Whereas the majority of research on Mindfulness-Based Interventions (MBIs) focuses on the role of meditation techniques in clinical outcomes, less is known about the contribution of social relationship factors. This project investigated how four types of relationships (early life relationships, current social support, and relationship with the instructor and group) affect clinical outcomes in MBIs.

Methods: One hundred and four individuals with mild-severe depression (73% female, M age = 40.28, range =18-65 years) were randomized into one of three 8-week MBIs in a 1:1 ratio: Standard Mindfulness-Based Cognitive Therapy (MBCT) or single component variants, focused attention (FA) or open-monitoring (OM). Clinical outcomes included the Quick Inventory of Depressive Symptomatology (QIDS), the Depression, Anxiety, Stress Scale (DASS), and the Positive and Negative Affect Schedule (PANAS). Early Life relationships were measured with the Childhood Trauma Questionnaire (CTQ), while pre-treatment relationships were measured with the Multidimensional Scale of Perceived Social Support (MSPSS). Relationships with the mindfulness instructor and therapy group members were measured with the Therapist Empathy Scale (ES), the Working Alliance Inventory (WAI) and the Therapeutic Factors Inventory (TFI). Using multiple linear regression with all treatment groups combined, relationship factors were entered as independent variables with clinical outcomes as dependent variables.

Results: Early life trauma predicted a pre- to post-treatment increase in QIDS depression (p<0.05). Additionally, lower baseline social support predicted greater improvements in depression (p<0.05); pre-treatment depression inversely correlated with baseline social support, suggesting that individuals with less social support were more likely to exhibit a greater change in depression (p<0.05). Furthermore, while social support did not significantly change pre- to post-treatment, positive changes in social support were associated with decreases in depression (p<0.05). Lastly, a greater degree of perceived instructor empathy and higher group therapeutic factor ratings related to installation of hope and learning to take responsibility for one’s own life predicted a decrease in PANAS negative affect (p’s<0.05).

Conclusion: These data suggest that different social factor have a critical impact on MBI treatment outcomes. Specifically, MBIs appear to be contraindicated for individuals with a history of childhood trauma and abuse. Conversely, MBIs may be particularly effective for depressed individuals with low levels of pre-treatment social support. Finally, consistent with previous research, therapist quality, interpersonal skills and group dynamics also impact outcomes. An understanding of the specific roles of these social factors can be leveraged to inform future clinical research, especially contraindications and therapist training, in order to maximize treatment efficacy of MBIs.

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“SMART CITIES” AND HOUSING EFFICIENCY: DESIGN ARCHITECTURE AND THE NEUROBEHAVIORAL RESPONSES OF ANXIOUS AND STRESSED ANIMAL IN ALTERNATE REARING ENVIRONMENTS

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As cities with a population exceeding ten million people proliferate (a megacity) it will become standard practice to house megacity inhabitants in densely populated urban housing projects. Within the present day urban project population, it has been estimated that a majority suffer from some level of anxiety and addiction (i.e., drug and alcohol). Add to this the urban wealth gap, and the social constructivist finds reasons to postulate that urban project dwellers are likely to face an increasing degradation of housing inequality. These vexing socio-economic characteristics argue for the advancement of design strategies to develop “Smart Cities.” A Smart City is one that evolves on the precept of using advanced technology and the sciences (i.e., data science, neuroscience, nanoscience, information science) to address the challenges of providing clean energy, health maintenance, public safety, and economic stabilization to its residents.

The behavioral neuroeconomics-based research presented in this manuscript is founded upon an integrative and translational approach between animal and human behavior to better understand the neural mechanisms underlying behavioral influences on the socio-economic development of “Smart Cities.” The basic science supporting the research effort is derived from a study of the neurobehavioral responses to stress exhibited by anxiety-bred Long Evans rats housed across alternate rearing environments. The first phase of two in this research rests upon an in vivo study. We begin with subjects that are bred with and without an anxiety trait. Subsequently, after insertion into a stressful environment we examine the gender-differentiated neurobehavioral responses across “social” (dense) and “isolated” rearing environments. Postmortem, the research focuses on the early-gene neural marker c-fos to observe whether, over time, the rats express an ability to overcome exogenous negative influences as they are gradually returned to a less hyper-anxious and stress-free environment. The empirical investigation is derived from a conditioned and sequential use of multivariate statistics, operations research and data science methods (e.g., heat maps to nonparametric artificial neural network modeling). By way of summary, from the in vivo phase of the study we find that socially integrated (dense environment) high-anxiety female rats develop a greater sensitivity to stress and, interestingly, return more easily to a balanced state than do their male counterparts. Further analysis of the c-fos protein revealed that sex and environment contributed most to the actualized variance in fear and contextual learning structures. The analysis also implicated greater stress vulnerability for the inclusive male population housed in dense living environments.

The second phase of the study presents an elementary translational model. The translational model engages state-of-the-art neuroeconomics to answer such questions as, is it possible to use rat brain models to tell us what is best for people? Or, can we use rat neural data to learn how to overrule the choices people make and, thereby, put them in a better place by doing so? For example, we know that dopamine can modulate synaptic plasticity (e.g., from depression to potentiation). What we postulate here is a computational method by which to translate the neurophysiological experiments on Long Evans rats to a hypothetical core neural circuit model. Such models have been examined for their strongly recurrent or attractor dynamics. Neuroeconomic contributions are drawn from extant research on the psychological and neural correlates of social decision-making in game theory and experimental economics. The contribution is intended to advance architectural design of the social and economic sub-systems within urban housing projects to better harmonize individual decision-making within the evolution of the “Smart City.”
THE ROLE OF PSYCHOLOGICAL FLEXIBILITY IN EXPLAINING THE RELATIONSHIP BETWEEN DEPRESSION AND STIGMA

Carter Davis, BFA, Brandon A. Gaudiano, PhD; Casey Schofield, PhD; & Lara Rifkin, BS

Psychological flexibility refers to attending to the present moment and being more accepting of internal experiences in the pursuit of valued goals. Previous research has linked mental health stigma to psychological inflexibility or avoidance of internal experiences, resulting in negative attitudes toward those affected by mental health problems. In the current study, 570 individuals participated in an online survey in which they completed measures of depression severity (Beck Depression Inventory-II, BDI-II), psychological inflexibility (Acceptance and Action Questionnaire-II, AAQ-II), and different types of mental health stigma (Depression Self-Stigma Scale, DSSS). Pearson correlations showed that the AAQ-II was significantly related to the BDI-II (r = -.62, p < .001), DSSS-Public subscale (r = -.17, p < .001), DSS-Treatment subscale (r = -.20, p < .001). Analyses based on the Preacher and Hayes (2008) model showed that psychological inflexibility statistically mediated the relationship between depression severity and public stigma toward others with depression (Coeff = .037, SE = .014, CI 95% = .0099, .0664), but not the relationship between depression and perceived stigma about receiving treatment for depression. Thus, one’s own depression severity increases the likelihood of holding stigmatizing attitudes toward others with depression, and this process appears to work through increased psychological inflexibility around a person’s own internal distress. In other words, avoidance of one’s own depressive feelings increases one’s negative views about others also suffering from depression. In contrast, the relationship between people’s increased depression and their negative perceptions about receiving mental health treatment is not dependent on their own level of psychological inflexibility. This suggests that negative attitudes about depression treatment may be influenced more by broader societal or cultural views. The findings are discussed within a contextual behavioral science model of stigma.
SHOULD I BE WORRIED ABOUT RUMINATING?: EXPLORING THE COMORBIDITY BETWEEN PEDIATRIC ANXIETY AND DEPRESSION

Stephanie Davis, PhD, Jennifer S. Silk, PhD, Laura J. Dietz, PhD, Dana L. McMakin, PhD, Ronald E. Dahl, MD, & Neal D. Ryan, MD

Anxiety and depression, two common disorders in childhood and adolescence, are highly comorbid. However, while the majority of depressed youth have a past history or current diagnosis of anxiety, only one third of anxious youth have experienced depression. To elucidate the substantial, but incomplete overlap between these disorders, this study examined whether youth with clinical diagnoses of depression and anxiety could be differentiated based on youth’s response to negative emotions experienced in real-life. The sample included 165 nine to 14 year-olds: 27 with diagnoses of depression (DEP), 76 with diagnoses of Generalized Anxiety Disorder (ANX), and 62 healthy controls (CON). None of the participants in the ANX group had diagnoses of depression, while 37% of participants in the DEP group had secondary diagnoses of anxiety. Questionnaire data was supplemented with ecological momentary assessment (EMA): over a 5 day call period, participants were asked to identify recent events that elicited negative emotions and report on how they handled these emotions. Hypotheses were tested using both categorical groups (DEP, ANX, CON) and continuous indices of depressive and anxious symptoms to examine the contribution of depressive symptoms above and beyond anxious symptoms (and vice versa). Findings regarding rumination differed based on whether categorical or continuous measures of anxiety and depression were used. While DEP youth had significantly higher levels of rumination than ANX youth, higher levels of anxious symptoms were associated with higher levels of rumination in analyses that did not control for concurrent depressive symptoms. Interestingly, while ANX youth reported a greater number of worries than DEP youth, these groups did not differ with respect to mean intensity of worry. Taken together, results suggest that anxious and depressed youth may utilize similar emotion regulation strategies. One clinical implication of these findings is that both youth with GAD and depression may benefit from more recent treatments specifically developed to target these patterns of negative unproductive thought.
EMOTION REGULATION AS A PREDICTOR OF JUVENILE ARREST

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The current study examines emotion regulation as a novel dynamic factor of juvenile arrest as it compares to known static and dynamic risk factors. Participants included seventh-graders at five urban public schools (n=420; M age =13; 53% male). The predictive relationship between adolescent self-, parent- and teacher-report of baseline adolescent emotional competence and arrest at 30-month follow-up was assessed. Stepwise logistic regression analyses revealed that teacher report of emotion regulation strategies (OR=.37, 95% CI=.18-.75, p<.01), past 6 month marijuana use (OR=2.97, 95% CI=1.06-8.34, p=.04), and minority status (OR=2.65, 95% CI=1.02-6.67, p=.04) were significant predictors of arrest. Findings indicate teacher report of emotion regulation competence in early adolescence may be an important consideration for prevention program development.
As developing axons grow towards their destinations, the axonal growth cone senses membrane-bound and secreted molecules through receptors localized on the growth cone’s surface. Upon ligand-receptor binding, signaling cascades within the growth cone result in cytoskeletal restructuring that drives attractive or repulsive responses to specific cues. This process of axon guidance is a crucial step in nervous system wiring and plasticity. The mechanisms of axon pathfinding are still not fully understood, and the full complement of tissues that play a role in guiding axons has yet to be elucidated. The meninges are layers of connective tissue that provides protection and support for the central nervous system. The meninges have been implicated in regulating the generation and migration of neuronal progenitor cells, thereby contributing to nervous system development, but their role in axon guidance has not been explored. Here, we examined the responses of different classes of spinal cord axons to the meninges by co-culturing embryonic nervous tissue explants with meningeal tissue in vitro. Our results show that spinal motor axons are attracted to meninges at a distance, and sensory axon growth is stimulated upon contact with meningeal tissue. Spinal commissural neurons are repelled from meninges, but after crossing the spinal cord midline (post-crossing), these axons lose responsiveness to meningeal repulsion. These in vitro responses to the meninges are consistent with the respective axon trajectories in vivo: pre-crossing commissural axons grow in the spinal cord gray matter, post-crossing axons grow adjacent to the meninges, motor axons cross the meninges to exit the spinal cord, and the central branch of sensory axons enters the spinal cord through the meninges. Thus, our results demonstrate that the meninges produces long- and short-range axon guidance cues, and they suggest that these cues shape axon trajectories in the developing spinal cord.
Every day we perform sequences of tasks that require monitoring the performance of individual sub-goals to reach a final end goal. This process often occurs in the absence of external cues indicating the amount of progress made towards the overarching goal. In such situations, one must internally monitor progress through the sequence. In previous fMRI and TMS experiments, we found that activation in the rostrolateral prefrontal cortex (RLPFC) progressively increased its activity over the course of a sequence of tasks. Specifically, participants repeatedly performed a sequence of four simple categorization tasks (e.g.: color, shape, shape, color). Further, single pulse TMS delivered to the RLPFC during the task sequences increasingly disrupted performance as the sequence progressed, mirroring the activation pattern. These results suggested that RLPFC may be necessary to resolve accumulated uncertainty at each position in the sequence, rather than representing serial position itself. We designed an experiment to explicitly test this hypothesis by breaking the confound between uncertainty and sequence position. Specifically, we provided “clues” to the participants as to the identity of the task they should be performing on approximately one third of the trials across positions. The clues serve to reduce the uncertainty on those trials. We used computational modeling to infer from subjects’ trial-by-trial choices their uncertainty about the task sequence. Preliminary results from fMRI participants suggest that RLPFC preferentially represents this uncertainty instead of a signal that simply monotonically increases through each position in sequence.
HEMORRHAGIC PROGRESSION OF CEREBRAL CONTUSIONS: ASSESSING RISK FACTORS

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Importance: Every year in the US 1.7 million people experience traumatic brain injury (TBI), resulting in 1.4 million emergency department visits, 270,000 hospitalizations, and 53,000 deaths. Cerebral contusions are a bruising of brain parenchyma that often expands post-injury, and are among the most common lesions associated with TBI.

Objective: To comprehensively assess hemorrhagic progression of contusions by analyzing the rate at which they expand depending on a variety of intrinsic and modifiable factors.

Design: This retrospective study examined all patients presenting with cerebral contusions at the Rhode Island Hospital trauma center from 2005-2013. Contusion volume was measured using GE Advantage Workstation on all axial CT scans within 72 hours of initial scanning, allowing calculation of contusion sizes and expansion rates.

Setting: Level-1 Trauma Center, Emergency Room Database, including: ICD-9 diagnoses, lab work, medications, discharge status.

Participants: 481 patients with cerebral contusions.

Main Outcomes/Measures: Contusion expansion was assessed quantitatively using the rate of expansion for each patient.

Results: Of 481 total patients, 362 (75.26%) experienced contusion growth, with an average expansion rate of 0.72 cm³/hr, while 119 (24.74%) experienced contusion reduction, with an average expansion rate of -0.21 cm³/hr. Patients were grouped by initial contusion size; 0-1, 1-5, or 5+ cm³. The groups had 195, 175, and 111 patients, respectively, with mean expansion rates of 0.12, 0.48, and 1.16 cm³/hr, respectively. One-way analysis of variance revealed significant differences in mean expansion rate between these groups, [F (1, 582) = 6.1 p=0.0024]. Post-hoc Tukey HSD tests found significant differences between the means of group 1 and group 3 (p = 0.0015), while no significant difference was found between groups 1 and 2, or 2 and 3 (p = 0.1305, p = 0.3467, respectively).

Conclusions/Relevance: These data suggest that contusions with small sizes expand at a significantly lower rate than larger ones, while intermediate-sized contusions were not found to expand at a significantly different rate. Future analysis will examine the effect of BAL and anticoagulants on contusion expansion to further identify vulnerable patient populations.
TRANSCRANIAL DIRECT CURRENT STIMULATION-AUGMENTATION OF VIRTUAL REALITY EXPOSURE FOR PTSD: A FOCUS ON METHODS

Causey Dunlap, BS, Mascha van’t Wout, PhD; Noah S. Philip, MD PhD; Benjamin D. Greenberg, MD PhD

Objective: The objective of the presented pilot study is to investigate the feasibility of non-invasive electrical brain stimulation in reducing psychophysiological arousal due to posttraumatic stress disorder (PTSD) using virtual reality exposure of trauma context. The current gold standard treatment for PTSD is exposure-based cognitive behavioral therapy (CBT). Although efficacious, meta-analyses have found that a substantial group of patients who undergo exposure-based CBT retain a PTSD diagnosis and symptoms, with combat-related trauma evidencing the lowest effect sizes. Thus, there is a pressing need to identify novel mechanisms to enhance the tolerability and efficacy of interventions for PTSD. Prior research by the authors demonstrates the potential for electrical brain stimulation to augment fear-relevant extinction learning and memory processes, the underlying mechanism of exposure, in PTSD. Moreover, study on the use and effectiveness of virtual reality for PTSD treatment is growing rapidly. The present study seeks to combine brain stimulation and virtual reality with the intention of utilizing stimulation-induced neuroplasticity to improve the effectiveness of VR based treatment. Ultimately this study may inform development of a VR-neuromodulation method to increase efficacy of exposure-based cognitive behavioral therapy for PTSD treatment.

Methods: A total of 20 male OIF/OEF Veterans with a diagnosis of PTSD will be recruited for this feasibility study. Ten participants will be randomized to receive active transcranial direct current stimulation (tDCS) during virtual reality exposure to combat-scenes of Iraq or Afghanistan. The remaining ten participants will receive sham stimulation during virtual reality exposure. Participants randomized to active tDCS will receive up to 25 minutes of 2 mA anodal tDCS over the left prefrontal cortex and cathodal stimulation in between the contralateral mastoid and EEG coordinate Oz while they undergo a VR session. Participants randomized to sham tDCS will receive up to 30 seconds of 1 mA anodal tDCS over the left prefrontal cortex and cathodal stimulation over the contralateral mastoid during the VR session. All participants will undergo six sessions total over the course of two weeks. In addition, participants will undergo one neuroimaging sessions at baseline and one neuroimaging session after completion of all VR-based exposure sessions. The virtual reality sessions are conducted using the Bravemind VR system, which allows for full immersion into a virtual Iraq/Afghanistan world using a head mount and headphones. During these virtual sessions the participants are presented with a standard continuous driving scenario in either Iraq or Afghanistan, dependent on the location of their trauma, where they encounter several stimuli including an armed insurgent, IED, and vehicle flip. The participant is presented with three identical eight-minute driving scenarios for a total of about 25 minutes. Psychophysiological measurements including heart rate and skin conductance will be measured throughout the 25 minute session. Immediate effects of tDCS during VR exposure on psychophysiology, mood, and PTSD symptoms will be assessed, as well as enduring effects at one-month follow-up. It is hypothesized that compared to a sham tDCS treatment, active tDCS will decrease psychophysiological arousal during VR-based exposure, and general PTSD symptom severity will be reduced. Moreover, we will evaluate neural changes in response to the tDCS-augmented VR-based experience using Magnetic Resonance Imaging (MRI). The purpose is to provide a necessary basis for understanding where and when neural changes may occur and why adjunctive tDCS treatment may be effective.
MALLEABILITY OF DISTRESS INTOLERANCE DURING SMOKING CESSATION TREATMENT

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Distress intolerance is a key vulnerability factor for the maintenance and relapse cigarette smoking. Yet, past work has not examined distress intolerance during smoking cessation treatment. The aim of the present study was to examine the effect of two smoking cessation interventions on changes in self-report and behavioral distress intolerance indices during treatment and following a quit attempt. Treatment-seeking smokers (N = 232) were randomly assigned to one of two 4-session smoking cessation treatment programs: Standard Cessation Program (SCP) or Smoking Treatment and Anxiety Management Program (STAMP). Quit dates were scheduled to coincide with the final treatment session. Distress intolerance was assessed at baseline and at each weekly session, via the Discomfort Intolerance Scale (DIS; higher scores indicate more intolerance for distress) and Breath Holding Duration Task (BH; shorter durations indicate more intolerance for distress). Smokers who received STAMP reported significant reductions in DIS scores and increases in BH duration over time, whereas non-significant changes were observed for the SCP group. Effects were significant after adjusting for baseline levels of the respective distress intolerance measure, nicotine dependence, and negative affectivity. Data suggest distress intolerance is malleable in the context of stress sensitivity reduction treatment, but not standard care.
Neuropsychiatric diseases are increasingly understood as disorders of neural circuits. Molecular mechanisms that may underlie aberrant circuit function have been difficult to study because of the cellular heterogeneity of brain tissue. We describe here a novel technique to obtain cell-type specific translational profiles of neurons projecting to a given brain region. Using a Herpes Simplex Virus (HSV) vector, we obtain high levels of expression of a transgene for a ribosomal-GFP fusion protein (Rpl10a-GFP) in neurons projecting to the striatum. Viral transduction of the dorsal striatum of C57/BL6 mice leads to robust transgene expression in neurons known to project to the striatum: layer V pyramidal neurons in the cortex, nigrostriatal projection neurons from the substantia nigra pars compacta, thalamostriatal afferent projections from the central median/parafascicular complex of the thalamus, and amygdala-striatal afferents. Immunoprecipitation of translated mRNAs from cortex of mice injected with either HSV-Rpl10a-GFP or HSV-GFP (control) recapitulates known markers of corticostratial neurons and also identifies novel markers for this cell population. ‘CircuitTRAP’ will allow for cell-type specific translational profiling of neural circuits in a wide range of normal physiological and pathophysiological states.
SENSITIVITY OF COMPONENT ATTENTIONAL MEASURES TO SUBTLE COGNITIVE CHANGES AND REAL-WORLD DRIVING PERFORMANCE IN EARLY ALZHEIMER’S DISEASE: A LONGITUDINAL EXAMINATION

Christina Figueroa, MS, Elena K. Festa, PhD, Brian R. Ott, MD & William C. Heindel, PhD

Objective: Distinct components of attention are differentially sensitive to early cognitive changes in Alzheimer’s disease (AD) and to real-world driving performance. This study examined the ability of neurocognitive tests of attention to: a) detect subtle cognitive changes in high functioning drivers with AD and b) predict current and evolving driving risk in this population.

Participants and Methods: Older drivers diagnosed with very mild (n=43) or mild (n=21) AD completed a standardized on-road test at baseline and 6 months. Tests of spatial orienting, alerting, inhibitory control, visual search, and visuomotor tracking were administered under single- and dual-task conditions at both time points, along with a standard neuropsychological battery.

Results: Repeated-measures ANOVAs with Time (0, 6 months) and Test Condition (single, dual) as factors revealed differential cognitive changes across the two groups: For very mild AD, accuracy under dual-task conditions for visuomotor tracking and visual search declined over 6 months; for mild AD, alerting under dual task conditions and inhibitory control under both single- and dual-task conditions declined over 6 months. Regression analyses also revealed that single-task alerting and orienting predicted current driving performance, while single-task inhibitory control performance predicted 6-month decline in driving.

Conclusions: In high-functioning drivers with AD, tests of attention were able to detect cognitive decline over 6 months and to predict current and evolving driving risk. Consistent with the presence of divided attention deficits early in AD, attentional measures under dual-task conditions were particularly sensitive to decline, with specific attentional components differing with disease severity. In contrast, single-task conditions that more effectively assess distinct attentional processes were more sensitive to driving performance. Component attentional measures may be useful for early detection and assessment of subtle cognitive decline, as well as driving risk.
CHANGE IN DEPRESSIVE SYMPTOMS FROM GESTATION TO POSTPARTUM IS ASSOCIATED WITH WOMEN’S DIURNAL CORTISOL

Allison Gaffey, MA, Margaret Bublitz PhD, Amy Salisbury PhD, Chrystal Vergara-Lopez PhD, Laura Stroud PhD

About 10-15% of women experience depression in the first 12 months postpartum (PPD). To better understand and treat PPD, it is critical to identify predisposing factors (e.g., prior depression) and associated biomarkers of risk within the period of transition to disorder. Depression appears to affect the hypothalamic pituitary adrenal (HPA) axis’ ability to regulate the stress hormone cortisol. Depression and stress during pregnancy are associated with changes in maternal cortisol. No known study has included prospective, repeated measures of depression to examine how pre- to postpartum changes are associated with altered maternal HPA activity. Women (N = 118, Mage = 26.6, Caucasian: 64%) were recruited based on SCID depression diagnoses and oversampled for current (34.6%) or past (19.5%) depression. Women completed the Inventory of Depressive Symptoms (IDS) in second and third trimesters and one month postpartum. Across all groups, pre- to postpartum IDS scores decreased on average. Saliva was collected 30 days post-birth on three days: upon waking, 30 minutes post-waking, and at bedtime, and was assayed for cortisol. The diurnal cortisol awakening response, evening levels, area under the curve, and daily slope were calculated. Analyses tested associations between change in pre- to PPD symptoms, and PPD symptoms alone, on postpartum cortisol. Controlling for age, a greater increase in symptoms was associated with higher evening cortisol (F(2,105) = 6.356, p = .002, R2 = .108) and a flatter slope (F(3,102) = 5.317, p = .002, R2 = .135). Greater PPD symptoms were also associated with higher evening cortisol and a flatter slope. Conversely, diurnal cortisol did not predict PPD. Thus, PPD may provoke alterations in cortisol rather than cortisol initiating greater PPD. While preliminary, the results encourage further research examining PPD onset and changes in the HPA axis. Such studies may also clarify the pathophysiological links between maternal depression, HPA activity, and potential dysregulation of fetal/infant stress responses.
AN EXAMINATION OF THE VALIDITY AND CLINICAL UTILITY OF THE WEIGHT MANAGEMENT FAMILY RESPONSIBILITY QUESTIONNAIRE

Laurie Gayes, MA, Elissa Jelalian, PhD

Pediatric obesity has increased significantly over the last 30 years and is a leading cause of preventable death in this country (Ogden, Carroll, Kit, & Flegal, 2012). Family-based behavioral obesity interventions are well-established treatments for pediatric obesity, and require families to manage many tasks related to weight control (e.g., shopping for healthy foods, determining portion sizes, choosing snacks, engaging in exercise). The aim of this study was to evaluate a questionnaire designed to assess division of responsibility among parents and adolescents for weight-management tasks. The Weight Management Family Responsibility Questionnaire (WMRQ) was adapted from similar measures of family management of diabetes (Anderson et al., 1990), cystic fibrosis (Drotar & Ievers, 1994), and asthma (McQuaid et al., 2001). This study is the first to examine the psychometric properties of this measure, as well as to examine its clinical utility for predicting weight loss in a pediatric obesity intervention. Obese adolescents and their parents participating in a 16-week behavioral intervention were administered the WMRQ at pre- and post-treatment. Other measures administered to test for convergent and divergent validity included feeding dynamics (Child Feeding Questionnaire), parenting style (Parent and Child Report of Parenting Inventory), and teasing (Perceptions of Teasing Scale). The WMRQ was scored both as a measure of number of items yielding a consensus between parent and child, and number of items indicating conflict over responsibility. Findings on internal reliability were high for both adolescent (0.79) and parent (0.82) report. Validity testing at baseline suggested partial support for the hypothesized association between the WMRQ and feeding dynamics, and a lack of support for an association between parenting styles and the WMRQ. Consistent with hypotheses of divergent validity, the WMRQ was not associated with teasing. Over the course of treatment, consensus on the teen being responsible for weight management tasks increased and conflict over responsibilities decreased. Furthermore, increased consensus on teen responsibility was associated with decreased weight status over the course of the intervention. Clinical implications for findings include support for this measure as a clinical tool in adolescent weight management interventions.
ASSESSING STABILITY AND DYNAMICS OF STOCHASTIC SPIKING NEURON MODELS

Felipe Gerhard, PhD, Wilson Truccolo, PhD

Point process generalized linear models (PP-GLMs) have become a popular choice to model the spiking activity in single neurons and neuronal networks. Specifically, for nonlinear Hawkes models, the conditional intensity function (CIF) is expressed as a function of previous spike history and exogenous inputs. Model parameters are typically estimated from electrophysiological recordings using maximum-likelihood methods. However, sampling activity from the stochastic CIF model reveals that simulated network activity is often unstable, and firing rates tend to diverge. As a consequence, simulated spiking patterns are neither physiological nor stationary in spite of these models passing common goodness-of-fit tests. This problem already occurs with models of single-neuron spike train recordings. Trivial solutions like the inclusion of an absolute refractory period are not satisfactory since, in most cases, the activity then converges to non-physiologically high rates.

Here, we derive stability constraints for general PP-GLMs. We are interested in the existence and stability of fixed points of the expected CIF dynamics (“mean firing rate”). We adopt a recently developed mean-field theory of neuronal dynamics based on a quasi-renewal (QR) approximation. The QR approximation decomposes the spike history effects into the contribution of the last spike and an average of the CIF over all spike histories prior to the last spike. After truncation of a moment-based expansion, this decomposition leads to an integral equation for the approximated CIF. Under stationarity conditions, steady-state firing rates are obtained as the fixed points (self-consistent) solutions to this integral equation. Analysis of the number of fixed points then leads to the classification of the model to exhibit either stable or divergent dynamics. In addition, the approach can reveal other aspects of the stochastic dynamics such as metastability. In case of multiple stable fixed points, fluctuations of the single-neuron dynamics predict an expected time horizon (“escape time”) until rates converge to non-physiologically high values. This metric can be used to estimate the probability of rates to remain physiological in a given time period, e.g., for simulation purposes.

We demonstrate our stability prediction framework using simulation examples and neurophysiological data sets. Finally, we discuss how to adapt PP-GLM estimation procedures to guarantee stability. Stabilized neuron models play an important role in the field of computational neuroscience and neuro-engineering where it is essential for network models to retain finite activity levels, e.g., to analyze statistical properties of model dynamics and to implement closed-loop applications.
WHAT DO WE KNOW ABOUT THE COURSE AND TREATMENT OF EATING DISORDERS IN PREGNANCY?

Nina Gonzales, MD & Cynthia L. Battle, PhD

Objective: While research is limited, emerging evidence suggests that eating disorders (Anorexia Nervosa, Bulimia Nervosa, and Binge Eating Disorder), may improve in pregnancy but worsen postpartum. Risks of eating disorders in the postpartum period include higher rates of postpartum depression, difficulty breastfeeding, and lower weight infants and toddlers. Pregnancy has potential as an opportune time for treatment and education, when women are considering the health of the fetus and may be more accepting of change. This review will summarize the literature on the course and treatment of eating disorders in pregnancy.

Methods: Authors reviewed the available empirical literature regarding the course and treatment of eating disorders in pregnancy.

Results: Recent empirical studies suggest that eating disorders may improve by the third trimester of pregnancy, but worsen postpartum. Few empirical studies have tested specialized treatments for eating disorders in pregnancy. Current clinical recommendations apply standard eating disorder treatment to the perinatal period, with the involvement of the woman’s prenatal provider as a central part of the treatment team.

Conclusions: Pregnancy may be a favorable time to treat eating disorders. Women may be more accepting of treatment and it may prevent risk of relapse postpartum. Future research is needed to evaluate treatment modalities that are effective in the perinatal population.
THE “HOW” AND THE “WHY” OF POST-FAILURE GOAL REENGAGEMENT: A NOVEL INTERVENTION STRATEGY

Eugenia Gorlin, MA, Bethany A. Teachman, PhD

The ability to reengage in adaptive goal-pursuit after a setback or failure is essential to human psychological well-being (e.g., Martin & Marsh, 2006). Yet this ability often eludes emotionally disordered individuals, who tend to get “stuck” in post-failure rumination, which in turn disrupts their goal-pursuits and perpetuates a vicious cycle of failure and distress (Lyubomirsky, Kasri, & Zehm, 2003). This study tested a novel intervention aimed to reduce post-failure rumination and enhance goal reengagement by combining motivation- and strategy-focused goal construal training after a failure. We further tested whether emotionally vulnerable or rumination-prone individuals are more or less likely to benefit from training.

Undergraduate students (N=262) with varying trait rumination levels completed an initial academic test battery (including reading comprehension and creative fluency subtests), and were given bogus negative feedback on their test performance to induce a failure experience. Participants were then randomly assigned to one of four training conditions: Why-only (in which they reflected on the value of improving their academic performance); How-only (in which they generated specific strategies for improving their academic performance); a Combined condition (in which they alternated between the “how” and “why” prompts above); and a “thinking-as-usual” Control condition. Participants then completed a second academic test battery, such that their task performance and self-reported rumination, negative affect, self-efficacy, and task motivation could be compared from pre- to post-training.

Results in the overall sample were mixed, with Combined and Control participants both showing some gains from pre- to post-training. Notably, among high-ruminative and high-symptom participants, Combined training yielded the greatest improvement in reading comprehension and rumination, as expected. Interestingly, the Why-only condition yielded the greatest improvement in self-reported task motivation among these high-ruminative and high-symptom participants. Results, though mixed, suggest this novel intervention may hold promise for enhancing failure resilience in emotionally vulnerable samples.
DEEP BRAIN STIMULATION IN PATIENTS WITH ESSENTIAL TREMOR: INVESTIGATING TREMOR REDUCTION AND MOTOR ADAPTATION

Julie Guerin, MSc, Shane Lee PhD, Minkyu Ahn PhD, Wael Asaad MD PhD

Essential Tremor (ET) is the most common movement disorder in adults. It is typically considered a mono-symptomatic disorder characterized by a debilitating involuntary action and/or postural tremor (4–8 Hz) that usually presents in the upper extremities. Recent research, however, has pointed to additional symptoms including cognitive deficits, mood and anxiety disorders, and gait and balance deficits. In addition, abnormal cerebellar function has consistently been associated with ET. Because the cerebellum has previously been shown to be critically involved in motor learning, we sought to investigate whether patients with ET demonstrate motor adaptation deficits. Motor learning deficits would confirm that ET is a more complex disorder beyond tremor, and while current treatment strategies including pharmacological intervention and deep brain stimulation (DBS) of the ventral intermediate nucleus (VIM) of the thalamus have demonstrated substantial efficacy in reducing tremor magnitude, further investigation into their effects on other symptoms would be warranted.

To investigate motor adaptation, we developed an adapted joystick version of the center-out task, which required subjects to move a cursor to one of eight peripheral targets that appeared randomly on screen. We quantified tremor magnitude and compared tremor in addition to learning among different trial types. On “rotation” trials, the mapping between physical joystick trajectory and on-screen cursor trajectory was rotated by 60 degrees in the counterclockwise direction, thus requiring visual-motor transformation adaptation. On “random” trials, the mapping was either rotated in the opposite direction or was rotated by a different angle, thus introducing unpredictability and making learning difficult. To test whether this task is a good metric for testing motor adaptation deficits, we tested 6 pre-DBS patients (10 sessions), 7 DBS-implanted patients (12 sessions in the DBS “on” state, and 12 in the “off” state), and 4 healthy age-matched controls (8 sessions) for preliminary analyses. To quantify tremor magnitude, we calculated the power of a 4–8 Hz band-pass filtered joystick data, and we used a low-pass filtered path length (total vector distance between each trial’s start and end positions) as a metric for adaptation. We compared path lengths in rotation trials to control trials to assess whether adaptation had occurred.

Our preliminary data suggest that ET patients demonstrate deficits in adapting to the rotation compared to controls. 7 of the 8 control sessions showed no significant difference in the path lengths between rotation trials and control trials, suggesting consistent adaptation effects. In ET patient sessions, however, 6/10 showed significantly higher path lengths, suggesting adaptation deficit. To investigate whether DBS influences motor adaptation, we made the same path length comparison in “on” versus “off” sessions. 10/12 “off” sessions showed adaptation via non-significant changes in path length, while only 6/12 “on” sessions showed adaptation. This suggests that despite tremor suppression in the “on” state, trial by trial error was higher, implying that the visual feedback of tremor is not necessarily underlying motor adaptation error.

Beyond recruiting additional patients and controls to re-test these effects, we are currently working to remove tremor feedback online from the cursor trajectories to isolate motor adaptation from the visual motor feedback, and are testing the efficacy of this task in the operation room during thalamic recording and stimulation procedures.
Perception and action interact in nearly every moment of daily life. Research demonstrates that performing an action toward an object can impact perceptual processing. For example, changes in orientation are detected more efficiently when relevant actions (i.e., grasps) are directed toward the target. Furthermore, it has been also shown that ease of action can enhance liking of a target stimulus; how ease of action influences visual perception, however, is lesser known. To address this question, right-handed participants were instructed to perform a grasp toward a Gabor patch, while simultaneously performing an orientation change detection task. On a given trial, the Gabor patch appeared on either the left or right side of the screen and was oriented to be $\pm 45^\circ$ from vertical. In addition, the Gabor patch could slightly change its orientation during action preparation. Because all subjects were right-handed, ease of grasping was easier and fluent towards the right-tilted object ($+45^\circ$). As a control, participants also performed the same orientation change detection task with pointing or perception. These served as a baseline for when an action is performed with no relevance to orientation (pointing) or when no action is performed. We found that participants performed best on the orientation discrimination task when grasping movements were prepared for right-tilted targets ($+45^\circ$). Therefore, we suggest that ease of action enhances perceptual sensitivity, but this is only the case when action features are relevant.
DEFINING THE ROLE OF CORTICOTROPIN RELEASING FACTOR BINDING PROTEIN IN ALCOHOL CONSUMPTION: A STRANGE CASE OF DR. JEKYLL AND MR. HYDE

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The corticotropin releasing factor (CRF) system has been implicated in alcohol use disorder (AUD). Therefore, identification of the exact contribution of each protein components holds the key to understand the biology and design effective AUD therapeutic strategies. Here we provide evidence for the functional involvement and therapeutic potential of targeting CRF binding-protein (CRFBP). CRHBP gene loss increased ethanol consumption in mice, but selective reduction of amygdalar CRHBP expression decreased ethanol consumption and hemodynamic activity in ethanol-dependent rats. To establish CRFBP role in receptor signaling, we showed that chimeric CRFBP C-terminal (10kD) was able to potentiate CRF-intracellular calcium release signaling. Finally, SNPs that may affect CRFBP(10kD) function were associated with greater risk for alcohol consumption and anxiety (rs10062367), while others, with reduced risk for anxiety (rs7718461,rs1053989). Taken together our data confirm the hypothesis CRFBP may play multiple roles in AUD and provide novel pharmacological targets for the treatment of alcoholism.
Increasing evidence supports the role of appetite-regulating pathways in alcoholism. In this set of studies, we tested the hypothesis that intravenous (IV) exogenous ghrelin administration acutely decreases endogenous serum leptin and insulin levels. Additionally, we explored possible correlations between changes in endogenous hormone serum levels and alcohol craving.

This was a double-blind, placebo-controlled human laboratory study. Non-treatment-seeking, alcohol-dependent, heavy-drinkers (n = 45) were randomized to receive IV ghrelin or placebo, followed by a cue-reactivity procedure, during which participants were exposed to neutral (juice) and alcohol trial cues. To determine the change in hormone levels, blood samples were collected at baseline and during the entire cue-reactivity experiment.

There was a main effect for IV ghrelin administration, compared to placebo, in reducing serum leptin levels [*P < .05]. Post hoc analysis showed significant differences in serum leptin levels at the alcohol trial [*P < .05] that persisted at the end of the experiment [*P < .05]. By contrast, there were no significant differences in serum leptin levels at the juice trial [P > .05]. This effect was specific for leptin, since there were no significant effects for IV ghrelin on other serum adipocytes levels analyzed, i.e.: resistin or visfatin [P > .05]. We found also a main effect for IV ghrelin, compared to placebo, in reducing serum insulin levels [*P < .05] and a time effect [***P < .001], but not ghrelin x time interaction [P > .05]. The change of serum insulin levels parallel a similar trend in reducing connective-peptide (C-peptide) levels in the ghrelin group compared to placebo [P = .076]. No similar effects were found for other incretins here analyzed, i.e.: glucagon-like peptide 1 (GLP-1) and gastric inhibitory peptide (GIP) [P > .05]. The reduction of serum leptin level at the alcohol trial negatively correlated with the increase in alcohol urge [P < .05], while urge to drink juice was not correlated with the leptin change at the juice trial [P > .05]. We did not find a correlation between the reduction of serum insulin and alcohol craving during the cue-reactivity experiment [P > .05].

Our findings represent the first human evidence that exogenous IV ghrelin administration results in reduction of endogenous serum leptin levels. Although ghrelin was found to reduce insulin level in alcohol-dependent individuals, the reduction of insulin did not correlate with changes in alcohol craving during the cue-reactivity procedure. We provided unique, yet preliminary evidence of ghrelin – leptin cross-talk in alcoholic individuals. We suggest that their relationship may play a role in alcohol craving and specifically changes in serum leptin levels can be used as possible biomarker to assess alcohol craving.
EFFECTS OF CEREBROVASCULAR RISK ON WHITE MATTER NETWORK CHARACTERISTICS IN MILD COGNITIVE IMPAIRMENT AND ALZHEIMER’S DEMENTIA

Elizabeth Hartman, PhD; Stephen Correia, PhD; Ryan Cabeen, MS; David Laidlaw, PhD; Paul Malloy, PhD; Stephen Salloway, MD; Sean Deoni, PhD

Objective: This study’s objective was to determine the effect of cerebrovascular (CV) risk on diffusion tensor imaging (DTI) based white matter (WM) networks in mild cognitive impairment (MCI) and Alzheimer’s dementia (AD) using graph theoretical analysis.

Background: AD and subcortical ischemic vascular disease (SIVD) are often comorbid. SIVD is related to CV risks, such as hypertension and diabetes. CV risk and consequent SIVD contribute to reduced WM integrity in patients with AD. Some have proposed that SIVD causes or exacerbates AD or that they share an upstream mechanism rather than being independent parallel processes. We examined whether the relationship between CV risk and AD reflects parallel versus interacting processes using DTI and graph theory. We hypothesized the latter; that CV risk would interactively impact both frontosubcortical WM networks typically affected by SIVD and temporo-limbic-parietal (TLP) WM networks affected by AD.

Participants and Method: Participants were MCI=16, mild AD=11, moderate-severe AD=6. CV risk was the sum of risk factors. Structural network models were created using whole-brain dMRI tractography and T1 MRI gray matter segmentation with Freesurfer. Quantitative analysis included global and local measures weighted by fractional anisotropy. Local frontosubcortical and TLP connections were selected using apriori gray matter areas. AD severity was estimated by total gray matter volume.

Results: CV risk showed no effect on global graph theory metrics. In frontosubcortical networks, higher CV risk associated with more network segregation and higher local connectivity/centrality. In TLP networks, CV risk associated with less segregation and lower local connectivity/centrality. Interaction analysis showed a more widespread and inconsistent effect of CV risk in more severe AD.

Conclusions: CV risk increased segregation and local connectivity/centrality of frontosubcortical WM networks typically affected in SIVD and had the opposite effect in TLP WM networks primarily affected in AD. These findings suggest a regionally specific interactive impact of CV risk on network connectivity in AD.
Youth involved in the juvenile justice system are shown to be at risk for emotional and behavioral problems. However, research with court-involved adolescents has often neglected to examine the mental health of their caregivers. This is alarming given that caregivers may also face particularly high rates of psychological distress, potentially influencing their children’s well-being and response to treatment. This sample consisted of 162 parent-adolescent dyads. The teens were identified by court officials (intake workers, drug court workers, Magistrates, etc.) and referred to the study to receive mental health treatment for a range of concerns (e.g., depression, anxiety, delinquency). Caregivers and adolescents completed surveys about their arrest history, substance use, mental health diagnoses and treatment, and family relationships. Using a clinical cut-off of the SCL-90 global severity index, our analyses were guided by examining group differences between caregivers meeting the cut-off (“distressed”) versus caregivers not meeting the cutoff (“non-distressed”) at the baseline assessment. Results indicated that 38% of caregivers met the clinical distress cut-off. Compared to non-distressed caregivers, distressed caregivers had significantly lower household incomes (p < .001) and lower educational attainment (50% vs. 33%; X² (2, N = 156) = 4.28, p = .039). They also were more likely to have a teen who identifies as a racial minority (31% vs. 18%; X² (1, N = 154) = 3.66, p = .056) and less likely to have a co-caregiver in the household (32% vs. 58%; X² (1, N = 156) = 10.52, p < .001). As expected, distressed caregivers had significantly greater parenting stress (p < .001) and were more likely to have received mental health treatment (54% vs. 24%; X² (1, N = 142) = 11.94, p < .001) and a psychiatric diagnosis (52% vs. 19%; X² (1, N = 134) = 16.26, p < .001). They also were more likely to have been arrested (32% vs. 15%; X² (1, N = 142) = 5.48, p = .019), but not incarcerated. Other factors that did not serve as indicators of distressed versus non-distressed caregivers included caregiver and teen age or gender, caregiver race or ethnicity, caregiver readiness to engage in treatment, and history of substance abuse treatment. Our findings revealed that more than one in three caregivers of court-involved youth are currently experiencing a high level of psychological distress. While many of these caregivers have been exposed to mental healthcare services previously, about half have not. Improved mental health screening and intervention that considers this population’s unique needs is recommended, including the possible use of family-based approaches as well as individualized treatment for the caregivers of court-involved youth.
The mental illnesses constitute 15% of the disease burden of the United States, yet research for new treatments is funded at a rate several times lower than that of disorders with similar burdens. Cure Alliance for Mental Illness is a social activist network that unites patients, families, clinicians, and scientists to educate the public and policymakers about mental illnesses as brain disorders, advocate for scientific research to understand mental illnesses, and work toward safe, effective treatments. Among our early projects is the generation of college chapters, which give students a chance to educate and advocate both on and off campus. Our inaugural chapter opened in the fall of 2015 at George Mason University, and has already begun to forge connections with Washington, DC, area policymakers, in addition to on-campus lectures and events, and educational activities in area K-12 schools. Another chapter is beginning at New York University in Fall of 2016. These pilot activities show the potential for engaging students in neuroscience, psychology, public health and other allied fields in advocating for research at the federal level on mental illnesses.
Stress generation in depression (i.e. the tendency for depression-prone individuals to experience more life stressors that are in part influenced by the individual) has been well established. However, more research is necessary to clarify the role of specific types of dependent life stressors in this effect. The current study extends the stress generation hypothesis by examining whether the content of dependent stressors is contingent upon the nature of the individual’s particular vulnerability. Childhood emotional abuse and interpersonal vulnerability factors were predicted to be associated with prospective interpersonal dependent but not non-interpersonal or independent stress. These interpersonal factors were examined as mediators of the association between childhood emotional abuse and interpersonal stress generation. Data were collected from 185 undergraduate participants (75.7% female, 56.2% white, Mage = 19.65, SD = 1.49) at two time-points, four months apart. At baseline, participants completed assessments of depressive symptoms, childhood abuse history, interpersonal risk factors (rejection sensitivity, excessive reassurance-seeking, and negative feedback-seeking), and a diagnostic interview for depression. At the follow-up assessment, participants completed a life stress interview. Childhood emotional abuse, but not physical or sexual abuse, prospectively predicted greater interpersonal stress, but not non-interpersonal or independent stress. Although both rejection sensitivity and excessive reassurance seeking were also associated with interpersonal stress generation, only rejection sensitivity mediated this relationship. These findings suggest that targeting interpersonal vulnerabilities in clinical settings, particularly rejection sensitivity for those with a history of childhood emotional abuse, may help to alleviate the occurrence of interpersonal stressors, thus possibly decreasing risk for depression.
NEUROPSYCHOLOGICAL ASSESSMENT WITHOUT UPPER LIMB INVOLVEMENT: SYSTEMATIC REVIEW OF ORAL ADAPTATIONS OF THE TRAIL MAKING TEST AND SYMBOL-DIGIT MODALITIES TEST

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Objective: The Trail Making Test (TMT) and Symbol Digit Modalities Test (SDMT) are used to assess attention and processing speed, but their utility is limited in populations with upper limb dysfunction. Oral adaptations of the TMT and SDMT have been developed, but a systematic investigation into their psychometric properties and clinical utility has not been conducted, which was the goal of this review.

Data Sources: Searches conducted in PubMed and PsycINFO, test manuals, and the reference lists of included articles.

Study Selection: Abstracts were independently reviewed by two investigators for the following criteria: reported on an oral variant of the TMT or SDMT; minimum sample size of 10; and written in English. Dissertations, book chapters, conference proceedings, studies with pediatric samples, and papers without abstracts were excluded.

Data Extraction: Articles meeting inclusion criteria were reviewed by one investigator who extracted information on demographic influences, test-retest reliability, construct validity, concurrent validity, predictive validity, responsiveness, and normative data. Data extraction was verified by a second investigator in a random selection of 10% of papers.

Data Synthesis: Strength of the evidence supporting each measurement property was rated on a 4-point scale based on the aggregate results of studies. 312 unique publications were identified, 137 of which met inclusion criteria. Results showed strong evidence for reliability and validity of the oral SDMT, moderate evidence for the oral TMT-B, and adequate to weak evidence for the oral TMT-A and Mental Alternations Test.

Conclusions: This systematic review graded the psychometric properties and clinical utility of oral adaptations of the TMT and SDMT. Results can inform the clinical assessment of attention and processing speed in individuals with upper limb disability.
DOES DIFFUSION TENSOR AND MYELIN IMAGING RELATE TO COGNITIVE STATUS IN ALZHEIMER’S DISEASE?

Jacob Jones, MS, Steve Correia PhD; Elizabeth Hartman PhD; Athene Lee PhD; Shawn Nelson Schmitt PhD; Steve Salloway MD; Paul Malloy PhD; Sean Deoni PhD

Objectives: Alzheimer’s disease (AD) is the most common neurodegenerative disorder in the world. Traditionally, AD was viewed as a disorder of the cerebral grey matter. However, it is now known that white matter changes are also common in AD. Brain imaging of white matter microstructural integrity has traditionally consisted of diffusion tensor imaging (DTI) metrics such as fractional anisotropy (FA) and radial diffusivity (RD). Deoni et al. (2008) developed a newer metric, myelin water fraction (MWF), which quantifies myelin integrity. The current study examined the relationship of MWF and DTI markers (FA and RD) of white matter integrity to cognitive status among an Alzheimer’s disease sample. We hypothesized that MWF, relative to traditional DTI metrics, would be a sensitive neuroimaging marker of cognitive functioning.

Participants & Methods: The sample (age 55-87) consisted of 14 elderly controls, 20 individuals with mild cognitive impairment (MCI), and 19 individuals with AD. All participants underwent MRI with DTI and multicomponent driven equilibrium single pulse observation of T1/T2 (mcDESPOT) for computation of MWF. Participants additionally completed neuropsychological tests of general cognitive functioning, language, processing speed, executive functioning, learning and delayed verbal memory. Tract-based spatial statistics (TBSS) were utilized to analyze: 1) group differences in white matter/myelin integrity and 2) the relationship between cognitive functioning and white matter/myelin integrity among individuals with cognitive impairment (AD and MCI). Age was statistically controlled for across all analyses.

Results: Analyses failed to find significant between-group differences (control, MCI or AD groups) in FA, RD and MWF. Within the cognitively impaired groups, higher values of both MWF and FA (greater integrity) were significantly related to better performance on tests semantic fluency, learning of a word list, and general cognitive functioning. Delayed memory performance was related to MWF only, but not to FA. In contrast, better processing speed was related to higher FA, but unrelated to MWF. Visual inspection revealed that cognitive functioning was generally correlated with FA in both posterior and frontal white matter regions, whereas the relationship between cognition and MWF was restricted to posterior regions. Cognition was not significantly related to either MWF or FA in the cognitively intact control group.

Conclusions: The current study supports the validity of MWF as a neuroimaging marker of cognitive functioning among individuals with cognitive impairment. The correlation and spatial distribution of the relationship between MWF and cognition overlaps substantially but not entirely with FA. Higher values of both FA and MWF (more intact white matter integrity) were correlated with better cognitive functioning. Additional longitudinal studies are needed to examine the utility of MWF as an early marker of AD.
WHITE MATTER INTEGRITY AND SELF-REPORTED SLEEP COMPLAINTS IN OEF/OIF/OND VETERANS WITH DEPLOYMENT-RELATED MILD TBI

Jacob Jones MS, Thomas Farrer PhD; Steve Mernoff MD; Megan Spencer PhD; Marie Sullivan MSW; Steve Correia PhD

Objectives: Acute and chronic sleep changes are common in mTBI. The current study included OEF/OIF veterans with (n=5) and without (n=8) deployment-related mTBI to examine the relationship between self-reported sleep quality and structural integrity of cerebral white matter regions (WM) important for sleep regulation.

Participants & Methods: Participants (age 22-35) underwent MRI with DTI and completed self-report measures of post-concussion symptoms, PTSD, depression, and sleep quality. Region-of-interest (ROI) analysis, based on the JHU Atlas, included measurement of fractional anisotropy (FA), mean diffusivity (MD) and radial diffusivity (RD) in regions involved in sleep neurocircuitry, including the right and left posterior thalamic radiations and pontine crossing fibers. Tractography analysis involved brainstem segment of the ascending reticular activating system (ARAS)

Results: Veterans with mTBI reported obtaining fewer hours of sleep and reported more symptoms of PTSD and depression. Compared to controls, the mTBI group showed increased FA in the pontine crossing fibers (.05<p<.10), but not the thalamic radiations. Self-reported hours of sleep significantly and negatively correlated with FA in pontine crossing fibers (r=-0.71, p=.01) for the entire sample and remained significant when controlling for depression (p=.02) and marginally significant when controlling for PTSD (p=.06). ARAS analysis showed no significant group differences in FA, number of fibers, or mean fiber length.

Conclusions: Decreased self-reported sleep duration was counter-intuitively related to increased FA in the pontine crossing fibers. This finding may be related to a small sample size. Alternatively increased FA could represent injury-related decrease in pontine crossing fibers. Investigation of the relationship between WM integrity and sleep duration in a larger sample of veterans is needed.
In the United States, 15.5 million children have witnessed domestic violence within the past year. A growing body of literature examines the effect of domestic violence on children, but little is known about the factors that contribute to a parent’s willingness to disclose violence exposure. Understanding why some parents are less willing to disclose domestic violence than are others is important because families cannot receive the help they need without sharing their experience with others. Learning which factors play a role in willingness to disclose would allow interviewers to ask parents about domestic violence in the best manner possible to elicit an honest response.

The current study includes 94 families with documented cases of moderate to severe domestic violence exposure in the past six months. Children ranged in age from 3 to 5 years and were racially and ethnically diverse. Sixty-eight percent of families had one parent living in the home and 49% of families consisted of married parents. Sixty-three percent of caregivers had no more than a high school degree. Children’s exposure to moderate to severe levels of domestic violence was determined by child protection record reviews. Parents also participated in an interview to assess childhood trauma that assessed for exposure to violence. Forty-eight parents disclosed child domestic violence exposure during the interview while 46 parents did not. Standard family information forms were completed to assess demographic factors that may contribute to a parent’s disclosure of domestic violence on the childhood trauma interview.

Results indicated that relationship factors contribute significantly to the disclosure of domestic violence while other sociodemographic factors (race, ethnicity, education, and income) play less of a role. Sixty-two percent of households with only one adult in the home disclosed domestic violence, while 24% of those with two or more adults living in the home disclosed (Chi-Square = 11.45, p < .001). Additionally, 60% of single caregivers reported domestic violence compared with 37% of married parents (Chi-Square = 4.45, p < .05). Paternal involvement also played a role in willingness to disclose domestic violence. Sixty-six percent of parents disclosed domestic violence when the father was no longer involved; whereas 42% of parents disclosed domestic violence if the father was involved in the child’s life (Chi-Square = 4.17, p < .05). These results highlight the importance of assessing a parent’s marital status and living environment when probing about issues of domestic violence. Parents whose partner is still involved in their children’s lives may face additional struggles and could face repercussions by disclosing violence. Future studies should focus on the role of each partner and also assess whether the interview location and context, as well as method of inquiry, further impacts willingness to disclose.
PREGNANT WOMEN SHOW GREATER PREFERENCE FOR SWEET VS. TOBACCO-FLAVORED E-CIGARETTES AND WATERPIPE TOBACCO

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Background. There has been a proliferation of available flavors for non-cigarette tobacco and nicotine products, yet little is known regarding perceptions and use of flavors in vulnerable populations. The impact of flavors on perceptions and use of tobacco/nicotine products is especially salient during pregnancy due to impact of maternal use on both mother and fetus, and potential for fetal toxicity from flavors as well as nicotine and combustion products. We investigated: (a) the impact of sweet vs. tobacco flavors on preferences for e-cigarettes (e-cigs) and waterpipe tobacco (WPT), and (b) the impact of flavor preferences on use of e-cigs and WPT in a diverse, low-income sample of pregnant tobacco users and controls.

Methods. 30 pregnant women (60% tobacco users; Mage=27; 67% minorities) were recruited from a larger study of perinatal smoking and fetal toxicity. Detailed interviews were conducted assessing preferences for and use of sweet (mint, cloves/spices, fruit, chocolate, alcohol, candy) vs. tobacco-flavored e-cigs and WPT.

Results. Rates of lifetime use of e-cigs and WPT in pregnant women were 40% and 80%, respectively; rates of use during pregnancy were 6% and 16%, respectively. Pregnant women showed increased preference for sweet vs. tobacco-flavored e-cigs (ps < .01) and sweet vs. tobacco-flavored WPT (ps < .001), with more pronounced preferences in current e-cig and WPT users (p ≤ .08). 90% of lifetime users endorsed use of sweet (vs. tobacco) flavors for both e-cigs and WPT. 100% and 80% of pregnancy users endorsed use of sweet (vs. tobacco) flavors for e-cigs and WPT, respectively. Preferences for sweet-flavored e-cigs and WPT were associated with greater use of e-cigs and WPT during pregnancy (rs > .32, ps ≤ .08) as well as greater intentions to use e-cigs and WPT after the baby is born (rs > .34, ps ≤ .06).

Discussion. Results highlight increased use of and preferences for sweet vs. tobacco-flavored e-cigs and WPT by pregnant women. Results also revealed links between preferences for sweet flavors and use and intention to use e-cigs and WPT during and after pregnancy. Results provide scientific data to inform regulation of flavored tobacco products in reproductive age women.
NEURAL ACTIVATION DURING MASKED AND UNMASKED EMOTIONAL FACE PROCESSING IN YOUNG ADULTS WITH BIPOLAR DISORDER

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Background: Despite our best treatments, bipolar disorder (BD) continues to be one of the most devastating psychiatric illnesses leading to high morbidity, mortality, and direct as well as indirect costs. Thus, there is a need to advance our understanding of the underlying neural mechanisms of BD in order to improve our ability to diagnose and treat BD. This is especially true for childhood-onset BD, in which children’s lack of verbal capacity to describe their symptoms often leads to a 10-15 year delay between the onset of symptoms and a BD diagnosis being confirmed or not. Moreover, studies show that up to one-third of adults with BD report their symptoms began in childhood. In this vein, prior work has shown that BD youth have aberrant brain and behavior interactions underlying emotional face processing. Now, we sought to take the next step in this line of research by examining these interactions underlying conscious and unconscious emotional face processing in young adults who were diagnosed with BD as children. We hypothesized that these BD young adults would have significantly altered prefrontal cortex (PFC)-amygdala-striatal activation during both explicit and implicit face processing compared to typically-developing controls (TDC) without psychopathology.

Method: This study was IRB-approved at Bradley Hospital and Brown University. Three groups of young adults (ages 18-30) were enrolled after informed consent: (1) those with BD type I or II (BD; n=31), (2) those with BD not otherwise specified (BD-NOS; n=12), and (3) TDC adults (n=59). All BD I, II, and NOS participants were prospectively followed from childhood to adulthood in Brown’s site of the Course and Outcome of Bipolar Youth (COBY) study. Participants’ 3Tesla MRI scan included an event-related functional MRI (fMRI) with a backwards-masked affective priming paradigm to examine implicit and explicit emotional face processing. Specifically, participants were instructed to rate how much they liked or disliked abstract shapes presented one at a time on a rating scale from one (dislike) to four (like) during four fMRI runs. Each shape was preceded by a priming stimulus consisting of either an emotional face (angry, happy, neutral, or fear) or a blank oval face. During two fMRI runs, the participant was aware of the priming stimulus as it was explicitly presented for 175ms. During the other two runs, the stimulus was implicitly presented for 11ms followed by a disordered face mask presented for 160ms.

Results: We found significant three-way interaction differences in brain activation in the frontal-temporal neural circuit, including the left middle frontal, the bilateral superior temporal, the parahippocampal, and the left fusiform gyri. Decomposing this further, we found significant group X awareness differences in the left fusiform and the right superior temporal gyri with BD-NOS participants having significantly less activation than BD or TDC participants. With respect to group X face type, we found significant differences in the bilateral middle frontal, the bilateral superior temporal, and the parahippocampal gyri. In general, these were driven by greater activation in BD participants than TDC participants when processing angry and happy faces.

Conclusions: Our data advance what is known about the neural mechanism of emotional face processing in BD in two important ways. First, we extended prior work demonstrating neural alterations in emotional face processing among BD youths by showing that these deficits persist into young adulthood. Second, our data suggest that these deficits are hard-wired, persisting during both conscious and unconscious face processing. Further work is required to determine if these brain and behavior alterations underlying emotional face processing—the most rudimentary aspect of emotional awareness and regulation—might be amenable to treatment by cognitive remediation or neurostimulation as potential non-medication treatments for BD.
DIFFERENTIAL RELATIONSHIP BETWEEN DEPRESSION AND WHITE MATTER INTEGRITY IN ADULT VERSUS CHILD ONSET TEMPORAL LOBE EPILEPSY

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Objective: White matter abnormalities occur in both temporal lobe epilepsy (TLE) and depression, but there is limited research examining the depression-white matter association in TLE. This study examined the relationship between white matter integrity (WMI) and depression and epilepsy-related variables in childhood vs. adult seizure onset.

Participants and Methods: Adults (N=20) with non-lesional TLE with and without depression (TLE+D; n=11; TLE-D, n=9) underwent diffusion tensor imaging (DTI). The sample was subdivided into childhood-onset seizures (COS; < 13 years; 4/11 with TLE+D) and adolescent/adult-onset seizures (AOS; 5/9 with TLE+D). Depression severity was assessed with the Hamilton Rating Scale for Depression. WMI was estimated based on fractional anisotropy (FA) and mean diffusivity (MD) calculated in frontal-temporo-limbic (FTL) regions in the JHU DTI atlas.

Results: Compared to COS, AOS showed lower FA in right uncinate fasciculus and higher MD in left hippocampus. There were no significant group differences in seizure-related variables. Within COS, WMI correlated significantly with depression severity (i.e., negatively with FA; positively with MD) in the corpus callosum, fornix, right cingulum, and bilateral superior longitudinal fasciculus. No significant WMI-depression correlations were found in FTL regions in AOS. COS had no associations between WMI and seizure-related variables. In the AOS group, the presence of seizures in past month was associated with lower FA in the fornix.

Conclusions: WMI in FTL regions are similar in COS and AOS, but are associated with depression in the COS group only. In the AOS group, WMI is associated with the presence of seizures in the past month. The results raise the possibility that COS impacts white matter development thereby increasing vulnerability to depression; whereas AOS WMI is alternatively more susceptible to current seizure severity. Epilepsy duration may also contribute to depression-WMI associations.
PUBLIC INSURANCE DURING PREGNANCY IS ASSOCIATED WITH ALTERED NEWBORN BEHAVIOR

Tessa Kehoe, BA, Chantelle Ward, BS, Maggie O’Reilly Treter, BA, Laura Stroud, PhD

In the United States, public insurance (i.e. Medicaid) covers almost half of all births, and with the Affordable Care Act there are continued efforts in place to improve birth outcomes for women enrolled in Medicaid (Daniel-Robinson, Cha, & Lillie-Blanton, 2015). Despite these efforts, many insurers fail to uphold these standards of coverage, and there continue to be disparities in care between publically and privately insured parties (Raglan, Anderson, Lawrence, & Schulkin, 2013; McCarthy 2015; Armstrong 2015). Early life conditions, including prenatal care can have lasting effects throughout the lifetime; however the more immediate effects on infant behavior are largely understudied (Currie & Rossin-Slater, 2014; Kuh & Shlomo 2004; Kuh et al., 2003). The objective of this study is to determine if insurance type during pregnancy is associated with altered infant outcomes at birth and in the first 30 days of life. We tested the hypothesis that the infants of women with public insurance throughout pregnancy may show altered behavior at day1 and day 30 compared with the infants of women with private insurance throughout pregnancy.

The sample consisted of 195 mother-infant pairs drawn from BAMBI, a larger study of behavior and mood throughout pregnancy and resulting infant outcomes. As part of the larger study, data were extracted from the maternal medical records during the timeframe of the pregnancy to establish a record of medical experiences throughout the pregnancy. Insurance status (i.e. public vs. private) was determined from this information; of the 195 participant pairs, 114 had public insurance (58%) and 81 had private insurance (42%). As another part of the larger study, infants were examined using the NICU Network Neurobehavioral Scale (NNNS) by certified examiners at postnatal days 1 and 30. The NNNS is a non-invasive exam that evaluates at-risk infants on a series of standardized subscales related to neurobehavioral performance (Lester, Andreozzi-Fontaine, Tronick, & Bigsby, 2014).

An independent samples t-test was utilized to determine if maternal insurance status was associated with infant NNNS performance at day 1 and 30. At both postnatal days 1 and 30, infants of mothers with public insurance had significantly less optimal scores than infants of mothers with private insurance. Specifically, at Day 1, infants of mothers with public insurance showed decreased quality of movement and ability to self-regulate, and increased stress signs and excitability vs. infants of mothers who had private insurance (t’s>2.07, p’s<.05). At Day 30, infants of mothers with public insurance showed increased stress signs, and non-optimal reflexes vs. infants of mothers with private insurance (t’s> 1.97, p’s<.05).

Our results show that public insurance status during pregnancy is associated with altered infant neurobehavioral outcomes immediately after delivery and persisting through the first postnatal month. These results have important implications for the continued development of public healthcare systems. Given the preliminary nature of results, future replications are needed. It is also of note that potentially confounding factors, such as socioeconomic status, were not considered in our analyses, and should be analyzed in future replications. Also of interest in future research would be analyses of prenatal and emergency care actually received during pregnancy in relation to insurance status and infant outcomes.
MOTIVES FOR DRUG USE IN BODY DYSMORPHIC DISORDER

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Background: Body dysmorphic disorder (BDD) is a common, severe, and distressing disorder. Lifetime rates of drug use disorders in BDD are high (17%-34%). Only one prior study has examined motives for substance use in BDD, finding that a majority of individuals with BDD use substances to alleviate BDD-related distress. No studies have examined motives to use drugs in BDD using a standardized measure.

Methods: This study examined associations between motives to use drugs and clinical correlates of BDD in 53 adults with BDD (32 with current BDD, 11 in partial remission, and 10 in full remission) who reported lifetime drug use and were asked to complete the Drug Use Motives Questionnaire (DUMQ). We examined associations among DUMQ subscale scores, which reflect three types of motives for drug use: 1) coping motives (i.e., using drugs to cope with negative affect), 2) social motives (i.e., using drugs for affiliative reasons), and 3) enhancement motives (i.e., using drugs to enhance positive affect). We also examined associations between these drug use motives and lifetime BDD severity, use of drugs because appearance concerns are upsetting, psychiatric comorbidity, and suicidality (e.g., history of attempted suicide).

Results: Among those subjects who reported a history of using illicit drugs, nearly half (47.2%) reported that they used illicit drugs because their body image concerns upset them: 15.1% reported that this was “sometimes” the case, 20.8% reported that this was “often” the case, and 11.3% reported that they “almost always” or “always” used drugs because their body image concerns upset them. Coping motives on the DUMQ were positively associated with the item using drugs because “body image concerns upset you” (r=.49, p<.001). Coping motives were also positively associated with history of a drug use disorder (r=.45, p<.001) and attempted suicide (r=.28, p=.046). Enhancement motives were positively associated with a history of a drug use disorder (r=.37, p=.006). Social motives were not significantly associated with BDD-related or other clinical variables. In regression analyses, controlling for age and BDD status (currently meeting partial or full DSM-IV criteria for BDD vs. full remission), using drugs because appearance concerns are upsetting, history of a drug use disorder, and history of attempted suicide contributed the most unique variance to coping motives for using drugs. History of a drug use disorder contributed the most unique variance to enhancement motives for using drugs.

Discussion: Nearly half of the participants who reported a lifetime history of using illicit drugs did so because their body image concerns upset them. As we previously found for alcohol use in individuals with BDD, BDD symptoms are strongly associated with coping motives for drug use. However, BDD symptoms are not significantly associated with enhancement motives or social motives for drug use. These findings suggest use of drugs to self-medicate BDD-related distress. These findings also suggest the importance of treating BDD symptoms in individuals with a substance use disorder. Further examination of drug use motives, including use of drugs to reduce BDD-related distress, will inform understanding and treatment of BDD.
EXAMINING DROPOUT RATES DURING COGNITIVE AND EXPOSURE-BASED TREATMENTS FOR ANXIETY: A META-ANALYTIC APPROACH

Joshua Kemp, MS, Aaron Lee, MS, Joshua Clapp, PhD, and Maria Mancebo, PhD

Despite strong empirical evidence supporting exposure therapy as a highly effective treatment for anxiety disorders it is consistently underutilized in clinical practice. A primary contributing factor to its underutilization is therapist concern about uniquely high rates of dropout. These concerns have led some to augment exposure therapy with anxiety control strategies such as breathing strategies or applied relaxation. Others have recommended that cognitive therapy be used to treat anxiety instead of exposure therapy. Cognitive therapy is thought to be a more palatable treatment for patients, and therefore less likely to lead to dropout. Although there are theoretical reasons to suggest cognitive therapy may lead to fewer dropouts than exposure therapy, no systematic examination of dropout rates for exposure and cognitive therapy has been conducted to date to confirm this common clinical assumption. The current investigation utilized a meta-analytic approach to assess differences in dropout rate between exposure-based and cognitively-based treatments for anxiety. Reasons for dropout were also compiled and analyzed to provide further insight into the problem of treatment dropout and potential methods for reducing attrition.

Direct comparisons of cognitive therapy and exposure therapy within randomized clinical trials were included. The primary search for studies utilized two electronic databases: PubMed (1/1/1980 to 12/1/2014) and PsycINFO (1/1/1980 to 12/1/2014). This yielded a total of 3202 studies (duplicates removed), which were screened down to a final sample of 25 studies. Of those identified for inclusion, eighteen provided sufficient information to calculate rates of dropout to be included in the primary analysis. Data were extracted by two independent coders using a standardized coding sheet, and inter-rater reliability was excellent.

The average length of treatment was 10.9 weeks, with sessions lasting an average of 78 minutes. The mean rates of dropout for exposure and cognitive therapy in this sample was 16.15% (SD = 12.62) and 13.76% (12.57), respectively. The comparison of dropout rates between exposure therapy and cognitive therapy for anxiety disorders yielded a null effect, Z = 1.24, p = 0.22. This suggests there was insufficient evidence to conclude that exposure therapy leads to reliably higher rates of dropout than cognitive therapy. Subgroup analyses revealed the exclusion of anxiety control strategies during exposure (e.g., arousal reduction and breathing retraining) did not significantly influence the discrepancy between exposure therapy and cognitive therapy, p = 0.45. The exclusion of behavioral experiments during cognitive therapy also did not significantly affect the discrepancy between exposure therapy and cognitive therapy, p = 0.60. Analysis of reasons for dropout revealed that treatment-related factors, such as adverse experience in treatment, played a much smaller role in dropout than hypothesized. Instead, environmental barriers such as transportation issues and scheduling conflicts comprised the large majority of reasons for dropout.

The current findings indicate a lack of evidence for a statistically reliable difference between exposure therapy and cognitive therapy on rates of dropout. Further, reasons for dropout seem to have much less to do with treatment-related factors than they do with environmental barriers. These findings counter the common clinical fear of temporary anxiety exacerbations leading to dropout during exposure. Temporary increases in anxiety are a necessary part of exposure, and typically serve as a strong indicator of optimal engagement with treatment activities. Future research should continue to study reasons for dropout and develop new treatment tools to help manage the influence of environmental barriers on dropout.
ELUCIDATING THE TRANSCRIPTIONAL NETWORKS THAT PRESERVE ADULT NEURAL STEM CELLS

Sun Kim, BS, Shleshma Dhakal, Abigail Brown, Trenton Woodham, Megan Gura, Ashely Webb, PhD

Cognitive decline is a major hallmark of aging, and occurs partly due to neuronal loss. Neural stem cells (NSCs) are an endogenous source of new neurons in the adult brain that persist in a quiescent state. In response to extrinsic/intrinsic cues, quiescent NSCs are activated for proliferation/differentiation. However, NSCs’ ability to exit quiescence and undergo neurogenesis in the adult declines with age. Currently, the molecular mechanisms underlying adult NSC quiescence are largely unknown. We hypothesize that the BMP (Bone Morphogenetic Protein) signaling pathway and a conserved “pro-longevity” transcription factor, FOXO3, regulate NSC quiescence, thereby preserving adult NSCs. We established an in vitro model of quiescence where treating adult mouse NSCs with BMP4 induces a rapid and reversible cell cycle exit. Intriguingly, we found that FOXO3 expression is strongly induced after three days of BMP4 treatment. We are currently investigating the functional role of FOXOs in NSC quiescence. In preliminary experiments, we treated Foxo3+/+ and Foxo3-/- NSCs with BMP4 and assayed their ability to enter quiescence. Consistent with strong induction of FOXO3 after prolonged BMP exposure (>24 hours), we found that FOXO3 is not required for activated NSCs to exit the cell cycle. Our results suggest that BMP signaling and FOXO3 are regulating two independent aspects of NSC quiescence: cell cycle exit and maintenance of quiescence.
TEMPERAMENT AS A MODERATOR OF INTERNALIZING BEHAVIOR PROBLEMS IN PRESCHOOLERS EXPOSED TO DOMESTIC VIOLENCE

Samantha J. Klaver, BA, Jennifer Gallagher, PhD, Audrey R. Tyrka, MD PhD, Ronald Seifer, PhD, Stephanie H. Parade, PhD

More than 7 million American children live in homes with ongoing severe domestic violence. In 90% of these cases, the children witness the domestic violence first-hand, either by being present during the altercation or seeing the physical and emotional aftermath. Exposure to domestic violence places children at risk for the development of behavior problems, yet children with less temperamental difficulties are often resilient in the face of domestic violence (Martinez-Torteya et al., 2009). However, no prior study has considered the contribution of social fear, a domain of child temperament related to shyness and inhibition in social situations, to emerging behavior problems in childhood. The current study examined links between domestic violence and internalizing and externalizing behavior problems in preschool-aged children, and considered the possibility that the child’s social fear moderates the effects of exposure to domestic violence on behavior problems.

The participants in the study included 187 children (88 male, 99 female). Children ranged in age from 3 to 5 years and were racially and ethnically diverse. 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. Of the participants, seventy-five children were exposed to domestic violence. In addition, ninety children had substantiated cases of moderate-severe childhood maltreatment, some of which included domestic violence exposure. Parents completed the Toddler Behavior Assessment Questionnaire (TBAQ; Goldsmith, 1996) to assess the child’s temperament, as well as the Child Behavior Checklist (CBCL; Achenback & Rescorla, 2000) to assess the child’s internalizing and externalizing behavior problems.

Regression analyses controlling for child age, ethnicity, and exposure to other forms of adversity including maltreatment were used to examine the link between exposure to domestic violence and child behavior problems. There were no main effects of domestic violence on internalizing or externalizing behavior problems. However, a significant interaction between domestic violence and social fear was found in the prediction of internalizing behavior problems (B = 2.92, SE = 1.38, p = .04). Domestic violence was positively associated with internalizing problems when social fear was high (B = 3.64, SE = 1.86, p = .05), but not when social fear was low (B = -1.49, SE = 1.83, p = .42). There was no significant interaction between domestic violence and social fear I the prediction of externalizing behavior problems.

The findings indicate that children with high social fear are more likely to experience internalizing behavior problems as a result of domestic violence exposure. Previous research has established that child temperament has effects on other child behavior aspects. In addition, our finding indicates that this predisposition to internalizing behavior problems may be increased in an environment with domestic violence, as the child may perceive the outward environment as unsafe, and turn inward. This finding that social fear moderates associations of domestic violence with behavioral outcomes poses many implications for both research and clinical interventions with children at risk.
SMOKING IN THE PRESENCE OF AN ALTERNATIVE DISTRACCTOR: ASSOCIATION WITH ELEVATED DIETARY RESTRAINT AND EXPECTANCIES

Michelle Kovacs, MA, Amanda M. Palmer, BA; Thomas H. Brandon, PhD

Prior research found that female smokers with elevated dietary restraint smoked more after a disinhibiting food event (Kovacs, Correa, & Brandon, 2014). The current study aimed to determine if those with elevated dietary restraint smoked merely to distract themselves from eating, or if the appetite/weight-control aspects of smoking played a role. 128 Female participants attended a laboratory session and were randomized to receive a milkshake prime (Prime condition) or not (No-Prime condition). All participants then received ad-lib access to several tempting foods, cigarettes, and a computer tablet with internet access. We utilized hierarchical regression analyses with condition, dietary restraint and the interaction between these two factors as predictors. Condition was predictive of total cigarette smoked. Specifically, those in the Prime condition smoked more (p < .05). Regardless of condition, several measures of expectancies predicted cigarette consumption (p’s < .05), and higher level of dietary restraint predicted shorter latency to smoke (p = .017). Importantly, latency to use the tablet was not predicted by level of dietary restraint or expectancies. Additionally, lower levels of trait mindfulness were associated with elevated dietary restraint and expectancies about cigarettes’ weight control properties. Consistently, lower levels of mindfulness were associated with elevated cigarette craving at baseline. Although dietary restraint and expectancies did not interact with condition to predict levels of smoking, the overall findings suggest that dietary restrainers attempt to prevent food consumption by turning to cigarettes, and that they choose to utilize cigarettes above and beyond preference for other salient distracting stimuli. Therefore, smoking appears to be more than just a distractor from eating, and is associated with strong beliefs about weight and appetite control. These findings can inform interventions aimed at the high-risk population of young adult female smokers. Interventions should be adapted for those who smoke for weight and appetite control purposes, and mindfulness-based strategies may prove especially useful.

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TEXT MESSAGE ACCEPTABILITY AND FEASIBILITY WITH SUICIDAL ADOLESCENTS

Maya Krek, BS, Adam Chuong, BA, Katherine Tezanos, BA, Megan Ranney, MD, Christopher Kahler, PhD, Anthony Spirito, PhD, Joel Solomon, MD, Shirley Yen, PhD

Background: Adolescent suicide is a tremendous public health concern. Risk is particularly high following discharge from an inpatient psychiatric admission when continuity of treatment is vulnerable. Texting has the potential to extend the reach of treatment, yet few studies have examined its application to suicidal adolescents.

Skills to Enhance Positivity (STEP) is an adjunctive skills training program developed to increase positive affect in teenagers and decrease suicidal thoughts and behaviors using mindfulness, gratitude, and savoring skills. In addition to in-person skills coaching sessions, teens receive 1 month of daily SMS upon discharge, with the option of extending the SMS for another 3 months. The messages contain mood-monitoring prompts and a skills reminder of their choice. The treatment as usual (TAU) group receive ‘healthy habit’ SMS for 1 month after discharge.

This study explores the acceptability and feasibility of the SMS and investigates predictors of responsiveness.

Methods: Participants were 13 to 18 year old hospitalized adolescents who were admitted due to suicide risk. Participants were randomly assigned to STEP (n=25) or TAU (n=26). Assessments were completed at baseline, 1 month and 3 month follow up intervals. Demographics, clinical symptoms, affect measures (e.g. Modified Differential Emotions Scale (mDES)), skills use (e.g. Five Facet Mindfulness Questionnaire (FFMQ)) and treatment satisfaction were among the questionnaires administered.

Results: Response rates were significantly higher in the STEP group (70.2%) than in TAU group (49.2%) (p = .004). The majority rated the SMS as helpful (84.7%) and opted for the SMS extension (52.17%). Mindfulness was the most frequently requested skill (76.2%). During the month of daily SMS, participants on average experienced a higher ratio of positive to negative emotions 73.8% of the time. Sex, age, parental income, and clinical severity had no correlation with response rates. In the STEP group, ethnic minorities had lower response rates (t=-2.1; p=.043), and FFMQ-non-judgmental sub-scores and mDES positive sub-scores were negatively correlated with response rates (FFMQ: R=-.46, p=.021; mDES: R=-.099, p=.037).

Discussion: The preliminary data indicates acceptability and feasibility of SMS skills coaching in suicidal adolescents. It is promising that adolescents with higher skills deficits and lower positive affect were especially engaged in the program.
EFFECTS OF M4 RECEPTOR MODULATION ON PARKINSONIAN MOTOR SYMPTOMS

Patrick LaChance, Kevin Bath PhD, Michael J. Frank PhD

Parkinson’s Disease is characterized by death of striatally projecting midbrain dopaminergic neurons. The resulting loss of striatal dopaminergic input leads to motor deficiencies including deficits in motor coordination and action initiation. These issues are compounded by a now disproportionate amount of striatal cholinergic innervation, contributed by cholinergic interneurons within the striatum, due to the relatively antagonistic effects of dopamine and acetylcholine on striatal neurons. A significant regulatory mechanism employed by the cholinergic neurons is autoinhibition via muscarinic M4 receptors, a negative feedback system that keeps excessive amounts of acetylcholine from being released. In the face of parkinsonian dopamine depletion, however, these autoreceptors become degraded due to overexpression of the protein RGS4. The result is increased striatal cholinergic tone, further exacerbating the dopamine-acetylcholine imbalance.

Rescuing M4 autoreceptor function could provide a useful mechanism for correcting this balance and reducing parkinsonian motor deficits. Such a hypothesis is supported by simulation of M4 modulation in the face of dopamine depletion in a computational model of basal ganglia function. However, the additional presence of M4 receptors on GABAergic striatal neurons complicates the effects of direct M4 modulation. Using a 6-OHDA mouse model and a pair of M4 modulating drugs, we seek to reveal a mechanism through which selective muscarinic modulation can help to alleviate parkinsonian motor symptoms, potentially providing a novel selective approach to anticholinergic medications in the treatment of Parkinson's Disease.
EFFECTS OF PRESTIMULUS BETA EVENTS ON TACTILE DETECTION: A HUMAN MEG AND MODELING INVESTIGATION

Robert Law, PhD, Shawn Tsutsui, Stephanie R. Jones, PhD

Beta frequency rhythms (15-30hz) are prominent throughout the brain, correlating with perception and attention as well as motor action and planning. Neural mechanisms that may link beta with perception, in particular, are not captured by contemporary models. In human somatosensory cortex, beta band magnetoencephalographic (MEG) spectral power in the prestimulus period inversely correlates with detection of a tactile stimulus. Moreover, the respective evoked potentials recorded after periods of high or low prestimulus beta power have distinguishable waveforms until about 100ms after stimulus onset. We use a detailed model of neocortical dynamics that accounts for the biophysics of MEG signal generation to provide a mechanism that links the prestimulus beta rhythms to these changes in evoked responses, offering a straightforward mechanistic account of the beta perceptual blocking effect.

Beta is typically event-like rather than temporally extended, and our results show that prestimulus spectral power differences correspond more strongly to differences in event density than to differences in individual event energy. Previous work also indicated that these beta events are largely subthreshold, driven by temporally overlapping bursts to proximal and distal dendrites from sources outside the somatosensory cortex. Taken together, these results raise the possibility that beta’s perceptual interference effect may result from the simple coincidence of an exogenously driven beta event with a tactile stimulus. We therefore model tactile stimuli occurring at several phases of a beta event as well as outside a beta event, finding that stimulation during a beta event recruits inhibition in superficial layers, which both blocks communication through these layers and generates current dipoles that qualitatively match early components of the event-related MEG signal. Our results generate testable hypotheses on the mechanisms linking beta rhythms and human sensory perception.
Patients with chronic pain are faced with limited therapeutic options. Moreover, the clinical diagnosis of pain is largely subjective. In order to identify novel therapeutics and objective diagnostic criteria, we seek to better understand the mechanisms of signal processing in the brain associated with pain. Our lab showed previously that a model of neuropathic pain enhances low-frequency power in somatosensory cortex (LeBlanc et al. 2014), and that cortical power is attenuated using a novel T-type calcium channel blocker with analgesic properties (LeBlanc et al. 2016), suggesting that cortical power correlates with neuropathic pain. Here, we test our hypothesis of cortical power modulation using EEG in three clinically relevant pain models and three classes of analgesics. Our data show increased power in primary somatosensory cortex (S1) and prefrontal cortex (PFC) in awake, freely-behaving rats with acute, inflammatory or neuropathic pain. In the neuropathic pain model, coherence between PFC and S1 is significantly increased at a late, but not early, time point during the development of nociceptive behavior. Treatment with ibuprofen (non-steroidal anti-inflammatory), pregabalin (calcium channel blocker) or mexiletine (sodium channel blocker) attenuates power and S1-PFC coherence. Our data suggest that cortical power correlates with pain, analgesia and the transition from acute to chronic pain.

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THE EFFECTS OF EARLY LIFE STRESS ON TELOMERE LENGTH: A META-ANALYSIS

Mateus Levandowski, MS, Kathryn K. Ridout, Samuel J. Ridout, Lindsay Gantz, Kelly Goonan, Daniella Palermo, Lawrence H. Price, Noah S. Philip, Audrey R. Tyrka

Background: Studies report telomere length is shortened or unchanged in persons with a history of early life stress (ELS). Telomere measurement technique, various types of early life stress studied in the extant literature, study population and size limit conclusive power in individual studies. This meta-analysis aims to clarify this relationship.

Methods: Included studies contained original data on telomere length from subjects with significant early life stress, which includes: physical or sexual abuse, parental death, homelessness or other socioeconomic environmental stressor. Studies also utilized standard methods to measure telomeres. Studies were identified from a search of Pubmed, PsycINFO, and Web of Science articles on February 1, 2016. Data regarding ELS, telomere length, demographics, and other study qualities were extracted by unblinded extractors using a structured form. Telomere measurements were converted into standardized mean differences. Primary and subgroup analyses were conducted using a continuous random effects model.

Results: 34 studies met the inclusion criteria; 27 with data available in the manuscript or provided via correspondence. The effect of ELS on telomere length, reported as Cohen’s d, was -0.274 (p < .0001, I² = 52%). Sensitivity analysis did not identify undue influence of a single study. The type of early life stress, telomere measurement technique, and source tissue were all significant moderators of the effect (all p <0.0001).

Conclusion: The effect of ELS on telomere shortening is robust. Further studies will determine whether telomere length and dynamics will serve a biomarker of general health or a primary target to evaluate physiologic sequelae and intervention efficacy.
A GENETICALLY ENCODED MARKER LABELS NEURONAL CELL-TYPES FOR BOTH LIGHT AND ELECTRON MICROSCOPIC ANALYSIS

Megan Leyrer, BS, Dan Berg; Kevin Briggman, PhD; David Berson, PhD

Constructing a connectome, a complete map of synaptic connections between neurons, is a primary goal of neuroscience. Arguably the best connectomic method uses computational 3-dimensional reconstruction of an electron microscopy (EM) volume to fully map synaptic connections with nanometer-scale resolution. However, identifying cell-types in an EM volume is far from trivial as EM techniques lack a dependable, genetic marker. Currently, some tools are available to label specific cells at the EM level, but they are either difficult to use, unreliable, or cause ultrastructure degradation unsuitable for EM analysis. As a result, to find a specific cell-type of interest in a EM volume, many, if not all, cells must be tediously reconstructed. Additionally, the acquisition and analysis of EM volumes are time consuming and produce 'big data' that is difficult to manage. To combat these challenges, researchers are forced to limit the scope of their studies to tiny volumes of tissue, increasing the probability of under-sampling and potentially excluding their cell-type of interest. In contrast to EM, Light microscopy techniques can easily exploit molecular-genetic tools to target cell-types of interest for analysis, but lack the resolution necessary to map synaptic contacts with ultrastructural detail. Therefore, an approach uniting light and electron microscopy techniques would provide a novel, powerful, tool to map the micro-circuitry of molecularly defined cell-types and target cell-types of interest for connectomic analysis.

Here we introduce a new method designed to utilize the molecular-genetic technologies available to label specific cell-types in mice for both light- and EM-level analysis. Genetic, temporal, and spatial targeting of a marker protein is achieved using a recombinant adeno-associated virus to deliver the Cre-dependent construct to a region of interest. The marker protein consists of a fluorescent protein (membrane-targeted green fluorescent protein -- mGFP) fused to an engineered ascorbate peroxidase enzyme, which is selectively expressed in virally infected, Cre-expressing cells. Preliminary results show strong expression of the marker protein in Cre-containing cells visualized using both light and electron microscopy. With this tool, we will be able to target single cells, or axon terminal fields of specific cell-types, for EM analysis. Furthermore, our method has the potential to expedite the acquisition, segmentation, and reconstruction of rare cell-types in EM volumes.
This poster describes a prototypical demonstration of a procedure that extends the basic contextual behavioral science of language and cognition into the area of therapist skill assessment and training. While expert-guided consultation and experiential training are increasingly recognized as essential ingredients in efforts to address global health challenges through clinical workforce development, public health needs remain unmet in part because the processes by which expertise is transferred are not understood with a degree of precision necessary for efficient regulation of scarce training resources. Relational Frame Theory (RFT) provides an empirically progressive analysis of symbolic behavior that precisely specifies the manipulable social conditions under which otherwise arbitrary stimuli acquire behavior regulatory functions (Hayes, Barnes-Holmes, & Roche, 2001). RFT comports with the evolution science of language development, has demonstrated clinical utility in predicting and influencing cognitive skills – including those involved in perspective-taking, and can be used to guide clinician behavior in the delivery of any psychosocial intervention (Villate, Villate, & Hayes, 2016; Wilson, Hayes, Biglan & Embry, 2014).

Therapist Agreement with Sensitivity to Context (TASC) is an assessment strategy informed by RFT whereby participant relational responses to contextual cues (i.e., videos of simulated therapy sessions) are compared to the relational responses of experts to those same stimuli. The TASC prototype presented in this poster was developed as a web-based competency assessment in Acceptance and Commitment Therapy (ACT) that was distributed to clinicians before and after participation in experiential training workshops (Long & Hayes, 2015). In TASC responses provided by 76 therapists of varying skill levels prior to ACT workshops, agreement with experts required participants to demonstrate a perspective-taking response of high relational complexity (i.e., “I see YOU seeing THAT process THEN which is DIFFERENT from THIS process I see HERE NOW”). Variability in the demonstration of this perspective-taking response was mildly associated with number of years spent practicing as a clinician and with self-rated familiarity with RFT – even while accounting for other ACT-consistent responses -- creating a regression model where R-squared = .155, p = .007. While this correlation was small, its specificity was notable, in that other therapist demographic and training-history variables did not display this relationship. This provides an empirical demonstration of the relevance of RFT to the development of clinical skill assessments that can be used to efficiently evaluate psychotherapy training practices.
THE IMPACT OF LIFETIME NON-SUICIDAL SELF-INJURY FREQUENCY ON SUICIDAL IDEATION

Roberto Lopez Jr., BA, BS

The interpersonal theory of suicide hypothesizes that for individuals to shift from experiencing suicidal desire (i.e. a yearning to die) to suicidal intent (i.e. a desire and some resolve to act on said yearning), they must first habituate to the emotional and physical pain associated with death (Joiner et al., 2012). Prior research demonstrated a link between NSSI and severity of suicidal ideation (SI), but the relationship has yet to be fully explored (Joiner et al., 2012). Therefore, the current study aimed to determine the impact of NSSI frequency on SI severity in psychiatric inpatients. In line with previous work relating NSSI frequency with the acquired capability for serious self-harm (Guan et al., 2012), lifetime NSSI frequency was hypothesized to predict SI severity in this group. A subsample of 71 inpatients from a larger study assessing suicide risk was used. Participants’ suicidality, NSSI frequency, Borderline Personality Disorder (BPD) symptomology and current Major Depressive Disorder (MDD) status were assessed using the Columbia Suicide Severity Rating Scale (CSSRS), a modified version of the Self-Injurious Thoughts and Behaviors Interview (SITBI), the McLean Screening Instrument for Borderline Personality Disorder (MSI-BPD) and the Structured Clinical Interview for DSM-IV (SCID-IV), respectively. BPD symptoms and MDD diagnosis were used as covariates in a logistic regression to account for their impact on SI severity. To test the influence of NSSI frequency on suicidal desire and intent, SI content was dichotomized: SI with desire and SI with desire & intent. The model was significant, $\chi^2(3) = 8.164$, $p < .05$, indicating that the set of predictors reliably distinguished between the two SI categories. In addition, it explained 18.2% (Nagelkerke R$^2$) of the variance and correctly classified 84.5% of cases. The Wald criterion demonstrated that lifetime NSSI frequency made a marginally significant contribution to prediction ($p = .051$). Neither MDD nor BPD symptomology significantly predicted SI severity. Individuals with higher frequencies of NSSI were 3.8 times more likely to endorse SI with desire & intent rather than SI with desire. Given our preliminary trend-level results, it appears as if NSSI frequency influences SI severity in individuals with concurrent MDD diagnoses and BPD symptoms. Therefore, it may be important to assess NSSI frequency in this subgroup and treat it to decrease the odds of acute SI.
Suicide is the third leading cause of death for adolescents (Bridge et al., 2008) with recent survey data showing 15.8% of 9-12 graders reporting past-year suicidal thoughts (Center for Disease Control and Prevention, 2012). The American Psychiatric Association and American Academy of Child and Adolescent Psychiatry have identified substance abuse as a major risk factor for adolescent suicide (Zhang and Wu, 2014). Use of alcohol, tobacco, and marijuana have been linked to increased suicidal ideation (Kim and Kim, 2010; Miller et al., 2011; Roberts et al., 2010; Swahn, 2010; Wichstrom, 2000; Zhang and Wu, 2014) and research has also found higher frequency and earlier onset substance use in adolescents who score high in risk taking behavior on a computerized behavioral task (Kim-Spoon et al., 2016). However, more research is needed to investigate how this relationship varies across different substances and how suicide and substance use relate to risk taking behavior. Participant were recruited from a large study at Bradley Hospital (R01MH105379, PI Nugent), exploring how (epi)genetics and social context affect an adolescent’s transition back into their community after an inpatient hospitalization for suicidal thoughts and behavior. The current descriptive study characterizes substance use measured by the Adolescent Alcohol and Drug Involvement Scale (AADIS) and the Simple Screening Instrument for Alcohol and Other Drugs (SSI-AOD), parent’s perception of their child’s alcohol using the Child Behavioral Checklist (CBCL), and risk taking behavior assessed with a computerized driving task (the stoplight task). The initial sample of 21 adolescents (18 females, 3 males) varied in age from 13-18 years (M=15.10, SD=1.81). Nearly 10% of participants reported their ethnicity as Hispanic or Latino. The majority of participants reported their ethnicity as White (81%), and the remainder reported their ethnicity as Black or African American (4.8%) or more than one race (9.5%). Nearly half of the adolescent participants (42.9%) reported engaging in some type of substance use, primarily alcohol and marijuana. Concordance between parent perceptions of their adolescent’s alcohol and drug use with adolescent self-reported use, varied across families. Out of the 4 adolescents reporting drug use other than tobacco and alcohol, 75% of parents were not aware that their adolescent was engaging in nonmedical substance use. Out of the 7 adolescents reporting alcohol use, 57% of parents reported that their adolescent was not drinking without parent approval. Among adolescents reporting any alcohol or substance use (N=9), 66.7% reported obtaining alcohol or drugs from friends, with most adolescents first using after the age of 15. These findings point to the importance of intervening early on given that adult substance abuse is strongly associated with early age drinking onset (Dawson et al., 2008). Although preliminary findings did not demonstrate differences in risk taking behavior based on substance use history, results are limited by a small sample size. Future research examining the associations between substance use, risk taking, and suicide will inform targeted interventions for adolescents suffering from substance use disorder with concurrent suicidal ideation.
THE ROLE OF ELABORATION IN PROCESSING PAST NEGATIVE EVENTS AND ITS IMPACT ON DYSFUNCTIONAL ATTITUDES

Eishita Manjrekar, BA, BS, Howard Berenbaum, PhD; Wenting Mu, MA

Dysfunctional attitudes are associated with depressive episodes and having a vulnerability to depression. In a sample of 398 college students, the present study examined: (a) how different thinking styles—characterized by varying levels of elaboration—influence dysfunctional attitudes when thinking about past negative events; and (b) how reflection and rumination might moderate this effect. Participants were assigned to a high elaboration, low elaboration, or control condition. In the high elaboration and low elaboration conditions, participants recalled past negative events through differentially elaborative writing tasks. In the control condition, participants completed a neutral writing task. Dysfunctional attitudes were measured following the manipulation using the Dysfunctional Attitudes Scale (DAS). Low elaboration was associated with greater dysfunctional attitudes. Furthermore, the impact of elaboration was particularly strong among individuals with high levels of reflection and rumination.
SLEEP HYGIENE AND SLEEP OUTCOMES IN A SAMPLE OF URBAN CHILDREN WITH AND WITHOUT ASTHMA

Sarah Martin, MA, Julie Boergers, PhD; Elizabeth McQuaid, PhD; Sheryl Kopel, MSc; Ronald Seifer, PhD; Robert Klein, MD; Daphne Koinis-Mitchell, PhD

Objective:
Sleep plays an important role in children’s health and sleep hygiene is an integral component to optimal sleep health. Socioeconomic disparities exist with respect to children’s sleep health and managing asthma may complicate sleep hygiene behaviors. This study aimed to assess sleep hygiene and environments of urban children with and without persistent asthma. We hypothesized that the added challenge of managing asthma would negatively effect sleep hygiene and ultimately sleep health in urban children.

Methods:
Data are from a larger study assessing asthma and sleep quality in urban children (R01 HD057220; PI, Koinis-Mitchell). Children with (N=216) and without asthma (N=130) from four urban districts who were 7-9 years old and from Black, Latino, or Non-Latino White backgrounds were included. Census block membership determined each family’s Neighborhood Risk Index. Poverty status was determined by an income-to-needs ratio. Parents completed valid sleep hygiene and sleep behavior questionnaires. Sleep duration was assessed via actigraphy over a 4-week period. Daytime sleepiness was assessed using a subscale of the Children’s Sleep Habits Questionnaire.

Results:
Healthy children had more optimal sleep hygiene (F(1,338) = 4.46, p=.04), but hygiene did not differ across groups when controlling for poverty (F(2, 315) = 2.35, p = .13). Higher neighborhood risk (B=-.04, p<.01) and poverty (B=-.16, p=.02) predicted poorer sleep hygiene above and beyond health condition. In children with asthma, controlling for neighborhood risk, sleep hygiene predicted sleep duration (B=.25, p<.001) and daytime sleepiness (B=-2.56, p<.001). In healthy children, sleep hygiene predicted daytime sleepiness (B=-1.75, p<.001), but did not predict sleep duration (B=.08, p>.05).

Conclusion:
Although the added stress of managing asthma may complicate sleep hygiene routines, urban stressors such as poverty and neighborhood risk may ultimately drive sleep hygiene. Consistent with past findings, hygiene promoted good sleep health in children with and without asthma even in the context of urban stressors and sleep hygiene may be more salient for children with asthma who are already at risk for poorer sleep. Examination of treatments targeting sleep hygiene behaviors in urban children is warranted.
CHARACTERIZING THE EFFECTS OF TSC1 MUTATIONS ON THALAMIC CIRCUIT FUNCTION

Rosa Martinez-Garcia, BS, Jeannie Smith, Shane R. Crandall, Mark Zervas, Barry W. Connors

Tuberous Sclerosis (TSC) is a developmental genetic disorder caused by mutations in TSC1 and/or TSC2. Neurocognitive signs in TSC patients include epilepsy, intellectual disability, and autism, but the altered cellular mechanisms underpinning TSC are poorly understood. One brain region implicated in the pathology of some TSC patients is the thalamus. Thalamic relay nuclei are functionally distinct clusters of excitatory neurons that project to the neocortex. Relay neurons also excite neurons of thalamic reticular nucleus (TRN), which in turn inhibit relay neurons. The laboratory previously generated a mouse model in which Tsc1 was deleted in ~70% of relay neurons on E12.5 (Normand et al., Neuron, 78:895, 2013). This mosaic deletion was sufficient to disrupt thalamic circuits and caused aberrant repetitive grooming and seizures. An unresolved question is how functional neural circuits are affected in this model. We tested whether mosaic Tsc1 deletion alters the intrinsic properties, synaptic function, and synaptic architecture of thalamic relay neurons. We first replicated previous results (Normand et al., 2013), confirming that Tsc1\(\Delta/\Delta\) (Thal) relay neurons have lower input resistance and reduced excitability. Action potentials of Tsc1\(\Delta/\Delta\) (Thal) neurons have larger amplitudes and faster rates of depolarization and repolarization. When firing in tonic mode, Tsc1\(\Delta/\Delta\) (Thal) neurons have shallower frequency vs. stimulus current slopes than those of wild type relay neurons. When firing in bursting mode, Tsc1\(\Delta/\Delta\) (Thal) neurons have increased intra-burst frequency compared to wild type relay neurons. Tsc1\(\Delta/\Delta\) (Thal) neurons also have ectopic expression of the calcium binding protein parvalbumin, which may affect thalamic physiology (Normand et al., 2013). Interestingly, Tsc1 deletion in relay neurons decreased the frequency of miniature excitatory postsynaptic currents and reduced the paired pulse depression of evoked synaptic responses in neurons of the TRN. Our results suggest that altered neurotransmission is likely caused by changes in presynaptic function, such as reduced release probability. Circuit dynamics can also be altered by changing the number and distribution of synapses. However, we observed no significant differences in excitatory or inhibitory synaptic markers in relay neurons or excitatory synaptic markers in TRN neurons. We are now testing how mosaic deletion of Tsc1 in relay neurons affects synaptic strength, dynamics, and network functions of the relay neuron-TRN circuit.
MATERNAL DEPRESSION SEVERITY WITH THE USE OF ANTIDEPRESSANT MEDICATION WITH AND WITHOUT HYPNOTIC TREATMENT: EFFECTS ON NEWBORN NEUROBEHAVIOR

Jennifer Mattera, BA, Kristen Stone, PhD, Cynthia Miller-Loncar, PhD, Dawn Johnsen, BA, Amy Salisbury, PhD

Objective: The prenatal use of psychotropic medications and maternal depression is associated with altered newborn neurobehavioral development. Additional use of hypnotic medication may contribute to lower depression severity. The purpose of this study was to examine the associations between prenatal antidepressant medications, with and without additional hypnotic use, maternal depression severity, and newborn neurobehavior in women diagnosed with a unipolar mood disorder during pregnancy.

Methods: 104 depressed, pregnant women were divided into three groups according to their prenatal medication use: 1) none (NoMeds, N=49); 2) antidepressants only (AD, N=40); 3) antidepressants plus hypnotics (medications taken at night for sleep disturbance: zolpidem, trazadone, amitriptyline; AD+HYP, N=15). Infant behavior was assessed at five time points during the first postpartum month (Days 2, 4, 7, 14, 30) using the NICU Network Neurobehavioral Scale (NNNS). Generalized Estimating Equations and cross-correlations were used to examine the effect of medication group, depression severity during pregnancy and the postpartum period, and time on infant neurobehavioral development.

Results: Women taking AD+HYP medication had higher depression severity scores in the 2nd and 3rd trimester than AD and NoMeds. However, they showed the greatest decline in scores from 3rd trimester to 1 month postpartum. There were significant group differences in the trajectory of newborn attention (p<.05), quality of movement (p<.02), and stress signs (p<.003) from birth through 30 days after delivery. The magnitude and direction of the effect between medication group and time was dependent upon depression symptom severity.

Conclusion: Collectively the pattern of results suggest that decreased depressive symptoms in the context of antidepressant medication treatment is associated with improved infant neurobehavioral outcomes by 30 days post-birth.

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PREDICTORS OF THE TRANSITION FROM SUICIDE IDEATION TO FIRST SUICIDE ATTEMPT OVER 12 MONTHS

Alexis May, MA, Sarah A. Arias, PhD, Edwin Boudreaux, PhD, Carlos Camargo, MD, DrPH, Ivan Miller, PhD

Previous suicide attempts are one of the strongest predictors of future attempts, however less is known about what predicts the transition from suicidal ideation to a first suicide attempt. This question is particularly important, as the majority of people who consider suicide never act on their thoughts (Kessler, 1999; Nock, 2012). Thus identifying which individuals with suicidal ideation are at greatest risk of attempting suicide is critical. Emergency department (ED) providers are regularly tasked with making this determination, though existing research provides limited information to assist in that process. Most evidence comes from cross-sectional studies and community studies (Borges et al., 2006; Borges et al., 2010) or predicts transition to attempt over long time periods (Conner et al., 2007; May et al., 2012).

The current study examined to what extent demographic, diagnostic, quality of life, or suicidality history variables predict the transition from presenting at an emergency department with suicidal ideation to a first time suicide attempt in the 12 months after the index ED visit. As a point of comparison, predictors of suicide attempts in the 12 months after the index ED visit among those with a history of suicide attempts were also examined.

Data from the Emergency Department Safety Assessment and Follow-up Evaluation (ED-SAFE) study were analyzed. The study consisted of 1,376 suicidal individuals presenting to 8 emergency departments across the country. They were followed for 12 months through telephone follow-up assessment (6, 12, 24, 36, and 52-weeks) and medical chart review (6 and 12-months). Of the participants, 402 presented with suicidal ideation, but without a history of suicide attempts and 974 reported a history of suicide attempt. Suicidality was assessed with the Columbia Suicide Severity Rating Scale (Posner et al., 2009).

Over the 12 month follow up period, 14% of participants with baseline suicidal ideation but no history of suicide attempt (i.e., ideators) and 24% of those with a previous history of suicide attempt (i.e., past attempters) reported making an attempt. Among ideators, less education (OR = 2.38), positive blood alcohol level (OR = 2.88) or toxicology screen (OR = 2.08) at baseline, ideation lasting over 1 hour at a time (OR = 2.25), and a history of interrupted suicide attempts (OR = 1.80) were associated with reporting a first time attempt during the 12-month follow-up period. Among past attempters, different factors predicted attempting during the 12 months after the index ED visit, these included being white (OR = 1.55), non-Hispanic (OR = 1.69), higher baseline suicide ideation severity (OR = 1.40), identifying a suicide method at baseline (OR = 3.87), having made a suicide plan at baseline (OR = 1.47), and lifetime and current nonsuicidal self-injury (NSSI; OR = 1.61-1.63). A lifetime history of many mental health diagnoses predicted attempts in both groups, with OR’s ranging from 1.68 to 2.56.

Results indicated that risk factors for transitioning to a first attempt differed from those for engaging in repeat attempts. Specifically, reporting less education, being under the influence of substances at the index ED visit, longer periods of ideation and a history of interrupted attempts were important predictors of first attempts, while race, ethnicity, having more severe suicidal ideation at baseline, thinking of a suicide plan and method, and engaging in NSSI were predictors of re-attempting. The current findings suggest that risk for suicide attempts may vary depending on suicide attempt history. The implication on risk assessment in emergency setting will be discussed.
Cells have a complex and multi-component protein quality control network to maintain the cellular proteome and ensure that proteins are correctly folded. Molecular chaperone proteins are integral players in protein quality control, helping to fold nascent polypeptides, refold misfolded or partially unfolded proteins, and target irreversibly misfolded proteins for degradation by the proteasome. The superfamily of AAA+ (ATPases associated with diverse cellular activities) proteins includes a diverse set of ATPases that share similar domain organization. This protein family also includes Hsp100 proteins, such as the chaperone Hsp104, which can disassemble amyloid fibers, and Lon, which has unfolding and proteolytic activities. Hsp104 is an ATP-dependent disaggregase that is involved in yeast prion propagation from mother to daughter cells and can mediate prion curing. Moreover, overexpression of Hsp104 cures yeast cells of mature amyloid fibers by catalyzing their disassembly. In the yeast model system [PSI+], we are studying amyloid formation by Sup35, a translation termination factor that aggregates to form amyloid fibers. We have developed a quantitative colorimetric assay, based on the accumulation of the metabolite 5-aminoimidazole ribotide, to distinguish between cells that contain amyloid and cells that have been cured of amyloid. To investigate substrate targeting and amyloid disassembly by Hsp100 family members, we have expressed native and mutagenized Hsp104 and Lon in the yeast [PSI+] model system. We are currently screening mutants for gain- and loss-of-function mutations that lead to altered prion propagation and amyloid clearance. This study provides new insight into chaperone-mediated disassembly of amyloids, which have been implicated in a variety of protein folding disorders, such as Alzheimer’s disease and Parkinson’s disease.
Target selection is strongly influenced by recent experience. For example, responses are facilitated when target features, such as color, are repeated (priming of pop-out; POP). Previous research indicates that POP leads to repetition suppression of the BOLD signal in regions associated with top-down attention, including the frontal eye fields (FEF) and intraparietal sulcus (IPS), as well as the lateral occipital cortex and fusiform gyrus. During a perceptual task, activation in these regions decreased when target colors were repeated compared to when they switched (Kristjansson et al., 2007). The authors interpreted this result in terms of perceptual reorienting, such that additional resources are required to switch attentional states when the search display changes. Importantly, however, many everyday tasks often involve multiple types of actions with different effectors (e.g., eye and hand). For instance, cooking dinner requires looking for and performing suitable actions toward specific ingredients. Here, we investigated whether the brain networks involved in this target selection bias are specific to the response used (effector-dependent) or if any of these regions impact target selection generally, regardless of the response mode (effector-independent). Using event-related fMRI paired with a color-oddity search task, we investigated the neural basis POP when participants were required make a saccade or reach to the odd colored target. The saccade and reach tasks were scanned in separate runs and participants maintained fixation with the effector not used for that run. We found that repeating target colors produced repetition suppression in brain areas involved in color processing (i.e., fusiform gyrus) and bottom-up attentional capture (i.e., right insula), and this was independent of the effector used. In addition to this effector-independent repetition suppression, we also identified a brain area involved in the effector-independent repetition enhancement. We observed that in the right superior parietal lobule, an area implicated in visuomotor coordination, showed increased activity when target colors were repeated for both saccades and reaches. We suggest that increased activity within this motor area might be driven by facilitated motor planning led by color priming. Furthermore, we found an interaction driven by repetition enhancement for saccades, but not reaches, in the right inferior parietal lobule, which has been shown to increase in activity with saccadic accuracy. In sum, we find that areas associated with attentional capture and color processing exhibit repetition suppression effects of color priming, independent of effector. Moreover, we demonstrate that POP produces both effector-specific and effector-independent repetition enhancement in regions related to motor control. Thus, our results suggest that the neural correlates of POP differ for perception and goal-directed action and can also be modulated by the effector used.
DIMINISHED AUTONOMIC RESPONSE TO SOCIAL PARTNERS IN INFANTS LATER DIAGNOSED WITH AUTISM SPECTRUM DISORDER

Carolyn McCormick, PhD, Stephen J. Sheinkopf, PhD, Todd P. Levine, MD, Linda Lagasse, PhD, Barry M. Lester, PhD

Background: The core behavioral symptoms of autism spectrum disorder (ASD) emerge developmentally and are not reliably observed within the first year of life (Jones et al., 2014). Even sensitive measures, like those generated from eye-tracking techniques, have not yet identified consistent reliable differences between children with and without ASD until the second year of life. Biological measures, such as respiratory sinus arrhythmia (RSA), hold great potential for detecting predictors of an ASD outcome before behavioral differences emerge. RSA is a measure of heart rate variability that indicates the body’s readiness to engage with environmental stimuli (Grossman & Taylor, 2007). RSA response patterns have been linked to social functioning in children with ASD (Sheinkopf et al., 2009). Differential patterns of RSA response may be part of the underlying biology of ASD and, therefore, be detectable within early infancy.

Objectives: To identify early patterns of behavioral and RSA responses in infants later diagnosed with ASD.

Methods: Two groups of infants were compared: infants with an ASD outcome (N = 8) and matched controls (N = 186). Infants were seen as part of their participation in the Maternal Lifestyle Study (MLS), a longitudinal study of the effects of drug exposures on long term developmental outcomes. At four months infants completed the face-to-face still-face (FFSF) protocol with their mother. The FFSF begins with the caregiver and infant in face to face interaction (play), followed by a period when the caregiver is instructed to face the infant relatively expressionless (still face), and ending with a reunion episode of normal face to face interaction (reunion). Infants were also observed in a face to face play interaction with a novel female examiner immediately following the caregiver interaction (stranger). ECG was collected to measure RSA. ECG post-processing incorporated automated artifact detection and correction routines. RSA was calculated from the resulting “cleaned” time series data using Porges’ method. Infant behaviors (passive-withdrawn, protest, object-environment, social monitor, and social positive engagement) were coded from video.

Results: A general linear mixed model of the FFSF paradigm revealed no significant group differences on RSA during interactions with the mothers between infants with an ASD outcome and controls. Both groups of infants demonstrated a decrease in RSA during the still face phase compared to the play phase (p <.05). No significant behavioral differences were detected. However, in response to play with a stranger, an ANOVA revealed that the infants with an ASD outcome had lower RSA than controls (p < .05). During the interaction with a stranger, lower RSA response was associated with more protesting behaviors (p <.01), whereas higher RSA response was associated with more social monitoring (p = .001).

Conclusions: Infants later diagnosed with ASD exhibited greater autonomic reactivity during interactions with an unfamiliar adult than did comparison infants. There were no differences between groups during interactions with mothers. Physiological dysregulation, as indicated here by a lower RSA response, may function as an early biological marker of difficulties with social interactions before differences in behavioral responses are detectable.
BIOLUMINESCENT OPTOGENETICS FOR THALAMIC BURST REGULATION

Elizabeth McDonnell, BA, Scott Cruikshank, PhD, Shane Crandall, PhD, Brian Higashikubo

The thalamus relays subcortical primary sensory information to cortex and serves as a hub for information flow between cortical areas. The thalamic reticular nucleus (TRN) sends inhibitory projections to relay cells in the thalamus and thus is an important mediator of the thalamocortical and cortico-thalamic-cortical dynamics that regulate normal perception and arousal. Thalamic cells can fire in burst or tonic mode; firing mode regulates normal information transmission but its dysregulation can lead to pathological states like epilepsy. The role of thalamocortical dynamics in these processes makes it an attractive target for modulation. Previous work in the lab describes a method for traditional optogenetic control of the TRN using viral expression of the light-sensitive cation channel ChR2. Using traditional optical stimulation and extracellular recording, the influence of stimulus duration on spike and burst probability was described for about 100 well isolated TRN neurons. We are developing a method for non-invasive optogenetic control of cells of the thalamus and TRN using bioluminescence to drive optogenetic elements. Bioluminescence is produced by the interaction of a bioluminescent enzyme, or luciferase, with its light-producing luciferin substrate. We have virally expressed a molecule of Gaussia luciferase tethered to the light-sensitive cation channel Volvox channelrhodopsin-1 (VChR1) to the TRN of wild-type mice. When activated by its luciferin coelenterazine (CTZ), this “luminopsin” uses bioluminescent light to drive VChR1 in expressing cells. In vitro whole cell recordings describe a small reversible depolarization following bath application of CTZ, and preliminary in vivo multielectrode data shows increased spiking in TRN following intraperitoneal injection of CTZ while simultaneously recorded putative relay cells show a decrease in firing rate, but an increase in burst rate after the same CTZ application. Ongoing and future experiments aim to systematically characterize this activity and manipulate the luminopsin to control the switch between burst and tonic modes in expressing TRN cells. This work provides proof of concept for the use of luminopsins as non-invasive drivers of optogenetic elements and could allow optogenetic modulation of thalamocortical circuits without external light delivery.
DEPRESSION AND ANXIETY MODERATE SEXUAL PARTNER CONCURRENcy INTENTIONS-BEHAVIOR AMONG STI CLINIC PATIENTS

Larissa McGarrity, MS, Theresa E. Senn, PhD, Jennifer L. Walsh, PhD, Lori A.J. Scott-Sheldon, PhD, Kate B. Carey, PhD, Michael P. Carey, PhD

Background: Sexual risk-reduction interventions are typically guided by theories that specify cognitive determinants of behavior, such as behavioral intentions. These theories are supported in epidemiologic research, and interventions shaped by these theories demonstrate efficacy, yet the relation between intentions and subsequent behavior is weaker than hypothesized. Research explaining the intentions-behavior gap can help to strengthen intervention designs.

Methods: Longitudinal data from a trial of STI clinic patients (N = 397; 56% male; 67% African-American, 19% White, 8% Latino; age: M = 28.49, SD = 9.47) were used in the analyses. Binary logistic regression tested whether the association between intentions and behavior for concurrent sexual partners differed based on depression/anxiety, as measured by the PHQ-4. Analyses controlled for demographic variables (i.e., sex, ethnicity, income) and partner concurrency at baseline.

Results: Intentions for partner concurrency were not associated with symptoms of depression/anxiety, r = .022, p = .629. However, symptoms of depression/anxiety moderated the association between baseline intentions and behavior at 3-month follow-up, B = -.435, SE = .136, p = .001. Among patients with fewer depressive and anxious symptoms (1 SD below the mean), lower intentions for partner concurrency were associated prospectively with reduced odds of partner concurrency, B = .621, SE = .179, p = .001; among patients with greater depressive and anxious symptoms (1 SD above the mean), intentions did not predict concurrency B = -.097, SE = .170, p = .569.

Conclusions: Psychologically distressed and non-distressed patients do not differ in the strength of their intentions for sexual partner concurrency; however, among those who are distressed, intentions are less likely to translate into subsequent behavior. Interventions that primarily target the hypothesized cognitive determinants of sexual behavior (e.g., behavioral intentions) may be less effective at altering health behaviors among vulnerable populations. Consideration of anxiety and depression in comprehensive risk-reduction programs may enhance intervention outcomes. Future research should examine why psychological distress appears to disrupt the intention-behavior link.
Gamma knife lesions within the anterior limb of the internal capsule are used for the treatment of severe, intractable obsessive compulsive disorder after all conventional treatments have failed. The lesions are designed to ablate aberrant striato-cortico-striatal circuitry involved in OCD. Our research team has been intensively studying this procedure since 1993. Originally, a single pair of bilateral lesions was made in the middle of the anterior limb of the internal capsule (IC) in the coronal plane. Results of that “single-shot” procedure did not appear promising after an average of nine months. In an attempt to improve therapeutic benefit, this same group of patients received a second pair of lesions, ventral to the first. After this “second shot,” patients demonstrated improvements gradually over the subsequent months. Based on these outcomes, the method used from the late 1990s to 2010 involved making two bilateral lesions in the lower half of the capsule 8-10mms rostral to the anterior commissure using a 4mm collimator and 180 Gray for each shot. After this “double-shot” procedure, there was meaningful clinical improvement in about 60% of these otherwise untreatable and functionally disabled OCD patients. Given that it appeared that the lower ventral “shot” of this procedure was necessary for clinical improvement, in the context of adverse effects in a few patients who had the “double-shot” procedure, some sites have started doing only the “single-shot” lesion in the ventral portion of the IC. Data from macaque histological tracings as well as from diffusion studies in humans have begun to identify the structural pathways coursing through the IC. However, there are no studies examining the functional connectivity of this region. Using publicly-available healthy control data from the Human Connectome Project, we examined differences in resting state functional connectivity between the dorsal and ventral regions of the internal capsule, using masks that are consistent with optimal placement of gamma knife lesions (either “double-shot” covering the bottom 2/3 of the IC, or “single-shot” covering the bottom 1/3 of the IC in the coronal plane). Analyses were carried out examining the relationship between these areas of the IC with the whole brain, as well as with delineated regions within the ventral prefrontal cortex. Results indicated that, consistent with structural connectivity findings, there is overlap between the connectivity of the dorsal and ventral IC lesions, likely due to individual variability. As expected, lesioning only the ventral IC spared a number of functional connections from the IC to the inferior and middle frontal gyrus, middle and lateral temporal gyrus, and posterior parietal regions. Furthermore, there were significant correlations between both internal capsule regions and the ventral prefrontal cortex (PFC) seeds, though there were more connections between the ventral IC and ventral PFC seeds. Understanding the connectivity of this region may help us improve our current targeting, as well as provide information about possible cortical targets for less invasive neuromodulatory treatments.
MPX-004 and MPX-007: NEW PHARMACOLOGICAL TOOLS TO STUDY THE PHYSIOLOGY OF NMDA RECEPTORS CONTAINING THE GluN2A SUBUNIT

Frank Menniti, PhD & Chris Fanger, PhD

GluN2A is the most abundant of the GluN2 NMDA receptor subunits in the mammalian CNS. Physiological and genetic evidence implicate GluN2A-containing receptors in susceptibility to autism, schizophrenia, childhood epilepsy and neurodevelopmental disorders such as Rett Syndrome. However, GluN2A-selective pharmacological probes to explore the therapeutic potential of targeting these receptors have been lacking. Here we disclose a novel series of pyrazine-containing GluN2A antagonists exemplified by MPX-004 (5-(((3-chloro-4-fluorophenyl)sulfonamido)methyl)-N-((2-methylthiazol-5-yl)methyl)pyrazine-2-carboxamide) and MPX-007 (5-(((3-fluoro-4-fluorophenyl)sulfonamido)methyl)-N-((2-methylthiazol-5-yl)methyl)pyrazine-2-carboxamide). MPX-004 and MPX-007 inhibit GluN2A-containing NMDA receptors expressed in HEK cells with IC50s of 79 nM and 27 nM, respectively. In contrast, at concentrations that completely inhibited GluN2A activity these compounds have no inhibitory effect on GluN2B or GluN2D receptor-mediated responses in similar HEK cell-based assays. Potency and selectivity were confirmed in electrophysiology assays in Xenopus oocytes expressing GluN2A-D receptor subtypes. Maximal concentrations of MPX-004 and MPX-007 inhibited ~30% of the whole-cell current in rat pyramidal neurons in primary culture and MPX-004 inhibited ~60% of the total NMDA receptor-mediated EPSP in rat hippocampal slices. GluN2A-selectivity at native receptors was confirmed by the finding that MPX-004 had no inhibitory effect on NMDA receptor mediated synaptic currents in cortical slices from GRIN2A knock out mice. Thus, MPX-004 and MPX-007 offer highly selective pharmacological tools to probe GluN2A physiology and involvement in neuropsychiatric and developmental disorders.
BACKGROUND: Cognitive impairment is common in heart failure (HF) and reduced functional capacity is one potential mechanism for the observed deficits. Higher levels of functional capacity have been associated with better cognition in HF but few studies have examined the impact of structured exercise programs. In some individuals, HF severity may prohibit sufficient physical exertion to derive functional and cognitive benefit from structured exercise programs. Examination of alternative interventions is therefore warranted.

Inspiratory muscle weakness has been implicated as an underlying mechanism of exercise intolerance in HF and thus may be indirectly associated with HF-related cognitive impairment. Inspiratory muscle training (IMT) is a well-established treatment that increases respiratory muscle strength through repeated inspiratory exercise. IMT has been consistently associated with improved functional capacity in HF at levels comparable to those seen with structured exercise programs, though no study to date has examined the potential effects of IMT on cognition in HF.

METHOD: This pilot study examines the effects of IMT on cognition and functional capacity in patients with HF through a 6-week sham-controlled IMT intervention. Participants are older veterans with clinically stable HF receiving care at the Providence VAMC. Baseline visit involves determination of participants’ maximum inspiratory pressure (MIP; a measure of functional capacity) followed by randomization to active- or sham-IMT. Active treatment is defined as setting the IMT device to a resistance of 30% MIP; sham is defined as setting the IMT device to a resistance of 5% MIP or lowest device setting. Participants are asked to complete 30-minutes of daily at-home breathing exercises and to keep a log of this. Participants attend weekly study visits to assess MIP and adjustments are made accordingly to their IMT device. Neuropsychological testing is completed at study baseline and end of study. It is hypothesized that those who complete 6 weeks of active-IMT will show improvements in MIP and neuropsychological testing at follow-up, and that cognition will improve as a function of gains made in functional capacity.

CURRENT STATUS: Ten participants have been screened to date; 7 have been randomized: 5 to active-IMT, 2 to sham-IMT. Five participants have completed the study fully (4 active-IMT, 1 sham-IMT) with no adverse events. The 1 sham participant may have received active treatment due to markedly low MIP. Two participants withdrew due to non-serious expected adverse events. The current small sample size precludes formal statistical analyses due to inadequate power. Graphical representation of pertinent findings are presented. Preliminary findings also indicate that a 6-week IMT intervention is a feasible and generally well-tolerated at-home intervention for older veterans with HF.
Deep Brain Stimulation (DBS) is frequently performed to treat Parkinson Disease (PD), which is the second most common neurodegenerative disease of the central nervous system after Alzheimer’s disease [1]. In recent years, adaptive, closed-loop DBS (aDBS) has been proposed to overcome the drawbacks [2] of conventional, open-loop DBS, which include side effects, battery consumption and manual parameter settings. In conventional methods [3], motor deficit is typically assessed by the Unified Parkinson's disease rating scale (UPDRS) and discrete movement tests. These, however, are subjective tests, that prevent the identification of more subtle behavioral motor markers. In addition, they measure un-naturalistic and discontinuous movements that may not generalize to the patients’ daily continuous limb movements. Lastly, using these tests makes it difficult to quantify varying motor impairments on a short time scale (i.e. several milliseconds to seconds). One requirement to implement aDBS is to identify specific neural features that can be reliably associated with time-varying continuous behavioral motor performance. In this study, we designed such a motor task, in which subjects track a moving target with a cursor controlled by a joystick. Two performance metrics were identified, including tremor value (TV), which quantifies physiological tremor, and vector difference (VD), which quantifies how well the patient tracks the moving object on an instant-by-instant basis. We observed that these metrics differentiate motor performance among healthy control subjects, patients in clinic, and intra-operative patients. The classification analysis between good and poor motor performance identified by VD and TV, demonstrated that the broad band frequency features (1-50 Hz) of local field potential (LFP) predicts behavioral motor performance with 70% and 76% accuracy, respectively.
EXPERIMENTALLY INDUCED MENTAL STRESS IS ASSOCIATED WITH MALADAPTIVE CARDIAC AUTONOMIC CONTROL IN PATIENTS WITH METABOLIC SYNDROME

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Metabolic syndrome (MetS) comprises metabolic abnormalities that substantially increase risk for chronic illnesses. Stress is closely linked to MetS; pathophysiological models often include dysregulated physiological and psychological stress responses. In an effort to further clarify the relationship between autonomic dysregulation and metabolic abnormalities, we used ambulatory impedance cardiography to examine indicators of cardiac autonomic control (CAC) in a sample of 50 adult primary care patients with and without MetS (N=25). Indices of independent sympathetic and parasympathetic cardiovascular control were assessed in the context of two psychological stressors (i.e., mental arithmetic and a health-related interview) and compared between experimental groups. We also calculated interdependent CAC measures, including cardiac autonomic balance (CAB; a measure of SNS and PNS reciprocity) and cardiac autonomic regulation (CAR; a measure of SNS and PNS co-activity) for additional between-group comparisons. These measures were then used to predict health status, and were examined in relation to self-reported treatment adherence and health behavior. Primary results revealed significant differences patterns of CAC between the two experimental groups. In particular, we noted greater sympathetic reactivity in MetS participants when discussing diet and medication concerns, F(14, 29) = 2.348, p = .025, partial \( \eta^2 = .531 \). In addition, CAR scores were higher among Met patients when discussing medication concerns, indicating greater co-activity in sympathetic and parasympathetic activity during this task, F(4, 172) = 4.641, p = .001, \( \eta^2 = .504 \). We also found that CAB scores were lower among MetS patients when discussing daily stressors, indicating imbalance between sympathetic and parasympathetic activation during this task, F(4, 172) = 2.619, p = .037, \( \eta^2 = .404 \). Additional findings offer preliminary evidence of a relationship between CAC and quality of life, and between CAC and medication adherence. These results provide further evidence that stress may be implicated in the maintenance of MetS through variations in CAC. Implications for future research are discussed including focus on prospective data collection in the service of enhancing diagnostic procedures.
THE RELATION BETWEEN AUTISM SYMPTOM SEVERITY AND FAMILY HISTORY OF PSYCHIATRIC AND NEURODEVELOPMENTAL DISORDERS

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Background: It is known that Autism Spectrum Disorder (ASD) is associated with family history of psychiatric disorders in addition to rates of autism and other neurodevelopmental disorders. Although epidemiological studies support a link between autism and familial mood and anxiety disorders (Smalley, McCracken, & Tanguay, 1995), studies disagree about which psychiatric disorders are most prevalent in families of those with ASD. Research shows a strong relation between positive family history and higher IQ or increased functional ability (Mazefsky, Williams, Minshew, 2008; Robinson, et. al 2014). However, studies have yet to examine how family psychiatric history may correlate to measures of autism severity.

Objective: To investigate whether the presence of psychiatric and neurodevelopmental disorder history in first- and second-degree relatives in a population of children and adolescents diagnosed with ASD is related to autism severity in the proband.

Methods: Participants were children and adolescents with ASD (n = 338, 3-17 years old) selected from a state-wide autism patient registry (80.5% male, mean age 9.94 years). ASD diagnoses were confirmed by the clinician administered Autism Diagnostic Observation Schedule (ADOS). Family history of psychiatric and neurodevelopmental disorders was obtained through parental interviews. The presence of psychiatric and neurodevelopmental disorders in first- and second-degree relatives were coded dichotomously and summed to create four composite variables (i.e, sum of psychiatric disorders and neurodevelopmental disorders in 1st and 2nd degree relatives). The psychiatric family history composite consisted of twelve disorders (e.g., mood and anxiety disorders) and the neurodevelopmental disorder composite consisted of ten disorders (e.g., ASD, Intellectual Disability). Estimates of proband symptom severity were based on the caregiver-completed Social Responsiveness Scales, 2nd Ed. (SRS-2) total T scores and the ADOS standardized severity score. Gender-controlled linear regression was used to investigate the relationship between family history of psychiatric and neurodevelopmental disorders and autism severity.

Results: First-degree family history of psychiatric disorders was related to increased symptom severity on the SRS-2 measure (β = .193, p = 0.001). There was no significant relation between first- or second-degree family history of neurodevelopmental disorders and SRS-2 severity measure, nor a significant relation between family history of neurodevelopmental disorders or psychiatric disorders and ADOS symptom severity. Follow up analyses of psychiatric disorders revealed that first-degree family history of depression was significantly associated with higher SRS-2 scores (t (288) = -3.085, p = .002) and a marginally significant association was present with history of anxiety and higher SRS-2 scores (t (291) = -1.964, p = .05), while remaining disorders did not hold significance.

Conclusion: The increase in presence of family history of psychiatric disorders in first-degree relatives was related to an increase in severity of social deficits in the autism spectrum measured by the SRS-2. This increase was reflected in the overall severity of social deficits and there was no significant relation of psychiatric family history to any one subscale score (social awareness, social cognition, social communication, social motivation, and restricted interests and repetitive behavior). These findings may implicate a positive psychiatric family history as a higher genetic liability toward autism symptom severity, but we also must consider the possibility that an increase in more “problematic” behaviors in children may relate to a reporting bias in parental psychiatric disorders such as depression or anxiety. Our results support existing research that stresses the importance of investigating psychiatric family history as a potential contributing factor to behavioral ASD phenotypes.
The Rhode Island Consortium for Autism Research and Treatment (RI-CART) is a unique state-wide academic-community partnership with the long term goal of advancing knowledge related to etiologic, biological and psychological mechanisms and treatments for individuals with Autism Spectrum Disorder (ASD). Through the collaborative efforts of basic and clinical scientists, clinicians and service providers, state agencies, and patients and their families we have now enrolled over 1,000 individuals (78% M, 22%F). Participants range in age from 2-65 and the racial and ethnic distribution of the sample is very similar to the most recent US Census estimates. Here we describe the methods that were successfully applied to create and maintain a statewide research network. We also present preliminary analyses on the data obtained thus far in relation to a number of variables including demographics, phenotypes and severity of symptoms, age-related outcomes, and co-occurring medical and neuropsychiatric/neurodevelopmental conditions. Finally, we discuss the challenges encountered thus far and propose approaches for future directions.
EVALUATION OF AN INTEGRATED ALCOHOL AND SEXUAL ASSAULT INTERVENTION: EXIT INTERVIEWS FROM A RANDOMIZED CONTROL PILOT TRIAL

Daniel Oesterle, BS, Kelly Ludew, Anna Strock, Lindsay Orchowski, PhD

Sexual assault is prevalent on college campuses. The vast majority of sexual assault is perpetrated by men against women using primarily coercive strategies (i.e., arguments or pressure) or by providing a potential victim with alcohol in order to lower her ability to resist. Many treatment interventions focus solely on alcohol reduction or sexual assault education. Such interventions fail to address the relationship of both components. Further, little is known about the effectiveness of integrated treatment interventions addressing both sexual assault and alcohol reduction. In addition, the efficacy, acceptability, and feasibility of integrated sexual assault and alcohol reduction interventions among high-risk samples of heavy drinking college men have not been assessed systematically. Reliable evaluations of scientific evidence are often achieved through randomized control trials. Further, results from randomized control trials are increasingly utilized in systematic reviews, translating to evidence based practice. Additionally, exit-interviews represent a unique way for researchers to assess participant perception of study design, intervention delivery and receipt, and the enhancement of intervention content. The present study examines participant (n=28) feedback from post-intervention interviews and assessments in a randomized controlled pilot trial of an integrated alcohol and sexual assault intervention, Project U-R SAFE, within a sample of heavy drinking college men at the University of Rhode Island.

Project U-R SAFE includes 3 treatment sessions: 1.) An individually administered interview that incorporates personalized normative feedback and motivational interviewing; 2.) a group workshop driven by social norms theory and bystander intervention techniques; and 3.) a booster session review of program material. Upon completion of 3 treatment sessions, participants were invited to participate in a final exit-interview reviewing the intervention. A credible non-active attention control intervention, General Health Promotion (GHP), was administered in a similar format to the proposed program, and served as the control group during the randomized pilot trial. The GHP condition included 3 sessions: 1.) An individually-administered 1-hour relaxation protocol, which has served as an active control addressing mindfulness and stress reduction; 2.) a group-based workshop addressing stress, general health concerns, and sleep; 3.) a group review of GHP (mindfulness/relaxation) material.

During the exit interview, participants completed an interviewer-administered Intervention Acceptability Survey (IAS) and questionnaire. Variables assessed include: ability to complete all sessions of the intervention, overall program satisfaction, and session-specific satisfaction. Additionally, participants completed assessments on their perceptions of: study procedures, future recommendations, and unhelpful or harmful aspects of the program. Participants rated usefulness of intervention content across eight (8) program constructs which include: 1.) learning more about self alcohol use, 2.) learning more about personal sexual experiences, 3.) learning more about having safe sexual experiences, 4.) strategies to reduce alcohol use, 5.) methods to build/improve relationships with sexual partners, 6.) building relationships with other men, 7.) methods of dealing with daily stressors, 8.) feedback and perspective of study facilitators.

Results presented include participant perception of content of intervention programming and acceptability. Results are also discussed in terms of their implications for future development of integrated interventions addressing reducing alcohol use and risk factors for perpetration of sexual assault.
SUICIDAL IDEATION IN ADOLESCENTS FOLLOWING INPATIENT HOSPITALIZATION: EXAMINATION OF CHRONICITY AND LABILITY OVER SIX MONTHS

Jessica Peters, PhD, Ethan Mereish, PhD; Shirley Yen, PhD; Joel B Solomon, MD; Anthony Spirito, PhD

Suicidal adolescents are highly heterogeneous in their presentations, and more information is needed about what clinical presentations represent greatest risk. Understanding suicidal ideation (SI) in adolescents, especially during the high risk time following hospitalization for suicide events, is a crucial component of improving risk assessment. Most studies rely on single assessments of SI, despite the potential for SI to vary considerably over time. The present study examined how indices of SI intensity and lability over a six-month period predict suicide and self-harm, as well as how they relate to other psychological factors, within a sample of 119 adolescents hospitalized for a suicide attempt or significant suicidal ideation.

SI was assessed at admission and weekly through a six-month follow-up, and indices were calculated for SI intensity (mean weekly level) and SI lability (mean squared successive difference across weekly ratings). SI intensity and lability were uncorrelated, suggesting these are orthogonal aspects of SI. Across the sample, SI intensity, but not lability, significantly predicted suicide attempts and nonsuicidal self-injury at follow-up, outperforming baseline single time point SI assessment but performing similarly to single time point SI assessment at follow-up. These findings suggest that SI intensity, but not lability, may be a risk factor for both suicide and self-harm.

Relationships between SI variables and affective lability and trauma history were also examined. Greater SI intensity was associated with a history of sexual abuse, and greater SI lability with higher levels of negative affect intensity and reactivity. Variables were also created capturing directional SI change to better understand the nature of SI lability: shifts from clinical levels of SI to subclinical levels of risk were counted as improvement shifts, and shifts from low to clinically significant risk were counted as worsening shifts. As expected, more worsening shifts were associated with greater SI reported at follow-up, but improving was not associated with SI at six months. While neither improvement or worsening shifts were associated with behavioral outcomes, a history of sexual abuse was associated with significantly higher rate of worsening shifts, and both negative affect intensity and reactivity were associated with significantly more improving shifts. Adolescents with greater negative affect lability may have been more likely to be hospitalized due to a relatively short-lived suicidal episode. Their distress may also be more responsive to coping skills than more stable and persistent negative affect. In contrast, sexual abuse appears to confer risk for more intense and recurrent SI. These findings highlight the potential importance of these factors, as well as the viability of examining both intensity and lability of SI in research.
BROWN’S NIMH-FUNDED R25 GRANT TO SUPPORT RESIDENT RESEARCH TRAINING: OVERVIEW AND 2015-2016 UPDATE

Katharine Phillips, MD, Audrey Tyrka, MD, PhD, Noah Philip, MD, Sara 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. This poster highlights the key components of the R25 program and provides an update on the R25 residents’ research projects and accomplishments.

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

In summary, the 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.
EVALUATING CLINICAL OUTCOMES IN A CHILD PARTIAL HOSPITAL SETTING: IMPROVEMENTS IN CHILD PSYCHOSOCIAL FUNCTIONING AND PARENTING BEHAVIORS

Teresa Preddy, PhD, Katharine E. Musella, BA, Stephanie Parade, PhD, Anne Walters, PhD

Although behavioral health services are frequently asked to demonstrate the effectiveness of the treatment they provide (Lennox, 1995; Granello, Granello, & Lee, 2000), there is a paucity of recent research focused on evaluating the effectiveness of child partial hospital programs. The limited focus on partial hospital program evaluation has remained consistent in the literature over the past two decades, despite increases in the utilization of partial hospital programs for children with severe psychiatric disorders (Kotsopoulos, Walker, Beggs, & Jones, 1996). The purpose of the current study is to provide preliminary evidence for the effectiveness of a child partial hospital program serving children with a range of psychiatric, social, and behavioral difficulties.

For the current study, clinical outcomes research was implemented in admission and discharge procedures in a child partial hospital setting. The program is a psychiatric hospital program for children ages 7-12 who are experiencing emotional, behavioral, or social issues that inhibit functioning at school, at home, or in the community. Children attend the program for six hours per day Monday through Friday and interventions include cognitive behavioral, behavioral, and family systems interventions. During admission, children participate in individual, group, milieu, occupational, family, and art therapies. Children also receive psychiatric services.

Parents, children, and the clinical team completed measures to assess child and family functioning at both admission and discharge. Parents completed the Family Check-up (adapted) and the Clinical Global Impression Scale (CGI). Children completed the Behavior Assessment System for Children-2 (BASC-2), the Children’s Depression Inventory (CDI), and the Screen for Child Anxiety and Related Disorders (SCARED). The clinical team also completed the CGI for each child.

Results suggested that approximately 69% of our patients are male and the average patient age is approximately 10 years old. The average length of admission is 24 days, although length of admission can vary widely (SD= 15.69; range= 2 to 144 days). Paired samples t-tests indicated that parents and clinicians report significant improvements in severity of illness as rated by the CGI from admission to discharge, t(51)=5.11, p< .001 and t(116)=2.10, p=.04, respectively . Results from the Family Check-up suggested that parents also reported significant improvements in child Emotional Problems t(67)=3.76, p< .001, Conduct Problems t(67)=6.33, p< .001, Hyperactivity t(67)=4.40, p< .001, and Peer Problems t(67)=3.65, p< .01. Parent reports also indicated improvements in parenting behaviors including significant increases in Parenting Warmth t(66)=4.18, p< .001, Limit Setting t(63)=3.40, p< .01, and Family Time t(66)=2.04, p< .05, and significant decreases in Negative Parenting Behavior t(63)=7.53, p< .001. Child reports suggested significant decreases in Depression t(107)=1.99, p=.05, Interpersonal Problems t(107)=2.57, p=.01, and Social Anxiety t(110)=2.64, p< .01.

Accordingly, results provide preliminary evidence that children and families participating in a child partial hospital program experience significant improvements in child emotional and behavioral functioning as well as improvements in parenting behaviors. These findings will be discussed in conjunction with non-significant findings (e.g., no significant change in child reported negative mood) to illustrate how the current research program can inform ongoing program development and clinical practice.
Motor neuron disease (MND) clusters into 3 groups, amyotrophic lateral sclerosis (ALS), spinal muscular atrophy, and primary lateral sclerosis, which have sporadic and genetic etiologies and generally abbreviated survival. Moreover, in ALS, motor system degeneration can co-occur with other neurodegenerative diseases including FTLD, AD, and PD/DLB. Post-polio syndrome (PPS) mimics MND due to selective impairment, degeneration, or death of motor neurons in spinal cord and brainstem. PPS is exceptional because it is linked to childhood poliovirus infection with survival and recovery, followed by recrudescence of progressive weakness, decades later in 25-40% of cases. A recent autopsy of PPS prompted us to review the RIH cases to assess common and distinguishing features of PPS vs ALS. The index case was a 68 year old man with a remote history of bulbar and cervical cord poliomyelitis. He developed slowly progressive upper extremity weakness several years prior to death, and died from a myocardial infarct. Autopsy revealed striking asymmetric atrophy and degeneration of ventral horns throughout the spinal cord, but most severe at cervical and thoracic levels. Bunina bodies were not detected. Brainstem motor nuclei exhibited subtle degeneration. Motor cortex and spinal nerve roots were intact. Despite modest atrophy of skeletal muscle, myofiber type grouping was present. Review of 5 other PPS cases from RIH revealed similar spectra of neurodegeneration and a notable absence of Bunina bodies and corticospinal tract degeneration in the spinal cord. In contrast, 5 cases of ALS selected from the same period had degeneration of spinal motor neurons with consistent presence of Bunina bodies, corticospinal tracts degeneration, and variable degrees of overlap with other neurodegenerative diseases, e.g. FTLD. Mechanistically, PPS is likely caused by progressive aging-associated decline in motor neuron survival in the context of a severely compromised but previously compensated motor unit function.
Introduction: Individuals with mild cognitive impairment (MCI) demonstrate deficits in instrumental activities of daily living (IADL) that place them at higher risk for dementia and mortality. The cognitive profiles, IADL deficits, and risk of progression differ between MCI subgroups of amnestic (aMCI) and non-amnestic MCI (naMCI), though many studies of functional decline have not examined these subgroups separately. This study aims to determine whether common neuropsychological tools, as well as ratings of patient anosognosia, are associated with IADL functioning differently in aMCI compared to naMCI.

Methods: Seventy-one individuals diagnosed with naMCI and 99 individuals diagnosed with aMCI underwent neuropsychological evaluation. Controlling for age, gender, and education, we examined if performance on neuropsychological tests predicted informant-rated IADL dysfunction. We also investigated the ability of patient anosognosia, as rated by clinician and informant, to predict informant-rated IADL dysfunction within MCI subgroups.

Results: Performance in cognitive domains of Attention/Processing Speed and Executive Functioning cross-sectionally predicted IADL independence in aMCI, but not in naMCI. Exploratory analysis with a subset of these individuals revealed that after accounting for an estimate of vascular burden, performance in Delayed Memory predicted IADL independence in the naMCI group, but not the aMCI group. Lastly, informant, but not clinician, ratings of patient anosognosia predicted IADL independence within the aMCI group only.

Conclusion: Neuropsychological performance on tests of attention/processing speed and executive functioning may better predict cognitive contributions to IADL dysfunction specifically in aMCI. After controlling for vascular burden, memory deficits may be the best cognitive indication of IADL dysfunction in naMCI. These results suggest that executive functions and memory, in addition to patient’s awareness of deficits, differentially predict early IADL dysfunction in subgroups of MCI, and can be used to formulate patient prognosis and recommendations on a more individualized basis.
FURTHER RESULTS FROM THE INVESTIGATION OF MULTIPLE EPISODES IN THE LONGITUDINAL COURSE OF BODY DYSMORPHIC DISORDER

Gene Quinn, PhD, Katharine Phillips, MD, Robert Stout, PhD

Background: This study prospectively examined the phenomenon of multiple episodes of body dysmorphic disorder (BDD) in a four-year observational study of the course of BDD. BDD is a common and often-severe disorder that consists of distressing or impairing preoccupation with nonexistent or slight defects in physical appearance. These results extend an earlier examination of the multiple episode course of BDD to include full remission as well as partial remission and multiple episode comorbid major depression (MDD).

Methods: The study followed 166 subjects who met full DSM-IV criteria for BDD at intake and had at least one year of follow-up data. The course of illness is tracked with Psychiatric Status Ratings, which are disorder specific, global 3- to 7-point ratings of disorder severity that have cutoff points for full DSM-IV criteria, partial remission, and full remission. Individual Psychiatric Status Ratings are assigned for each week of follow-up, providing summaries of course and allowing calculation of time to remission and relapse.

Results: As an individual's illness progressed, some subjects had a tendency to cycle between episodes of full-criteria BDD and full or partial remission, whereas others did not. A greater number of full-criteria BDD episodes significantly predicted more subsequent full remissions (HR 4.5, p=0.007) and partial remissions (HR 3.3, p<0.0001) of BDD. However, a greater number of full-criteria BDD episodes did not significantly predict full relapse (HR 1.2, p=0.82) or partial relapse (HR=1.3, p=0.40) of BDD. For comorbid MDD, the number of full-criteria BDD episodes significantly predicted more full remissions of MDD (HR=2.2, p=0.005) and partial remissions of MDD (HR=2.6, p<0.001) as well as more full MDD relapses (HR=2.1, p=0.004), but did not predict more partial relapses of MDD (HR=1.08, p=0.78).

Conclusions: For individuals whose illness progresses as a series of partial remissions and relapses, each successive full-criteria BDD episode increases the likelihood of both full and partial remissions from BDD, but not that of full or partial relapses of BDD. Thus, for individuals with a cycling course of BDD, the course of illness over time generally becomes more favorable. However, successive full-criteria BDD episodes increase not only the likelihood of full or partial comorbid MDD remission, but also that of full MDD relapse. They do not increase the likelihood of partial MDD relapse.
Previous research has shown that non-suicidal self-injury (NSSI) is a risk factor for suicide (Groschwitz et al., 2015). However, there remains little research on adult psychiatric inpatient populations with and without a history of a suicide attempt (SA) and a number of NSSI variables, such as the need for medical attention due to NSSI, the number of NSSI methods used, and how much an individual predicts they will engage in NSSI in the future. One study has found that inpatient adolescents who engage in NSSI and have attempted suicide require more medical attention due to injuries caused by their NSSI than adolescents who engage in NSSI but have never attempted suicide (Tanner, Hasking, & Martin, 2015). Other research has found that adults who engage in NSSI and have attempted suicide use a greater number of NSSI methods compared with adults who engage in NSSI but have never attempted suicide (Victor & Klonsky, 2014). The present study builds on previous research in this area by examining multiple NSSI variables, including the need for medical attention due to NSSI, the number of NSSI methods used, and an individual’s prediction that they will engage in NSSI in the future, among a group of adult psychiatric inpatients (N=126) with a history of NSSI and a suicide attempt (NSSI+SA group; n=87) or a history of NSSI and no suicide attempt (NSSI-only group; n=39). These individuals were recruited as part of a larger ongoing study of novel risk factors for suicide. While the individuals in the NSSI-only group had never attempted suicide, they may have expressed a history of or current suicidal ideation. It was hypothesized that individuals in the NSSI+SA group would have more severe NSSI characteristics than individuals in the NSSI-only group. The differences between the two groups on a number of variables in the Self-Injurious Thoughts and Behaviors Interview (SITBI; Nock, Holmberg, Photos & Michel, 2007) were examined using a series of independent samples t-tests. It was found that individuals in the NSSI+SA group (M=2.51, SD=5.41) require more medical attention when they engage in NSSI compared with individuals in the NSSI-only group (M=0.79 SD=3.31); t(122) = 2.17, p = .03, d = .38. It was also found that individuals in the NSSI+SA group (M=4.90 SD=2.45) use a greater number of methods when they engage in NSSI compared with individuals in the NSSI-only group (M=3.13, SD=2.18); t(124)= 3.97, p < .01, d =.78. Finally, individuals in the NSSI+SA group (M=2.22, SD=1.50) predicted that they will engage in NSSI in the future at a higher rate than individuals in the NSSI-only group (M=1.44, SD=1.57); t(123) =2.67, p < .01, d = .54. These results suggest that individuals who engage in NSSI and have a history of a suicide attempt have more severe NSSI characteristics than individuals who engage solely in NSSI. Therefore, individuals with NSSI and a suicide attempt may require more intensive and targeted treatment for their NSSI.
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, LDN, Stephanie Parade, PhD

Introduction: Previous research has found that adverse childhood experiences (ACES, e.g. abuse, neglect, witnessing domestic violence) are strongly linked to physical and mental health problems throughout the lifespan (Dube et al., 2003; Bellis et al., 2014). Moreover, individuals raised in poverty are more likely to experience multiple adverse experiences during childhood (Child Trends, 2013). 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.

Research question: How do adverse childhood experiences, as compared to current life stressors experienced during pregnancy, affect maternal health in the prenatal period?

Method: Data were drawn from an ongoing study of ACES and maternal-child health. The current report includes 45 pregnant women over the age of 18. Participants were recruited during their pregnancy from Women, Infants, and Children (WIC) clinics across Rhode Island as well as Women and Infants Hospital. In this sample, 38% of women identified as white, 66% were unemployed, and 44% reported that they would be raising the child as a single parent. As part of a prenatal assessment, participants completed a series of questionnaires. Maternal health in pregnancy was measured using a self-report questionnaire in which participants endorsed current and past medical problems. The Adverse Childhood Experiences Questionnaire (Felitti et al., 1998) was used to measure ACES in childhood. The total number of ACES endorsed was used for data analysis. The measure of current stressors experienced during pregnancy was adapted from the ACES measure along with other life stress measures, and a total score was calculated for data analysis.

Results: Correlational analyses show a significant association between ACES score and current adult stressors (r= .509, p <.01). ACES were significantly correlated with current health conditions (r = .365, p <.05), but the correlation between current stressors and current health conditions did not reach significance (r = .24, p = .125). 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 at a trend level, over and above the effect of current stressors (r = .287, p =.073).

Discussion: Results suggest that women with 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. The prenatal period is a critical time for mothers especially since maternal health in pregnancy impacts infant health and development. The findings illustrate the importance of addressing adverse childhood experiences, as the longstanding risks for maternal health continue into the prenatal period.
LIFE EVENTS AND ADOLESCENT OBESITY: METABOLIC AND BEHAVIORAL PATHWAYS

Lisa Ranzenhofer, PhD; Vania Kasper, MD; Wendy Hadley, PhD; Kately Chopy, RD; Gustavo Gonzalez, Elissa Jelalian

There is a hypothesized link between life adversity and obesity, and both biological and behavioral pathways have been proposed to explain these links. To investigate each of these pathways, we conducted a retrospective chart review in 44 patients seen in a tertiary-care adolescent weight management clinic in order to examine relationships among life adversity, weight-related behaviors, metabolic syndrome (MetS) components, and body mass index (BMI, kg/m²). Self-report questionnaires administered during adolescents’ baseline visit were used to assess stressful life events and weight-related behaviors, and standard medical procedures were conducted to evaluate anthropometric indices and metabolic syndrome components (blood pressure, fasting glucose, triglycerides, HDL cholesterol, and waist circumference). All data were extracted from the electronic medical record and questionnaire database for visits occurring between August 13, 2015 and February 9, 2016. Forty-four adolescents (14.54±1.85years, BMI 37.83±9.91) completed a baseline evaluation. Over half (54.6%) of the sample experienced either the death of a parent or close friend and nearly one third (30.2%) reported failing one or more subjects in school. Controlling for age and depressive symptoms, there was a significant relationship between adolescents’ total life events score and BMI (standardized Beta = 0.36, p = 0.02, R²model =0.48). Controlling for age and BMI, greater life events score was also associated with greater sedentary activity (standardized Beta = 0.49, p < 0.01, R²model =0.21), greater high-calorie food intake (standardized Beta = 0.48, p < 0.01, R²model =0.31), and marginally associated with greater self-reported stress eating (standardized Beta = 0.34, p = 0.07, R²model =0.18). Life events score was not associated with exercise or healthy food intake (p’s > 0.5), nor any MetS component. It is possible that behavioral pathways are more salient in explaining the link between adverse life events and obesity, or precede the involvement of metabolic pathways. Implications for future research and clinical practice will be discussed.
ASSOCIATION BETWEEN MOLECULAR MARKERS OF NEUROENDOCRINE FUNCTION AND CELLULAR METABOLISM WITH EARLY LIFE STRESS AND PSYCHOPATHOLOGY

Kathryn Ridout, MD, PhD, Stephanie H. Parade, PhD, Linda L. Carpenter, MD, Lawrence H. Price, MD, Noah S. Philip, MD, H-T Kao, MD PhD, Barbara Porton, PhD, Audrey R. Tyrka, MD PhD

Background: There is strong evidence linking early life stress and psychopathology to alterations in neuroendocrine function. Many of the cellular effects of neuroendocrine activity are exerted through intracellular glucocorticoid receptor (GR) signaling. Cellular levels of GR are strongly dependent on promoter methylation of the GR gene, NR3C1. Thus, NR3C1 methylation may be a mechanism by which early experiences or psychopathology exerts effects on neuroendocrine function. Mitochondria are key to cellular responses to stress and recent evidence suggests that they may have a role in the development of psychopathology. In adults with a history of early life stress or psychopathology, mitochondrial DNA copy number (mtDNAcn), an indirect measure of mitochondrial replication, is increased. Similar results are observed in mouse models after chronic stress or extended glucocorticoid administration. In mice with dysfunctional mitochondria, neuroendocrine responses to restraint stress are altered, suggesting a link between mitochondria and stress-induced neuroendocrine function. There have been no studies examining the links between early stress and psychopathology, NR3C1 methylation, and mtDNAcn.

Methods: Adults (n=395) free of current substance use and lifetime bipolar, obsessive-compulsive, or psychotic disorders were included. Medical conditions and prescription medication other than oral contraceptives were exclusionary. Participants completed diagnostic interviews and questionnaires to characterize early life stress (maltreatment and parental loss) and psychiatric symptoms. mtDNAcn was measured from whole blood DNA using qPCR. Pyrosequencing was used to detect NR3C1 methylation. Age, gender, ethnicity and telomere length were included as covariates given prior literature regarding their effects on mtDNAcn. Subjects were categorized into four groups: no early stress and no lifetime psychopathology (n=136); early stress but no lifetime psychopathology (n=89); lifetime psychopathology but no history of early stress (n=46); and both early stress and lifetime psychopathology (n=124). Associations of mtDNAcn and NR3C1 methylation were examined using partial correlations and general linear models were used to predict the effects of early stress/psychopathology on mtDNAcn and NR3C1 methylation, both controlling for covariates. Multiple regression and bootstrapping procedures outlined by Preacher and Hayes tested NR3C1 as a mediator of effects of psychopathology/early stress on mtDNAcn.

Results: There was a significant negative association between mtDNAcn and GR methylation (r = -.254, p < .001), after controlling for relevant covariates. Results of unconditional models testing early life stress and psychopathology as predictors of mtDNAcn revealed a positive association between psychopathology and mtDNAcn (B = .063, SE = .022, p = .005). During conditional testing, psychopathology became less strongly associated with mtDNAcn when NR3C1 methylation was included in the model (B = .051, SE = .022, p =.022). Methylation partially mediated the link between psychopathology and mtDNAcn (B = .0125, SE = .0051, CI: .0022 - .0229). While the early stress/psychopathology grouping was a significant predictor of mtDNAcn (F = 4.93, p = .002), early life stress was not a significant predictor of mtDNAcn in regression analysis when psychopathology was also included in the model (p > .05).

Conclusions: This is the first study examining associations between cellular neuroendocrine function and mtDNAcn in healthy adults. This unique sample is free from such potential confounders as medications and medical illness, and raises the possibility that GR signaling may be part of a mechanism by which mtDNAcn is altered in psychopathology.
CHILDHOOD MALTREATMENT AND METHYLATION OF FKBP5

Kathryn Ridout, MD, PhD, Stephanie H. Parade, PhD, Alison Paquette, BA, Carmen J. Marsit, MD, Ronald Seifer, PhD, Audrey R. Tyrka, MD PhD

Background: A growing body of evidence suggests that alterations in the stress response system may be a mechanism by which childhood maltreatment alters risk for psychopathology. FK506 binding protein 51 (FKBP5) binds to the glucocorticoid receptor and alters its ability to respond to stress signaling. Previous work has shown that methylation of the FKBP5 gene (FKBP5) at intron 7 is decreased in adults with a history of childhood maltreatment and that a genetic variant of FKBP5 affects the degree of methylation. Decreased FKBP5 intron 7 methylation is associated with increased glucocorticoid induction of FKBP5 expression and decreased glucocorticoid receptor sensitivity. Studies of subjects with later traumas did not exhibit FKBP5 methylation changes, suggesting a role of developmental stage at the time of exposure in FKBP5 methylation. The aim of the present study was to examine the impact of childhood maltreatment and an FKBP5 genetic variant on FKBP5 methylation in a sample of impoverished preschool-aged children. This is the first study to specifically examine FKBP5 epigenetic changes with maltreatment exposure in this age group.

Methods: One hundred seventy-four families, including n=69 with child welfare documentation of moderate-severe maltreatment in the past six months, participated in this study. Families of children with no indicated case of maltreatment within the past six months served as the control group. Children ranged in age from 3 to 5 years, and were racially and ethnically diverse. Structured record review and interviews in the home were used to assess a history of maltreatment, other traumas, and contextual life stressors, and a composite variable assessed the number of exposures to these adversities. Methylation of FKBP5 intron 7 CpG sites was measured from saliva samples via sodium bisulfite pyrosequencing.

Results: Maltreated children had lower levels of methylation at intron 7 FKBP5 CpG sites (p<.05). Children with lifetime contextual stress exposure showed lower levels of methylation at CpG1 (p=.064) and an interaction with the FKBP5 polymorphism that approached significance (p=.082). A composite adversity variable was associated with lower levels of CpG1 methylation (p<.05).

Conclusion: These data are consistent with previous work in adult populations and suggests that epigenetic changes associated with childhood maltreatment may start soon after the exposure. It has been proposed that FKBP5 methylation may be a mechanism through which adverse exposures in young children contribute to alterations in the stress response system and to bio-behavioral outcomes. Our results suggest that childhood maltreatment decreases FKBP5 methylation, which would be consistent with this proposed mechanism. Future extensions of work with this population could examine the relationship of FKBP5 methylation to glucocorticoid levels and responsiveness and behavioral outcomes.
EFFECTS OF TRANSCRANIAL MAGNETIC STIMULATION THERAPY ON HEART RATE VARIABILITY IN DEPRESSION

Samuel Ridout MD, Noah Philip MD, Audrey Tyrka MD/PhD, Matt Niedzwiecki MD, Benjamin Greenberg MD/PhD, Jennifer Barnes MD, Lawrence Price MD, Linda Carpenter MD

Background: Heart rate variability (HRV) is altered in patients with major depressive disorder (MDD), and reflects a pathological imbalance in sympathovagal tone. Little is known about how neuromodulation may affect the autonomic nervous system. The present report describes an interim examination of the effects of therapeutic repetitive transcranial magnetic stimulation (rTMS) on HRV in a sample of clinically depressed patients who completed a course of rTMS therapy.

Methods: HRV data (LabChart 8 Pro) were acquired on MDD patients who received an acute course of rTMS (i.e., left sided, high frequency stimulation using standard parameters). Baseline data were acquired at quiet seated rest during the first clinic visit prior to rTMS and follow-up data after the last rTMS treatment. MDD Severity was measured using the Inventory of Depressive Symptoms-Self Report (IDSSR). The ratio of low frequency (LF) to high frequency (HF) was calculated as the primary outcome measure, using within-subjects paired t-tests for pre- and post-treatment changes.

Results: Eight patients (n=8, age 59±9 years) completed 34±9 sessions of rTMS. HRV as indexed by LF/HF ratio was reduced after rTMS (p=.051), which was driven by an increase in LF (p=.02) and reduction in HF (p=.03) domains. Treatment significantly reduced depressive symptoms, from 45±11 to 26±16 with (p=.01); only one patient demonstrated no improvement.

Conclusions: These preliminary results in a small clinical sample suggest a significant impact of TMS therapy on sympathovagal balance. Future work will expand this clinical sample and investigate the underlying mechanism by which TMS impacts the sympathovagal balance.
EXPLORING PARENT- AND CHILD-REPORTS OF FUNCTIONAL IMPAIRMENT IN YOUTHS WITH OBSESSIVE-COMPULSIVE DISORDER

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Obsessive-Compulsive Disorder (OCD) is a debilitating mental illness that is prevalent in 1-2% of youth populations (Rapoport et al., 2000). Research suggests that children with more severe OCD exhibit higher degrees of functional impairment, specifically in familial, academic, and social domains (Piacentini et al., 2003; Piacentini & Jaffer, 1999; Storch et al., 2010; Valderhaug & Ivarsson, 2005). However, report of impairment seems to differ depending on the informant, with parents reporting higher levels of OCD-related dysfunction than their children (Piacentini et al., 2003). Additionally, some research suggests that parents’ report of impairment differs according to their child’s gender and that girls may be more likely to report more impairment than boys (Valderhaug & Ivarsson, 2005). Therefore, the current study examined the relationship between parent- and child-report of functional impairment in youths with OCD. Participants were 52 treatment-seeking youths with OCD enrolled in the Brown Longitudinal Obsessive Compulsive Study. Parents and children reported on OCD symptom severity and related impairment in family, academic and social domains. It was hypothesized that symptom severity would be positively associated with both child- and parent-reports of functional impairment. It was also predicted that parents would report greater OCD-related impairment than their children. Finally, it was hypothesized that parents and youths would report greater functional impairment in girls than in boys for all domains.

Overall parents reported higher levels of impairment than the children self-reported at a trend level (t = -1.852, p = .070). For specific domains, a significant difference between parent- and child-report was found only in school functioning, with parents reporting greater dysfunction than children (t = -2.075, p = .043). Consistent with hypotheses, a significant association was found between OCD symptom severity and both parent- (r = .648, p<.000) and child-reports (r = .569, p<.001) of youth functional impairment. Finally, there were no significant differences in parent or child report of overall functioning according to gender (all ps > .05). These findings provide valuable information for parents of children with OCD. Parents reported significantly greater impairment in academic-related functioning, indicating that parents may perceive more interference in their child’s academic success due to OCD symptoms than children. Conversely, parents and children reported similar degrees of impairment in familial and social domains. The association between OCD severity and overall functional impairment supports the abundance of previous research finding that children who present with more acute OCD experience the most disruption in their daily functioning. Finally, no significant differences were found regarding child gender, suggesting that gender does not influence perception or report of functional impairment. Although the study yielded important results, there are limitations of this research. The sample was predominately white (92.3%) and analyses did not account for potential differences in OCD-related impairment due to developmental stage. Future research, using more diverse samples, should investigate how developmental stage relates to parent and child report of OCD symptom severity and functional impairment.
OUTCOMES OF A FAMILY VISITING PROGRAM - DO THEY DIFFER BY ETHNIC GROUP?

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Healthy Families America (HFA) is an evidence-based family visiting program that is funded through the Maternal, Infant, and Early Childhood Home Visiting Initiative (MIECHV) (U.S. Department of Health and Human Services). HFA is grounded in the belief that establishing early, sustained, and nurturing relationships are fundamental for healthy child development (Healthy Families America (HFA) Program Model Overview). The HFA program model is designed to “promote positive parent-child relationships and healthy attachment” and is “strengths-based, family-centered, culturally sensitive, and reflective” (Healthy Families America (HFA) Program Model Overview). HFA targets low income families, single parents, parents with adverse childhood experiences, and parents with drug/substance abuse issues (Healthy Families America (HFA) Program Model Overview).

The current report focuses on understanding if there are ethnic group differences (Hispanic and Non-Hispanic) in the amount of support parents participating in the HFA family visiting program provide their child in the home environment. To measure this, we used the Infant/Toddler HOME Inventory to assess the level of support in the home environment (Caldwell & Bradley, 2003). The Infant/Toddler HOME Inventory consists of six subscales rated by an observer: Parental Responsivity, Acceptance of Child, Organization of the Environment, Learning Materials, Parental Involvement, and Variety in Experience (Caldwell & Bradley, 2003).

The sample for the present study consisted of 125 caregivers between the ages of 15 and 41 years (M = 24 years, SD = 5.35 years). Caregivers were enrolled in HFA and completed an assessment that included the HOME inventory when their child was approximately 12 months of age. A vast majority of caregivers were women (98%). Most caregivers (97%) in this study received public assistance. For this study, 30% of caregivers identified as Non-Hispanic and 70% of caregivers identified as Hispanic. Caregivers had a wide range of educational attainment: 47% of caregivers did not have a high school degree, 32% reported having obtained a high school degree or equivalent, 18% reported receiving some education or training beyond high school, and 3% reported having a bachelor’s degree or higher. Forty percent of caregivers’ infants were male and 60% were female.

No significant differences were observed between Hispanic (M = 9.36, SD = 1.23) and Non-Hispanic (M = 9.11, SD = 2.17) families in Parents’ Responsivity (t(123) = -.645, p = .520); Hispanic (M = 5.74, SD = 1.25) and Non-Hispanic (M = 6.21, SD = 1.64) families in Acceptance of Child (t(123) = -1.766, p = .080); Hispanic (M = 5.21, SD = 0.93) and Non-Hispanic (M = 5.05, SD = 0.98) families in Organization of the Environment (t(123) = -.898, p = .371); Hispanic (M = 6.94, SD = 1.74) and Non-Hispanic (M = 6.68, SD = 2.05) families in Learning Materials (t(123) = -.720, p = .473); Hispanic (M = 4.05, SD = 1.45) and Non-Hispanic (M = 3.76, SD = 1.49) families in Parental Involvement (t(123) = -1.030, p = .305); and Hispanic (M = 3.54, SD = 1.25) and Non-Hispanic (M = 3.47, SD = 1.28) families in Variety in Experience (t(123) = -.270, p = .787).

Results indicate that there were no differences between ethnic groups in the amount of support that parents who were participating in HFA provided to their infants in the home environment. To determine how effective HFA is in promoting a supportive home environment, future studies should examine whether there are differences in the home environments of families participating in HFA and families in a control group that is not receiving HFA services. Additionally, future work should include repeated assessments of the HOME over time to help understand how HFA potentially contributes to change in the home environment and if this differs by ethnic group.
CARDIAC ANXIETY IN PATIENTS WITH PERIPARTUM CARDIOMYOPATHY

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Introduction: Cardiac anxiety is a psychological condition characterized by cardiac specific-fear, avoidance behaviors, and excessive cardiac symptom monitoring. It has been associated with cardiovascular morbidity, physical inactivity and patient-reported disability. However, the severity of cardiac anxiety in women diagnosed with peripartum cardiomyopathy (PPCM) remains unknown. Methods: Women with PPCM (N=74) were enrolled in the Peripartum Cardiomyopathy Quality of Life Registry and completed an internet-based questionnaire. Cardiac anxiety was assessed with subscales (Fear, Avoidance, Heart-Focused Attention) from the Cardiac Anxiety Questionnaire (CAQ). PPCM patients’ CAQ scores were compared to published CAQ mean scores from other studies (patients with defibrillators [ICD, n=205], inherited Long QT Syndrome [LQTS, n=12] and sudden cardiac arrest [SCA, n=182]) using one-way ANOVA and Tukey's HSD. Results: PPCM patients had a mean age of 35.0 (SD 5.8) years; time since diagnosis 2.5 years. Cardiac fear significantly differed between groups F(3,461) = 18.71, p = <0.001 as PPCM patients had greater cardiac fear than ICD (p = <0.001), LQTS (p = 0.02), and SCA survivors (p = <0.001). Behavioral avoidance also significantly differed between groups F(3,461) = 8.00, p = <0.001. PPCM patients had greater behavioral avoidance than LQTS (p = <0.001) and SCA (p = 0.004) patients but not ICD patients (p=0.17). Finally, heart-focused attention significantly differed between groups F(3,461) = 34.77, p = <0.001. PPCM survivors reported greater heart focused-attention than ICD (p = <0.001) and LQTS (p = 0.008) patients but not SCA survivors (p=0.30). Conclusion: Cardiac anxiety is more severe in women with PPCM compared to other cardiac patient samples. Attention to cardiac anxiety symptoms should be considered to facilitate early detection and treatment. Further research is needed to fully understand the impact of cardiac anxiety on clinical outcomes.
A DEVELOPMENTAL ROLE FOR REM SLEEP IN THE NEURAL PROCESSING OF COMPLEX SOCIAL EMOTIONS

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Objectives: Adolescence represents a period of profound psychosocial development, one requiring accurate, parental independent, processing of complex emotional signals. In adults, REM sleep physiology specifically low levels of gamma EEG activity reflecting reduced adrenergic tone—optimally recalibrates limbic brain function, one benefit of which is superior next-day discrimination of complex social emotions. Despite developmental shifts in both sleep and affective processing, when and how such sleep-dependent emotional brain mechanisms emerge during the human lifespan remains unknown.

Methods: 31 healthy males—22 adolescents (age: 12.1–15.9) and 9 young-adults (age: 18.0–21.1) obtained a PSG-recorded night of sleep, followed the next morning by an fMRI scan while performing an affective task requiring the discrimination of “Threatening” (anti-social) from “Affiliative” (pro-social) face stimuli. Analyses focused on the limbic related anterior insular cortex (AIC) and dorsal anterior cingulate (dACC), testing the hypothesis that decreasing REM gamma EEG activity—reflecting lower REM adrenergic tone—adaptively supports accurate neural discrimination of complex social emotions in a age dependent developmental manner.

Results: Statistical mixed models established that both age and REM sleep gamma power independently (p’s<.03) predicted emotional discrimination ability in limbic-related dACC and AIC, with increasing age and lower REM gamma associated with superior emotional discrimination ability. Most critical, however, a significant age-by-REM gamma interaction (p’s<.01) emerged in both regions. Only low REM gamma power was associated with the development of superior socioemotional threat across age.

Conclusion: These results reveal a developmentally sensitive interaction between REM sleep and the emergence of accurate socioemotional processing within the adolescent brain. Specifically, lower REM gamma—reflecting reduced adrenergic activity—promoted superior discrimination of social cues with increasing developmental age, while higher adrenergic REM sleep gamma activity stunted this normal age-related trajectory. Thus, atypically REM sleep gamma activity during adolescence, potentially indicative of high stress-related adrenergic tone, may lead to a neural signature of hypervigilance and a failure to appropriately disambiguate threatening from affiliative signals. More generally, these findings establish a REM-sleep process that may beneficially improve psychosocial functioning, enabling the adaptive ability to avoid threat while identifying and engaging with prosocial cues. They further highlight the essential need for sleep during adolescent development—particularly late morning REM sleep—in support of healthy emotional functioning.

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CAUSAL MANIPULATION OF SOMATOSENSORY NEURAL DYNAMICS USING ALPHA AND GAMMA-BAND TRANSCRANIAL ALTERNATING CURRENT STIMULATION AND IMPLICATIONS FOR PERCEPTION

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Alpha and gamma band oscillatory activity in the sensory cortices are thought to play mechanistic roles in the gating of sensory information. Specifically, alpha-band activity (7-14Hz) has been associated with inattention to task-irrelevant sensory signals (Jones et al. J Neurosci. 2010, Sacchet et al. J. Neurosci. 2015) and gamma-band activity (30-80Hz) has been associated with enhancing the processing of task-relevant sensory signals (Siegel et al. Nature Neurosci 2014). Here, we used a custom-designed combined EEG (based on the Open Ephys architecture, see poster by Black et al.) and transcranial alternating current stimulation (tACS), a non-invasive technique for presenting electrical oscillatory activity to the brain to examine the causal role of these dynamics in human sensory perception. Participants performed a tactile detection task before and after tACS stimulation to primary somatosensory cortex (SI) at either alpha (7-11Hz) or gamma-band (40Hz) frequencies. tACS was localized anatomically to near the hand area of SI on the cortical hemisphere contralateral to the hand used for the tactile detection task. We analyzed changes in behavioral performance as well as changes in event-related potentials (ERPs) and event-related spectral dynamics (ERSP) before and after 10 minutes of tACS and between alpha and gamma-band stimulation conditions. Distinct elements of the ERPs and ERSPs were modulated by alpha and gamma-band stimulation in contralateral SI but not ipsilateral SI. Investigation of the influences of these causal changes on somatosensory perception is ongoing. These preliminary results suggest that tACS can causally modulate functionally relevant oscillatory rhythms and ERPs in sensory cortex with distinct influences of alpha versus gamma band stimulation.
I present initial evidence for a replicable methodology and framework (NIMT) that aims to elucidate clinically-relevant causal relationships between neurophysiological and experiential processes. In this methodology, expert meditators working directly as research-collaborators with neuroscientists use a neurofeedback display to employ a systematic procedure for discovering, formulating and refining meditation strategies (NIMTs) that modulate the chosen neurofeedback signal. NIMTs are subsequently introduced to hypothesis-blind groups to assess the influence of the NIMT on the targeted neurophysiological signal and relevant behavioral measures. This methodology offers neurofeedback-independent modulation of targeted neurophysiological signals with important implications for clinical treatment.

In our proof-of-concept experiment, we developed a NIMT for deactivating PCC activity by drawing on expert meditator’s verbal descriptions of the experiential correlates of PCC activity reported in previous experiments. We use fMRI to compare PCC activity and functional connectivity during this PCC-NIMT and a control meditation (focused attention on the breath). Degree of PCC deactivation following 20 minutes of the meditation with the PCC-deactivation NIMT is compared to performance on a demand-avoidance task.
NEIGHBORHOOD CHARACTERISTICS AS A PREDICTOR OF ACTUAL AND PERCEIVED NORMS AMONG HIGH SCHOOL STUDENTS

Chloe Sarapas, BA, Miryam Yusufov, Lindsay Orchowski, PhD

Introduction: Drawing on prior research suggesting that the density of alcohol outlets moderates the effectiveness of social norms marketing addressing alcohol on college campuses, it is feasible that the characteristics of neighborhoods surrounding high schools play a role in establishing student norms regarding sexual violence. Accordingly, the present study explores how the density of adult outlets (i.e. strip clubs, adult paraphernalia shops) and violence-related resource centers near a high school influences actual and perceived norms regarding sexual violence among students.

Method: We utilized geospatial coding to determine the density of adult outlets and violence-related resource centers within a 3-mile radius of selected Rhode Island high schools. Drawing upon data from 9th-12th grade respondents across 12 public and charter high schools (N=2239), we examined whether the density of adult outlets and violence-related resources was associated with students’ actual and perceived norms.

Results: Accounting for participant demographics, a series of linear regressions suggested that students’ beliefs varied as a function of neighborhood characteristics. Specifically, students attending schools located near a greater number of adult outlets were less likely to be bothered when peers used the words gay or lesbian in a mean way; however, those attending schools located near a higher number of resource centers were more likely to be bothered by homophobic teasing. A negative correlation was observed between density of adult outlets around a school and the extent to which students were bothered when their peers were bullied, and the opposite was true in regard to resource centers and student beliefs about bullying. Students attending schools with a high density of violence-related resources were more likely to report that it was wrong to pressure someone to have sex.

Analyses also suggested that student perceptions of peer norms varied as a function of the density of neighborhood outlets around a school. Specifically, students attending schools located near more adult outlets were less likely to think that their peers would respect someone who stepped in to address sexual violence, and the opposite was true for students attending schools located near higher numbers of resource centers. Likewise, perceptions of their peers’ beliefs about bullying varied according to how many adult outlets and resource centers near which their school was located.

Discussion: Findings suggest that the characteristics of the neighborhood in which a high school is located might influence student norms and perceptions of peer norms. In particular, the density of adult outlets and resource centers appears to be related to students’ personal beliefs and their (mis)understanding of their peers’ attitudes toward sexual violence. Current findings point to the importance of taking into consideration a particular school’s surroundings when designing prevention and intervention programs, as well as the necessity of continued research on how actual and perceived norms might be influenced by the characteristics of the neighborhood in which their high school is located.
A MODULAR, CLOSED-LOOP PLATFORM FOR INTRACRANIAL STIMULATION
IN PEOPLE WITH NEUROLOGICAL DISORDERS

Anish Sarma, ScB, Britni Crocker, Sydney S. Cash, MD, PhD, Wilson Truccolo, PhD

Neuromodulation systems based on electrical stimulation can be used to investigate, probe, and potentially treat a range of neurological disorders. The effects of ongoing neural state and dynamics on stimulation response, and of stimulation parameters on neural state, have broad implications for the development of closed-loop neuro-modulation approaches. We describe development of a modular, low-latency platform for pre-clinical, closed-loop neuromodulation studies with human participants. We illustrate the uses of the platform in a stimulation case study with a person with epilepsy undergoing neuro-monitoring prior to resective surgery. We demonstrate the efficacy of the system by tracking rare power fluctuations in a low-frequency band to trigger intracranial electrical stimulation, and show that the response to stimulation depends on the neural state.
NEURAL CIRCUITS UNDERLYING ALCOHOL REWARD MEMORY

Kristin Scaplen, PhD, Hayley A. Bounds, Tyler G. Ekins, Nicholas J. Mei, Reza Azanchi, Karla R. Kaun, PhD

Animals are innately wired to seek reward and avoid punishment. Aberrant regulation of the reward neural circuitry underlying these behaviors, can lead to many maladaptive and pathological behaviors including those attributed to addiction. A compact genome, small but sophisticated brain and impressive array of neurogenetic tools make Drosophila an ideal model for studying the neural circuitry mechanisms underlying reward. Specifically, Drosophila are an excellent model for understanding how alcohol acts on the brain’s reward circuits because of their robust motivated response for alcohol and the remarkable similarity that exists in reward circuitry. Here we demonstrate how circuits underlying alcohol-induced increases in locomotion modulate circuits required for the rewarding properties of alcohol intoxication.

In Drosophila, both the reward memory for alcohol intoxication and acute locomotor effects of alcohol require an associative central brain structure called the mushroom bodies (MB) and dopamine. Recent anatomical work report that subsets of MB dopaminergic axons and dendrites of output neurons tile the MB creating multiple semiautonomous compartments that comprise feed-forward and feedback circuits necessary for associative learning. Using a combination of intersectional and thermogenetics, we identified a simple circuit that is necessary for alcohol reward memory expression and a separate circuit required for the regulation of alcohol-induced hyperactivity. We describe how dopaminergic modulation of the mushroom body mediates the acquisition and expression of memories for alcohol intoxication and propose mechanisms for how these alcohol-related circuits interact. This work provides valuable insight to the dynamic qualities of memory and how the long lasting reward memories for alcohol intoxication are formed.
A MOBILE SELF-HELP TREATMENT FOR OBSESSIVE COMPULSIVE DISORDER

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Obsessive-compulsive disorder (OCD), characterized by recurrent intrusive thoughts or images and associated compulsive behaviors or mental rituals, is a common and impairing disorder affecting 1.6% of the United States population (Kessler et al., 2005). Though several studies attest to the efficacy of therapist-guided cognitive-behavioral therapy with exposure and response prevention (ERP) as a first-line treatment for OCD (Fisher & Wells, 2005; Foa et al., 2005; Simpson et al., 2006), many patients remain untreated due to financial and/or time constraints, as well as a lack of trained clinicians in the community (Crits-Cristoph et al., 1995; Mataix-Cols & Marks, 2006; Eisen et al., 2006). Although self-guided ERP via workbooks or web-based programs have shown promise in reducing symptom severity and improving quality of life (Greist et al., 2002; Marks et al., 1998; Tolin et al., 2007), patient compliance remains low (Kenwright et al., 2005). There remains a critical need to develop innovative alternative strategies to increase patient adherence to self-directed ERP. Therefore, the present study examined the feasibility, acceptability, and preliminary efficacy of a mobile health application (mHealth app), Live OCD Free, designed to assist patients with self-directed ERP. It was hypothesized that if participants reported using the app regularly and engaging in exposure exercises and ritual prevention often, OCD symptom severity, work and social impairment, and quality of life, would improve by the end of the 12-week treatment.

Adults with mild to moderate OCD symptoms were included in an ongoing open trial (target N = 30) where they were asked to use the Live OCD Free app at least one hour per day over 12 weeks, without any therapist intervention. Participants completed a battery of self-report questionnaires at pre- and post-treatment including measures of patient satisfaction and app utilization, OCD severity (Yale-Brown Obsessive Compulsive Scale), functional impairment (Sheehan Disability Scale) and quality of life (Quality of Life Enjoyment and Satisfaction Questionnaire). Planned data analysis is as follows: Feasibility and acceptability will be assessed using descriptive statistics. In order to assess the impact of the self-help intervention on OCD severity, quality of life and interference in daily functioning, a series of repeated measures ANOVAs will be conducted on pre- and post-treatment scores. To provide a sense of whether our self-help intervention produces similar degrees of pre- to post-treatment change as other self-help interventions for OCD, treatment effect sizes will be calculated and compared with effect sizes reported in leading studies of ERP treatment outcome in OCD. Results will suggest if self-guided ERP through a mobile app can be successful in treating mild to moderate OCD, and thus be a valid treatment option for those in the community who cannot access therapy with a clinician.
META-ANALYSIS OF TREATMENT OPTIONS FOR PATHOLOGICAL SKIN-PICKING

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INTRODUCTION: Pathological skin-picking (PSP) is a repetitive body-focused behavior that is associated with significant distress and/or impairment. While individual randomized controlled trials (RCTs) suggest benefit of specific interventions, there has been limited systematic evaluation of behavioral and pharmacological treatments or their collective benefit.

METHOD: The present study examined the current state of treatments for PSP using meta-analytic techniques and explored factors that may moderate treatment efficacy. Following a comprehensive literature search, nine trials were identified that met inclusion criteria, three of which included a control condition.

RESULTS: A fixed effects meta-analysis found a large overall effect size (g = 1.13, p < .001), which was comprised of large effects for behavioral treatments (g = 1.19, p < .001), lamotrigine (g = 0.98, p < .001), and selective serotonin reuptake inhibitors (g = 1.09, p < .001). Clinician-rated measures did not exhibit significantly different effect sizes from self-rated measures; however, self-rated measures of severity exhibited larger treatment effects relative to self-rated measures of impairment [Q(1) = 4.63, p = .03]. Treatment type, trial length, and trial methodological quality were not significant moderators of the size of treatment effects. Publication bias was not identified. For controlled trials, the comparative efficacy of treatments for PSP was in the moderate range (g = 0.47, p = .03).

CONCLUSIONS: Taken together, findings suggest that individuals who seek treatment for PSP experience benefit; however, the benefit of treatment appears less robust when compared to a control condition. Overall, the meta-analysis illuminated a lack of systematic study of treatments for PSP, highlighting the need for additional randomized controlled trials and inclusion of multiple informants in assessment.
INHIBITORY SYNCHRONY: A POTENTIAL MECHANISM FOR ENHANCEMENT OF FEEDFORWARD SENSORY PROCESSING

Hyeyoung Shin, PhD, Stephanie Jones, PhD, Christopher Moore, PhD

Gamma oscillations (30–80 Hz) have been repeatedly linked with success in perceptual encoding. Previous studies have shown that the gamma component in the local field potential (LFP) is a signature of the synchronization of fast-spiking (FS) interneurons. We hypothesize that synchronization of FS spiking can lead to enhancement of sensory encoding by fine-temporal modulation of pyramidal gain. To test this hypothesis, we employ chronic extracellular electrophysiology and record from mice performing a vibrissae stimulation detection task. This allows us to compare the neural dynamics underlying hit (perceived) and miss (not perceived) trials for perceptual threshold level stimuli. We present preliminary evidence that in the barrel cortex, feedforward FS synchrony (within ~20ms of stimulus onset) is more likely to be evoked on hit trials. Further, putative pyramidal units showed enhanced gain on hit trials at ~40ms with regard to stimulus onset. This timing (i.e. 20ms post FS synchrony) coincides with the beneficial window of opportunity created by FS synchrony, as predicted by previous studies of FS-gamma. These emerging data lend support to the idea that efficient recruitment of feedforward inhibitory synchrony can enhance neocortical processing of excitatory input.
PORTABLE TRANSCRANIAL MAGNETIC STIMULATION

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This project is concerned with the development of a wearable transcranial magnetic therapeutic device that employs a mechanism of rotating permanent magnets. The device is intended for the enhancement of brain injury rehabilitation. Rare earth magnets are mechanically rotated to generate time-varying magnetic fields on specific injured areas of the brain. Each therapeutic probe consists of two neodymium disc magnets arranged in a concave position toward the brain and enclosed in a customized 3D-printed housing. The magnet holder is rotated with a DC motor controlled by a microprocessor and a pulse width modulator for the desirable rotational speed, timing, and treatment protocol. The components are integrated in a lightweight helmet suitable for frequent rehabilitation sessions over a prolonged period of time or for at-home use. The effectiveness of the low-level, mechanically varied magnetic field therapy will be further studied in future clinical investigations.
EXAMINATION OF THE TRAIL MAKING TEST – PART B EFFICIENCY SCORE IN A LONGITUDINAL CLINICAL SAMPLE

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Objective:
The Trail Making Test – Part B (TMT-B) is a commonly used executive functioning measure with a known floor effect, limiting ability to distinguish impairment among individuals unable to complete this task in the standard time limit (300sec). We previously proposed the TMT-B Efficiency Score (TMT-Be), which captures performance variability among examinees who fail to complete the task. The present study examines TMT-Be in a longitudinal clinical sample.

Participants & Methods:
Data were collected via record review of veterans who underwent ≥2 neuropsychological evaluations. Thirty veterans (mean age T1: 68±8.8) unable to complete the TMT-B during at least one evaluation were identified (mean days between visits =615). Two scoring systems were utilized to examine performance variability: TMT-Be (accounts for number of attempted/unattempted moves, errors, time) and TMT-B Prorated Score (TMT-Bpr [Heaton et al., 2004]; estimates time to completion based on circles completed at 300sec).

Results:
TMT-Be and TMT-Bpr were highly correlated at each time point [rs(29)≥.97, p<.001]. However, TMT-Be had more acceptable skewness and kurtosis, providing greater variance than TMT-Bpr.

Conclusions:
TMT-Be and TMT-Bpr are highly correlated, indicating concurrent metric validity, but TMT-Be demonstrated a more normal distribution, suggesting it better captures performance variability in a clinical sample and provides sufficient variance for examining executive functioning in individuals unable to complete TMT-B.
INTERGENERATIONAL CONTINUITIES IN FAMILY CONFLICT PREDICT ADOLESCENT AND ADULT ADAPTIVE AND MALADAPTIVE OUTCOMES

Jessica Solis, MA, Drew Rothenberg, MA, Andrea Hussong, PhD, Laurie Chassin, PhD

Researchers continue to provide compelling evidence for the intergenerational transmission of externalizing, internalizing, and substance use behaviors within families (Capaldi et al., 2012; Kim et al., 2009; Pears et al., 2007). While previous work has proffered several potential individual factors in these intergenerational relationships—genetics (Limosin et al., 2005), temperament (Iacono et al., 1999), parenting (Bailey et al., 2009), etc.—less is known about how family environments relate to the persistence of behavior across generations (Silberg et al., 2012). Specifically, family conflict stands out as a promising contextual factor in the intergenerational continuity of maladaptive behavior (Rothenberg et al., 2014). Therefore, the current study tested whether parents and adolescents within families that demonstrated high conflict across generations had higher maladaptive and lower adaptive behaviors than parents and adolescents in families with intergenerational discontinuities in family conflict.

The sample included 220 families from a multi-generational, high-risk, longitudinal study (Chassin et al., 1991) of parents (G1s) and targets (G2s) followed from adolescence (age M=13.2) to adulthood, and of these targets’ children (G3s; age M=12.5 years). Family conflict was measured by mother, father, and adolescent reports in G1-G2 families (Wave 1) and by G2 target, G2 target’s spouse, and G3 adolescent report in G2-G3 families (Wave 6). Family environment was then classified into one of five intergenerational patterns: most adverse (i.e., parent and adolescent report high conflict across G1-G2 and G2-G3 families), adverse (i.e., either parent or adolescent report high conflict across G1-G2 and G2-G3 families), resilient (i.e., parent and adolescent report high conflict in only G1-G2 family), vulnerable (parent and adolescent report high conflict in only G2-G3 family), and favorable (parent and adolescent report low conflict in G1-G2 and G2-G3 families). Internalizing and externalizing symptoms, substance use, and parenting measures were reported by G2 targets (N=220) and G3 adolescents (N=119) in wave 6.

ANCOVAs controlling for SES (see Figures 1 and 2) showed that G2s had higher internalizing and externalizing behavior and less parental consistency if families reported the most adverse levels of conflict in their G1-G2 and G2-G3 families as compared to peers from other intergenerational family environments. Similarly, G2s from adverse and most adverse families reported more lifetime drug dependence symptoms and less parental monitoring than those from other families. Additionally, G3s self-reported higher levels of lifetime alcohol consumption and consequences and past year drug and alcohol consequences and dependence symptoms if families reported the most adverse levels of conflict in their G1-G2 and G2-G3 families as compared to the other family environments. Moreover, G3s from adverse and most adverse families had more self-reported externalizing behavior and lifetime drug consequences and parent-reported internalizing behavior than those from other families.

Results indicate that intergenerational conflict can predict adaptive and maladaptive outcomes in both generations above and beyond SES. Evidence also suggests that G3s from families where there has been conflict across multiple generations are at heightened risk for maladaptive outcomes despite direct exposure to only one conflictual household. These results have important implications for policy and intervention efforts regarding intergenerational associations.
Despite the serious nature of suicidality, research indicates low rates of treatment-seeking in individuals reporting suicidal thoughts and behaviors (Barnes, Ikeda, & Kresnow, 2005; Kisch, Leino, & Silverman, 2005). Little if any prior work, however, has investigated suicidal individuals’ perceptions regarding their own capacity to effectively seek psychiatric care. Given previously-reported relationships between suicidality and both reduced help-seeking and maladaptive coping strategies (Horwitz, Hill, & King, 2011; Piquet & Wagner, 2003), the present study hypothesized that participants reporting histories of suicidality would endorse lower levels of confidence in their ability to seek mental health treatment compared to non-suicidal participants. A sample of 124 adult psychiatric hospital inpatients, part of a larger study identifying novel risk factors for suicide, completed the Self-Efficacy to Seek Mental Health Care (SE-SMHC) scale (Moore, Schofield, van Rooyen, & Andersson, 2015). Since total scores (possible scores ranging from 9 to 90) were not normally distributed within our sample, non-parametric analyses were employed. A Mann-Whitney U test revealed that participants reporting a history of suicidal ideation (n=108, M=65.34, SD=16.66) scored significantly lower on the SE-SMHC scale than those with no history of suicidal thoughts or behavior (n=16, M=75.25, SD=11.02), U=568.50, p=0.03, Cohen’s d=0.70. In addition, we examined self-efficacy for treatment-seeking among individuals reporting histories of suicidal ideation but no suicide attempts (SI-only) and those reporting histories of both suicidal ideation and attempts (SI-SA). A Kruskal-Wallis test revealed that the difference in SE-SMHC scores among the non-suicidal, SI-only (n=45, M=65.87, SD=17.19), and SI-SA (n=63, M=64.97, SD=16.40) groups approached significance, $\chi^2(2)=4.97$, p=0.08. The present study suggests that individuals with a history of suicidal thoughts have a reduced confidence in their ability to effectively obtain psychiatric care. It is unclear, however, if this limited self-efficacy influences suicidality directly, or if it reflects experience with the current mental health care system. Given our preliminary trend-level result, a history of attempted suicide may also influence self-efficacy to seek psychiatric care at a statistically significant level in the larger sample that we plan to obtain. Our findings extend previous research, suggesting that individuals with histories of suicidal ideation are not only less likely to seek psychiatric care, but also may doubt their ability to do so. It is thus important that families, medical providers, and other social supports provide these individuals with assurance and encouragement to obtain mental health treatment during times of crisis.
THE VALIDITY OF THE SOCIAL RESPONSIVENESS SCALE IN CHILDREN WITH OCD

Elyse Stewart, BA; Christine Conelea, PhD; Hannah Frank, BA; Jennifer Freeman, PhD; Abbe Garcia, PhD

Obsessive-Compulsive Disorder (OCD) and Autism Spectrum Disorders (ASD) have some similar clinical characteristics, most notably symptoms of repetitive or stereotyped behaviors (American Psychiatric Association, 2013). Previous research has shown high prevalence of autistic spectrum traits in both children and adults with OCD (Ivarsson & Melin, 2008; Bejerot, Nylander & Lindstrom, 2001). Establishing a differential diagnosis in younger children may be challenging as developmental limitations could hinder their ability to report on the more cognitive aspects of OCD. There is also little research on evaluating social characteristics specific to OCD in younger children. A widely used measure to assess social deficits, most specifically autistic traits, is the Social Responsiveness Scale (SRS; Constantino & Gruber, 2005). This parent-report measure is an effective screening tool for ASD and assists clinicians in making a more informed diagnosis (Booker & Starling, 2011). Given the overlap of repetitive behavior problems in OCD and ASD, the SRS was examined in relation to OCD severity in a pediatric population who did not meet diagnostic criteria for ASD. We hypothesized that SRS scores would be positively correlated with OCD severity.

Participants (N=119) were children ages 5 to 8 years enrolled in the Pediatric Obsessive-Compulsive Disorder Treatment Study for Young Children (POTS Jr.), a multi-site randomized controlled trial testing the efficacy of family-based Cognitive Behavioral Therapy. All participants had a primary DSM-IV diagnosis of OCD and a clinician-rated Children’s Yale-Brown Obsessive-Compulsive Scale (CY-BOCS; Scahill et al., 1997) score of 16 or greater. Pervasive Developmental Disorder(s) (PDD), including Asperger’s Syndrome, were exclusion criteria for this study. Both the CY-BOCS and the SRS were collected upon presentation.

Results indicated that the CY-BOCS total severity score (M=25.55, SD=4.23) was positively correlated with the SRS total t-score (M=58.29, SD=11.21; r=.21, n=119, p=.02), including the SRS subscales of Social Motivation (M=59.90, SD=12.53; r=.24, n=119, p=.01) and Autistic Mannerisms (M=65.94, SD=12.64; r=.21, n=119, p=.02). This supports previous research regarding the prevalence of social impairment in OCD and suggests that OCD severity is associated with social deficits. Additionally 50.42% of this study’s population had a 65 or greater t-score on the Autistic Mannerisms subscale. It is likely that this finding reflects the presence of repetitive behaviors in both OCD and ASD, suggesting that this measure may not accurately discriminate between compulsions and stereotypes. This highlights the importance of using other assessment strategies (e.g., functional assessment) when assigning diagnoses and planning treatment in young children with repetitive behavior problems. Further research is necessary for more precise measures delineating between OCD and ASD symptoms.
RELATIONS BETWEEN ALPHA POWER AND THE STABILITY OF MOTION-INDUCED BLINDNESS

Hsin-Mei Sun, PhD, Marina Inyutina, Rufin VanRullen, PhD, Chien-Te Wu, PhD

Motion-induced blindness (MIB) refers to a phenomenon in which a static target spontaneously disappears and reappears into consciousness when superimposed on a global moving pattern, despite the fact that it is constantly present in the display. The MIB paradigm has been used as a powerful tool to study visual awareness since it can produce conscious as well as unconscious perception within the same task. However, the neurophysiological correlates of the perceptual target disappearance during MIB remain unclear. Therefore, in the present study, we examined the dynamics of brain oscillations associated with the perceptual target disappearance due to MIB, which would help us to better understand the neural process that distinguishes the neural representation of a perceptually suppressed stimulus from the conscious representation of the same stimulus. Twenty-two participants performed a MIB task while their EEG was recorded. During the task, participants reported the perceptual disappearance and reappearance of a dot target (the MIB condition) by pressing and releasing a response key. We also included a control condition, which simulated the MIB condition with physical disappearance and reappearance of the dot target. The duration of the target disappearance in the control condition was based on the actual target disappearance durations recorded from the MIB condition. The average time between a physical disappearance and the key press in the control condition was used to estimate the onset time of the illusionary target disappearance in the MIB condition. We then tested whether power fluctuations in different frequency bands before the estimated MIB onset would predict the length of MIB. Our results showed a positive correlation across participants between alpha power before the estimated MIB onset and MIB duration ($r = 0.45, p = 0.04$), indicating that participants with stronger alpha power were also the participants who experienced longer MIB. However, no such correlations were found between the power activity in other frequency bands (e.g., delta, theta, beta, gamma) and the length of MIB. Therefore, the results suggest that alpha dynamics plays an important role in the changes in perceptual state and may help shape our visual experience.
Motor neurons have a unique cellular phenotype because their cell bodies remain within the CNS while their axons extend out into the periphery. This distinct projection pattern relies on various cellular and molecular signaling pathways to regulate motor neuron migration, axonal growth and guidance. To advance our understanding of motor circuit formation, we need to elucidate the functions of molecules expressed by motor neurons during development. We have found that a cell adhesion molecule, Transient Axonal Glycoprotein type-1 (TAG-1), is a fundamental, multifunctional regulator of motor neuron development and circuit formation. Multiple neural cell types transiently express TAG-1 during development, and while TAG-1 is expressed on motor neuron cell bodies and axons during early stages of differentiation and axon outgrowth, the function of TAG-1 in motor neurons is not known. An examination of TAG-1 knockout (KO) mice revealed three major defects in motor neurons: (1) motor axon bundles (ventral roots) are expanded, (2) motor neuron cell bodies aberrantly leave the spinal cord, and (3) motor axons have severe guidance defects and invade dorsal root ganglia. The severity of defects in motor axon bundling, guidance, and cell migration indicate that TAG-1 is integral to motor circuit formation. Utilizing a combination of novel genetic tools in mice, whole embryo imaging, and in vitro assays, we will continue to investigate the molecular mechanisms of TAG-1 function in motor circuit formation. Our data provides valuable insights into the complex developmental functions of cell adhesion molecules. Understanding the molecular mechanisms that regulate normal neuronal development will inform therapeutic approaches for neuronal repair and could aid in the diagnosis and treatment of diseases that result from brain mis-wiring.
ACCURACY OF THE HOSPITAL TRIAGE LOS ANGELES MOTOR SCALE IN IDENTIFYING EMERGENCY LARGE VESSEL OCCLUSION ON CTA

Prasanna Tadi MD, Pranav Reddy MSIII, Pemmasani Sravanthi MD, Nasir Fakhri MD, Matthew Siket MD, Mahesh Jayaraman MD, Ryan McTaggart MD, Shadi Yaghi MD, Ali Saad MD, Jason T Machan PhD, Brian Silver MD

CT angiography (CTA) is now the gold standard for rapid identification of acute stroke caused by an emergency large vessel occlusion (ELVO) and increasingly emergency departments are utilizing a direct from EMS stretcher-to CT process to minimize time to diagnosis of acute ischemic stroke. However, the incidence of false positive pre-hospital stroke activations is high and the addition of CTA of the cerebrocephalic vasculature to a standard NCCT(non-contrast CT scan) triples the radiation exposure. A pre-hospital stroke severity scale, such as the Los Angeles Motor Scale (LAMS) may have utility in selecting the appropriate patients needing CTA and improve its overall yield in patients suspected of having an acute ischemic stroke. We reviewed 249 consecutive CODE STROKE activations at a single academic emergency department in a comprehensive stroke center over a 3.5 month period since institution of a LAMS cutoff of >4 to trigger CTA acquisition. Data was acquired for the entirety of the sample and only the physical exam data was reviewed by three neurovascular attending physicians independently for LAMS score analysis. Shrivat-Fleiss weighted and Standard kappa coefficients were used to estimate the inter-rater reliability between pairs of raters on LAMS scores. Standard kappa coefficients estimated reliability crossing the clinically meaningful threshold of 3 or less vs. 4-5, as well as physician judgment as to whether a stroke was present. Shrivat-Fleiss weighted kappa coefficients between pairs of raters on LAMS scores were 0.67, 0.55, and 0.62. Kappa coefficients for pairs of raters when LAMS were dichotomized as <3 vs. 4-5 were 0.64, 0.50, and 0.71. Kappa coefficients between pairs of raters for assessment of stroke were 0.33, 0.47, and 0.16. These results suggest that, while reliability statistics retain validity in the model, clinically meaningful disagreements were evident between raters. In our study, LAMS had clinical utility in selecting patients with acute ischemic stroke for the appropriate combined CT/CTA imaging modality when used by LAMS trained medical personnel. We validated the LAMS in an in-hospital rather than pre-hospital cohort and suggest that it has clinical utility in selecting patients for the combined CT/CTA imaging package. Its accuracy and ease-of-use makes LAMS an ideal clinical tool to rapidly assess acute stroke patients in screening for ELVO and for patients eligible for emergency mechanical thrombectomy while preserving judicious and appropriate radiation exposure. Limitations of this study include retrospective evaluation of findings and a relatively small sample size. Appropriate training is required to ensure accuracy of LAMS scoring by providers.
LEFT ATRIAL ENLARGEMENT AND CRYPTOGENIC STROKE

Prasanna Tadi, MD, Mayra Montalvo Perero, MD; Shadi Yaghi, MD

Introduction: Despite extensive evaluation, no definite cause is identified in 30-40% of ischemic stroke patients. Left atrial dysfunction or “cardiopathy” have been shown to be associated with ischemic stroke risk, a relationship independent of atrial fibrillation. Our aim was to determine the association of Left Atrial Enlargement (LAE) with cryptogenic stroke.

Methods: We conducted a retrospective study where we reviewed the medical records of 261 ischemic stroke patients admitted to Rhode Island Hospital between January 1st 2010 until August 31st 2015. LA size from 2D Echocardiography was categorized as normal LAE, mild LAE, moderate, and severe LAE.

Results: We identified 236 patients with ischemic stroke; 85 cryptogenic stroke and 151 of known non-cardioembolic etiology. In the non-cryptogenic cohort 73 adults had large vessel disease and 58 had small vessel disease. For the entirety of the group, the mean age was 67 with 45% males. Patients with cryptogenic stroke were more likely to have moderate to severe LAE when compared to patients with known non-cardioembolic etiology (p = 0.0061).

Conclusion: Moderate to severe left atrial enlargement, a biomarker of atrial cardiopathy or dysfunction, is more prevalent in patients with cryptogenic stroke than strokes of known etiology, suggesting that this may constitute one of the stroke mechanisms in this patient population. Clinical trials are needed to improve stroke prevention strategies in patients with cryptogenic stroke and evidence of atrial cardiopathy.
Case Report:
A 23-year-old female with a history of migraines and tobacco use was brought to the emergency department with a two-hour history of acute onset right sided hemiplegia and expressive aphasia. The differential diagnosis for acute onset right sided hemiplegia and expressive aphasia includes: stroke, demyelinating disease, metabolic disorders, and psychiatric disease. Due to the acute onset of symptoms and objective findings on neurologic exam, the most likely diagnosis was thought to be stroke. The clinical syndrome was localized to the contralateral middle cerebral artery (MCA) territory. Her head CT showed hypodensity of the left caudate, lentiform and insula, highly suspicious for an acute left MCA infarct. CT angiography showed total occlusion of the left supraclinoid internal carotid artery and left M1 segment with mild collateralization of the left M2 segment. There was no evidence of hemorrhage on head CT and no contraindications for thrombolytic therapy. The patient received intravenous thrombolytic therapy which when given within 4.5 hours from onset improves the chances of good functional outcome. Since the patient had a large vessel occlusion and she was within 6 hours from onset, she subsequently underwent mechanical thrombectomy for removal of a left M1 occlusion. She had an excellent response to therapy, with minimal residual aphasia on examination. In the process of evaluation a transthoracic echocardiogram was done which demonstrated a large (over 5cm) size mass in the left atrium prolapsing into the left ventricle. The mass was suspicious for myxoma. A cardiac MRI was done which showed a lobulated amorphous 4.9 x 2.4 x 2.5 cm mobile left atrial mass consistent with myxoma which appeared to be attached to left atrial wall immediately inferior to the os of left atrial appendage, a small part of it extending into left atrial appendage. Given the size of the patient's stroke presentation and recent thrombolytic therapy for ischemic stroke the risk of intracranial bleeding was considered and surgery was delayed. The patient subsequently had another small embolic event which demonstrated no significant gross deficits although there were some associated visual changes. Given the recurrence of the episode, the risk of intracranial bleeding was thought much lower than the risk of third embolic phenomenon and therefore the decision was made to proceed with surgery for cardiac tumor resection. Intraoperative findings revealed that the tumor occupied 80% of the left atrium. Pathological analysis confirmed atrial myxoma. Atrial myxoma is a rare cause of stroke in the younger population. It is a benign cardiac tumor arising from the subendocardial mesenchymal cells. Incidence of cardiac tumors ranges from 0.001% to 0.3% in autopsy studies and a 0.15% incidence in major echocardiographic series. With atrial myxomas, early identification of the cause is of utmost importance to improve outcome and avoid residual disability. Definitive treatment needs to be done with surgical resection.
“I’M GLAD THAT I GOT HIV—I CAN TEACH HER:” A QUALITATIVE STUDY OF FAMILY HIV PREVENTION PRACTICES WITH MOTHERS LIVING WITH HIV AND THEIR ADOLESCENT CHILDREN

Nicholas Tarantino, MA & Jamee Carroll

Due to treatment advances, mothers living with HIV (MLH) increasingly have the opportunity to raise their children into adolescence and beyond. Many, however, face significant social and behavioral challenges to parenting and family life. Such challenges may contribute to the intergenerational transmission of risk for HIV infection which has been speculated to occur in families of MLH. For the purposes of understanding how to reduce this vulnerability and promote healthy families, our study examined the effects of maternal HIV infection on several established family-based targets of intervention for youth HIV prevention. This includes mother-adolescent relationship quality, communication about sex and HIV, and parental monitoring. We also wanted to demonstrate how mother-to-child HIV disclosure may influence family processes in a way that is protective of adolescent HIV risk. Four focus groups with 15 MLH and 13 in-depth interviews with HIV-negative adolescent children of MLH were conducted. Participants were low-income, primarily African American, and from an urban setting in the southeastern United States. MLH ranged in number of years they had been living with the virus from less than a year to 17 years (M = 13, SD = 9). All adolescents were aware of their mother’s HIV status. The semi-structured focus group and interview protocols were organized by questions related to HIV prevention targets and the disclosure experience. Using a theoretical thematic analysis, several themes emerged from the qualitative data such as the protective effect of HIV infection on adolescent risk behavior and mother-adolescent communication about sex and sexual risks; mother-adolescent attachment disruption due to maternal substance abuse history; and problems related to continuing the mother-to-son HIV disclosure process. A complete thematic map of the findings is presented and example excerpts from the data are highlighted. Findings are discussed in the context of adapting evidence-based HIV prevention interventions for MLH and their adolescent children.
CUES TO FACILITATE WORD LEARNING IN TYPICALLY DEVELOPING CHILDREN AND CHILDREN WITH ASD

Elena Tenenbaum, PhD, Dima Amso, Stephen J. Sheinkopf

Attention to a speaker’s mouth predicts successful word learning and higher language ability among typically developing (TD) children and children with autism spectrum disorder (ASD) (Tenenbaum, Amso, Abar, & Sheinkopf, 2014; Young, Merin, Rogers, & Ozonoff, 2009). We explored whether we can facilitate word learning by pushing attention to the mouth of a speaker by pointing (Experiment 1) or holding the object near the mouth (Experiment 2).

In Experiment 1, children with ASD (n = 19, 14 male, 5 female, M = 47.67 months, SD = 12.73) and language matched TD participants (n = 17, 12 male, 5 female, M = 20.29 months, SD = 6.89) participated in a word learning task. Trials included baseline in which two objects appeared on the screen, familiarization in which the speaker provided a label for the target object (e.g. “Hey, it’s a dax! Do you see the dax? What a great dax!”), and test in which the two objects reappeared after the instructions, “Look at the dax!” Participants saw 6 trials. On half the trials, the speaker pointed to her mouth while labeling the object. In experiment 2, children with ASD (n = 24, 20 male, 4 female, M = 69.14 months, SD = 21.17) and language matched TD children (n = 23, 16 male, 7 female, M = 30.47 months, SD = 20.36) saw three trial types. On Far trials, the speaker held the object off to the side (as in Experiment 1). On Near trials, the speaker held the object close to her mouth while labeling it, and on Cover trials, the speaker held the object in front of her mouth.

In Experiment 1, pointing to the speaker’s mouth increased attention to that region of the face (proportion of tracked time spent fixating the mouth on Point trials: M = .27, SD = .20; No Point trials: M = .21, SD = .20; Paired sample t-test: t(32) = 1.81, p = .08). Contrary to predictions, pointing to the speaker’s mouth did not facilitate word learning among TD or ASD participants. Difference scores between proportion of time spent fixating the target at test minus proportion spent fixating the target at baseline were in fact lower in the pointing condition than in the baseline condition (Point: M = -.03, SD = .19; No Point: M = .06, SD = .24; t(33) = 1.93, p = .06). In Experiment 2, TD and ASD participants increased attention to the target at test on Near trials (One sample t-test >0, t(40) = 2.77, p <.01) but not on Far or Cover trials (Far: t(41) = 1.34, ns, Cover: t(42) = .96, ns).

Manipulating social cues during object labeling had either detrimental (pointing to the speaker’s mouth) or facilitative (holding the target object near the mouth) effects on novel word learning. Results are discussed in the context of mechanisms underlying connections between social attention and language learning. These findings have implications for refining language therapies for infants and children with emerging speech.
PERCEIVED SEXUAL PERMISSION FROM THE MEDIA: RACIAL AND GENDER-DEPENDENT VARIATIONS

Sneha Thamotharan MA, David Barker PhD, Esther Henebeng BS, Chris Houck PhD

Exposure to sexual content in mass media (e.g., magazines, movies, music, and television) has been linked to adolescents’ attitudes about and increased engagement in sexual behavior, with significant racial and gender differences being observed. However, little information exists on whether adolescents perceive sexual permission from the media and whether this perception of permission differs by race, gender and their interaction.

Method: Participants consisted of early adolescents (mean age = 12.94, SD = 0.53) engaging in a sexual risk prevention intervention for youth with mental health symptoms or engaging in risk behaviors. Slightly less than half of the participants were female (n = 191, 47%). Ethnic and racial backgrounds were diverse with 37% reporting Hispanic decent (n = 152), followed by Euro-American (n = 100, 25%), African-American (n = 96, 24%), and Other (n = 61, 15%). Participants completed a computer assisted self-interview that included the Perceived Sexual Permission from the Media (PSPM) scale. This scale was dichotomized to reflect adolescents who did or did not believe that mass media approved sex for adolescents.

Results: Of the total sample (N = 409), 106 (26%) endorsed believing that mass media approved sex for adolescents. A logistic regression was performed to ascertain racial and gender differences in adolescents’ perceived sexual permission from the media. There was a significant main effect for race (p = .04), no main effect for gender (p = .11), and a near significant interaction between the two (p = .07). Compared to their Euro-American peers, African American (Odds Ratio[OR] = 0.26, p = 0.02) and Hispanic (OR = 0.37, p = 0.02) females were less likely to believe that mass media approved sex for adolescents. Further, for African American early adolescents, males were more likely than females to perceive sexual permission from the media (OR = 5.89, p = .01). A similar, near significant difference was also found for Hispanic early adolescents, with males again more likely than females to perceive sexual permission from the media (OR = 2.82, p = 0.08).

Conclusions: Results reflect a small proportion of early adolescents perceive sexual permission from the media, which is somewhat discrepant from previous findings on the effects of exposure to sexual media on adolescents’ engagement in sexual risk behavior. Results also suggest that there are differences among racial and gender subgroups, especially with regard to minority females. These differences are particularly striking given that African American female youth often have the highest rates of STIs/HIV. Understanding why minority females may not see mass media as shaping their sexual beliefs despite evidence that their behavior is influenced by the media may help identify novel approaches to communicating to minority youth about sexual messaging in the media.
AN APPROACH TO CIRCUITS IN PSYCHIATRIC DISEASE: INTERROGATING ACTIVITY IN A THALAMUS-SPECIFIC KNOCKOUT OF TSC1

Brian Theyel, MD, PhD & Barry Connors, PhD

Advances in genetic manipulation and new ways of exploring neurocircuitry are enhancing our ability to detect relevant changes in the brains of mice with mutations associated with Psychiatric disease. Here, we present an experiment in which we combine an imaging technique and single-cell recordings to interrogate neurocircuitry in such a mouse. Initial results suggest a difference between wild-type and mutant mice, but more data need to be collected for statistical analyses. In this mouse, TSC1, highly penetrant for autism in humans, is knocked out in only a subset of thalamocortical relay cells, yet this is sufficient to yield repetitive grooming and seizures, suggesting that this is disease-related circuitry. We are using this paradigm to characterize changes in inputs from thalamus to cortex at the level of individual cells and network level simultaneously. Such a project demonstrates the potential for the combination of these techniques, alongside traditional slice physiology, to examine how a specific circuit change related to Psychiatric pathology leads to effects both at the level of neuron-neuron communication, as well as at the network level. The first of its kind, this work gives us circuit specificity and information about circuit perturbations relevant to disease that could be used to directly inform neuromodulatory experiments in humans.
THE ROLE OF INTERPERSONAL RISK FACTORS IN THE PREDICTION OF SUICIDAL IDEATION IN A SAMPLE OF MULTIPLE SUICIDE ATTEMPTERS: AN ECOLOGICAL MOMENTARY ASSESSMENT STUDY

Zoe Trout, BA, Evelyn M. Hernandez, Richard T. Liu, PhD, Evan M. Kleiman, PhD, Matthew K. Nock, PhD

Self-injurious thoughts and behaviors have been predominantly studied using retrospective self-report measures. This methodology is limited, however, in its ability to capture the temporal nuance of suicidal ideation (SI) in relation to its risk factors, as such ideation is likely to fluctuate in response to environmental changes and stressors, and may present fleetingly.

In the present study, Ecological Momentary Assessment (EMA) was used to examine Joiner’s interpersonal theory of suicide (2005), which identifies perceived burdensomeness and thwarted belongingness as two central risk factors predicting SI. EMA offers an ideal design for assessing these constructs with high temporal resolution as it is less likely to be biased by retrospective reporting and can better capture contextual variables that affect these thoughts. Despite these advantages, few studies have utilized EMA to assess suicidality (Davidson, Anestis, & Gutierrez, 2016); this study is the first to examine Joiner’s theory and the associated risk factors using EMA, providing novel insight into these risk factors as they vary on a daily basis and predict SI.

Participants were 36 adults ages 18 to 45 (71% female; 68% white; Mage =23.93, SD = 5.01) who reported making at least two suicide attempts in the past year. Participants completed an assessment of perceived burdensomeness, thwarted belongingness, and SI on their smartphones each night for an average of 15.56 days (SD = 11.29).

Results demonstrated considerable day-to-day variation in each of these variables. Burdensomeness and thwarted belongingness were each concurrently associated with SI, while the interaction between burdensomeness and thwarted belongingness was non-significant. Neither burdensomeness nor thwarted belongingness, nor the interaction between the two predicted SI the next day. These findings demonstrate partial support for Joiner’s theory, but suggest limitations in the ability of these risk factors to predict SI in the short term among a high-risk sample.
PREDICTING HUMAN EPILEPTIC SEIZURES FROM INTRACORTICAL MICROELECTRODE ARRAY SIGNALS

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The need for new therapeutic interventions to treat pharmacologically resistant focal epileptic seizures has led recently to the development of closed-loop systems for seizure control. Once a seizure is predicted/detected by the system, electrical stimulation is delivered to prevent seizure initiation or spread. So far, seizure prediction/detection has been limited to tracking non-invasive electroencephalogram (EEG) or intracranial EEG (iEEG) signals. Here, we examine seizure prediction based on local field potentials (LFPs) from a small neocortical patch recorded via a 10×10 microelectrode array implanted in a patient with focal seizures. We formulate the seizure (ictal) prediction problem in terms of discriminating between interictal and preictal neural activity. Using convolutional neural networks (CNNs), we show that periods of preictal activity can be successfully discriminated (80% detection; no false positives) from periods of interictal activity several (2 – 18) minutes prior to seizure onset. CNN input features consisted of the spectral power of LFP channels (1-second time windows) computed in 50 frequency bands (0 – 100 Hz; 2 Hz steps). Our preliminary results show that intracortical LFPs may be a promising neural signal for seizure prediction in focal epilepsy.
EFFECTS OF CONFLICT-DRIVEN ATTENTION ON HIGH AND LOW LEVEL VISUAL PROCESSING

Kerstin Unger, PhD, Rebecca Waugh, MA, Michal Worden, PhD

Compatibility effects in selective attention tasks are typically reduced following incompatible trials compared to compatible trials, an observation termed congruency sequence effect (CSE). Relatively little is known about the nature of the attentional mechanisms that are engaged in response to recent conflict between incompatible stimulus and/or response representations. In particular, the existing literature remains controversial as to whether conflict-induced attentional mechanisms operate at early (or only later) stages of visual processing and work preferably through enhancement of target information or also by suppression of distractor information. In this study, we examined the relative contribution of these mechanisms using a modified spatial flanker paradigm with face and house stimuli as targets and distractors. Individually defined regions of interest (ROIs) included Fusiform Face Area (FFA), Parahippocampal Place Area (PPA), and regions within early visual cortex corresponding to the spatial locations of the target vs. the peripheral distractors. Behavioral results showed the expected compatibility effect as well as conflict adaption following incompatible trials. Imaging data indicated that the BOLD response in distractor regions was reduced following incompatible compared to compatible trials, whereas activity was enhanced for the center target. Furthermore, FFA activation to face targets was reduced following incompatible trials with face distractors compared to trials with house distractors. We observed a qualitatively similar albeit weaker effect for the PPA’s response to house targets following incompatible trials including houses vs. faces as distractors. These findings suggest that conflict-induced attentional mechanisms modulate processing in early and higher-level visual areas via both suppression and enhancement.
Background: Exposure-based therapy for PTSD uses tenets of extinction learning to reduce symptoms by repeated exposure to feared stimuli without the occurrence of feared consequences. Abnormalities in fear extinction is thought to be a core component of posttraumatic stress disorder (PTSD). Successful extinction learning relies on the generating of a novel safety memory that competes with the original fear memory. Prior research points to the ventromedial prefrontal cortex (vmPFC) as a potential site for extinction success, consolidation, and subsequent retention of extinction memory. Pursuing to augment extinction learning in itself and/or the consolidation of labile safety memories immediately after extinction may provide clinical benefits. In two different studies we explored whether 1) transcranial direct current stimulation (tDCS) during extinction of a conditioned stimulus (CS) can augment extinction of a second CS in healthy volunteers, and 2) tDCS during extinction training or during immediate extinction reconsolidation, improved extinction recall in Veterans with warzone-related PTSD.

Methods and Results: We administered a 2-day Pavlovian fear conditioning, extinction, and recall paradigm while continuously recording skin conductance. Participants in both experiments received 2 mA tDCS for 10 minutes with the anodal electrode placed over EEG coordinate FA3 and the cathodal electrode over the contralateral mastoid. For experiment 1, 26 participants received active tDCS during extinction of a first conditioned stimulus, and 18 participants received active tDCS during extinction of a second conditioned stimulus. Results showed a significant interaction between timing of tDCS during extinction blocks and changes in skin conductance reactivity over late extinction trials. These data indicate that tDCS was associated with accelerated late extinction learning of a second conditioned stimulus after tDCS was combined with extinction learning of a previous conditioned stimulus. No significant effects of tDCS timing were observed on early extinction recall. In the second experiment, 14 Veterans with PTSD received active tDCS starting at the onset of extinction learning, and 14 Veterans with PTSD received tDCS starting immediately after extinction completion during extinction reconsolidation. Results revealed that Veterans who received tDCS immediately following extinction training showed borderline significant lower skin conductance reactivity to previously extinguished stimuli during early recall compared to Veterans who received tDCS during extinction training, generating a medium effect size (Cohen’s d’= 0.34). There was no significant effect of tDCS on skin conductance during late extinction.

Conclusions: Taken together the results of these two studies not only show that tDCS can influence extinction learning and memory processes, but more importantly, tDCS appears to have a time-dependent effect in relation to extinction learning and recall. Namely, tDCS during extinction learning may influence subsequent extinction, but tDCS during extinction consolidation, i.e. after extinction learning, may enhance extinction memory. This is relevant for designing clinical tDCS applications.
LINKING OBJECTS TO ACTIONS: ENCODING OF TARGET OBJECT AND GRASPING STRATEGY IN PRIMATE VENTRAL PREMOTOR CORTEX

Carlos Vargas-Irwin, PhD, Jonas B. Zimmermann, PhD, Lachlan Franquemont, PhD, Michael J. Black, PhD, John P. Donoghue, PhD

Ventral premotor cortex (PMv) is a key node in the parieto-frontal network specialized in transforming visual information representing the shape of objects into hand postures best suited for grasping them. It remains unclear how PMv networks can flexibly link percepts of objects affording multiple grasp options into a final desired hand action. Here, we use a relational encoding approach to track the functional state of PMv neuronal ensembles in macaque monkeys through the process of passive viewing, grip planning, and grasping movement execution. We used objects affording multiple possible grip strategies. The task included separate instructed delay periods for object presentation and grip instruction. This approach allowed us to distinguish responses elicited by the visual presentation of the objects from those associated with selecting a given motor plan for grasping. Neural data was analyzed using the spike train similarity space algorithm (SSIMS) recently developed by our team. Mapping neural data into a SSIMS projection is done without any information regarding behavioral condition (unsupervised dimensionality reduction). Instead, the method relies on the intrinsic properties of the neural data and does not require an explicit model of the relationship between neural activity and external variables. The SSIMS algorithm begins by embedding the neural data into a high-dimensional pairwise similarity space, and then projects the data into a more compact (low-dimensional) representation, which facilitates statistical analysis as well as data visualization while still capturing the relationship between individual data points. A neural activity pattern is represented by a single point in the resulting SSIMS projection. The distance between points denotes the degree of similarity between the activity patterns they represent. Two identical firing patterns correspond to the same point in this space; the more different they are, the farther apart they lie in the SSIMS projection.

Our results show that PMv continuously incorporates information related to object shape and grip strategy as it becomes available, revealing a transition from a set of ensemble states initially most closely related to objects, to a new set of ensemble patterns reflecting unique object-grip combinations. These results suggest that PMv dynamically combines percepts, gradually navigating toward activity patterns associated with specific volitional actions, rather than directly mapping perceptual object properties onto categorical grip representations. Our results support the idea that PMv is part of a network that dynamically computes motor plans from perceptual information.
HIGH RATES OF MENTHOL USE IN PREGNANT SMOKERS: A PRELIMINARY REPORT

Chrystal Vergara-Lopez, PhD, Allison Gaffey, MA, Margaret Bublitz, PhD, Raymond Niaura, PhD, Laura Stroud, PhD

Background: Smoking during pregnancy is one of the most widespread prenatal insults in the world, and has known causal associations with perinatal and neonatal morbidity. Reducing rates of smoking during pregnancy is a major public health goal. Despite links between menthol cigarette use and reduced quit rates, little is known about use of menthol cigarettes in pregnant smokers. Further, although racial/ethnic minorities (particularly black women) show a disproportionate use of menthol cigarettes, few studies have investigated racial/ethnic variation in menthol cigarette use during pregnancy.

Method: We investigated rates of menthol cigarette use in two racially/ethnically diverse cohorts of pregnant smokers recruited between 2006-2010 (Cohort I) and 2012-2015 (Cohort II). Cohort I included 83 pregnant mothers (Mage=25, SD=5; 51% minorities); Cohort II included 73 pregnant mothers (Mage=26, SD=5; 60% minorities). Average cigarettes per day, menthol cigarette use, quit status, race/ethnicity and other demographics were assessed by structured interviews over pregnancy. Quit status was verified by saliva cotinine and breath CO in Cohort I.

Results: High rates of menthol use were found in both cohorts (84% of pregnant smokers in Cohort I; 89% of pregnant smokers in Cohort II). Rates of menthol cigarette use were similarly high across all race/ethnicity groups in both studies (Cohort I [whites: 75%; blacks: 94%; Hispanic: 89%; Other/multi-race: 100%]; Cohort 2 [whites: 83%; blacks: 91%; Hispanic: 95%; Other/multi-race: 86%]); menthol and non-menthol users also did not differ in socio-economic status or age. In Cohort I, menthol smokers were less likely to quit (20% quit) over pregnancy compared to non-menthol smokers (38% quit) (p=.16).

Conclusion: We found extraordinarily high rates of menthol cigarette use in pregnant smokers, with little variability by race/ethnicity or socio-economic status in two Northeast cohorts between 2006 and 2015. Given known fetal morbidity from maternal smoking, consideration of effects of tobacco and menthol on the next generation is warranted in evaluating regulation of menthol in cigarettes.
PREGNANT SMOKERS SHOW ALTERED MATERNAL SENSITIVITY AND BEHAVIOR

Chantelle Ward, BS; Tessa Kehoe, BA; Stephanie Parade, PhD; Laura Stroud, PhD

While the number of mothers who smoke throughout pregnancy is on the decline (Tong et al., 2013), at least half of women who smoke continue smoking throughout their pregnancy (Ebrahim et al., 2000). Women who smoke during pregnancy are more likely suffer from externalizing disorders such as conduct disorder (CD) and attention deficit hyperactivity disorder (ADHD) during childhood and to engage in antisocial behavior than non-smokers (Kodl & Wakschlag, 2004). Given the differences between those who smoke during pregnancy and those who do not, it follows that differences in child-rearing behavior may exist. Smoking during pregnancy is correlated to lower levels of maternal nurturing behavior and higher levels of physical punishment (Fergusson et al., 1998). In 2002, Wakschlag and Hans examined parenting characteristics as moderating variables between prenatal smoking and development of child behavior problems and found that the level of maternal responsiveness significantly affected whether boys whose mothers smoked prenatally later developed conduct disorder. We sought to elaborate on previous research regarding differences in maternal parenting characteristics of non-smokers, quitters and smokers throughout pregnancy.

145 families participating in the Behavior and Mood of Babies and Mothers 2 (BAMBAM2) study were included in this analysis. The study included n=37 smokers, n=18 quitters and n=90 non-smokers. Mothers ranged in age from 18-37 years (M=26 years) and the majority (50%) had a high school degree or less. Mothers were racially diverse (44% white, 26% Black, and 30% other races). 39% were Hispanic. Approximately half of infants were male.

At 6-months of age, mothers and their infants engaged in a Free Play Task to assess maternal behavior and sensitivity. Maternal behavior and sensitivity was coded by the lead author using the Parent Caregiver Involvement Scale (Farren et al., 1986) and the Emotional Availability Scales (Biringen et al., 1988).

Individual maternal behavior scales were examined for links to study group using ANOVAs. There were significant differences in maternal sensitivity between groups (F = 3.57, p = .031), such that smokers were less sensitive than quitters (p = .025) and non-smokers (p = .021). A significant difference in amount of positive regard mothers displayed toward their infants were also detected between groups (F = 3.39, p = .036), with non-smokers showing higher amounts than smokers (p = .011). Overall acceptance towards their infants also yielded significant differences between groups (F = 4.29, p = .016), such that smokers displayed lower acceptance towards their infants than non-smokers (p = .045) and quitters (p = .005). Lastly, maternal enjoyment yielded significant differences between groups (F = 3.11, p = .048), with smokers having displayed a lower amount of enjoyment with their infants when compared to quitters (p = .017). There was no significant difference in behavioral and sensitivity ratings between non-smokers and quitters.

Smokers were found to be less sensitive, less accepting, and to display lower enjoyment with their newborns compared to quitters and control mothers. There were no significant differences in maternal behavior between non-smokers and quitters. Previous research has shown prenatal smoking results in a more irritable, highly aroused infant. The findings from the present study suggest differences in parenting characteristics between smokers and quitters/non-smokers may exacerbate the negative effects of prenatal smoking on infant behavior. Results have implications for education and prevention efforts with pregnant and postpartum smokers and also for elucidating pathways underlying the intergenerational transmission of smoking.
EXPLORING THE TIC SUPPRESSION PARADIGM IN YOUTH WITH TIC DISORDERS

Brianna Wellen, BA & Christine Conelea, PhD

Tic disorders are characterized by involuntary motor movements and/or vocalizations, often onset between the ages of 4-6 years, and become the most severe at ages 10-12 (Bloch & Lechman, 2009). Although tic disorders are primarily attributed to neurobiological dysfunction, research has demonstrated that context influences tic expression, such that tics can be exacerbated or alleviated by certain environmental situations (Himle et al., 2005). Self-reported measures indicate that individuals tic more frequently when they are tired or in social situations and less frequently when concentrating or relaxed (Conelea & Woods, 2008). In order to empirically study conditions under which tic rates change, Himle and colleagues (2004) developed a tic suppression paradigm involving direct observation of tics under different conditions. The paradigm typically compares a baseline condition (tic freely) to a reward condition (earn points for suppressing tics). Over 10 studies have used this methodology and collectively demonstrate that adolescents and children tic significantly less when rewarded for suppressing tics. Although there is a large body of research to support this paradigm, these studies do not have much power individually (average N = 9). The aim of the current project is to review the literature and calculate overall effect sizes, combining data from multiple trials.

An initial search reveals that there are at least 6 peer-reviewed articles investigating the tic suppression paradigm that report enough data to include in the effect size analysis. Preliminary analyses using these articles indicate a combined N of 72 participants, and that tics per minute were very high during the baseline condition (M = 12.03) and much lower during the reward condition (M = 3.14). Further analyses will be conducted using this sample, an in-depth review of the literature will be performed to include any studies published in the interim, and methodology will be discussed in detail.

Discussion will situate results in the current research, specifically addressing contextual factors implicated in tic expression. It will further address implications of these results for future research examining tic suppression.
A PRACTICAL COMPARISON OF THE SIEMENS TIM TRIO AND SIEMENS PRISMA FIT SCANNERS FOR ANATOMICAL AND FUNCTIONAL MRI

Westlin, C., BA, Bedard, P., PhD, Guediche, S., PhD, Luthra, S., Walsh, E., PhD, Yan, P., PhD, Sanes, J., PhD, Dickstein, D., MD, Worden, M., PhD

Magnetic resonance imaging is a widely used technology that reveals both functional and anatomical information. Recently, the MRI Research Facility at Brown University upgraded our scanner from the Siemens 3T Tim Trio to the Siemens 3T Prisma Fit. In order to assess implications for ongoing research studies, we investigated how the scanner upgrade impacted various MRI modalities, including anatomical signal-to-noise ratio (SNR), resting state fMRI connectivity, and task-based fMRI. We found a significant increase in anatomical signal-to-noise ratio values for the new Prisma Fit scanner compared to the old Tim Trio scanner, as well as a significant increase in resting state fMRI connectivity measures for comparable brain regions. However, we found no significant increase for task-based fMRI. The results suggest that the new Prisma Fit scanner allows for higher quality anatomical images (in terms of image noise or image resolution) using similar scan times or the ability to acquire equivalent quality images in less time. Similarly, resting state results suggest that the new scanner allows for better connectivity detection due to the reduction of noise in the data. Finally, task-based fMRI likely showed no significant difference because SNR is adequate at standard spatial resolutions on both scanners. Although not tested, we would expect the increased SNR levels to allow fMRI studies to be done at higher resolutions at which image SNR becomes a limiting factor.
The rubber hand illusion is a somatic-perception illusion in which individuals attribute a sense of ownership to a rubber arm in a visible place where their arm that is covered could plausibly be. The experimenter induces the illusion by stroking both the participant’s covered real arm and the rubber arm synchronously. Previous studies have shown that when this illusion is induced, subjects seem to perceive the rubber arm as part of their body. Variability in the ability to induce the rubber hand illusion and in the strength of the illusion has been observed between subjects, but there is little data indicating why this variability exists. Here, we investigate potential resting-state network characteristics associated with variability in the rubber hand illusion by assessing correlations between rubber hand illusion susceptibility scores in 12 participants with functional connectivity measures during resting-state fMRI acquisitions. Our results provide initial evidence suggesting that individual differences in rubber hand illusion susceptibility scores are associated with greater connectivity between the left intraparietal sulcus and the anterior cerebellum, a region thought to be involved in somatotopic motor representation and motor control.
EVALUATION OF PROGRAM FIDELITY FOR WAVE ONE OF A RANDOMIZED CONTROLLED TRIAL OF THE YOUR VOICE YOUR VIEW SEXUAL VIOLENCE PREVENTION PROGRAM FOR HIGH SCHOOL YOUTH

Miryam Yusufov, MS, Daniel W. Oesterle, George Andoscia, Lindsay M. Orchowski, PhD

Introduction: There is often wide variability in the reported effects of interventions. Effectiveness can vary across studies, sites, and providers. A factor often insufficiently considered is the fidelity of the treatment or program provided. Assessment of fidelity is needed to ensure that the program and treatment protocol is delivered as intended. Further, monitoring treatment fidelity throughout study implementation reduces attrition. Fidelity is particularly important in treatment studies conducted at multiple sites, to ensure that treatments are delivered in a standardized manner across sites and to reduce the possibility of ‘site by treatment’ interactions. Notably, conclusive statements about treatment effects cannot be made without attention to treatment fidelity. Therefore, the present study evaluated program fidelity of a randomized controlled trial of a sexual violence prevention program designed for high school students. External raters evaluated fidelity of facilitator adherence to study protocol, along with ratings of individual-facilitator presentation style, among 76 intervention sessions.

Methods: A total of five distinct intervention sessions were conducted with the following characteristics: Session 1 (n=23), Session 2 (n=20), Session 3, boys (n=12), Session 3, girls (n=8), Session 4 (n=4), and “Lunch & Learn” (n=9). One external rater noted adherence to program fidelity on a dichotomous scale (i.e., yes/no). The number of domains assessed varied by session type (i.e., Session 1, 16; Session 2, 23; Session 3-girls, 18; Session 3-boys, 20; Session 4, 21; “Lunch & Learn”, 18). The same external rater noted style for Facilitator 1 and 2 on a four-point Likert scale (1=strongly disagree, 2=disagree, 3=agree, 4=strongly agree). Style was examined along the following observable characteristics: being warm/inviting, confidence in answering questions, eye contact, articulation, enthusiasm, confidence in material, language, spontaneity, vocal variety, appropriateness, and physical behavior.

Results: Average session fidelity was 98.93% for Session 1, 91.74% for Session 2, 93.06% for Session 3 (girls), 94.86% for Session 3 (boys), 100% for Session 4, and 96.83% for “Lunch & Learn”. Mean style ratings for Facilitator 1 were as follows: 3.93 (session 1), 3.98 (session 2), 4.00 (session 3, girls), 3.97 (session 3, boys), 3.93 (session 4), and 3.90 (“lunch & learn”). Mean style ratings for Facilitator 2 were high as well: session 1 (M=3.93), session 2 (M=3.96), session 3, girls (M=4.00), session 3, boys (M=3.98), session 4 (M=3.94), and “lunch & learn” (M=3.95). Chi-square analyses revealed no significant differences in mean style scores between Facilitator 1 and 2. Overall style means across sessions ranged from 3.93 to 4.00.

Discussion: Findings suggest strong treatment fidelity and high ratings for facilitator style across multiple domains. Such adherence to treatment protocol may warrant more conclusive statements about treatment effectiveness upon study completion. Future evaluations of treatment fidelity for this program are warranted. Results are also discussed in terms of their implications for researchers and clinicians.
PATHWAY LASSO: ESTIMATE AND SELECT SPARSE MEDIATION PATHWAYS WITH HIGH DIMENSIONAL MEDIATORS

Yi Zhao, PhD & Xi Luo, PhD

In many scientific studies, it becomes increasingly important to delineate the causal pathways through a large number of mediators, such as brain mediators. Structural equation modeling (SEM) is a popular technique to estimate the pathway effects, commonly expressed as products of coefficients. However, it becomes unstable to fit such models with high dimensional mediators as predictors, especially for a general setting where all the mediators are causally dependent but the exact causal relationships between them are unknown. This paper proposes a sparse mediation model using a regularized SEM approach, where sparsity here means that a small number of mediators have nonzero mediation effects between a treatment and an outcome. To address the model selection challenge, we innovate by introducing a new penalty called Pathway Lasso. This penalty function is a convex relaxation of the non-convex product function, and it enables a computationally tractable optimization criterion to estimate and select many pathway effects simultaneously. We develop a fast ADMM-type algorithm to compute the model parameters, and we show that the iterative updates can be expressed in closed form. On both simulated data and an real fMRI dataset, the proposed approach yields higher pathway selection accuracy and lower estimation bias than other competing methods.
NEURAL ENSEMBLE ACTIVITY CHARACTERIZES SLEEP, ACTIVE MOVEMENT, AND MOVEMENT OBSERVATION STATES IN PRIMATE MOTOR CORTEX

Jonas B. Zimmerman, PhD, Carlos E. Vargas-Irwin, PhD and John P. Donoghue, PhD

Detection of behavioral states is an important feature of any brain-computer interface suitable for 24h operation. Periods of sleep can resemble rest in local field potentials or movement when comparing firing rates. Here we demonstrate distinct representations of action, action observation, rest, and sleep periods in a low dimensional neural state space. We recorded simultaneous ensemble neural activity from primary motor cortex, and dorsal and ventral premotor areas from the rhesus macaque while the monkey was engaged in a reach to grasp task, observed an experimenter perform the same task, and during sleep. In accordance with previous experiments, we found that overall neural activity is decreased during sleep compared to movement, observation, and rest in all three areas. Nevertheless, short periods of high neural activity occur during sleep, with firing rates comparable to movement periods. We used spike train similarity measures and dimensionality reduction techniques to project ensemble activity during movement, action observation, rest, and sleep into low-dimensional neural state spaces. In all areas, active movement trials cluster separately from observation trials during object contact. Rest in inter-trial periods constitutes another cluster. Periods of sleep again constitute a separate cluster, with some overlap with resting periods. Whereas both action observation and movement trials exhibit a distinct pattern of cycles in neural state space, such organization does not seem to occur in sleep periods. Transient increases in firing rates occur during all the behaviors investigated, yet we can distinguish between different behavioral states using unique signatures in neural dynamics. Automatic detection and classification of such states will be a valuable tool for calibration of closed-loop BCIs.