Abdelmessih, Peter
Board 1, Session 1
PI: Bodfish, Jim

Altered neural processing during the execution of complex sensorimotor behavior in autism

Peter Abdelmessih ,Robin L. Shafer, Eli Solomon , Mark H. Lewis, Karl M. Newell , James W. Bodfish.

Stereotyped behavior consists of rhythmic, repetitive movement Precedes complex, goal-directed behavior in typical development (TD) Considered maladaptive, abnormal in autism spectrum disorder (ASD) Associated with low motor complexity Complex, adaptive movements are mediated by sensorimotor integration Sensorimotor integration may play a role in the expression of motor stereotypy

Visuomotor EEG Task: Participants track a moving target on screen with a computer mouse Random start position and direction of motion 8 blocks (4 feedback, 4 no feedback), 32 trials/block Feedback: Target & cursor are present for the duration of the trial No Feedback: Cursor & target are present initially, disappear mid-trial, reappear at the end. Participants keep moving without visual cues.

Both ASD and TD show reduced error and increased motor complexity when visual feedback is available Motor complexity is negatively correlated with severity of clinical stereotypy in ASD ASD and TD show increased alpha neural complexity when visual feedback is available No group differences in alpha complexity

Individuals with ASD have abnormal sensorimotor processing that may indicate use of compensatory neural mechanisms Low motor complexity is associated with greater clinical stereotypy

Arceneaux, Jerome
Board 2, Session 2
PI: Grueter, Brad A.

Temporal Dynamics of Cocaine-Induced Drug-Reward Behavior in TLR4-Deficient Mice

Jerome S. Arceneaux, Daniel T. Kashima, Carrie A. Grueter, and Brad A. Grueter

Substance use disorders (SUDs) affect more than 7% (19.7 million people) of the US population. While men are twice as likely to develop SUDs, women are more sensitive to the negative consequences of drugs of abuse and have increased propensity of relapse to drug-seeking behavior. Toll-like receptor 4 (TLR4), a component of the innate immune system, is implicated in drug-related behavior. However, the contribution of TLR4 to the temporal components of cocaine experience is largely unknown.

To determine the contribution of TLR4 to cocaine-induced behavior, the behavioral properties of wildtype (WT) and TLR4 knockout mice (TLR4.KO) were compared following cocaine exposure. Locomotor sensitization and place conditioning assays were used to elucidate how TLR4 modulates cocaine-induced behavior.

We find that TLR4 deficiency results in differential expression of cocaine-induced locomotor sensitization between males and females. While both male and female TLR4.KO mice had reduced locomotor responding during the development of cocaine sensitization, female TLR4.KO mice exhibited robust enhancement of sensitization expression following a challenge dose of cocaine. In addition, female TLR4.KO mice had prolonged retention of associative memory following cocaine exposure and displayed reinstatement following a subthreshold dose of cocaine.

Taken together, these results suggest TLR4 contributes to behavioral adaptations in response to cocaine experience.

Badivuku, Hana
Board 3, Session 1
PI: Niswender, Colleen

Characterization of Rett Syndrome Model Mice by Electroencephalography

Hana Badivuku, Susmita Chennareddy, Robert W. Gould, Nicole M. Fisher, Rocco C. Gogliotti, Carrie K. Jones, Colleen M. Niswender

Rett syndrome (RTT) is a neurodevelopmental disorder characterized by loss of hand use, intellectual disability, motor dysfunction, speech impairment, apraxia, central apneas, and seizures. It has been determined that loss-of-function mutations in the methyl CpG binding protein 2 gene (MECP2) result in RTT, and mice lacking the Mecp2 gene exhibit phenotypes similar to those seen in RTT patients. Unfortunately, direct modulation of MeCP2 is challenging because neurons require precise levels of MeCP2, leading to narrow safety margins. As a result, research efforts at the Vanderbilt Center for Neuroscience Drug Discovery (VCNDD) are focused on targeting neurotransmitter receptors downstream of MeCP2. This study aimed to characterize RTT model mice by quantitative electroencephalography (EEG) to establish baseline differences that could serve as biomarkers in future pharmacological studies.

This study involved the surgical implantation of EEG transmitters in mice at six weeks of age. Thirteen mice were selected - six wild-type females and seven Mecp2+/- females - and were housed individually throughout the duration of the experiment. EEG recordings began at eight weeks of age and continued every other week for forty-eight hours until the mice were twenty weeks of age. Sleep staging was scored manually via Neuroscore to determine the periods in which each mouse was in active wake, quiet wake, slow-wave sleep (SWS), or paradoxical (REM) sleep. Analysis of quantitative EEG (qEEG) parameters, activity, and temperature was also performed by Neuroscore software.

We found significant differences in the sleep-wake architecture of Mecp2+/- mice compared to wild-type mice. Mecp2+/- mice experienced reduced REM sleep and fewer bouts of REM sleep during the light phase of each recording, as well as decreased activity and temperature during the dark. qEEG analysis revealed increased theta waves during both SWS and REM sleep, as well as decreased delta waves during SWS when compared to the wild-type mice.

In summary, we report an overall reduction in REM sleep in Mecp2+/- mice that persists from eight to twenty weeks of age and is consistent with what has been observed in RTT patients. The resulting decrease in the overall duration of REM sleep in Mecp2+/- mice could potentially contribute to deficits in fear learning and novel object recognition that we have reported. Decreased delta power during SWS corresponds to decreased sleep quality, which may impact memory consolidation. Additionally, the diminished ability of Mecp2+/- mice to regulate body temperature is consistent with an impaired autonomic nervous system. Future studies will test the ability of novel compounds to normalize these EEG phenotypes of Mecp2+/- mice. This work was supported by R01 MH113543 and CDMRP/DoD award W81XWH-17-1-0266.

Bailey, Kathryn
Board 4, Session 2
PI: Lambert, Joseph

Training Caregivers to Implement Trial-Based FCT to Treat Severe Challenging Behavior in a Home Setting

Kathryn M. Bailey, Cassandra M. Standish, Joseph M. Lambert

Severe challenging behavior in individuals with intellectual and developmental disabilities (IDD) is a persisting challenge for the caregivers and communities that surround these individuals. Key stakeholders in these individuals' lives, including their caregivers, teachers, and other staff, may face issues like burnout due to this problem behavior. Behavioral intervention is often implicated in supporting these individuals and those that care for them. However, certain access barriers may exist when it comes to behavioral intervention for this population. Thus, a main issue in behavioral intervention research is the need to train indigenous implementers in the natural environment of persons with disabilities. Caregivers may be able to implement function-based interventions to treat their childrens' severe challenging behavior in a home setting. Certain function-based interventions, like functional communication training (FCT), are designed to increase adaptive communicative behaviors and can effectively reduce problem behavior. Functional communication training is an empirically validated differential reinforcement of alternate behaviors intervention developed by Carr and Durand (1985) that involves first identifying the function of challenging behavior, and then reinforcing an alternative, but functionally-equivalent communicative response while placing problem behavior on extinction. However, FCT is typically implemented by teams of trained implementers, and can be an expensive process for families in terms of both time and funding. Adapting interventions, like FCT, into trial-based formats may increase their feasibility and acceptability in naturalistic settings. Currently, there is a lack of research on the effects of caregiver implemented trial-based FCT in home settings on children's severe and challenging behaviors.

Three caregivers of children with IDD and severe challenging behaviors were systematically trained in implementing trial-based FCT procedures with their children to validate the results of a previous trial-based functional analysis. Using a reversal design (A-B-A-B), we analyzed the impact caregiver-implemented trial-based FCT had on latency to challenging behavior in the participants' children, as well as the extent to which parents were able to implement the intervention to fidelity.

Preliminary results suggest that caregiver-implemented trial-based FCT is effective in reducing severe challenging behavior in a naturalistic setting. Caregivers can be trained as primary interventionists for their children at home using a systematic training procedure.

These results suggest that training natural implementers in FCT procedures at home is feasible and effective, which has implications for reducing access barriers to behavior analytic services and function-based interventions like FCT.

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Burton, Jane
Board 5, Session 1
PI: Ramachandran, Ramnarayan

Neuronal frequency selectivity in the inferior colliculus and cochlear nucleus of the awake behaving macaque monkey

Jane A. Burton, Ramnarayan Ramachandran

Frequency selectivity relates to the ability to process complex signals and can be measured through perceptual auditory filters. Numerous previous studies have characterized behavioral and neuronal filters, but comparisons have been problematic. Behavioral filters show broader tuning compared to cochlear and auditory nerve fiber tuning, but these estimates are highly dependent on the methodology used for measurement. Two prevailing thoughts on the substrate of perceptual filters are as follows: (i) they have their basis in the auditory periphery; and (ii) they evolve across the auditory pathway. To test between these two hypotheses, we compared simultaneously measured behavioral and neuronal filters in two important subcortical auditory stations: the cochlear nucleus (CN) and inferior colliculus (IC).

Three macaque monkeys were trained to detect tones in steady state broadband noise and in spectrally notched maskers of varying notch width. Single unit responses were isolated in the CN and IC and were recorded simultaneously with the behavioral responses. During the single unit recordings, the frequency of the signal to be detected was the characteristic frequency (CF) of the isolated unit. Signal detection theoretic methods were used to determine psychometric thresholds and receiver operating characteristics were used to measure neurometric thresholds. Psychometric and neurometric tone thresholds in notched-noise were used to derive perceptual and neuronal auditory filters, respectively, using the rounded exponential fit. Filters were characterized by the equivalent rectangular bandwidth (ERB).

Behavioral and neuronal filters increased in bandwidth with increasing CF. Behavioral and neuronal bandwidths were significantly correlated and not significantly different from each other for single units recorded in the CN and in the IC. Neuronal filter bandwidths were variable across units and structures, possibly reflecting heterogeneity of neuronal encoding strategies.

These findings support a model in which behavioral frequency selectivity is established early in the auditory pathway. These data form the baseline for ongoing studies of macaques with noise-induced hearing loss and future studies of emerging hearing loss therapeutics.

Casale, Ellen
Board 6, Session 2
PI: Hodapp, Robert

School Administrators & Special Education: A National Survey of Knowledge, Perspectives, & Training

Ellen G. Casale, Sarah E. Blumberg, Robert M. Hodapp

Now more than ever, administrators are under increased pressure to improve educational outcomes of all students as federally mandated in the Every Student Succeeds Act (ESSA, 2015) and the Individuals with Disabilities Education Improvement Act (IDEIA, 2004). This responsibility is amplified within the national administrator accreditation standards (e.g., National Education Leadership Preparation standards or Professionals Standards for Educational Leaders). The purpose of this ongoing survey is to gather information from a national sample of school administrators to gather information about administrators': a) demographics; b) prior work/teaching experience; c) education and training; d) perceptions, practices, and barriers related to special education; and e) concerns. Descriptive results and correlates of special education practices have implications for both the special and general education fields.

Data were collected from October 2018 to August 2019 from building-level school administrators across the nation in a web-based survey. Univariate and multivariate analyses were completed in order to answer the following research questions: : 1) To what extent are school administrators prepared to deal with an oversee the implementation of special education processes?; 2) To what extent do administrators implement strategies to support the special education processes?; 3) Are there correlates of administrators who implement a large number of special education practices, or report having a high level of special education content knowledge?

Current results represent administrators from 11 states representing administrators at both the elementary and secondary levels representing ages from 26 to 63. Many administrators reported never to rarely having experiences with persons with disabilities in their post-baccalaureate training and are satisfied with their special education staff. Additional results will be available at the time of presentation.

Cassidy, Margaret
Board 7, Session 1
PI: Woynaroski, Tiffany G.

Relations Between Sensory Responsiveness and Broader Symptomatology in Children with and without Autism

Margaret Cassidy, Jacob I. Feldman, Yupeng Liu, Neill Broderick, Mark T. Wallace, Tiffany G. Woynaroski

Autism spectrum disorder (ASD) has historically been characterized by deficits in social communication and by the presence of restricted and repetitive patterns of behavior, interests, and activities (RRBs). Individuals with ASD may also present with co-morbid language and intellectual impairments. The most recent diagnostic criteria for ASD now additionally recognize differences in patterns of responding to sensory stimuli (i.e., sensory responsiveness) as a core characteristic of ASD. Clinically, these differences in sensory responsiveness can be characterized as hyperresponsiveness (i.e., over-responding to sensory stimuli), hyporesponsiveness (i.e., under-responding to sensory stimuli), and sensory seeking (i.e., craving of certain sensory stimuli). It has been proposed that differences in sensory responsiveness, particularly early in life, may produce cascading effects on broader development, potentially causing or contributing to the constellation of deficits that have conventionally considered the core characteristics of ASD. Previous research indicates that children with ASD present with significantly more of these symptoms compared to their typically developing (TD) peers, and that these patterns of sensory responsiveness are associated with concurrent ASD and related symptoms in early childhood (e.g., in children ≤ 8 years old). The present study examines sensory responsiveness in school-aged children and adolescents with ASD. Specifically, we explored (a) whether between-group differences are present in sensory responsiveness in ASD and well-matched TD peers, (b) whether there are associations between patterns of sensory responsiveness and broader ASD and related symptoms, and (c) whether those associations are moderated by group.

Preliminary analyses were conducted on 26 older children and adolescents with ASD (aged 8;0-21;11) and 26 TD controls matched on sex and chronological age. The measures collected and used in statistical analyses include parent report measures of sensory responsiveness (i.e., the Sensory Experiences Questionnaire [SEQ] and Sensory Profile [SP]), core ASD symptomatology (i.e., the Social Communication Scale [SCQ] and Social Responsiveness Scale [SRS]), adaptive functioning (i.e., the Vineland Adaptive Behavior Scales [VABS]), social emotional wellbeing (i.e., the Behavior Assessment System for Children [BASC]), and a battery of norm-referenced and standardized language assessments (i.e., the Clinical Evaluation of Language Fundamentals [CELF-4] and Receptive/Expressive One Word Picture Vocabulary Tests [ROWPVT/EOWPVT]).

Preliminary results indicated that groups significantly differed in all three patterns of sensory responsiveness, with large effect sizes (d's = 3.4, 2.7, and 1.7 for hyporesponsiveness, hyperresponsiveness, and sensory seeking, respectively). Additionally, patterns of sensory responsiveness were correlated with several metrics derived from measures of other core and related symptoms of ASD. For example, across groups increased sensory seeking symptoms were associated with greater language impairments on the CELF (r = 0.36), increased social communication difficulties on the SCQ (r = 0.61) and SRS (r = 0.63), increased restricted and repetitive behaviors on the SRS (r = 0.68), increased incidence of anxious behaviors (r = 0.42) and other internalizing behavior problems (r = 0.48), and more severe communication deficits on the VABS (r = 0.45). These aforementioned metrics were also highly correlated with increased hyporesponsiveness (r's = 0.37 - 0.90) and hyperresponsiveness (r's = 0.47 - 0.80). None of the associations were moderated by group.

This study extends prior work to show that differences in sensory responsiveness that are linked with core and related ASD symptomatology persist in older children and adolescents on the autism spectrum. Preliminary results indicate that associations between sensory responsiveness and social communication and language symptoms are particularly robust. Final results, along with limitations and implications for theory and clinical practice, will be presented at the VKC Science Day.

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Centanni, Sam
Board 8, Session 2
PI: Winder, Danny

An insular-BNST neural circuit regulates ethanol forced abstinence-induced negative behavioral affect

Samuel W Centanni, Bridget D. Morris, Joseph R. Luchsinger, Tracey L. Fetterly, Danny G. Winder

Negative affective states are associated with a wide range of psychiatric diseases including depression, anxiety, and drug addiction; however, our current understanding of the underlying neural circuitry, and therapeutic targets to improve treatment outcomes and diagnosis are limited. Here we used a multifaceted circuit-based approach in preclinical models to elucidate a neural circuit that controls negative affect following alcohol withdrawal, a reliable predictor of relapse. We define mechanisms to mitigate dysfunction in these pathways, with the goal of improving diagnostic tools and treatment outcomes.

We used a two-bottle choice mouse model of chronic ethanol drinking followed by forced abstinence (CDFA) in combination with whole-cell electrophysiology, fluorescent in situ hybridization, immunohistochemistry, chemogenetic/optogenetic circuit manipulations, behavioral assessments for negative affect, and in vivo calcium measurements with fiber photometry.

CDFA mice consume up to 20 g/kg/day of ethanol, even in the presence of the aversive tastant quinine. Moreover, CDFA reliably produces a negative affective phenotype in protracted abstinence. CDFA increased neuronal activity in a key region regulating affective state, the bed nucleus of the stria terminalis (BNST), evidenced by increases in c-fos expression, glutamate release, and behavior-correlated in vivo calcium activity during tests for negative affect. Next, using a channelrhodopsin-assisted mapping strategy, we identified the insular cortex (insula), a region involved in regulating interoception, as a dense, functional, excitatory input to the BNST. Chemogenetically inhibiting insula neurons with hM4Di mitigated the abstinence-induced phenotype, thus implicating this region in negative affect. Using an anterograde strategy for transsynaptic targeting of Cre in combination with the Cre-dependent Gq-coupled chemogenetic DIO.hM3Dq, we specifically activated BNST neurons receiving inputs from the insula, as indicated by a robust increase in c-fos expression. hM3Dq activation increased latency in the novelty suppressed feeding task (NSFT), a measure of affective state. To determine the functional relevance of the insula inputs to BNST in regulating affective behaviors, ongoing experiments are measuring insula terminal calcium release in the BNST during affective behavioral tests with GCaMP in the insula and a fiberoptic in the BNST.

Together, these data point to a novel neural insula-BNST pathway strongly involved in regulating negative affect, and we begin to delineate the dysfunctional state of this pathway in abstinence. A more holistic understanding of affective circuitry will open the door for developing highly effective diagnostic tools and targeted therapeutics for treating negative affect in abstinence.

Chennareddy, Susmita
Board 9, Session 1
PI: Niswender, Colleen

Differential expression pattern of HSPA6 in Rett syndrome

Susmita Chennareddy, Sheryl A. Vermudez, Nicole M. Fisher, Yuta T. Moxley, Rocco Gogliotti, Colleen Niswender

Rett syndrome (RTT) is a neurodevelopmental disorder that is clinically characterized by developmental regression, cognitive deficits, loss of ability to speak, stereotypic hand movements, and apneas. Approximately 95% of individuals presenting with typical RTT exhibit loss-of-function mutations in the methyl-CpG binding protein (MeCP2) gene; however, ~5% of RTT patients are MeCP2-mutation negative. MeCP2 is a methyl reader protein, and RNA-sequencing analysis comparing MeCP2 mutation-positive and negative temporal cortex autopsy samples has identified 784 genes that are similarly affected in both populations. Among the most significant was the heat shock protein (HSP) family A member 6 (HSPA6) gene. HSPA6's response to cellular stress is unique from other HSPs, as it localizes to sites of active transcription instead of protein degradation machinery. Paradoxically, HSPA6 disruption is also one of the most conserved findings in idiopathic autism and Alzheimer's disease; however, the protein is not expressed in rodents, and its exact function remains poorly understood.

To examine how loss of MeCP2 impacts HSPA6 expression, we obtained HAP1 cells engineered to have a nonsense mutation in the MeCP2 locus (Horizon). Cultured parental and MeCP2 knock-out cells were then heat shocked at 42°C for 2 hours before being returned to 37°C for recovery. Cells were harvested at progressive points between 0 and 24 hours. Western blot analysis was performed using antibodies against HSPA6 (1:1000, OriGene) and tubulin (1:5000, Abcam). All values were compared relative to cells without heat shock.

Expression of HSPA6 protein was induced by 2 hour heat shock in both HAP1 Parent and MeCP2 mutant cell lines. Baseline HSPA6 expression was low in non-heat shocked samples, as well as throughout the two hour heat shock. Conversely, expression increased substantially 0.5-2 hours after heat shock in both cell lines. Interestingly, in all three trials, HSPA6 expression was induced faster, with a higher magnitude, and for a longer duration in HAP1 parental cells relative to MeCP2 mutant cells.

The HSPA6 response to heat shock was diminished in MeCP2 mutant cells relative to controls. One possible explanation arises from closer examination of the heat shock response. During heat shock, HSP expression is induced in a manner that requires SWI/SNF dependent chromatin remodeling. MeCP2 associates with the catalytic component of the SWI/SNF, and we hypothesize that pathological MeCP2 mutations impact the ability of this complex to epigenetically regulate the HSPA6 promoter. Future directions of this study will explore differences in mRNA expression and methylation between parental and mutant MeCP2 cell lines and the impact of an HSPA6 transgene on RTT phenotypes in mice.

Chen, Siqi (Alice)
Board 10, Session 2
PI: Miller, David

Branched-Actin Promotes Presynaptic Elimination in GABAergic Neurons

Siqi Chen, Andrea Cuentas-Condori, and David M. Miller, III

Synaptic plasticity is one of the underlying mechanisms for learning and memory and dysregulated synaptic pruning is linked to human neurological disorders. Our studies of remodeling C. elegans GABAergic neurons, have revealed a critical role for the actin cytoskeleton in synapse elimination. Dorsal D (DD) GABAergic motor neurons initially form synapses with ventral muscles which then relocate to dorsal muscles during early larval development (1). The DD remodeling scheme, however, is normally blocked in Ventral D (VD) GABAergic motor neurons by the COUP-TF/unc-55 transcription factor. The Miller lab has previously used neuron-specific expression profiling to identify unc-55-regulated transcripts and global RNAi to show that one of these candidates, ARX-5/p21, a component of the Arp2/3 complex, promotes removal of the presynaptic apparatus in remodeling VD neurons (2). Because the Arp2/3 complex nucleates assembly of branched actin networks, this finding suggests that actin polymerization drives synapse elimination. Here, we used cell-specific RNAi to show that arx-5/p21 is required for removal of presynaptic domains in the native DD remodeling program.

We used the flp-13 promoter to drive co-expression of arx-5 sense and antisense strands specifically in DD neurons. Two expression plasmids were co-injected, one expressing the arx-5 sense strand and cytosolic mCherry and the other expressing the arx-5 antisense strand and nuclear-localized GFP. We used SNB-1::GFP/Synaptobrevin to visualize DD neuron presynaptic terminals. DD cells showing both cytosolic mCherry (red) and nuclear GFP (green) should express double-stranded RNA (dsRNA) for cell-specific knockdown of arx-5.

In wild-type DD neurons, few SNB-1::GFP puncta are retained on the ventral side at the L4 stage due to remodeling. In contrast, DD neurons that express arx-5 dsRNA retain substantially more ventral SNB-1::GFP fluorescence ($p<0.01$, $N=13$) than wild type. Thus, our results suggest that the Arp2/3 complex acts cell-autonomously in DD neurons to promote presynaptic removal.

My study suggests that F-actin is required for synaptic elimination in DD neurons. However, little is known about the mechanisms that direct the removal of presynaptic proteins. Some studies suggest not only the localization of actin polymerization in the active zones, but also bring up the questions of actin polymerization function (3,4). Importantly, F-actin is shown to drive bulk endocytosis at presynaptic terminals (5). This raises the interesting hypothesis that F-actin driven bulk endocytosis is involved in promoting synaptic elimination in DD neurons. One limitation in my study, however, is that it is hard to predict the extent of impact of p21/arx-5 knockdown on actin dynamics. We could confirm the role of Arp2/3 complex in promoting DD remodeling using the native and tissue-specific fluorescence (NATF) strategy (6).

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Ciriegio, Abagail
Board 11, Session 1
PI: Compas, Bruce

The Association Between Cognitive Function, Coping with Stress, and Levels of Distress in Offspring of Patients with Huntington's Disease

Abagail E. Ciriegio, Lisa Hale, Anna C. Pfalzer, Katherine McDonel, Heather Riordan, Sarah Moroz, Daniel O. Claassen, Bruce E. Compas

Huntington's disease (HD) is an autosomal dominant neurodegenerative disease characterized by progressive deficits in cognitive function, motor function, and psychiatric symptoms. More specifically, it has been established that HD is marked by deficits in executive function including working memory early in disease pathology (You et al., 2014). Offspring of HD patients are faced with high levels of stress due to increased caretaking responsibilities, observing the painful decline of their parent, and the uncertainty of their own gene status, as each offspring has a 50% chance of inheriting the Huntingtin gene mutation. Given their risk for inhering the mutant gene, associated impairment in cognitive and executive function, and possible impairment in the ability to manage the myriad of stressors that they face, offspring of patients with HD are at risk for heightened levels of anxiety, depression and other psychiatric symptoms. In the current study, we examined the association of cognitive function, coping with stress, and levels of distress in adolescent and young adult offspring of HD patients.

In a sample of adolescent and young adult offspring of HD patients (n=22) with a mean age of 17.73 years (SD=5.60), we assessed auditory and visual working memory using the List Sorting Task from the NIH Toolbox Cognition Battery (Gershon et al., 2010). The Youth Self Report (Achenbach & Rescorla, 2001) and Adult Self Report (Achenbach & Rescorla, 2003) were used to assess symptoms of Mixed Anxiety/ Depression (mean T Score of 58.9, SD=8.4). Secondary control coping (acceptance, cognitive reappraisal, distraction) was measured using the Responses to Stress Questionnaire (Conner-Smith et al., 2000). Direct and indirect associations among working memory, coping, and symptoms of anxiety/depression were tested using PROCESS Version 3.3 (Hayes, 2018).

The direct association between working memory and levels of anxiety/depression approached significance (β=-.37, p=.09). Working memory was significantly and positively associated with secondary control coping (β=.44, p=.04). Secondary control coping was significantly and negatively associated with levels of anxiety/depression (β=-.54, p=.02). The indirect association between working memory and levels of anxiety/depression through secondary control coping was significant (b=-.21, SE=.12, 95% CI (-.52, -.03)). The direct association between working memory and levels of anxiety/depression was non-significant when secondary control coping was included in the model.

This study provides the first evidence that both deficits in working memory, and the ability to manage stress are associated with increased levels of anxiety and depression in offspring of HD patients. Our findings suggest two potential targets to help at-risk adolescents and young adults: improving working memory and promoting complex cognitive coping strategies.

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Conley, Alexander
Board 12, Session 2
PI: Newhouse, Paul

Cognitive and Electrophysiological Measures of a Phase 1 Single Ascending Dose Study of the Muscarinic Positive Allosteric Modulator VU319

Alexander C. Conley, Alexandra P. Key, Jennifer U. Blackford, P. Jeffrey Conn, Craig Lindsley, Carrie Jones, Paul A. Newhouse

The development of neurotransmitter based cognitive enhancers for Alzheimer's disease have focused recently on allosteric modulation, as a way of reducing potential drug-limiting toxicities that have been the hallmark of earlier orthosteric compounds. VU319 is an experimental positive allosteric modulator of the M1 muscarinic acetylcholine receptor that has recently begun clinical testing in healthy volunteers. Cognitive tasks and event-related potentials (ERPs) were used during the randomized, double-blind, placebo-controlled Single Ascending Dose study of VU319 to identify early markers of efficacy and target engagement. VU319 is an investigational new drug that has not been approved by the FDA for any use.

VU319 was given orally to 40 healthy volunteers aged 18-55 years in five dose escalating cohorts of eight participants, in which six received VU319 and two received placebo. Cognitive and electrophysiological tasks were examined pre-dosing and at 5 hours post-dose. The tasks were selected for their sensitivity to cholinergic tone. Cognitive tasks tested spatial and sustained attention, episodic and working memory, perceptual vigilance and psychomotor speed. Tasks recorded by EEG tested auditory and visual attention using oddball tasks, and an incidental memory task in which participants passively observed novel and repeated complex image.

The analysis suggests a trend for improvements in cognitive and ERP performance on the higher doses of VU319 compared to placebo. Participants on the highest dose of VU319 appeared to respond faster to targets on the continuous performance test compared to participants on placebo (effect size $d = 1.2$). Additionally, participants who received the higher two doses of VU319 exhibited larger incidental memory response(greater amplitudes to repeated vs. novel images) compared to placebo ($d > 0.8$).

We conclude that these preliminary results suggest potential enhancement of the cholinergic system in healthy adults following a single dose of VU319. These early results indicate potential measures that are sensitive to target engagement by VU319 and support the examination of multiple doses of VU319 in healthy volunteers or patients

Conrad, Benjamin
Board 13, Session 1
PI: Price, Gavin

Neural mechanisms of digit processing in kindergartners: An fMRI study

Benjamin N. Conrad, Gavin R. Price

Number symbol processing is a critical foundation for math achievement. Evidence in adults suggests preferential engagement of a "Number Form Area" (NFA) in the ventral occipito-temporal cortex (vOTC), during the processing of Arabic numerals compared to other symbols, and that the function of this region relates to individual differences in calculation ability. It is currently unknown, however, 1) when preferential processing of the NFA develops, 2) what mechanisms drive category specificity in the NFA, and 3) how NFA function relates to behavior in children.

We address these questions using fMRI in typically-developing kindergartners who performed a symbol classification task. Participants (n=46, Mean age 6.1±0.4yo) saw digits, letters, or scrambled symbols, deciding whether they "knew the name" of the stimulus. Analyses included traditional univariate measures of activation levels in the NFA in response to each condition, multi-voxel pattern analysis (MVPA) to look at representational distinction in voxelwise activity patterns across the NFA, and region to region task-based connectivity measures using beta-series correlations.

We found no evidence for preferential processing of digits in the NFA in relative activation level, nor in representational distinction via MVPA. Similarly, we found no evidence of differences across symbol categories in NFA-to-parietal connectivity, as would be predicted from a biased-connectivity account of vOTC functional development. In a brain-behavior correlation, a significant negative association was observed between digit-related activity in the NFA and digit naming speed ($r = -0.52$, $p < 0.001$), with higher performance related to lower activation to digits relative to other symbols. The relationship remained significant ($p < 0.02$) after controlling for letter naming speed.

This finding suggests NFA function is relevant for digit recognition in kindergarten, albeit in the opposite direction than expected. Overall, our results are not easily reconcilable with prior findings in adults, suggesting a complexity to NFA development which requires further investigation, including longitudinal assessment of NFA functional maturation.

Consoli, David
Board 14, Session 2
PI: Harrison, Fiona

Synaptic glutamate dysfunction underlies epileptic activity and cognitive decline in early amyloid pathology

David C. Consoli, Jordyn M. Wilcox, Shilpy Dixit, William P. Nobis, James M. May, Fiona E. Harrison

The gene encoding the amyloid precursor protein (APP) is located on chromosome 21 leading to amyloid abnormalities in patients with Down Syndrome due to APP triplication. The co-occurrence of subclinical epileptic activity amidst early amyloid pathology has recently been highlighted as a significant hinderance to cognitive development. Altered epileptogenic signaling results from pathological synaptic glutamate dysfunction that could be a valid treatment target for cognitive improvement in patients with Down Syndrome.

Young (12-16 weeks old) APP/PSEN1 and wild-type mice were treated with kainic acid, an agonist for the glutamatergic kainate receptor, twice per week for up to 8 weeks. Low doses (≤10 mg/kg) of kainic acid were used to avoid overt seizure behavior. Epileptogenic signaling was measured via telemetry EEG systems weekly for up to 6 weeks. Learning and memory were assessed using Morris water maze to explore changes in hippocampal function. Deficits in synaptic transmission and plasticity were studied via tetanus-induced long-term potentiation in hippocampal slices from kainic acid treated wild-type and APP/PSEN1 mice.

APP/PSEN1 mice were more susceptible to the effects of kainic acid. They showed greater numbers of altered epileptogenic signaling events without observable seizure behavior and were more likely to die in the days following administration. The surviving APP/PSEN1 mice showed memory impairments during reversal learning in the Morris water maze. Five days of low-dose kainic acid administration was sufficient to disrupt long term potentiation in both wild-type and APP/PSEN1 mice.

Chronic mild disruption of glutamatergic systems led to changes in cognitive ability and greater susceptibility to epileptogenic events in young mice with co-occurring mild amyloid pathology. Treating hyperexcitability in Down Syndrome patients may help protect cognitive development across their lifespan.

Crandall, Madison
Board 15, Session 1
PI: Yoder, Paul

Children with Autism Spectrum Disorder May Learn from Caregiver Verb Input Better in a Certain Engagement State

Madison Cloud Crandall, Kristen Bottema-Beutel, Jena McDaniel, Linda R. Watson, Paul J. Yoder

Building a generative vocabulary is an important treatment goal for children with autism spectrum disorder (ASD). Theory suggests that it may be more challenging for children to acquire verbs than nouns that are object labels. One way adults might facilitate verb learning in children with ASD is using verbs in utterances that map onto the child's current attentional focus (in follow-in utterances) when they are engaged in a special state of joint engagement, higher order supported joint engagement (HSJE). We thus asked, "does HSJE with caregiver follow-in verb input (HSJE+FV) predict later child expressive verb vocabulary in children with ASD?"

We conducted a longitudinal correlational design with three measurement periods using a sample of twenty-nine toddlers with ASD. Videos of parent-child free play sessions from Time 1 were coded for parent linguistic responses with verbs (follow-in utterances) and engagement state. Generalized linear models using full maximum likelihood estimates of the coefficients and robust standard errors were utilized to test the relation between parents' verb input in follow-in utterances in HSJE and later child verb expressive vocabulary, as measured by number of words produced from the action word section on the MCDI.

Caregiver verb input in follow-in utterances presented during HSJE accounted for a significant, large amount of variance in later child verb vocabulary; $R^2 = .26$. This relation remained significant when controlling for early verb vocabulary or verb input in other states. Other types of talk in follow-in utterances in HSJE did not correlate with later verb vocabulary.

To our knowledge, these findings are the first to confirm a prediction that follow-in verb input presented in one engagement state (HSJE) is differentially associated with later child expressive verb vocabulary. Unfortunately, verbs are a commonly over-looked aspect of language development for children with ASD. This correlational study is a step in a program of research designed to identify how verb input might be best provided to support the verb acquisition of children with ASD.

Cuentas-Condori, Andrea
Board 16, Session 2
PI: Miller, David

C. elegans neurons have functional dendritic spines

Andrea Cuentas-Condori, Ben Mulcahy, Siwei He, Sierra Palumbos, Mei Zhen, David M. Miller, III

Mammalian neurons display specialized postsynaptic protrusions or dendritic spines that receive input from presynaptic terminals. Dendritic spines are important signaling compartments in which molecular components of the postsynaptic apparatus can be dynamically reorganized in response to presynaptic stimuli. Spines are thus key cellular structures for integrating presynaptic input and for remodeling circuits during learning and memory. In the original electron microscopic reconstruction of the C. elegans nerve cord, John White and colleagues reported that a subset of neurons extends "short branhces" to neuromuscular junctions. Recently, postsynaptic receptors have been shown to localize to spine-like protrusions from ventral cord neurons raising the possibility that C. elegans has functional postsynaptic spines.

We have used a combination of super-resolution microscopy, high-pressure freezing electron microscopy, live-imaging and genetic manipulation to firmly establish the occurrence of functional dendritic spines in C. elegans.

Our analysis reveals striking parallels with dendritic spines in mammals. In both cases, dendritic spines (1) are structurally defined by a dynamic actin cytoskeleton; (2) appose presynaptic dense projections; (3) localize postsynaptic receptor clusters, ER and ribosomes; (4) display calcium transients triggered by presynaptic activity; (5) respond to developmental and activity-dependent signals that regulate spine density.

This work is important because it establishes a new in vivo model for studies of dendritic spine biology in a genetically-tractable organism. In addition, dendritic spines occur in C. elegans GABAergic neurons that undergo a developmentally-regulating remodeling program in which the presynaptic actin cytoskeleton is dramatically reorganized to create functional postsynaptic spines. Thus, we can now investigate the cell biological pathways that direct spine assembly in a synaptic remodeling mechanism that is critical to circuit function.

Daly, Claire
Board 17, Session 1
PI: Woynaroski, Tiffany

Automated Vocalizations of Infants at High- and Low- Risk for ASD: A Proposed Stability and Validity Study

Claire M. Daly, Jacob I. Feldman, Bahar Keceli-Kaysili, Sarah M. Bowman, Pooja Santapuram, Kacie Dunham, Alexandra J. Golden, Tiffany G. Woynaroski

Theory and past research suggest that metrics of early vocal development, including the frequency, duration, complexity, and reciprocity (parent-child exchange) of early vocalizations, are useful for predicting language development in a number of clinical populations. However, vocal development has historically been measured and derived in the laboratory via conventional behavior sampling approaches that are extremely time-intensive (and thus costly) to collect and code. As a result, such measures have little potential to translate to use in clinical practice. Recent work in our lab (Woynaroski et al., 2017; Harbison et al., 2018) has shown that novel, automated approaches to measuring vocal development are psychometrically sound and valid for predicting prelinguistic and linguistic development of preschool-aged children with autism spectrum disorder (ASD). However, no work to date has been done on these automated analyses of vocalizations in infants at heightened risk for ASD, leaving many questions about the stability and validity of such metrics in early development in this population.

The proposed study will extend the aforementioned work to evaluate automated indices of vocal development in infants at heightened genetic risk for receiving a future diagnosis of autism or language/communication impairment based on their status as infant siblings of individuals who are already diagnosed with the disorder (Sibs-ASD; n=35) and a control group of infants at relatively lower, general population-level risk for autism (Sibs-TD; infant siblings of typically developing children; n=35). Various indices of vocal development will be derived via automated analysis of extant data that was collected in the Biobehavioral Approaches in Neurodevelopment Laboratory at Vanderbilt University Medical Center (PI: Woynaroski). We will analyze the stability of these metrics using G and D studies (see Sandbank & Yoder, 2014) and the validity of these metrics using correlations to other metrics of pre-/linguistic development.

If vocal samples have not yet been processed by the LENA Research Foundation by Science Day, anticipated results will be presented.

The present project represents T0/preclinical research necessary to identify the measures of vocal development with sufficient psychometric support for use in a future T1/translational research project involving Sibs-ASD. The planned project will evaluate the indirect effects of an early communication intervention on distal social, communication, and language skill via midpoint infant vocalization by which early intervention may facilitate language and social development in infants at heightened risk for ASD. Clinical implications will also be discussed.

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D'Archangel, Micah
Board 18, Session 2
PI: Cutting, Laurie

Visuospatial Learning in Children with Neurofibromatosis Type 1 and Reading Disability: Navigating a Virtual Reality Water Maze

Micah D'Archangel, Stephanie Del Tufo, Laura Barquero, Laurie Cutting

Difficulty with reading ability is found in both individuals with Neurofibromatosis type 1 (NF1), a genetic disorder, and Reading Disability (RD) a developmental disorder. However, individuals with NF1 also commonly exhibit impaired visuospatial performance (North, 2000), while those with RD do not (Diehl et al., 2014). Across animal models of human disorders, the Morris Water Maze (Costa et al., 2002) is the most common measure of spatial learning and memory. While both the mouse and human model of NF1 have been reported to have difficulty performing the Water Maze task, no study to date has compared the performance of those with NF1 to those with RD. Therefore, in the current study, we examined the group differences in Water Maze performance between those with NF1 and RD in an effort to better understand the spatial learning differences between these populations.

Children and adolescents (Age=11.97yrs, SD=3.44) with either NF1 who had evidence of reading difficulty (n=14) or RD (n=7), performed a virtual reality Morris Water Maze. Participants took part in nine trials: two practices with a visible target platform, six with an invisible platform, and one probe trial with no target. Across all trial types, participants' float time, time in the target zone, and time in the target quadrant were measured. Multi-level mixed effect linear regression models were used to analyze the difference in group performance across all 6 learning and probe trials.

There was a significant 3-way interaction of group x performance measure x learning trial. Follow-up analyses revealed that the effect of group differed across all three performance measures. Float time was longer for the RD group than the NF group. The percentage of time individuals spent in the target zone was significantly greater for RD at the beginning of the learning trials, but by the end of the learning trials the group with NF spent more time in the target zone. The reverse was true for the percentage of time individuals spent in the target quadrant. Significant differences were also found during probe trials, driven by greater float time and time in the target quadrant by the RD group than the NF group.

These findings suggest distinctions in learning and target finding strategies between groups. Specifically, individuals with RD demonstrate adaptation over the course of learning trials, while those with NF1 struggle. This research may inform future targeted learning intervention strategies.

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DiCarlo, Gabriella
Board 19, Session 1
PI: Wallace, Mark

Autism-linked dopamine transporter mutation alters striatal dopamine neurotransmission and dopamine-dependent behaviors

Gabriella E. DiCarlo, Jenny I. Aguilar, Heinrich Matthies, Kyle E. Bundschuh, Fiona E. Harrison, Alyssa West, Parastoo Hashemi, Freja Herborg, Mattias Rickhag, Hao Chen, Ulrik Gether, Aurelio Galli, Mark T. Wallace

The dopamine transporter (DAT), a presynaptic membrane protein, regulates the temporal and spatial availability of the neurotransmitter dopamine (DA) by rapidly clearing released DA from the synapse. The precise regulation of synaptic DA by the DAT fine-tunes the phasic nature of the DA signal, which is required for reward processing and behavioral learning. Dysregulation of the DA system has been implicated in various neuropsychiatric disorders, including Autism Spectrum Disorder (ASD). A de novo mutation in the SLC6A3 gene resulting in a threonine to methionine substitution at site 356 (DAT T356M) was recently identified in an individual with ASD. Our group sought to determine the impact of this variant on transporter function, dopamine homeostasis, and mammalian behavior.

For all experiments, both male and female mice homozygous for the DAT T356M variant (DAT T356M+/+ mice) and their wildtype littermates were used. We used carbon fiber amperometry to quantify DA release and reuptake kinetics in striatal slices. To understand the impact of DA mishandling on DA homeostasis, we used immunoblotting and high performance liquid chromatography. A battery of behavioral tasks was used to explore the impact of the DAT T356M variant on behaviors associated with ASD (e.g. social deficits, repetitive behaviors, hyperactivity, etc.). Finally, drugs targeting the DAT were used to determine the reversibility of the observed behavioral changes.

DAT T356M+/+ mice displayed significant impairments in the uptake of released DA and reduced total tissue content of DA. Immunoblotting revealed down regulation of the DA synthetic pathway. DAT T356M+/+ mice exhibited a number of behavioral changes corresponding with the behavioral characteristics of ASD. These behavioral changes included reduced social preference, repetitive behaviors, and profound increases in spontaneous locomotor activity. Antagonism of the DAT reduced the observed hyperlocomotion in DAT T356M+/+ animals, suggesting that DAT-mediated leak of DA may underlie hyperactivity in these animals.

This research provides new evidence for a role of DAT dysfunction (specifically anomalous DA efflux) in the behavioral changes typically associated with ASD and ADHD and presents the exciting possibility of a potential mechanistic underpinning for these behavioral changes. Our model suggests that blockade of the DAT may improve behavior via reduction of DAT-mediated DA efflux. Importantly, this work provides a rigorous model for studying the impact of genetic variants on both transporter physiology and behavior from the structural to the mammalian level, a task that is becoming increasingly important with the now-common use of whole exome sequencing in the clinic and the drive to practice precision medicine.

Dillehay, Kelsey
Board 20, Session 2
PI: Kaiser, Ann

Mindfulness-Based Interventions for Stress Reduction in Caregivers of Children with Disabilities

Kelsey M. Dillehay, Ann P. Kaiser

In comparative studies, parents of children with developmental disabilities report higher levels of stress than parents of typically developing children (Baker et al., 2003; Baker-Ericzen, Brookman-Frazee, & Stahmer, 2005; Hayes & Watson, 2013; Theule, Wiener, Tannock, & Jenkins, 2013; Miranda, Tárraga, Fernández, Colomer, & Pastor 2015). Interventions to reduce caregiver stress are implemented in group and individual format, vary in dosage, and include interventions such as behavioral parent training, psychoeducational programs, cognitive behavioral therapy for parents, and mindfulness-based interventions (Frantz, Hansen, & Machalicek, 2017). There is emerging evidence that supports using mindfulness training to reduce stress in parents and caregivers who are raising children with disabilities (Jones, Hastings, Totsika, Keane, & Rhule, 2014; Jones et al., 2018). The purpose of this review was to evaluate studies in order to build a framework for future research employing mindfulness as an evidence-based intervention to reduce stress in caregivers of children with disabilities.

A review of literature search was conducted and studies meeting the following inclusion criteria were included in this review: (a) mindfulness intervention for parents or caregivers, (b) outcome measures included parent stress reduction or increased well-being, (c) child disability was developmental, intellectual, or behavioral, and (d) the study was peer reviewed. Studies were excluded for the following: (a) quasi-experimental or pre-post design, (b) caregiver's children were not school age, or older than 22-years old, and (c) results included parent report of mindfulness effectiveness without intervention. A coding system was developed to analyze quality indicators, methods and design, internal and external validity, and an estimate of the risk of bias.

The mean caregiver age was 40.80 years old and most participants had at least a high school diploma and an annual income slightly above average. The dosage of intervention varied from 1.5-2.5 hour sessions for six to eight weeks. The primary outcome measures were assessed through the Parenting Stress Index (PSI) and the Center for Epidemiological Studies Depression Scale (CES-D). The majority of studies indicated an acceptable quality of internal and external validity and a low to medium risk of bias. Selection and detection biases were prevalent throughout the studies.

Mindfulness interventions were effective for reducing stress in caregivers of children with disabilities. This should be considered an emerging evidence-based practice because of limitations such as a lack of blind assessors, the use of only self-report measures for stress outcomes, and little evidence of feasibility/acceptability in populations other than middle to upper-middle class samples. Studies were of acceptable quality and indicated a low to moderate risk of bias that showed positive implications for parenting stress.

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Douglas, Ashli-Ann
Board 21, Session 1
PI: Bethany Rittle-Johnson

Promoting Parents' Early Numeracy Input

Ashli-Ann Douglas, Bethany Rittle-Johnson

Preschoolers whose parents provide numeracy input frequently tend to have better numeracy knowledge than their peers whose parents provide numeracy input infrequently (e.g. Elliott et al., 2017). However, very little of parents' numeracy input to their preschoolers is about advanced early numeracy concepts (Ramani et al., 2015). Additionally, parents' numeracy input is often related to their belief about the importance of numeracy for their children (Douglas et al., 2019). The current study examined whether parents' input and child-centered belief about magnitude comparison, an advanced early numeracy concept, could be promoted by providing parents with related information. The study also examined how the context of play and child gender affect parents' magnitude comparison input.

Sixty parents and their three- to five-year old children (53% boys) were recruited to engage in a twenty-minute, videotaped parent-child interaction. Parents were predominantly mothers (75%), white (83%), and well educated (76% of mothers and 80% of fathers had at least a bachelor's degree). Parents completed questionnaires on their academic beliefs about their preschooler immediately before and about one week after they participated in the parent-child interaction. They played two card games with their child during the interaction, received some information about magnitude comparison, and then played the two card games again. Parents' magnitude comparison talk during the interaction was coded in 10-second intervals.

A paired sample t-test indicated that parents rated magnitude comparison as significantly more important for their child after receiving related information. A two-way repeated measures ANCOVA was used to examine whether parents' magnitude comparison input differed across time and context of play, controlling for child gender. There was a significant main effect of context on parents' input about magnitude comparison. However, there was no significant main effect of time, though there was a significant interaction effect of time and child gender. Specifically, the magnitude comparison input provided by parents of girls increased significantly across time, but the magnitude comparison input provided by parents of boys did not change.

The current study continues efforts to identify effective ways to promote parents' early numeracy input. Though the study's main hypotheses were only partially supported, it offers insightful findings on the malleability of parents' numeracy input and beliefs. First, the current study indicates that parents' beliefs about early numeracy concepts are malleable. Second, encouraging parents to play a specific card game (i.e. War) with their preschooler effectively promotes frequent parent magnitude comparison input. Third, future research on promoting parents' early numeracy input should consider child gender given that we successfully promoted magnitude comparison input among parents of girls but not boys.

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Du, Jennifer
Board 22, Session 2
PI: Conn, P. Jeffrey

mGlu1 and M4 Receptor Activation Modulates Corticostriatal Signaling and Enhances Motor Learning

Jennifer J. Du, Samantha E. Yohn, Craig W. Lindsley, P. Jeffrey Conn, Daniel J. Foster

Motor learning is the improvement of motor skills through practice, in which these actions initially require high cognitive demand but eventually become almost automatic with repetition. While changes in corticostriatal signaling from the primary motor cortex (M1) to the dorsolateral striatum (DLS) are thought to play a key role in this process, the specific mechanisms underlying motor learning remain unclear. Given the cooperative role that the metabotropic glutamate receptor subtype 1 (mGlu1) and the M4 muscarinic acetylcholine receptor have been previously demonstrated to play in modulating striatal signaling, we hypothesize that these receptors work together to induce synaptic plasticity at M1-DLS synapses and ultimately facilitate motor learning.

To isolate the motorcortical inputs to the striatum, we performed viral injections of Channelrhodopsin-2 into the M1 of C57BL/6J mice. We then prepared brain slices from these mice and recorded field excitatory postsynaptic potentials (fEPSPs) evoked by light stimulation in the DLS. To assess motor learning, we used the rotarod test and measured latency to fall for 4 trials/day for 7 days using the following treatment groups: vehicle control (10% Tween 80), positive allosteric modulator (PAM) of the M4 receptor (1 mg/kg VU'154), mGlu1 PAM (30 mg/kg VU'4909), and mGlu1 PAM (30 mg/kg VU'4909) + M4 antagonist (1 mg/kg VU'625).

Bath application of a group I mGlu receptor agonist (50 µM DHPG) induced a long-term depression (LTD) of fEPSPs that was blocked in the presence of either a negative allosteric modulator (NAM) of the mGlu1 receptor (3 µM VU'650) or M4 antagonist (3 µM VU'720), revealing that this form of corticostriatal plasticity requires intact signaling through both mGlu1 and M4 receptors. Furthermore, mice dosed with the mGlu1 PAM on the rotarod test showed an increased latency to fall compared to the vehicle control mice, indicating that mGlu1 receptor activation can improve the acquisition of motor skills. Interestingly, this effect was blocked upon pre-treatment with the M4 antagonist, which suggests that both mGlu1 and M4 receptor activation is required for motor learning.

Taken together, these data show that the induction of LTD in the striatum is dependent upon both mGlu1 and M4 receptor activation, with the mGlu1 receptor ultimately expressing an M4-dependent facilitation of motor learning. Continued investigation into the importance of M4 for mGlu1 effects on motor learning will allow us to identify the specific mechanisms by which motor learning occurs.

Dunham, Kacie
Board 23, Session 1
PI: Woynaroski, Tiffany

Stability of Metrics of Audiovisual Integration in Children with Autism Spectrum Disorder

Kacie Dunham, Jacob I. Feldman, Margaret Cassidy, Yupeng Liu, Evan Suzman, Prachy Mahbub, Julie G. Conrad, Alexander Tu, Pooja Santapuram, David M. Simon, Neill Broderick, Mark T. Wallace, Tiffany Woynaroski

Children with autism spectrum disorder (ASD) demonstrate atypical responses to multisensory stimuli. For example, relative to typically developing children, children with ASD demonstrate wider temporal binding windows (TBWs) for audiovisual stimuli and limited perceptual gains when presented with audiovisual versus auditory-only stimuli. There is increased interest in exploring whether metrics of multisensory integration may be valid for predicting language and communication development and/or sensitive to effects of interventions targeting language and communication outcomes. However, we currently know little about the stability of commonly used metrics of multisensory integration. This is important because the stability of a metric places a ceiling on its validity. This study tested the stability of several metrics of audiovisual speech perception and integration and determined the number of observations needed to reach acceptable levels of stability for these metrics.

Eleven children (7 male; Mage = 10.5 yrs) with ASD completed psychophysical tasks, including a simultaneity judgment task for audiovisual speech, McGurk effect tasks, and listening in noise tasks, as well as an event-related potential (ERP) task that indexed response to audiovisual versus auditory only speech and an eye tracking task that measured attention to audiovisual speech. Participants completed these tasks twice within one week. Generalizability (G) and Decision (D) studies were conducted to evaluate the stability of each metric and the number of observation periods needed to obtain stable estimates for each metric of interest (i.e., $g \geq 0.8$).

Eye gaze metrics had high stability, with proportion of gaze to the mouth (g for a single observation = 0.91) and to the eyes (g = 0.87) reaching acceptable stability in a single observation. The stability of psychophysical tasks was mixed. The most stable metrics were TBW for audiovisual speech (g = 0.74) and Pa/Ka McGurk illusions (g = 0.90); these metrics are acceptably stable after two observations and one observation, respectively. Ba/Ga McGurk illusions (g = 0.37) and whole-word recognition of audiovisual speech presented at -3dB SNR (g = 0.18) and -6dB SNR (g = 0.22) were less stable, requiring 6 or more observations to achieve acceptable stability. ERP metrics demonstrated the most variable stability, with only P2 amplitude reaching acceptable stability (g = 0.90) in one observation.

These results indicate that the stability of metrics from tasks tapping multisensory integration is variable and that the psychometrics of commonly used measures must be examined at the metric level. Additionally, repeated observations may be required to obtain acceptably stable estimates, and thus to increase the likelihood of detecting effects of interest, as it relates to multisensory integration in children with ASD.

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Failla, Michelle
Board 24, Session 2
PI: Cascio, Carissa

Characterizing co-occurring conditions by age at diagnosis in autism spectrum disorders

Michelle D. Failla, Kyle L. Schwartz, Shikha Chaganti, Laurie E. Cutting, Bennett A. Landman, Carissa J. Cascio

Individuals with autism spectrum disorders (ASD) experience a significant number of co-occurring medical conditions, yet little is known about these conditions beyond prevalence. We hypothesized that individuals with ASD experience an increased burden of co-occurring conditions as measured by duration and frequency of visits related to co-occurring conditions. We expected that age of ASD diagnosis (early, <7; late, >7) would be associated with different co-occurring conditions.

Medical record data was pulled from an anonymized database (Vanderbilt University Medical Center) for 3097 individuals with ASD and 3097 matched controls. Co-occurring conditions were characterized using a novel tool (pyPheWAS) to examine presence, count, and duration of each condition.

We identified several categories of co-occurring conditions in ASD: neurological (epilepsy, sleep disorders); psychiatric (mood disorders, adjustment/conduct disorders, suicidal ideation), and developmental. Early ASD diagnosis was associated with epilepsy-related conditions, whereas a later diagnosis was associated with psychiatric conditions. The onset of psychiatric conditions differed by age at ASD diagnosis (early [mean=0.916 years] compared to late [mean= -0.378], W=16408, p=6.723e-07).

Our work confirms individuals with ASD are under a significant medical burden, with increased duration and frequency of visits associated with co-occurring conditions. Adequate management of these conditions could reduce burden on individuals with ASD.

Farag, Mariam
Board 25, Session 1
PI: Alexandra (Sasha) Key

Behavioral and attentional modulation in response to facial emotional stimuli in adolescents on the Autism Spectrum

Mariam Farag

Children and adolescents with autism spectrum disorders (ASD) exhibit core impairments in several areas of social competence. Identifying social cognition processes underlying social behavior is necessary for development of treatments that would have generalizable outcomes. One of the most important and early emerging skills in social cognition is being able to understand the emotional cues provided by facial expressions of social partners. While prior studies have established that persons with ASD exhibit only subtle differences in basic face perception processes, less is known about their higher-order abilities, such as emotional expression recognition. Using electroencephalogram imaging techniques and event related potentials, the current study focused on the N2 modulation in response to inhibition, and the P3 modulation in response to attention.

Following the procedures of Taylor et al. (2018), participants were presented with a randomized series of emotional facial stimulus, showing angry and happy faces. Each face was framed in a different color, and the participants were asked to press a button when they saw their target color, which established a go and no/go task. The participants were told their target color before data collection started. The task had an inhibition and a vigilance condition.

P3 in the frontal and central regions was used as a marker for the vigilance condition, and although typical populations displayed higher brain activation in response to happy faces, a similar pattern was not observed in the ASD subjects. In addition to the attentional modulation in response to emotion, it was also observed that in typical population, brain activation in response to inhibition of angry faces was significantly greater than what was observed for happy faces (Taylor et.al, 2017). Within the ASD subjects, there was no significant difference observed between the inhibition in response to angry or happy faces, as measured through the N2 peak. A higher amplitude was used as a reference for increased processing.

The observed patterns of significance could possibly be due to the smaller sample size, given that data collection is ongoing. Although, significant differences were not established for tree out of the four conditions, the mean amplitudes appear to show similar patterns that is comparable to typical population. This in congruence with previous literature as increasing difficulty was reported in response to emotions such as fear and anger. This study served to fill a gap in the literature about the higher order processing in adolescents with autism through emotional analysis linked with behavior. Future studies aim to use this baseline data as a comparable reference to track the success of intervention programs aimed at improving attention.

Feldman, Jacob
Board 26, Session 2
PI: Woynaroski, Tiffany

Audiovisual Multisensory Integration in Children with Autism Spectrum Disorder: Associations with Broader Symptomatology

Jacob I. Feldman, Margaret Cassidy, Julie G. Conrad, Kacie Dunham, Wayne Kuang, Yupeng Liu, David M. Simon, Alexander Tu, Neill Broderick, Mark T. Wallace, Tiffany G. Woynaroski

Sensory differences, in particular differences in audiovisual integration, have been well documented in children with autism spectrum disorder (ASD) and are hypothesized to potentially underlie the core- and related-deficits observed in this clinical population. However, the extant literature is presently limited by a lack of studies that (a) compare groups across levels of stimulus complexity (social vs non-social stimuli specifically), and (b) explore associations between metrics of audiovisual integration and the broad range of ASD and related symptoms. The proposed study will attempt to address these gaps by (a) comparing children with ASD and well-matched controls on tasks tapping multisensory integration across both social and non-social stimuli, (b) evaluating associations between metrics of audiovisual integration and measures of core and related ASD symptoms, including language and intellectual ability, and (c) evaluating whether the aforementioned associations vary according to group. Participants completed a battery of psychophysical tasks that assess multisensory integration in response to social stimuli, via a task based on the McGurk illusion (wherein participants are presented with an audio "ba" dubbed onto a visual "ga", which elicits an illusory percept of "da" or "tha" upon integration) and in response to non-social stimuli, via a task based on the sound induced flash illusion (SIFI; wherein one visual flash is presented with two auditory beeps at a range of stimulus onset asynchronies, which elicits an illusory flash percept upon integration). The derived metrics of audiovisual integration included the number of reported McGurk illusions and the number of reported SIFI illusions at a 50ms auditory delay. Participants' parents completed surveys that quantified concurrent autism symptom severity (Social Communication Questionnaire [SCQ] and Social Responsiveness Survey-2 [SRS-2]), as well as social and communication ability (Vineland Adaptive Behavior Scales-2). Participants also completed a neuropsychological battery that included the Leiter International Performance Scale-3 (a measure of nonverbal intelligence), the Receptive and Expressive One-Word Picture Vocabulary tests, and the Clinical Evaluation of Language Fundamentals. To answer the first research question, a 2 (group; ASD, TD) by 2 (social vs. nonsocial) ANOVA was carried out. To answer the second and third research question, a series of multiple regression analyses was conducted.

A significant main effect of group indicated participants with ASD perceived fewer illusions than TD participants. There was no main effect of stimulus type. A significant interaction effect was present; Follow up analyses indicated groups differed moreso in their perception of the social illusion (McGurk illusion) vs nonsocial illusion (SIFI). Significant correlations were observed between all of the clinical measures and our metric of audiovisual integration of social stimuli (i.e., perception of the McGurk illusion), with moderate-large effects. No significant correlations were observed between any of the clinical measures and our metric of audiovisual integration of nonsocial stimuli (i.e., perception of the SIFI illusion)

This study is among the first to comprehensively evaluate multisensory integration in children with ASD. Results suggest that children with ASD show a reduced magnitude of multisensory integration across both social and non-social stimuli, but that diminished integration of social stimuli specifically may be most strongly linked with ASD and related symptomatology. Implications for research, theory, and practice will be discussed.

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Feller, Jessica
Board 27, Session 1
PI: Ramachandran, Ramnarayan

Effect of noise exposure on the detection of modulated tones in modulated noise by nonhuman primates

Jessica Feller, Michelle Valero, Chase Mackey, Lakshmi Veerapaneni, M. Charles Liberman, Troy Hackett, Ramnarayan Ramachandran

Typical psychophysical and physiological experiments use steady state signals; however, signals and maskers in the real world are temporally modulated. The ability to process such real-world stimuli is impaired in humans with hearing loss. These may be the basis for the finding that humans with even mild sensorineural hearing loss have difficulty understanding speech presented in noisy environments. Further, the anatomical and physiological correlates of these deficits are at present unknown. Animal models, in which controlled noise exposures, invasive assays of central integrity, and direct and indirect assays of cochlear integrity are possible, could allow these physiological and anatomical correlates to begin to be established. To this end, we examined behavioral performance and cochlear histology in non-human primates before and after noise exposure causing hearing loss.

Monkeys performed a Go/No-Go tone detection task in the presence of 76 dB SPL continuous, sinusoidally amplitude modulated (SAM) broadband noise (BBN) at 10 or 40 Hz. We chose 10 Hz modulations - and 40 Hz modulations based on the temporal integration times estimated from modulation masking release. Tone frequencies were 1-16 kHz and were sinusoidally amplitude modulated at the same frequency as the noise (either 10 or 40 Hz). Differences in modulation phase between the tone and noise varied from 0 to 315 degrees in steps of 45 degrees. We also explored the effect of modulation depth of the masker by varying masker modulation depth from 0 (unmodulated) to 1 (fully modulated) at six modulation depths. These data were obtained for three normal hearing (NH) monkeys and two monkeys exposed to either a 141 or 146 dB SPL 50 Hz band of noise centered at 2 kHz for four hours, which caused a permanent threshold shift (PTS). Further, cochlear histology was assessed in terms of inner and outer hair cell counts, and counts of ribbon synapses per inner hair cell.

NH subjects showed lower SAM tone detection thresholds in SAM BBN (modulated-tone in modulated-noise; MTMN) when the modulations were anti-phase. This threshold reduction, or MTMN phase sensitivity, was 20 - 35 dB for 10 Hz modulations, and was lower (10 - 20 dB) for 40 Hz modulations, which is close to the highest frequency of temporal integration. After noise exposure that caused PTS, the MTMN phase sensitivity was reduced for both 10 and 40 Hz modulations compared with NH subjects. The MTMN phase sensitivity decreased with increasing noise exposure. For PTS subjects, the largest reduction in MTMN phase sensitivity occurred at, or one octave above, the center frequency of noise exposure. Reductions in MTMN phase sensitivity in the PTS subjects did not correlate with audiometric changes. Increases in the modulation depth of the masker caused increases in the modulated-tone detection threshold. These changes were not significantly different from similar changes in NH subjects. Cochlear histology confirmed large-scale, frequency-place specific hair cell loss and inner hair cell ribbon synaptopathy in the PTS subjects. There was a weak trend toward a correlation between the amount of outer hair cell loss and the reduction in MTMN phase sensitivity for the 10 Hz modulation, and a significant correlation for the 40 Hz modulation.

Noise exposure causing PTS caused some changes in the ability to process time-varying signals in time-varying maskers. Changes in MTMN phase sensitivity at 40 Hz modulation frequency were reflective of outer hair cell loss; ongoing experiments with purely synaptopathic noise exposures will reveal the effectiveness of such behaviors in assessment of synaptopathy.

Fisher, Nicole
Board 28, Session 2
PI: Niswender, Colleen

A point mutation associated with developmental delay and epilepsy leads to loss-of-function of the mGlu7 receptor

Nicole M. Fisher, Aditi Buch, Vincent Luscombe, Rocco G. Gogliotti, P. Jeffrey Conn, Colleen M. Niswender

Whole-exome sequencing studies have recently identified several point mutations in the metabotropic glutamate receptor 7 gene (GRM7, mGlu7) in children with undiagnosed neurological disease. mGlu7 is a G protein-coupled receptor that is expressed in neurons and regulates neurotransmitter release. Because mGlu7 knockout mice exhibit seizures and deficits in associative learning, we hypothesized that point mutations identified in these patients would lead to loss of mGlu7 activity. This study sought to characterize one mutation, mGlu7-I154T, which affects the mGlu7 extracellular domain.

Wildtype and mGlu7-I154T receptors were expressed heterologously in HEK293A cells. Expression was assessed by Western blot and on-cell ELISA while receptor function was measured in a thallium flux assay. mGlu7-I154T mice were generated and studied using a combination of biochemical, electrophysiology and behavioral approaches.

In HEK293A cells, the mGlu7-I154T point mutation resulted in diminished receptor dimerization, reduced surface trafficking and reduced total expression. Decreased expression was confirmed in vivo by analysis of tissue from mGlu7-I154T mice. The functional response of mGlu7-I154T cell lines in a thallium flux assay was significantly decreased, but could be normalized by pre-application of a positive allosteric modulator.

These findings demonstrate that the mGlu7-I154T point mutation leads to receptor loss of function, providing proof-of-concept evidence that mGlu7 dysfunction can cause disease in humans. Future studies will compare phenotypes of mGlu7-I154T mice with those previously shown in mGlu7 knockout mice, and test the ability of positive allosteric modulators to normalize physiology and behavior in this model. This work was supported by NIMH grant F31 MH113259, R01 MH113543 and CDMRP/DoD award W81XWH-17-1-0266.

Flook, Elizabeth
Board 29, Session 1
PI: Blackford, Jenni

Altered threat processing in patients with AUD during early abstinence

Elizabeth A. Flook, Meg Benningfield, Marisa M. Silveri, Danny G. Winder, Jennifer Urbano Blackford

Despite efficacious treatments to achieve sobriety, over 50% of patients with alcohol use disorder (AUD) relapse within a year post-treatment. The high relapse rate is thought to result from persistent neuropsychological effects of chronic alcohol use leading to heightened negative affect and stress sensitivity for weeks or months after detoxification. Despite evidence that stress is a major trigger for relapse, little is known about the processing of stressful stimuli, such as threat, in abstinence. The purpose of this study is to better understand the changes in threat processing during early abstinence in patients with AUD.

Fifteen patients with AUD in early abstinence (30-180 days of sobriety) and 20 healthy controls participated in the study. fMRI was used to measure threat processing during a cued anticipation task with three conditions: unpredictable threat, predictable threat, and predictable neutral. Data were analyzed with a repeated measures ANOVA in SPM12 using a flexible factorial model with group (patient/healthy control) and cue (unpredictable/predictable threat/predictable neutral) as factors. Whole brain voxel-wise analyses were performed for the main effect of group, main effect of cue type, and group x cue type interaction (cluster corrected $p < 0.05$).

There were prominent main effects of group, with greater activation to cues for patients in the anterior insula, posterior insula, BNST, and fusiform gyrus. In contrast, healthy controls showed greater activation in multiple prefrontal cortical regions including the dorsal anterior cingulate cortex, rostral anterior cingulate cortex, and orbitofrontal cortex. Main effects of cue type were observed in the hippocampus and cerebellum. For the group x cue interaction, patients showed greater activation to the unpredictable relative to the predictable threat cues in multiple subcortical regions including the amygdala, hippocampus, anterior insula, and posterior insula.

These results provide initial evidence for altered threat processing during early abstinence. Hyperactivity in limbic regions found in patients was especially pronounced for the unpredictable threat cues, which is important because an aversive response to unpredictability is a hallmark of anxiety disorders. These results suggest a neurobiological basis for the increased negative affect and stress sensitivity seen in early abstinence, and treatments targeting this system might promote long-term abstinence.

Gonzalez, Hernan
Board 30, Session 2
PI: Englot, Dario J.

Nucleus basalis MRI functional connectivity abnormalities in patients with temporal lobe epilepsy

Hernan F.J. Gonzalez, Saramati Narasimhan, Kanupriya Gupta, Graham W. Johnson, Keshav B. Kundassery, Kristin E. Wills, Victoria L. Morgan, Dario J. Englot

Recent studies have shown that temporal lobe epilepsy (TLE) patients demonstrate altered functional connectivity of subcortical arousal structures, such as the thalamus and brainstem, and this altered connectivity is related to neurocognitive deficits and seizure frequency. Additionally, prior animal work has shown that activity of cholinergic neurons of the basal forebrain is suppressed during consciousness impairing seizures (Motelow et al. 2015). We hypothesize that recurrent ictal events incite interictal connectivity disturbances of the nucleus basalis which may relate to diffuse network problems and comorbidities of TLE. In this study, we examine whether nucleus basalis exhibits abnormal network connectivity in TLE patients as compared to healthy controls.

We evaluated 40 adult unilateral TLE patients and 40 matched healthy controls using functional MRI (fMRI) to measure resting-state functional connectivity between nucleus basalis and neocortex. Functional connectivity was calculated between regions of interest using partial correlation. To understand alterations of network properties of nucleus basalis ipsilateral and contralateral to the epileptogenic temporal lobe we calculated graph theory measures (positive node strength, negative node strength, clustering coefficient). We then related nucleus basalis connectivity and graph theory network measures to disease severity.

Functional connectivity of the bilateral nucleus basalis with frontoparietal neocortex was lower in patients as compared to healthy controls ($p<0.01$, paired t-test). Patients with greater frequency of consciousness impairing seizures had more abnormal connectivity between nucleus basalis and frontoparietal neocortex ($r=-0.429$, $p<0.01$, Pearson correlation). Next, we examined the network properties of the individual nucleus basalis (ipsilateral and contralateral to the epileptogenic temporal lobe). Both ipsilateral and contralateral nucleus basalis displayed lower positive node strength and lower clustering coefficients in TLE patients as compared to controls ($p<0.05$ for all, paired t-test). However, only the ipsilateral nucleus basalis displayed larger negative node strength in TLE patients as compared to controls ($p<0.01$, paired t-test). Additionally, of all 114 brain regions examined in the study, the ipsilateral nucleus basalis displayed the greatest decrease in clustering coefficient as compared to controls. Interestingly, higher ipsilateral nucleus basalis clustering coefficient (i.e. closer to healthy control values) was associated with higher verbal IQ and higher performance on tests of verbal memory ($r=0.38$-0.40, $p<0.05$ for both, Pearson correlation).

The nucleus basalis exhibits abnormalities of functional connectivity and network properties in TLE patients as compared to healthy controls. Greater aberrations of these measures are associated with greater seizure frequency and worse verbal neurocognition. These results are the first to demonstrate abnormal connectivity of nucleus basalis in TLE which may lead to an improved understanding of the widespread long-term effects of seizures on brain networks in TLE.

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Giorgione, Ryanne
Board 31, Session 1
PI: Gilmer, Mary Jo

Exploration of Parent Communication Preferences about Child's Cancer

Ryanne Giorgione, Emily Litzow, Austin Darling, Mary Jo Gilmer

Parents of children in need of palliative care face many communication challenges. While the National Cancer Institute (2018) recommended parents try to be gentle, open and honest with their children about cancer, questions remain about who should be involved, how a child should be told, and when to communicate details. The American Academy of Pediatrics (2017) advocates for children to participate fully in communication, but little research has explored strategies and preferences of parents of children diagnosed with cancer.

The larger pilot study explored communication styles and preferences among children (ages 7-17 years) with cancer and their parents/caregivers through a cross-sectional, qualitative design. Results from the parent interviews are shared in this report. Based on those results of our focus group study in 2016, researchers developed interview questions and recruited 10 mothers and 4 fathers at least 6 months after a cancer diagnosis. Researchers conducted in-depth interviews with each participant between January-June 2017. After the audio-recorded interviews were professionally transcribed, researchers used content analysis, and reached consensus on themes that emerged from the data.

Two themes and eleven sub-themes emerged from the parent interviews related to telling children about their cancer diagnosis: 1) Communicating with children about their cancer diagnosis/prognosis with sub-themes of how to tell, who should tell, changes in prognosis, who should be included, and talking with the whole family; and 2) Thoughts about and responses to diagnosis and treatment with sub-themes of what child understands, side effects of treatment, parent emotional regulation, how parents cope, and how children cope. A father said, "I think [the child] appreciates when people address her [...] because she's intelligent [...] and she knows she's important [...] and that would make her feel important as an individual."

Data reveal communication preferences described by parents of children with cancer. Parents appreciate a step process throughout the duration of their treatment in how providers communicate with them and their children. Results of this study show a need for use of culturally and developmentally appropriate, evidence-based educational materials to 1) equip providers and 2) best inform parents on how and what to communicate concerning their child's disease. Developmental, cultural, and individual differences have global implications for awareness of and sensitivity to communication preferences in the face of serious disease.

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Gray, Laura
Board 32, Session 2
PI: Malow, Beth A.

Parent satisfaction with sleep education for children with autism spectrum disorder provided by community educators

Laura Gray, Lydia L. MacDonald, Kemberlee Bonnet, David Schlundt, Beth A. Malow

Sleep education to address insomnia in children with autism spectrum disorder and their parents can be effective but often inaccessible. In conjunction with a quasi-experimental pilot study, we assessed parent reactions to and satisfaction with a 15-week sleep education program offered by community providers trained and supported by sleep specialists. We also investigated chaos and order among families who participated in the sleep education.

At the conclusion of the sleep education program, we conducted a telephone interview with at least one parent in each of 26 families who completed the program. Interviews were transcribed verbatim then coded and analyzed using an inductive/deductive qualitative methodology. Transcripts were coded using a hierarchical coding system and analysis of the coded data was used to create a conceptual framework.

Four themes and multiple subthemes emerged from the parent interviews. Themes included: 1) Factors related to disrupted sleep; 2) program implementation; 3) intermediate outcomes, and 4) impacts. Factors related to disrupted sleep included subthemes of environmental, parent and child factors related to disrupted sleep. Program implementation included subthemes of facilitators and barriers to program implementation. Intermediate outcomes included family harmony and family engagement. Impacts included improved sleep and parental increase in sleep literacy. One parent noted: "We have ... a visual schedule and we even have timers set. We have sorta [sic] looked at bedtime a little bit differently."

Families of children who have ASD and sleep problems are able to identify sources of sleep problems, articulate effects of child's disrupted sleep, and appreciate benefits of community-based sleep education programs that offer research-based strategies for improving child sleep. Families may benefit from support aimed at structuring family routines. Our framework identifies barriers and facilitators that may be useful in enhancing the impact of sleep interventions.

Hart, Emma
Board 33, Session 1
PI: booth, amy

Executive function and vocabulary disparity

Emma Hart, Margaret Shavlik, Amy Booth

Evidence suggests that children from low-income families develop smaller vocabularies in comparison to those from higher-income families (e.g., Hart & Risley, 1995), with repercussions for future language and academic achievement (Walker, Greenwood, Hart, & Carta, 1994). Quality and quantity of parent-child verbal interaction, and children's individual word learning skills (Booth, 2018), may explain vocabulary disparity. Exploring the contributions of executive function (i.e., inhibitory control, working memory, and cognitive flexibility) to vocabulary variance may also offer insight. Like vocabulary, executive function (EF) seems to be influenced by poverty-related circumstances (Shonkoff, 2011) and is predictive of later cognitive performance (St. Clair-Thomspon & Gathercole, 2006). Additionally, early language capacities and EF are reportedly correlated (Slot & Von Suchodoletz, 2018). Therefore, we analyze the relationship between EF skills (EF), word learning skills (WRDLRN), and accumulated vocabulary (VOC) to understand how EF and WRDLRN interact, and to what extent EF uniquely contributes to variance in VOC. We predicted that EF would account for some variance, given its relevance to cognitive performance and relationship to early language capacities.

One hundred seventy-five (71 boys) two- and three-year-olds (Mage = 2.97 years, SD = 0.32, range = 2.38 - 3.90) completed measures of EF (MEFS; Carlson, 2017) and VOC (PPVT; Dunn & Dunn, 2007). Task performance on gaze following, whole object assumption, the mutual exclusivity assumption, shape bias, and syntactic bootstrapping were compiled into WRDLRN composite scores.

To account for missing data, we used multiple imputation. The following analyses use the resulting pooled values. Since EF and VOC ($r = .47$, $p < .001$), and EF and WRDLRN ($r = .46$, $p < .001$) were significantly correlated, we ran a linear regression to predict VOC variance based on EF and WRDLRN. EF and WORDLRN significantly explained 28.8% ($R2 = .29$) of the variance in VOC, $F(2, 127) = 25.7$, $p < .001$. Furthermore, both EF ($\beta = .36$, $t(174) = 4.23$, $p < .001$) and WRDLRN ($\beta = .25$, $t(174) = 3.37$, $p < .001$) significantly predicted VOC. Furthermore, EF uniquely explained some of the variance in VOC (above and beyond the influence of WRDLRN), $sr = .32$, $p < .001$.

Our results indicate that EF significantly and uniquely contributes to vocabulary variance among young children. Given the long-term implications of disparities in early vocabulary, researchers should explore the intricacies of this relationship, since EF may be a missing link.

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Hessling, Alison
Board 35, Session 1
PI: Schuele, Melanie

Narrative Intervention for School-Age Children: A Single-Case Research Study

Alison Hessling, Melanie Schuele

Narrative interventions are effective for children with a variety of disabilities (e.g., Gillam, Gillam, & Reece, 2012). Because children with specific language impairment (SLI) have deficits in oral language, they may benefit from interventions to explicitly learn narrative skills in academically-relevant contexts. This study extends the research on narrative intervention by evaluating the effect of a standard treatment protocol, Story Champs (Petersen & Spencer, 2012), on personal narrative generations of school-aged children with SLI.

Four second grade, 8- to 9-year-old boys with SLI participated in this multiple baseline across behaviors single case design study that was repeated across participants. Each one-on-one Story Champs intervention session involved eight steps across two intervention segments: story retell and personal narrative generation. The interventionist provided systematic scaffolding (visual and verbal supports) that were faded within each session. Two to three individualized story grammar elements per participant were targeted sequentially across the weeks of intervention based on each participant's individual needs identified in baseline. The dependent variable probe was administered at the beginning of each twice-weekly session and story grammar targets were scored on a four-point rubric. Maintenance data was collected two and three weeks post-intervention.

A functional relation between the Story Champs intervention and the dependent variable was observed for two participants. A functional relation was not observed for the other participants due to the lack of stability in data across the story grammar elements. Despite the variability in data, clear changes in behavior (above baseline performance) concurrent with the introduction of intervention were demonstrated for the majority of story grammar elements for each participant.

Results provide preliminary evidence for the efficacy of individually administered Story Champs intervention for improving narrative skills for children with SLI. Participants demonstrated growth for some story grammar targets concurrent with the introduction of intervention. This study extended the research on narrative intervention by validating the effectiveness of a commercially-available, standard narrative treatment protocol, Story Champs. Validation of Story Champs for specific clinical populations is important as the standard treatment protocol provides structure for clinicians through provision of guidelines for scope, intensity, and duration. The study findings demonstrating the effectiveness of the intervention as well as increased implementation fidelity associated with standard treatment protocols are critical to achieving change for individual children with disabilities. Future research will systematically evaluate clinicians' implementation of Story Champs as well as further research on distal outcome effects and maintenance of change.

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Hong, V. Emily
Board 36, Session 2
PI: Cutting, Laurie

The Link Between Reading Strategies and Executive Functions in Text Comprehension

V. Emily Hong, Tin Q. Nguyen, Sage E. Pickren, Laurie E. Cutting

Executive functions (EF) play a key role in reading comprehension (RC). Difficulties while reading text aloud, as indexed by oral reading errors (or miscues), have also been linked to poor EF, which likely in turn hinders RC. Students may potentially rescue the impact of miscues on RC via reading strategies, including comprehension-monitoring inconsistencies and self-correcting miscues. Prior studies have shown that, when reading passages are experimentally embedded with inconsistent information, more efficient comprehension-monitoring is related to better EF, especially in skilled RC. Yet, what remains elusive is whether the ability to self-correct miscues while reading aloud contributes to students' comprehension-monitoring performance and is related to students' EF skills (Research Question 1). Another key aspect of RC is whether students are able to distinguish central versus peripheral textual information. Whether self-correcting miscues related to central versus peripheral information in text contributes to students' comprehension-monitoring performance is less explored, especially in relation to EF (Research Question 2).

Fifty participants (ages 9-15) read three 300-word expository passages about science and animals. Each participant read one baseline text and two texts that were experimentally manipulated to tap comprehension-monitoring. These two experimentally-manipulated passages were embedded with inconsistent information about the topic. The inconsistent information was either placed in adjacent sentences (near condition) or separated by several sentences (far condition). After reading the text aloud, students were asked whether they were aware of any contradictory/inconsistent information introduced in the text as an estimation of their comprehension-monitoring performance. Miscues and unprompted self-corrections were recorded as students read aloud. Students' EF was measured using Digit Span (working memory), Elithorn Maze (plan/organize), and Matrix Reasoning and Block Design (reasoning). Better versus worse comprehenders (High-RC; Low-RC) were defined by median split based on students' performance on the Gates-MacGinite Reading Test.

Our results were consistent with prior findings in that the High-RC group versus the Low-RC group was better able to detect inconsistencies in the text more often (i.e., had better comprehension-monitoring performance) and had higher EF. While there were no statistically significant differences between the overall ability to self-correct miscues between reader groups, there was an interaction between High- versus Low-RC groups and EF abilities. Specifically, students in the Low-RC with worse EF self-corrected and detected inconsistencies in the text significantly lass often than students in the High-RC group (Research Question 1). Additionally, students with Low-RC tended to self-correct more miscues related to peripheral versus central information. Interestingly, among the Low-RC group, those with higher EF exhibited more self-correcting and detecting inconsistencies related to both central and peripheral information (Research Question 2).

Reading strategies, such as monitoring text inconsistencies and self-correcting miscues, support RC. Our study extends on this link by highlight the contribution of EF, whereby less skilled readers with strong EF may be able to leverage these skills to facilitate reading strategies, potentially facilitating restoration of RC.

Horvath, Patricia
Board 37, Session 1
PI: Monteggia, Lisa

MeCP2 regulated miRNA, miR-101a, regulates excitatory/inhibitory synaptic functioning

Patricia M. Horvath, Michelle K. PIazza, Ege T. Kavalali, Lisa M. Monteggia

Accumulating evidence suggests the importance of micro-RNA (miRNA) species in brain development and function, with miRNA dysregulation being implicated in certain neurodevelopmental disorders including Rett Syndrome (RTT). The majority of RTT patients have loss of function mutations in Methyl-CpG-Binding-Protein-2 (MeCP2). RTT is primarily seen in females and is characterized by 6-18 months of normal development followed by pronounced regression in speech, fine motor skills and respiratory function, among other symptoms. Work in rodent models suggests that these phenotypes are driven by synaptic dysfunction in the central nervous system. MeCP2 has long been regarded as a transcriptional regulator, but recent studies have also directly linked its function to miRNA biogenesis. Given the growing evidence that miRNAs can regulate broad synaptic processes, it is possible that miRNA dysregulation could underlie some of the synaptic dysfunction seen following MeCP2 loss. Investigation of multiple MeCP2 regulated miRNAs revealed higher expression of miRNA-101a (miR-101a) in MeCP2 knockout animals relative to controls. In the present study, we sought to characterize the role of hippocampal miR-101a in synaptic phenotypes related to Rett Syndrome.

miR-101a expression in wild type primary hippocampal cultured neurons was selectively increased via infection with a miR-101a overexpression vector or decreased via treatment with a miR-101a inhibitor. Target RNA expression was quantified with qPCR to confirm treatment efficacy. Whole-cell patch-clamp electrophysiology was used to assess synaptic function following miR-101a manipulation. Both spontaneous and evoked vesicle release were measured at excitatory and inhibitory synapses.

Overexpression of miR-101a led to opposing effects on spontaneous excitatory and inhibitory neurotransmission in hippocampal cultures. Compared to control, neurons overexpressing miR-101a showed higher frequency of mEPSCs but lower frequency of mIPSCs. The increase in mEPSC frequency appears to be mediated by an increase in excitatory synapse number. Furthermore, overexpression increased inhibitory evoked response to low frequency 0.1 Hz stimulation but did not affect excitatory evoked response. Preliminary data also suggests that miR-101a inhibition leads to a modest increase in mESPC frequency.

The regulation of miRNAs by MeCP2 may be an important factor in the etiology of RTT. miR-101a in particular is a promising target, as its dysregulation in wild type neurons has been shown to result in synaptic abnormalities consistent with general hyperexcitability characteristic of RTT. Interestingly, both overexpression and inhibition of miR-101a increase the frequency of excitatory spontaneous vesicle release in the hippocampus. This suggests a dosage sensitivity similar to that seen in MeCP2 regulation, in which deletion and duplication both lead to similar phenotypes. Further work is necessary to characterize the relationship between pathological MeCP2 dysfunction and the regulation of miR-101a.

Ioannou, Sara
Board 38, Session 2
PI: Corbett, Blythe

Avoidant Behavior in Males and Females with ASD

Sara Ioannou, Blythe A. Corbett

Avoidant behavior can be found in youth with anxiety disorders, as a method to avoid anxiety-provoking stimuli. Avoidant behavior-particularly social avoidance-is connected to ASD as well; youth may attempt to avoid anxiety-inducing social situations, including separation from caregivers (separation anxiety). The Multidimensional Anxiety Scale for Children -2 (MASC-2; March 2013) includes subscales for both Harm Avoidance and Separation Anxiety/Phobias. Notably, the Harm Avoidance subscale correlates only with the Separation Anxiety/Phobias subscale, highlighting the relationship between these constructs. This study aims to clarify differences in anxiety across sex on the autism spectrum, focusing specifically on avoidant behavior.

Participants were aged 10-13 and had IQ scores above 70. Diagnoses were confirmed with the Autism Diagnostic Observation Schedule Second Edition (ADOS-2). Ninety-five parents of TD youth (56 male children, 39 female children) and 133 parents of youth with ASD (99 male children, 34 female children) completed the MASC-2 Parent; correspondingly, 95 TD children (54 male, 41 female) and 131 children with ASD (98 male, 33 female) completed the MASC-2 Self. Using independent t-tests, Harm Avoidance and Separation Anxiety/Phobias subscales were compared between males and females within diagnostic groups, and between TD and ASD participants within sex.

Within the ASD group, parents of males reported higher Separation Anxiety ($t(131)=3.81$, $p<0.001$) and Harm Avoidance ($t(131)=2.75$, $p=0.007$) than parents of females with ASD. Like their parents, male participants with ASD also self-reported higher Separation Anxiety ($t(129)= 2.26$, $p=0.02$) and Harm Avoidance ($t(84.45)= 3.68$, $p <0.001$) compared to females with ASD. Conversely, within the TD group scores did not differ across sex for parent-or-self -report (all $p>0.05$). When comparing between diagnostic groups, males with ASD showed significantly higher Separation Anxiety than TD males, by both parent ($t(148.03)=-8.06$, $p<0.001$) and self-report ($t(150)=-2.81$, $p=0.006$). Females with ASD self-reported significantly less Harm Avoidance than TD females ($t(69.51)=3.57$, $p=0.001$) and there was no difference per parent report between TD females and females with ASD (all $p>0.05$).

Within the ASD group, avoidant behavior (whether separation or general harm avoidance) was higher in males than females. Furthermore, when comparing males across diagnostic groups, separation anxiety was higher in males with ASD. While there is a large body of literature on social avoidance in ASD, current results underscore the necessity of continuing to explore avoidance in ASD more broadly, particularly among males. Avoidance may be seen as a method of coping with feared stimuli (avoidant coping); thus, fear could serve as a target for interventions (e.g., exposure/response prevention , cognitive behavioral therapy). Future work can investigate such interventions for youth with ASD.

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Jaramillo, Anel
Board 39, Session 1
PI: Winder, Danny G.

Exploration of parabrachial control of the extended amygdala during stress

Anel A. Jaramillo, Tracy L. Fetterly, Sam W. Centanni, Danny G. Winder

Preclinical studies demonstrate a role for the Bed Nucleus of the Stria Terminalis (BNST), a region of the extended amygdala, in modulating anxiety-like behavior and stress-reward integration. The BNST receives a large excitatory input from the Parabrachial Nucleus (PBN) a region implicated in arousal, aversion, and sensory processing. Ex vivo slice electrophysiology and analysis of Fos expression demonstrate that global chemogenetic inactivation of PBN terminals decreases stress-induced neuronal activity in the BNST (Fetterly et al., 2019).

To specifically investigate the role of PBN glutamatergic afferents on in vivo BNST activity and anxiety-like behavior, we utilized a fiber-photometry approach during the stress-evoking Novelty Suppressed Feeding Task (NSFT). C57BL/6J female mice with unilateral injections of the calcium sensor AAV9-hSyn-jGCaMP7f-WPRE and a fiber optic in the BNST demonstrated enhanced BNST calcium transient amplitude at the time of food approach. To investigate whether chemogenetic manipulation of the PBN altered NSFT behavior, males and females from a CalcaCRE mouse line (Calca is the gene that encodes CGRP and CGRP-expressing neurons in the PBN project to the BNST) received bilateral injections of excitatory hM3D DREADD (AAV5-hSyn-DIO-hM3D(Gq)-mCherry) or control virus (AAV5-hSyn-DIO-mCherry) in the PBN.

Chemogenetic activation of the PBN increased the latency to obtain food during NSFT. Additionally to assess the impact of PBN signaling on BNST in vivo activity, the mice also received a unilateral injection of AAV9-hSyn-jGCaMP7f-WPRE and a fiber optic implant in the BNST. Chemogenetic activation of the PBN enhanced and produced a left-ward shift in BNST in vivo calcium transients during food approach but not in controls (i.e., saline, viral controls). Lastly, to investigate manipulation of PBN-innervated BNST (BNSTPBN) neurons in NSFT, male and female C57BL/6J mice received bilateral injections of the anterograde AAV1-hSyn-CRE in the PBN and hM3D DREADD (or control virus) in the BNST. Specific activation of BNSTPBN increased latency to obtain food in females but not males.

These data suggest that global PBN activation increases latency to obtain food in the NSFT while changing BNST activity and furthermore implicate a sex-specific role within the BNST-PBN circuitry. Given that males and females differentially respond to therapeutic intervention for maladaptive stress response, these data have the potential to provide insight to the circuitry mediating these sex-specific effects in an anxiety-like state.

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Jones, Dorita
Board 40, Session 2
PI: Key, Alexandra

Language abilities in young children with Down syndrome are associated with multiple stages of speech processing in the brain.

Alexandra P. Key, Courtney Wright, Dorita Jones, Ann Kaiser

Children with Down syndrome often experience difficulties with language acquisition (Yoder & Warren, 2004), attributable at least in part to inefficient processing of spoken inputs. Auditory event-related potentials (ERP) offer a noninvasive means to document multiple stages of information processing with millisecond-level precision and without requiring an overt behavioral response, minimizing confounding effects of intellectual disability. This study examined whether neural differences in syllable- and word-level speech processing could account for variance in individual differences in expressive and receptive language abilities of preschoolers with Down syndrome.

Sixteen children with Down syndrome, ages 2 to 4 years (M=3.69, SD=0.66) participated in the study. Auditory ERPs were recorded during two passive listening paradigms using natural speech stimuli: (1) consonant differentiation (voice onset time and place of articulation contrasts), previously established as sensitive to individual differences in typical language abilities and predictive of later developmental outcomes (Molfese et al., 2005), and (2) auditory incidental memory paradigm, a novel task assessing the extent of spontaneous engagement with and processing of the word-level novel spoken inputs. Conversational samples were collected from each participant in two settings: with a familiar (parent) and novel (examiner) partner. The two interactions were audio-recorded and transcribed to quantify the number of utterances and individual spoken words. Standard scores from norm-referenced tests (Mullen Scales of Early Learning, Preschool Language Scales) further characterized receptive and expressive language ability of the study participants. Different examiners administered and scored ERPs and standardized language tests.

Evidence of consonant differentiation was observed for the P1-N1-P2 responses only to the voice onset time contrast (/ba-pa/). Greater N1 and P2 amplitude differences between the consonants were associated with a larger number of utterances, words and variety of different words spoken (r=.583-.752) during the parent-child interaction. A similar trend was observed for verbal output during the language sample with an unfamiliar examiner (r=.489-.523). In the incidental memory task, children with Down syndrome demonstrated the expected "old/new" memory response (more positive parietal amplitudes between 500-900ms in response to repeated nonwords than the stimuli heard once). Correlation analysis indicated that better auditory incidental memory was associated with higher receptive language standard scores (r=.749).

Our study provides new support for the hypothesis that language difficulties in Down syndrome may be due in part to atypical processing of spoken inputs. Extending prior work, we demonstrated that not only the early perceptual stages (indexed by the obligatory P1-N1-P2 responses) but also the later higher-order cognitive processing (the "old/new" response) of auditory stimuli may be relevant for expressive and receptive language abilities in children with Down syndrome. Identification of these specific neural processes, which can be measured noninvasively and without behavioral responses, offers a new way to characterize individual differences in language functioning of children with Down syndrome. Future studies will examine whether these neural responses may serve as the predictors of language treatment outcomes.

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Keller, Mary Alice
Board 41, Session 1
PI: Bodfish, James

Developing an Observational Receptive Language Assessment for Minimally Verbal Children with Autism

Mary Alice Keller, Anne Marie Tharpe, James Bodfish

Thirty percent of children with autism fail to develop useful speech. The majority of previous research studies on language ability in autism have included only verbally fluent participants. Because many minimally verbal children are not able to fully participate in standardized testing, the receptive language abilities of minimally verbal children with ASD have been under-studied. The purpose of this study was to develop an observational measure of receptive language that is psychometrically sound and feasible to administer to minimally verbal children.

Ten preschool-aged children with autism participated in this study (age range = 2 - 4 years). The sample included two language subgroups: (a) phrase speech (n=5), (b) minimally verbal (n=5). Participants were phenotyped in terms of ASD severity, cognitive ability, and language ability. Participants were administered a set of three receptive ability presses (response to name, identification, and direction following). A standard prompt sequence with delays was used during the administration of the presses. Presses were videotaped and then coded for latency to correct response, and prompt level required for correct response. A trained observer coded 20% of all sessions.

Feasibility: Administration time for the full set of receptive ability presses time for all children was under 5 minutes. Repeated administration (between 3 - 7 sessions) of the receptive ability presses were completed for 10 participants. The protocol could be successfully completed on all days for all participants (100%), and visual inspection of the data indicated that 1 of the 10 participants (10%) showed clear ceiling effects on all receptive ability press trials while the majority of participants (90%) showed neither floor nor ceiling effects. Stability: Analysis of test-retest results for the preschool sample indicated significant stability over time ($r = 0.86$, $p < .01$). Additionally, visual inspection of the repeated administration data (3 - 7 sessions) revealed stability (+/- 1 SD) for seven of the ten children (70%). Discriminant validity: The phrase speech and minimally verbal subgroups were compared on the receptive ability presses using the prompt-level metric. This analysis confirmed a significant difference in level of prompt dependence between groups ($t = 4.56$, $p = .002$).

The results suggest that our observational measure of receptive ability is feasible for use with minimally verbal children with ASD, is stable over time for most participants, and discriminates between subgroups of children with ASD. These results are promising given the lack of research on receptive language in these groups. Replication of these results with larger samples and also additional psychometric analyses is warranted.

Khera, Zain
Board 42, Session 2
PI: Lagrange, Andre H.

Characterizing the cortical expression and localization of the GABA-A receptor's gamma-2 and delta subunits during early development

Zain Khera, Anjana Hassan, Kirill Zavalin, Andre H. Lagrange

Pentameric GABA-A receptors are the primary source of inhibitory signaling in the mammalian brain, but are they are excitatory during brain development. The gamma-2 and subunits of the pentameric GABA-A receptor, determine many of its functional properties as well as its localization in neurons. Because the majority of GABA-A receptors in the mammalian brain also possess either one gamma-2 subunit or one delta subunit, any given GABA-A receptor can be sharply distinguished by the presence of either subunit. For instance, GABA-A gamma-2 receptors tend to congregate at the synapse, exhibit greater peak currents, and desensitize quickly, whereas GABA-A delta receptors are localized extrasynaptically, exhibit smaller peak currents, and have minimal fast desensitization.

Using immunohistochemistry, we characterized the localization and expression of these two subunits in mouse cortex from embryonic day 16 to postnatal day 26.

Gamma-2 expression remained high throughout the forebrain, even during embryonic development. At E18, the ventricular zone possessed gamma-2 expression, but expression was absent in the subventricular and intermediate zones. Unlike gamma-2, delta was low throughout the cortex until P5, when cell bodies with delta began to appear, especially in layer 4 and the subplate. Later in development, the expression of delta became diffuse in layer 4 while rest of the cortical layers possessed delta-positive cell bodies. In mice expressing GFP driven by the dlx5 promoter, the majority of GFP+ interneurons in the cortex were also found to be delta-positive through colabeling.

These results shed light on the cell- and region-specific regulation of GABAergic signaling during the important developmental window including late embryonic life and early postnatal life, when neurons are migrating to their final location, cortical layers are being defined, and circuits are forming.

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Klemencic, Mark
Board 43, Session 1
PI: Corbett, Blythe

BMI status of adolescents with Autism Spectrum Disorder and Typical Development

Briana K. Horrocks, Mark E. Klemencic, Rachael A. Muscatello, Yasas Tanguturi, Blythe A. Corbett

Physical health is regularly assessed via medical exams throughout childhood and the lifespan. Screening of physical health can lead to early detection and intervention of potential or emerging health issues by examining height (HT), weight (WT), heart rate (HR), blood pressure (BP), and body mass index (BMI). BMI-for-age, calculated using age, weight, and height, is used to assess size and growth patterns and can be used as a proxy for an individual's percentage of body fat. The Center for Disease Control (CDC) categorizes weight according to the following percentiles: underweight (< 5th), healthy weight (5th to < 85th), overweight (85th to < 95th) and obese (> 95th) (Centers for Disease Control and Prevention National Center for Chronic Disease Prevention and Health Promotion, 2018). The objective of this study was to examine the general health status of 228 pre-to-early pubescent 10-to-13-year old children with autism spectrum disorder (ASD, N = 133) or typical development (TD, N = 95) who are participants in a longitudinal study assessing pubertal development.

HT and WT were measured directly by a study physician. BMI was calculated as weight in kilograms over height^2 and age- and sex-adjusted according to CDC guidelines. BMI percentile categories were also based on CDC recommendations. Measures were compared between the ASD and TD groups and further examined based on age and sex (male, female). Associations were examined between significant indices and possible associated factors through Pearson and Spearman correlational analyses.

Although there was a trend toward significance in that children with ASD showed higher average weight (mean = 108.70, SD = 41.77) compared to TD children (100.31, SD = 3.61), it did not reach statistical significance ($F(1,222) = 3.49$, $p = 0.06$. However, there was a significant difference in BMI percentile ($F(1,222) = 5.94$, $p = 0.02$), with average BMI percentile for ASD children at 65.48 compared to that of the TD children, which was 54.99. Statistical analyses also revealed significant positive correlations between BMI and pubertal stage at assessment and BMI and medication use.

In this study of health status of pre-to-early pubescent children with ASD and TD, most indices were comparable. However, children with ASD had significantly higher BMI percentiles compared to age-matched TD peers. These findings suggest that children with ASD may have an elevated risk of developing weight-related health concerns. Future studies should examine the relationship between BMI and potential contributing factors, including physical activity, diet, and family medical history.

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Kopke, Danielle
Board 44, Session 2
PI: Broadie, Kendal

Carrier of Wingless (Cow) Regulation of Drosophila Neuromuscular Junction Development

Danielle L. Kopke, Shannon N. Leahy, Dominic J. Vita, Sofia C. Lima, Zachary L. Newman, Kendal Broadie

The first Wnt signaling ligand discovered, Drosophila Wingless (Wg; Wnt1 in mammals), plays critical roles in neuromuscular junction (NMJ) development, regulating synaptic architecture and function. Heparan sulfate proteoglycans (HSPGs), consisting of a core protein with heparan sulfate (HS) glycosaminoglycan (GAG) chains, bind to Wg ligands to control both extracellular distribution and intercellular signaling function. Drosophila HSPGs previously shown to regulate Wg trans-synaptic signaling at the NMJ include the glypican Dally-like Protein (Dlp) and perlecan Terribly Reduced Optic Lobes (Trol). Here, we investigate synaptogenic functions of the most recently described Drosophila HSPG, secreted Carrier of Wingless (Cow), which directly binds Wg in the extracellular space. At the glutamatergic NMJ, we find that Cow secreted from the presynaptic motor neuron acts to limit synaptic architecture and neurotransmission strength. In cow null mutants, we find increased synaptic bouton number and elevated excitatory current amplitudes, phenocopying presynaptic Wg overexpression. We show cow null mutants exhibit an increased number of glutamatergic synapses and increased synaptic vesicle (SV) fusion frequency based both on GCaMP imaging and electrophysiology recording. We find that membrane-tethered Wg prevents cow null defects in NMJ development, indicating that Cow mediates secreted Wg signaling. It was shown previously that the secreted Wg deacylase Notum restricts Wg signaling at the NMJ, and we show here that Cow and Notum work through the same pathway to limit synaptic development. We conclude Cow acts cooperatively with Notum to coordinate neuromuscular synapse structural and functional differentiation via negative regulation of Wg trans-synaptic signaling within the extracellular synaptomatrix.

Kumar, Anivarya
Board 45, Session 1
PI: Park, Sohee

Association of Rubber Hand Illusion and Subjective Experience of Anomalous Self

Anivarya Kumar, Lénie Torregrossa, Moustafa Hadi, Andrea Prada, Sohee Park

Abnormal body ownership and flexible body boundary characterize schizophrenia but these experiences are also prevalent in individuals who may be at risk for schizophrenia. Previous research indicates that abnormalities of the bodily self can be quantified via a multisensory procedure known as the Rubber Hand Illusion (RHI) task. We investigated the subjective and phenomenological reports of self-disturbances in relation to an objective measure of abnormal body ownership as quantified by the RHI in college students.

RHI procedure was administered 47 college students who also completed the Inventory of Psychotic-Like Anomalous Self-Experiences (IPASE) and the Schizotypal Personality Questionnaire (SPQ). RHI was induced by simultaneously brushing the participant's hidden left hand and the visible rubber hand for 4 minutes. Before and after brushing, participants were asked to indicate the location of their hidden left forefinger on a ruler. This provided an objective measure of the proprioceptive drift that may occur during the brushing.

We found that proprioceptive drift and IPASE score were significantly correlated ($r=0.36$, $p<0.0463$). There was also a positive correlation between IPASE score and the positive syndrome of the SPQ ($r=0.37$, $p<0.0462$).

Participants who reported self-disturbance as measured by the IPASE showed a greater proprioceptive drift in the RHI. Thus, it seems possible to link phenomenological reports of self-disturbances to an objective measure of flexible body boundary. Moreover, IPASE and positive schizotypy were correlated in this sample, which suggests that those at risk for psychosis experience self-disturbances. Given the important role of the temporoparietal junction on body representation and schizophrenia, future studies should examine the effects of stimulation of this brain region on symptoms of schizophrenia.

Kunda, Maithilee
Board 46, Session 2
PI: Kunda, Maithilee

Towards a New Technology-based Theory of Mind Intervention for Adolescents on the Autism Spectrum

Roxanne Rashedi, Mandy Zi, Shiyao Li, Chris Ketchum, Phil Chen, Christine Kim, Tengyu Ma, Maithilee Kunda

We are working to design a new, technology-based intervention for teaching theory of mind and social reasoning skills to middle school students on the autism spectrum. Towards this goal, we have been conducting user studies to investigate both theory of mind reasoning as well as proficiency with and attitudes towards educational technology in adolescent participants on the spectrum. We acknowledge many collaborators on this project, including: Gautam Biswas, Amy Kinsman, Pablo Juarez, Shitanshu Mishra, Marian Rushdy, Amy Swanson, and Zack Warren.

Our research follows several threads: 1) Design of a naturalistic and engaging theory of mind curriculum, based on students' watching, analyzing, and answering questions about social content in video clips from movies and television shows. 2) Development of an educational technology that will both test students' knowledge in a game-like environment and also provide visual scaffolds for students to improve their theory of mind reasoning skills. 3) Investigation of interaction and gaze patterns of students on the spectrum engaging in an existing, science-oriented educational technology. 4) Investigation of gaze patterns of students on the spectrum watching video clips and answering questions about social content. 5) Development of a computational cognitive model of theory of mind reasoning in the context of answering questions about social content in video clips.

We will present preliminary results from all five of the above activities. 1) We have collected a corpus of 200 video clips containing interesting social content, and are working to develop questions for each clip. 2) We are designing the educational technology for students based on principles from gamification and user-centered software design. 3-4) We have collected data on both educational technology usage and on social question answering from around 20 participants on the autism spectrum and 15 neurotypical participants. 5) We are creating an ontology of social reasoning knowledge and inference mechanisms towards the development of a computational cognitive model.

We present several possibilities and advantages of the educational technology we are developing, and also present hypotheses and preliminary results based on our user studies. We discuss our findings in the context of the importance of theory of mind in social reasoning and the need for further interdisciplinary research and interventions geared towards improving theory-of-mind skills in individuals on the autism spectrum.

Lancaster, Zoi
Board 47, Session 1
PI: Rittle-Johnson Bethany

Child Mathematical Talk Reflects That of Their Parents

Zoi Lancaster, Ashli-Ann Douglas, Bethany Rittle-Johnson

Preschool children's ability to correctly compare magnitudes predict their advanced mathematical skills for up to five years later (Rittle-Johnson et al., 2017). Parents may be able to support their children's growing magnitude comparison skills during play by discussing the relative size of numbers (e.g. by identifying which of two numbers or amounts is bigger). The current study aimed to compare the frequency and accuracy of children's magnitude comparison to the frequency of their parents' magnitude comparison during a play session. Likewise, we aimed to identify if parents' self-reported frequency of engaging their children in magnitude comparison activities at home was related to the accuracy of their children's magnitude comparison during a play session.

Participants were forty-five preschoolers (M = 4.38, SD =.65) along with a parent. Children were 60% male and 83% white. Parents were mostly mothers (73%) and had at least a bachelor's degree (80%). Dyads were videotaped playing two card games before and after listening to a description of magnitude comparison, including its' lasting effects on children's later math skills. Additionally, parents completed a survey about one week after their play session to report the frequency of parent-child play at home. Parents' and children's magnitude comparison talk were coded separately in 10-second intervals.

Parents talked about magnitude comparison during 26% of the 10-second intervals (SD = 8%) while children talked about magnitude comparison during 18% of the intervals (SD = 9%). Additionally, children's magnitude comparison statements were often accurate (throughout 84% of intervals during which they compared magnitudes; SD = 15%). Parents reported providing input about magnitude comparison at home once per week on average (M = 3.03, SD = 1.48). Children's age and the duration of the play session were controlled for in further analyses. The frequency of parents' and children's magnitude comparison talk were significantly correlated, $pr(40) = .74$, $p < .001$. Likewise, the frequency of parents' magnitude comparison talk was correlated with the accuracy of children's magnitude comparison, $pr(40) = .66$, $p < .001$. However, the frequency of home magnitude comparison was not significantly correlated with the accuracy of children's magnitude comparison during the play session, $pr(32) = -.11$, $p = .53$

Findings suggest that the accuracy and frequency of a child's magnitude comparison talk is strongly related to the frequency of their parent's. This suggests that the more parents discuss magnitude comparison in a given context, the more a child will compare magnitudes accurately. Future research should focus on parent-child magnitude comparison interactions in the home setting to gain more knowledge on activities that support children's magnitude comparison skills.

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Lee, Hyeon-Seung
Board 48, Session 2
PI: Park, Sohee

the predictors and mediators of improvement following virtual reality based social skill training

Hyeon-Seung Lee, Lenie Torregrossa, Megan Ichinose, Laura Adery, Heathman Nichols, Joshua Wade, Dayi Bian, Eric Granholm, Nilanjan Sarkar, Sohee Park

Social impairment is a core feature of schizophrenia. It is present throughout the course of the illness from the premorbid stage and resistant to treatments (Green et al, 2008). Given the important role of social deficits in poor outcome, it is imperative to improve social functioning in individuals with schizophrenia (SZ) but currently available pharmacological and psychosocial interventions have not proven to be very effective. However, recent technological advances have enabled the use of virtual reality (VR) to develop novel psychiatric interventions. We have previously reported preliminary feasibility and acceptability findings from a new VR-based social interaction training program that suggests the benefits of simulating and rehearsing social interactions situations in VR (Adery et al, 2018). In the present study, we evaluated predictors and mediators of the clinical outcome of this VR-intervention.

18 outpatients with schizophrenia completed 10 sessions of the social VR training over the course of 5 weeks. At each session, participants were asked to approach and interact with avatars by making appropriate conversations to accomplish social 'missions'. There were 12 different missions varying in difficulty levels and social settings (café, bus stop and shop). Symptoms (BPRS, SAPS, SANS), emotion recognition (BLERT and a novel facial emotion recognition task), social functioning (Social Functioning Scale) and cognitive functioning (IQ, CogState) were examined in relation to the VR game performance at pre- and post-treatment. Multivariate regression models with backward elimination method were used to verify significant predictors of the outcome. Lastly, mediation analyses were evaluated using bootstrapping (n=5000) to specify the relationship between predictors and behavioral changes.

Negative symptoms, especially alogia, anhedonia and asociality improved significantly by post-assessment. Additionally, attention and emotion recognition improved. Within the VR game, number of incorrect responses declined significantly throughout the training period. In multivariate regression models, baseline and changes in social functioning scores predicted clinical symptom improvement. Furthermore, IQ mediated the relationship between performance change in high-difficulty sessions and improvement in alogia. Alogia improvement mediated the relationship between interpersonal communication changes and VR performance.

Simulation-based social skills VR training game improved clinical symptoms, especially negative symptoms, via changes in social functioning and emotion recognition in schizophrenia. These results suggest that VR-based social skills training may be an effective social intervention method. Although the small sample size limits the scope of our conclusion, the results of the present study illustrate the potential power of technology-based psychiatric interventions.

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Lee, Chung
Board 49, Session 1
PI: Taylor, Julie

Evaluating skills and behavioral change among students with intellectual and developmental disabilities enrolled in Next Steps at Vanderbilt

Chung Lee, Tammy L. Day, Julie Taylor

Across the United States, postsecondary education (PSE) options for young adults with intellectual and developmental disabilities (IDD) are emerging, yet there is little research evaluating the ways in which students benefit from these programs. In the current study, we examined whether students in Next Steps at Vanderbilt - an inclusive higher education program for students with IDD - experienced improvements in self-determination, adaptive functioning, social skills, and executive functioning across the first year of the program.

Participants included 27 18- to 25-year-olds who began the Next Steps at Vanderbilt program between the years of 2014 to 2017. The participants averaged 20.27 years of age (SD = 2.10) at the start of the study. Two-thirds (66.7%) were male and most (66.7%) had an Autism Spectrum Disorder and/or Intellectual Disability. Student outcome measures were collected by parent- and self-report at two time points - the beginning (Time 1) and end (Time 2) of students' first year in Next Steps at Vanderbilt. The following measures were collected: Brief-A (executive functioning; Roth et al., 2005); Vineland Adaptive Behavior Scales - 2nd Ed. (adaptive functioning; Sparrow et al., 2005); Social Skills Improvement System Rating Scales (social skills; Gresham & Elliott, 2008); and the Arc Self-Determination Scales (self-determination; Wehmeyer & Kelchner, 1995).

Changes in student outcomes from Time 1 to Time 2 were examined using paired t tests. The Vineland adaptive behavior composite significantly increased from Time 1 to Time 2 ($M = 66.80$, $SE = 1.56$ for Time 1; $M = 70.60$, $SE = 1.62$ for Time 2), $t(26) = -2.51$, $p < .05$. Significant improvements were observed for the Communication domain ($M = 63.71$, $SE = 2.45$ for Time 1; $M = 70.04$, $SE = 2.23$ for Time 2), $t(26) = -2.81$, $p = .009$, and Socialization domain ($M = 73.82$ for Time 1, $SE = 1.92$; $M = 79.79$, $SE = 2.27$ for Time 2); ts (26) = -2.81 and -2.59, respectively, $ps < .05$. Self-determination skills also significantly increased from Time 1 ($M = 92.22$, $SE = 2.73$) to Time 2 ($M = 97.03$, $SD = 2.81$); $t(26) = -2.46$, $p = .02$. There were no statistically significant changes in overall executive functioning (parent or self-report) and social skills.

Findings of the present study suggested that participating in Next Steps at Vanderbilt was associated with improvements in adaptive functioning and self-determination. Promising directions for future research include examining student development across multiple PSE programs to determine which components are most effective, as well as examining post-school outcomes such as employment, community engagement, and independent living.

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Liang, Shih-Yuan
Board 50, Session 2
PI: Schuele, C. Melanie

"Does It Make Sense" A Comprehension Monitoring Intervention to Improve Reading Accuracy: A Single-Case Design Study

Shih-Yuan Liang, C. Melanie Schuele

Shared book reading is often recommended to teachers and parents to support beginning readers. However, teachers and parents are seldom instructed on how to respond to children's reading errors (Evans, Barraball, & Eberle, 1998). Most adults view oral reading as an accuracy task rather than an opportunity to guide children in monitoring their comprehension and applying effective word-solving strategies. Adults interrupt and supply the correct words at points of difficulty more often with struggling readers than with adequate readers. Immediate word supply is considered generally effective feedback; however, it does not help struggling readers develop self-monitoring or advance their decoding skills.

We conducted a single-subject, multiple probe design across four second-grade struggling readers (including three English Language Learners) to gauge the functional relation between a comprehension monitoring strategy and self-correction behaviors in independent oral reading. Each participant received three weekly one-on-one sessions across 9 weeks. In the baseline condition, the interventionist supplied the word to the child immediately at points of miscues (business-as-usual). In the intervention condition, the interventionist implemented the Does It Make Sense comprehension monitoring intervention (Liang & Schuele, 2017), which involved 4 to 5 steps per 20- to 30-minute lesson. Through explicit modeling, the interventionist demonstrated the strategy: she read to the end of each sentence/clause regardless of accuracy, and posed the question "Does it make sense?". If her oral rendering of text made sense, she put a check mark by the ending punctuation and continued reading. If not (i.e., she intentionally made errors), she scanned the sentence quickly, identified misread words, and applied word-solving strategies to repair her understanding. The child was engaged in employing this simple comprehension monitoring strategy in a modeling-guided practice-independent practice structure. The primary dependent variable, self-correction proportion, was derived from a 4-minute reading task administered twice weekly. A distal dependent variable, oral reading fluency, was derived from a 1-minute reading task administered once weekly.

All participant demonstrated increased use of self-correction behaviors. The mean self-correction proportion increased from baseline at 14% (range = 10% to 20%) to intervention at 34% (range = 27% to 45%). The percentage of non-overlapping data ranged between 0% to 81%. The strength of intervention effect was subject to participants' English proficiency and automatic word recognition.

Findings confirm a functional relation and support that when interventionists delay giving feedback until the end of each sentence, children are more likely to monitor their own errors and attempt self-correction. By contrast, immediate word supply to struggling readers was not effective in promoting reading for understanding and text reading accuracy. Feedback that promote long-term retention and skill transfer across contexts will be discussed.

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Litzow, Emily
Board 51, Session 1
PI: Gilmer, Mary Jo

Exploration of Child Communication Preferences about Cancer

Emily Litzow, Lauren E. Smith, Austin Darling, Ryanne Giorgione, Amanda Feldman, Katie Beard, Terrah Foster Akard, Mary Jo Gilmer

In providing pediatric palliative care, communication is often a challenge among children, families, and healthcare providers. The American Academy of Pediatrics recommends that children participate in conversations to the fullest extent possible. The National Cancer Institute (2016) advises parents to have open and honest communication about cancer with their children, but questions remain about what, how, and when to communicate. Minimal research has explored communication preferences and strategies of children diagnosed with cancer. This pilot study explored communication styles and preferences among children (ages 7-17 years) with cancer through a cross-sectional, qualitative design.

Following a study conducted in 2016 using focus groups with children with cancer, researchers developed interview questions and recruited children (N=8) at least 6 months after initial cancer diagnosis. Researchers conducted in-depth audio-recorded interviews with each participant between January-June 2017. The interview questions centered around children's opinions about how a cancer treatment should be communicated. For example, one question used was, "The doctor just told Kim's parents that she has cancer. Who do you think should tell Kim that she has cancer? Her parents or the doctor?" The recorded interviews were transcribed verbatim and three researchers used content analysis, reaching consensus on themes that emerged from the data.

Results document communication preferences and styles described by children with cancer throughout the disease trajectory. Five themes emerged from the interviews related to telling children about their cancer diagnosis: How to tell, who should tell, changes in prognosis, side effects of treatment, and who should be included in the disclosure. For example, one 14-year-old girl said, "They should talk to their parents and let their parents tell them." Participants' preferences varied by age, gender, and diagnosis. Children in this study demonstrated complex understanding of their disease/prognosis and the impact of their cancer diagnosis on their family system.

Quality communication during cancer diagnosis and treatment is challenging and requires healthcare providers' knowledge of children's developmental needs and preferences. Results of this study reveal a need for use of developmentally appropriate, evidence-based educational materials to 1) equip providers and 2) best inform parents on how and what to communicate about their child's disease. Data show that children want to be included in conversations about their diagnosis/prognosis. Children's cultural and developmental differences have global implications for awareness of and sensitivity to communication preferences in the face of serious disease.

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Liu, Talia
Board 52, Session 2
PI: Lense, Miriam

Increasing Parent-Child Social Interactions in Preschoolers with and without ASD through Song Books

Talia Liu, Danielle Dai, Benjamin Schultz, Christina Liu, Miriam Lense

Providing natural opportunities that scaffold interpersonal engagement is important for supporting social interactions for children with ASD. The familiar, predictable, and reinforcing context of musical activities may provide a platform for the development of social interaction skills. For example, children with ASD showed increased eye gaze and turn-taking with therapists during music therapy versus play therapy (Kim et al., 2008). Beyond impacts on children's behavior, musical activities may also support children's interaction partners in providing opportunities for and being receptive to moments of validated social engagement. We assessed the impact of a musical context on child and parent behavior during book sharing interactions.

Thirteen children with ASD (10 male, M = 41.8 months) and sixteen typically developing (TD) children (10 male, M = 35.6 months) were videotaped during a 5-minute picture book and a 5-minute songbook activity with their parents. A five-second partial interval coding schema (Klimenko, 2007) assessed parents' and children's visual attention towards the books and their partner. Frame-by-frame interpersonal movement activity was extracted from videos.

For the children's visual attention, a 2x2 ANOVA revealed a significant main effect of diagnostic group, $F(1,27) = 4.34$, $p = 0.047$. TD children looked significantly more at the book/parent than children with ASD. There was also a significant main effect of activity, $F(1,27) = 8.36$, $p = 0.007$. Children spent significantly more time looking at the books/parent during songbooks than picture books. For the parents' visual attention, a 2x2 ANOVA revealed a significant main effect of activity, $F(1,27) = 22.36$, $p < 0.0001$, indicating that parents demonstrated significantly greater gaze toward their child during songbooks than during picture books. Correlations showed that children are generally stable in their visual attention across activities; the effect is evident in both children with ASD ($r = 0.74$, $p = 0.004$) and TD children ($r = 0.66$, $p = 0.007$). The same effect is seen in parents of TD children ($r = 0.64$, $p = 0.008$) but not parents of children with ASD ($r = 0.38$, $p = 0.19$). Analyses of interpersonal movement coordination (Granger causality) during song vs. picture book activities are ongoing.

Songbooks, as compared to picture books, appeared to create a context that scaffolded parent-child engagement. Children increased sustained attention to the books and parents increased eye gaze toward their children during songbook versus picture book activities. Parents' increased gaze to their child during the songbook activity may have impacted their movement coordination with their child. Song activities may be accessible activities that support parent-child engagement due to their familiarity and predictability.

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Liu, Yupeng
Board 53, Session 1
PI: Woynaroski, Tiffany

Atypical Multisensory Integration is Linked with Reduced Looking to Faces in Children with Autism

Yupeng Liu, Jacob I. Feldman, Pooja Santapuram, Margaret Cassidy, Kacie Dunham, David Lewkowicz, Neill Broderick, Mark T. Wallace, Tiffany G. Woynaroski

Typically developing children often look to the talking face of their communication partner, in particular in early childhood when they are latching onto their native language and continuing in later years when they are presented with an unfamiliar or non-native language. In contrast, children with autism spectrum disorder (ASD) commonly present with reduced looking towards the face of their communication partners. It has been proposed that children with ASD may avoid looking towards faces because they have difficulty integrating the audiovisual cues from the talking face. A number of studies have demonstrated that children with ASD display differences in their integration of auditory and visual speech cues relative to their typically developing peers. For example, children with ASD may show a diminished magnitude of integration in response to McGurk stimuli (i.e., wherein an audiovisual illusion is commonly caused by the integration of mismatched auditory and visual speech cues in typically developing children). Children with ASD may also integrate auditory and visual speech cues over a wider window of time, or present with extended temporal binding windows (TBWs), relative to typically developing peers. This pilot project explored the degree to which these previously reported differences in (a) magnitude of multisensory integration and (b) TBWs for audiovisual speech correlate with looking behavior in children with ASD.

Participants completed a McGurk task and a simultaneity judgement (SJ) task to index magnitude of multisensory integration and temporal binding for audiovisual speech, respectively. During the McGurk task, participants were presented with mismatched audiovisual stimuli (i.e., auditory "pa" + visual "ka", a combination that frequently induces a percept of "ta" of "ha" in typically developing individuals) and asked to report their perception. In the SJ task, children were presented with auditory and visual speech cues at various stimulus onset asynchronies (SOAs) and asked to report whether they perceived the stimuli to occur at the "same time" or "different times". Within 24 hours of completing the aforementioned psychophysical tasks, participants were presented with remote eye tracking tasks, wherein they viewed 50 sec monologues produced in native (English) and non-native languages (Spanish) with adult-directed speech.

Preliminary analyses indicate that magnitude of multisensory integration as indexed by the percent of reported McGurk fusion is positively correlated with looking to the face during the native monologue ($r = 0.28$) and, more strongly, with looking to the face during non-native speech ($r = 0.65$). TBWs were not significantly associated with looking behavior.

Results thus far lend some empirical support to the hypothesis that differences in multisensory integration may account for a tendency not to look to the face in children with ASD. Looking behavior appears to covary with magnitude of multisensory integration moreso than temporal binding of audiovisual speech cues, and associations are most apparent under challenging listening conditions (e.g., when children are presented with non-native speech). Additional research is needed to draw conclusions about the direction, or causal nature, of the correlations that have been observed. It is possible that early differences in multisensory integration lead to generalized differences in looking behavior. Alternatively, it is possible that a tendency not to look towards faces, over time, could produce cascading effects on multisensory development in this clinical population.

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Luderman, Lauryn
Board 54, Session 2
PI: Knapik

The role of ERC1 in patterning of neuromuscular junctions and trigeminal nerve innervation of craniofacial muscles

Lauryn N. Luderman, Daniel S. Levic, Ela W. Knapik

Cranial muscle and motor nerves form specialized connections known as neuromuscular junctions (NMJs) through which the cranial motor neurons induce contractions of innervated muscles, and ultimately, movement of the craniofacial structures. Defects in muscle innervation or NMJ may contribute to defects in jaw movements found in craniomandibular disorders; however, the molecular mechanisms controlling these processes during development are poorly understood. In this study, we aim to investigate the function of ERC1 as a potential new molecular component to axon outgrowth and NMJ maturation.

We utilized a forward genetics screen to identify a zebrafish craniofacial mutant carrying a nonsense mutation in erc1b. Live imaging and whole-mount immunofluorescence was used to further investigate the craniofacial phenotype of erc1b mutants.

Zebrafish erc1b mutants display craniofacial malformations compared to wild-type (WT) siblings. Whole-mount immunofluorescence reveal erc1b mutants have significant defects in craniofacial muscle organization, including muscle length. Using a transgenic line to live image the cranial motor nerves in the developing zebrafish, it was observed erc1b mutants have trigeminal motor axon pathfinding defects compared to WT siblings. To further investigate axonal growth, time-lapse imaging of developing embryos was performed. Compared to WT siblings, trigeminal motor axons in erc1b mutants failed to cross the midline over the imaging period. Because erc1b mutants have defects in motor axon outgrowth and muscle organization, whole-mount immunolabeling was used to visualize the NMJ. In both WT siblings and erc1b mutants, pre- and postsynaptic NMJ components colocalize. However, erc1b mutants have defects in NMJ patterning, including size and number of NMJs compared to WT siblings.

These results indicate loss of zErc1b protein is associated with defects in cranial nerve outgrowth, craniofacial muscle organization, and NMJ patterning. Further experiments will be to determine the cell autonomous function of zErc1b in trigeminal motor neurons and craniofacial muscles and its effect on NMJ maturation. By explaining molecular mechanisms regulating craniofacial NMJ development, this study will advance the understanding of developmental mechanisms that may underlie jaw movement defects such as those in trigeminal and craniomandibular disorders.

Lytle, Marisa
Board 55, Session 1
PI: Booth, James

A longitudinal neuroimaging dataset on multisensory lexical processing in school-aged children

Marisa Lytle, Chris McNorgan, James R. Booth

Recent years have shown a rapid increase in open science initiatives and tools for reproducibility in neuroimaging research, including new standardized processing pipelines, organization systems, and open access data repositories1. Data sharing is a core component of transparent and reproducible neuroscience, improving access to raw data for additional analyses and replicating reported results. Sharing of large neuroimaging datasets also improves the field by allowing researchers with less resources access to datasets that require substantive funding to acquire.

Here we describe the open access dataset entitled "Longitudinal Brain Correlates of Multisensory Lexical Processing in Children" hosted on OpenNeuro.org2. This dataset examines reading development through a longitudinal neuroimaging and behavioral approach, including diffusion-weighted and T1-weighted structural magnetic resonance imaging (MRI), task based functional MRI, and a battery of psycho-educational assessments and parental questionnaires. Neuroimaging, psycho-educational testing, and functional task behavioral data was collected from 188 typically developing children when they were approximately 10.5 years old. Seventy children returned approximately 2.5 years later, of which all completed longitudinal follow-ups of psycho-educational testing, and 49 completed neuroimaging and functional tasks. At T1 participants completed auditory, visual, and audio-visual word and pseudo-word rhyming judgment tasks in the scanner. At T2 participants completed visual word and pseudo-word rhyming fMRI tasks in the scanner.

This dataset was organized in accordance with the Brain Imaging Data Structure (BIDS) and has been made publically available on OpenNeuro.org, a public repository for raw neuroimaging data. Data quality metrics, reviewed using the MRIQC tool3, fell within expected ranges based on other similar datasets. The dataset descriptor for this project has been uploaded as a preprint to psyarxiv.com and is under review at Scientific Data4.

This dataset will serve as a resource to the field of educational neuroscience and researchers examining reading development. The dataset allows for nuanced analyses of brain behavior interactions, structural / functional comparison, as well the examination of different sensory modalities of lexical processing. Our hopes in making this data publically accessible are to aid in openness, reproducibility, and reliability in neuroimaging research.

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MacDonald, Lydia
Board 56, Session 2
PI: Malow, Beth

Behavioral Sleep Education for Children with Autism and Insomnia: Partnership with Community Practices

Lydia MacDonald, Whitney Loring, Amanda Wyatt, Diane Fawkes, Laura Gray, Beth A. Malow

Insomnia is common in children with autism spectrum disorder (ASD). Due to time constraints, pediatricians may impart only limited information to parents on sleep education. Building the capacity of community therapists to provide sleep education within the context of their ongoing care is practical and time-effective for families. We describe a collaborative program whereby academic sleep physicians and psychologists provide training to community therapists in behavioral sleep interventions. These therapists then deliver education to parents of children with ASD and insomnia, who, in turn, implement behavioral strategies with their children.

Pilot pre/post behavioral study examining the effectiveness of providing sleep education to parents of children with ASD with sleep onset delay (30 minutes or longer). Pediatricians referred families to community therapists we had trained in sleep education. The intervention consisted of a 90-minute in-person session followed by two shorter weekly sessions conducted in-person or by phone. Parents completed baseline and post-intervention surveys including the Children's Sleep Habits Questionnaire (CSHQ; standard and four-factor modified for ASD) and the Family Inventory of Sleep Habits (FISH). Children wore actigraphy at baseline and post-intervention. Wilcoxon signed rank tests were performed to determine change with the intervention.

31 children completed the intervention (mean age = 6.6 years; standard deviation, SD = 2.7). FISH improved from 46.1 (SD = 5.6) to 50.0 (SD = 3.7; p =0.000). Standard CSHQ showed improvements in sleep onset delay (p = 0.000), bedtime resistance (p = 0.001), night wakings (p= 0.002) and sleep duration (p= 0.007). Four-factor CSHQ showed improvements in sleep initiation and duration (p = 0.000) and sleep anxiety and co-sleeping (p = 0.001). Sleep latency (minutes) measured by actigraphy improved from 55.9 (SD = 19.9) to 44.8 (SD = 16.9; p = 0.04).

Improvements were documented in sleep habits and parent-reported and objective measures of sleep in children with ASD after receiving sleep education. This work demonstrates a successful partnership among parents, community pediatricians, community therapists, and academic sleep physicians and psychologists.

Mackey, Chase
Board 57, Session 1
PI: Ramachandran, Ramnarayan

Deficits in Temporal, but not Spatial, Resolution Correlate with Pathophysiological Cochlear Changes in Noise Exposed Macaques

Chase Mackey, Jennifer McCrate, Michelle Valero, Jessica Feller, Namrata Temghare, Alejandro Tarabillo, M. Charles Liberman, Troy Hackett, Ramnarayan Ramachandran

Deficits in temporal and spatial processing associated with sensorineural hearing loss have been well characterized in humans. Animal models that afford the possibility of controlled noise exposures, cochlear histology, and central neurophysiology can establish causal links between noise exposure history, perceptual deficits, cochlear pathophysiology and central changes. To establish such links, we characterized temporal and spatial resolution in a non-human primate model of noise-induced hearing loss.

Monkeys performed a Go/No-Go tone detection task in the presence of 76 dB SPL unmodulated broadband noise (BBN). Signal detection theoretic methods were used to calculate behavioral accuracy (probability correct) as a function of tone level in all conditions. In the SAM noise condition, BBN was modulated at 10-150 Hz. In the spatially separated condition, BBN was separated (45° or 90°) from the tone. Tone frequencies were 0.5-32 kHz. These data were obtained in a normal hearing group, and another group exposed to noise for four hours at 141 or 146 dB SPL 50 Hz band of noise centered at 2 kHz (permanent threshold shift model, PTS). One subject was exposed to a 120 dB SPL octave-band noise (2-4 kHz, temporary threshold shift model, TTS).

Normal-hearing subjects showed lower tone detection thresholds in SAM BBN (Modulation masking release, MMR), and for noise that was spatially separated from the tone (Spatial release of masking, SRM) relative to BBN co-localized with the tone. MMR was highest for low noise modulation frequencies (~10-20Hz) and decreased to match the threshold in BBN at high (~100 Hz) noise modulation frequencies. SRM increased with spatial separation between the tone and noise. After noise exposure, PTS subjects showed frequency-specific deficits in MMR that correlated with audiometric change, while SRM was abolished at all frequencies. The TTS subject showed frequency-specific deficits in both tasks. Cochlear histology confirmed large-scale hair cell loss and inner hair cell ribbon synaptopathy in the PTS subjects, and inner hair cell ribbon synaptopathy without hair cell loss for the TTS subject. The PTS subjects' deficits in MMR showed significant correlation with the amount of outer hair cell loss and synaptopathy. The TTS subject's deficit in MMR correlated with synaptopathy. Deficits in SRM did not correlate with cochlear pathophysiology in any subjects.

: Behavioral deficits in temporal resolution, indexed by MMR, are more reflective of cochlear damage than SRM, and potentially a better behavioral assay of cochlear pathology. Deficits in SRM, while caused by peripheral pathology, are probably reflective of central changes in response to cochlear insult. Clinical diagnostics and therapeutics may benefit from consideration of these results when assessing noise-induced and hidden hearing loss.

Manz, Kevin
Board 58, Session 2
PI: Grueter, Brad

Heterosynaptic GABAB receptor function within feedforward microcircuits gates glutamatergic transmission in the NAc core

Kevin M. Manz, Andrew G. Baxley, Zack Zurawski, Heidi E. Hamm

Complex circuit interactions within the nucleus accumbens (NAc) facilitate goal-directed behavior. Medium spiny neurons (MSNs) mediate NAc output by projecting to functionally divergent brain regions, a property conferred, in part, by the differential projection patterns of D1- and D2 dopamine receptor-expressing MSNs. Glutamatergic afferents to the NAc direct MSN output by recruiting feedforward inhibitory microcircuits comprised of parvalbumin (PV)-expressing interneurons (INs). Furthermore, the GABAB heteroreceptor (GABABR), a Gi/o coupled G protein-coupled receptor, is expressed at glutamatergic synapses throughout the mesolimbic network, yet its physiological context and synaptic mechanism within the NAc remains unknown. Here, we explored GABABR function at glutamatergic synapses within PV-IN embedded microcircuits in the NAc core.

We utilized (a) transgenic D1tdTomato BAC transgenic mice to differentiate D1 and D2-expressing MSNs, (b) triple transgenic PV-Cre-cChR2-D1tdTomato mice to optically stimulate PV-expressing neurons in the NAc, and (c) SNAP25D3 transgenic mice in which the C-terminus of SNAP25 is truncated to reduce GPCR-directed targeting of presynaptic SNARE proteins. Each mouse line was used to perform ex vivo whole-cell patch clamp electrophysiology and optogenetics experiments.

We found that presynaptically-expressed GABABR recruits a non-canonical SNAP-25-dependent signaling mechanism to reduce glutamatergic synaptic efficacy at D1(+) and D1(-) [putative D2] MSN subtypes. This pathway is NEM-insensitive, independent of N- and P/Q-type voltage-gated calcium channels (VGCCs), adenylyl cyclase/PKA, mGluRs, and GPCR-activated Kir channels, and functionally distinct from presynaptic CB1 receptors group II mGluRs. Presynaptic GABAB heteroreceptor function is targeted by circuit-wide elevations in neuronal GABA. Furthermore, PV-INs, a robust source of neuronal GABA in the NAc, heterosynaptically target GABABR to selectively modulate glutamatergic transmission onto D1(+) MSNs.

These findings elucidate a new mechanism of feedforward inhibition and refine mechanisms by which GABAB heteroreceptors modulate mesolimbic circuit function. Understand microcircuit mechanisms regulating NAc circuit function will hopefully yield novel therapeutic targets for the treatment of addiction.

Merritt, Jonathan
Board 59, Session 1
PI: Neul, Jeffrey

Creation and characterization of the Mecp2-R294X mouse model

Jonathan Merritt, Bridget Collins, Kirsty Longley, Jessica Lee, Jeffrey Neul

Rett Syndrome is a severe neurodevelopmental disorder primarily caused by mutations in the X-linked gene Methyl-CpG Binding Protein 2 (MECP2). More than 30% of Rett cases result from nonsense mutations in MECP2. For these patients, nonsense suppression therapy might be a way to significantly alter the course of the disorder. In nonsense suppression therapy, pharmacological agents are used to readthrough a premature termination codon and restore full-length protein expression in pursuit of phenotypic rescue. In an effort to provide a platform for preclinical validation of this approach to therapy, we have created a new mouse model of Rett Syndrome with a common mutation seen in patients, R294X, introduced into the endogenous Mecp2 locus by CRISPR-Cas9 directed mutagenesis. Gross characterization has shown R294X mice develop phenotypes typically seen in mouse models of Rett Syndrome. However, the unique presence of truncated MeCP2 protein in R294X mice results in delayed onset and reduced severity of these phenotypes compared to an existing Mecp2-R255X mouse model. To validate the R294X mouse for preclinical studies of nonsense suppression, we sought to determine if readthrough agents could rescue full-length MeCP2 protein production in this model. As a proof-of-concept, we treated fibroblasts from R294X mice with G418, a known readthrough compound, and found this intervention was sufficient to yield full-length MeCP2 protein in vitro. Daily intraperitoneal administration of G418 was similarly able to restore full-length MeCP2 protein expression in vivo. Ongoing experiments are focused on investigating if chronic treatment with readthrough agents is sufficient to improve the phenotypes observed in R294X mice. Demonstrating therapeutic efficacy of nonsense suppression in the R294X mouse model will provide a rational basis for conducting further preclinical testing and patient trials of clinically relevant read through drugs.

Miceli, Alexandra
Board 60, Session 2
PI: Weitlauf, Amy

Reducing Disparities in Early Identification of Autism: Preliminary Results from Aim 1 of a Trial of Novel Telemedicine Tools

Alexandra Miceli, Amy Weitlauf, Amy Nicholson, Laura Corona, Caitlin Reichstein, Zachary Warren

Long waiting lists contribute to delayed diagnosis of autism spectrum disorder (ASD). Telemedicine holds promise for increasing access to diagnostic evaluations necessary for accessing early intervention. However, no study has examined parent and clinician feedback on parent-implemented ASD tele-assessment tools. Our objective was to evaluate parent and clinician feedback on acceptability and feasibility of parent-implemented tele-assessment.

Participants included 48 children (18-36 months; m=30 months, sd=.35 months) and a primary caregiver. Children had diagnoses of ASD, developmental delay (DD), or typical development (TD). Participants and caregivers entered an assessment space and were connected with a licensed clinician through a wall-mounted screen. Clinicians then coached caregivers through administration of a tele-assessment tool. At the end of the visit, caregivers and clinicians completed the Acceptability, Likely Effectiveness, Feasibility, and Appropriateness Questionnaire (ALFA-Q) about the procedure.

We compared parent and clinician ALFA-Q scores on four items: acceptability ("Telemedicine screening would be an acceptable method for the assessment of ASD risk in toddlers"), appropriateness ("Telemedicine screening would be an appropriate assessment for children across a spectrum of impairment (i.e. low vs. high)"), need ("The problem of limited availability of assessment services is an important problem and is large enough to justify the use of telemedicine screening"), and endorsement ("I would recommend the use of telemedicine screening to others"). On a scale of 1-5, with 5 being most positive, both parents and clinicians indicated high levels of acceptability (Parent: mp=4.27, sdp=0.64; Clinician: mc=4.60, sdc= 0.49). Parents gave moderate-to-high ratings of telemedicine assessment as appropriate for children across a spectrum of impairment (mp=3.97, sdp=0.93), whereas clinician scores were moderate (mc=3.47, sdc = 1.05). Both parents and clinicians indicated that limited assessment availability supported the need for telemedicine (Parent: mp=4.54, sdp=0.68; Clinician: mc=4.95, sdc=0.20). Parents and clinicians said they would recommend telemedicine screening method to others, with both groups reporting similarly high mean scores (Parent: mp= 4.57, sdp=0.65; Clincian: mc=4.64, sdc=0.52).

Results indicate that parent-implemented tele-assessment of ASD yielded acceptable levels of parent and clinician approval. Stakeholders may consider telemedicine screening for ASD with parent involvement to be appropriate, especially given limited access to expert comprehensive assessment services. However, modest clinician ratings of its utility across the spectrum suggest that it may be best utilized with children with a clear diagnostic profile rather than for any child with ASD-related concerns. Further research will continue to refine the tele-diagnostic process in order to determine how it can best be utilized by clinicians.

Morton, Ian
Board 61, Session 1
PI: Schuele, Melanie

Complex Syntax Production in 5-Year-Old Children with Specific Language Impairment and Typical Language Development

Ian Morton, Ana Delgado, Dr. Melanie Schuele

Children with specific language impairment (SLI) produce less complex syntax (CS), omit more markers of CS, and produce fewer types of CS than same-aged peers (e.g., Barako Arndt & Schuele, 2012; Owen & Leonard, 2006). Further research is needed to develop a full picture of the complex syntax produced by children with SLI. We compare the complex syntax produced by five-year-old children with SLI to the complex syntax produced by same-aged peers with typical language development (TD). Diessel (2004) asserted that early-emerging CS productions (e.g., matrix clauses with fixed word-pairings like I think) precede later-emerging CS productions (e.g., matrix clauses that follow a NP-VP constructional schema like She remembered). We hypothesized that children with SLI would produce less later-emerging complex syntax as compared to same-aged peers. We address two research questions. Do children with SLI produce fewer instances of each complex syntax type in their spontaneous spoken language as compared to TD same-aged peers? Do children with SLI produce less later-emerging complex syntax than TD same-aged peers?

Spontaneous spoken language samples of 26 children (age M= 5;4) were selected for analysis. All participants' typical language status was verified by performance within normal limits on norm-referenced language measures. Language samples were collected using the Hadley Interview Protocol for Eliciting Text-Level Discourse (Hadley, 1998). Child utterances were coded for 11 types of CS (Schuele, 2009). Variables were derived to answer our research questions: Research Question 1: CS TYPE PRODUCTION = frequency of tokens for each CS type produced in 144 utterances. Research Question 2: LATER-EMERGING CS PRODUCTION = frequency of utterances with later-emerging CS in 144 utterances.

Research Question 1: Compared with children with TD, children with SLI produced fewer subordinate clauses ($t(24) = 2.33$, $p = .014$; Hedge's g =.86 [large]); full propositional complements ($t(24) = 3.02$, $p = .003$; Hedge's g =1.21 [very large]); and wh- finite complement clauses ($t(24) = 3.24$, $p = .002$; Hedge's g =1.27 [very large]). Research Question 2: Children with SLI produced less later-emerging subordinate conjunction clauses than children with TD ($t(24) = -1.9553$, $p = .031$; Hedge's g =.97 [large]). Children with SLI produced less later-emerging complement clause productions than children with TD ($t(24) = -1.82$, $p = .035$; Hedge's g =.76 [large]).

Our results support previous findings that five-year-old children with SLI produce fewer instances of CS types in their spontaneous spoken language than same-aged peers. Additionally, we found that children with SLI produce fewer instances of later-emerging CS than same-aged peers, providing preliminary evidence that later-emerging CS is especially challenging for children with SLI.

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Mueller, Carlyn
Board 62, Session 2
PI: Forber-Pratt, Anjali

Claiming disability?: Exploring adolescent disability knowledge and identity development

Carlyn Mueller

The goal of this study is to understand, in part, how opportunities to reflect on and develop disability identity with other people with disabilities shapes each individual and their self-understandings.

This study draws from a critical research tradition, which seeks "not just to study and understand society but rather to critique and change society" (Merriam, 2009, p. 34). The first stage of the project involves reflection from disabled adults on their educational experiences and disability awareness in school. The second part of the study involves interviews of adolescents with disabilities discussing their current knowledge of disability and relationship to disability communities. They will be brought the "findings" from disabled adults' experiences in school as potential sources of connection. Finally, students engage in a photovoice project (Wang & Burris, 1997) identifying places in their school or community where disability issues are ignored or encouraged. The study was conducted in a large city in the Pacific Northwest, including a large public high school. 4 adults with autism and/or learning disabilities and 4 students with intellectual disabilities, autism and/or learning disabilities participated in the study.

Common themes included the need for adult role models with disabilities in childhood, a sense of being "the only one" in school who shared either their visible disability or internal sense of disability identity, and a pervasive lack of support for developing or encouraging disability identity. Disabled adults described isolation from the disabled community they felt as children, and the incredibly emotional, positive experiences they had when "re-united" (or, in some cases, united for the first time) with this community in adulthood.

This study contributes to the theoretical and methodological conversations around experiences of disability in a few important ways. First, it centers individual meaning-making around disability as the major source for both data collection and understanding. This is the intolerable cost of disability research that treats individuals with disabilities as a subject under study and intervention, rather than capable of creating community and solidarity, negotiating power and stigma, and articulating the changes that need to be made to make their communities more inclusive. Understanding these ideas about identity could potentially lead to developing spaces that support positive disability identity, with far-reaching impact on people with disabilities.

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Muñoz, Valerie
Board 63, Session 1
PI: Lense, Miriam

The Effect of Musical Play on Interactions Between Children with ASD and their Parents

Olivia Boorom, Meredith Watson, Rongyu Xin, Valerie Muñoz, Miriam Lense

Although a growing body of research is examining connections between music and social development in children with autism spectrum disorder (ASD), there is limited research investigating musical play in parent-child interactions. Parent-child play interactions offer an important avenue for supporting children's social development. Shared engagement and parent responsiveness to children's focus during play are associated with children's social and language development (Gulsrud et al., 2016). Musical play may support interactions because it is familiar, reinforcing, and predictable, which may help children attend to activities and provide parents with an accessible way to be responsive (Lense & Camarata, 2018). However, musical play may also impede interactions due to its sensory and repetitive components. The present study examines whether the use of musical play/toys during parent-child play is related to children's attention and parental responsiveness.

Twelve parent-child dyads of preschoolers with ASD were video recorded for ten minute play sessions that included both musical and non-musical toys (8 male children; M=40.75 months). Videos were coded using a 5-second partial interval schema for engagement in musical play, as well as use of musical toys apart from musical play (e.g., building with drums). Additionally, children's attentional leads and corresponding parental physical toy play or verbal responses were identified. Wilcoxon Signed Rank tests compared differences between children's leads and parental responsiveness during musical and non-musical activities.

Children with ASD spent 34.3%±14% of time engaged in musical play and an additional 18.3%±11% of time engaged with musical toys apart from musical play. Overall, parents showed similar responsiveness to children's musical play/musical toy leads (65.0%±15.9%) versus non-musical leads (58.2%±17.0%) ($V=57$, $p = 0.18$) but this differed by type of responses. In response to children's musical vs. non-musical leads, parents provided significantly more physical play responses ($p=0.03$) and significantly fewer verbal responses ($p=0.003$).

While there are substantial individual differences in ASD children's use of musical toys and play during a parent-child free play, engagement with musical play/toys impacted parental responsiveness. Parents provided more physical play responses when their child engaged with musical play/toys potentially due to the familiarity and accessibility of musical activities. Parental verbal responses may be reduced during active musical play perhaps due to the competing auditory stimuli. Results have implications for incorporation of music into therapy including using musical activities to support parents in following their children's leads and providing responsive input. Follow-up analyses with an expanded sample size will further address different types of play leads and responses.

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Muscatello, Rachael
Board 64, Session 2
PI: Corbett, Blythe

Interactions Between the Hypothalamic-Pituitary-Adrenal Axis and Autonomic Nervous System as Predictors of Depressive Symptoms in Children with ASD

Rachael A. Muscatello, Emily McGinn, Sara Ioannou, Justin Andujar, Blythe A. Corbett

The hypothalamic-pituitary-adrenal (HPA) axis and autonomic nervous system (ANS) are involved in physiological arousal response and regulation, and independently, have been implicated in negative behavioral health outcomes, including internalizing disorders. Previous research to identify associations with physiological dysregulation and internalizing symptoms in ASD has produced inconsistent findings, and little attention has been paid to the interactions of the distinct, yet interrelated, HPA axis and ANS. The current study examined physiological regulation and interactions in children with ASD and typical development (TD). The extent to which the individual systems, as well as the interactions between them, predicted parent-reported internalizing symptoms in children with ASD was investigated.

In 111 children, ages 10-to-13 years, with ASD (N=64) and TD (N=47), diurnal rhythm of the HPA axis was measured via salivary cortisol, collected at home over 3 days, four times per day. Baseline respiratory sinus arrhythmia (RSA) and pre-ejection period (PEP) were collected in the lab via electrocardiography and impedance cardiography to examine PNS and SNS regulation, respectively. Parents completed the Child Behavior Checklist (CBCL), and the Withdrawn/Depressed, Anxious, and Internalizing subscales were included in analyses. ANOVAs compared group differences, and hierarchal multiple linear regression examined the extent to which physiological variables and their interactions predict internalizing symptoms.

Consistent with previous research, children with ASD showed elevated evening cortisol compared to TDs ($F(1,108)=10.09$, $p=0.002$). There were no significant group differences in baseline RSA or PEP (all $p>0.05$); however, the ASD group reported higher scores on CBCL subscales Withdrawn/Depressed ($t(109)=-8.56$, $p<0.001$), Internalizing ($t(85.10)=-8.87$, $p<0.001$), and Anxious ($t(109)=-6.36$, $p<0.001$). No significant main effects of physiological variables on CBCL subscales were seen using hierarchal linear regression while controlling for age, IQ and gender (all $p>0.05$). However, controlling for demographics and main effects, there was a significant interaction for cortisol and RSA, which accounted for 9% of the unique variance in Withdrawn/Depressed symptoms in ASD ($\Delta F(1,42)=5.51$, $p=0.03$). Post hoc analysis revealed that ASD participants with low evening cortisol showed a negative trend association between RSA and withdrawn symptoms ($t(92)=-1.89$, $p=0.06$).

The results extend previous findings on physiological dysregulation in ASD to reveal the presence of unique interactions, which predict parent-reported symptoms of depression. Children with high PNS regulation and low evening cortisol showed the fewest symptoms. In contrast, hyper-arousal in the HPA axis and/or PNS was associated with elevated depressive symptoms, even in the presence of more adaptive physiological regulation in the other system. The findings underscore the importance of examining arousal across multiple systems to more accurately identify response profiles associated with behavioral outcomes in ASD.

Nagabhushan Kalburgi, Sahana
Board 65, Session 1
PI: Bodfish, James

Children with autism produce a unique pattern of EEG microstates during an eyes closed resting state condition

Sahana Nagabhushan Kalburgi, Sasha Key, Carissa Cascio, James W. Bodfish

Individuals with Autism Spectrum Disorders (ASD) demonstrate robust differences in large scale brain network connectivity at rest in fMRI studies compared to their typically developing (TD) peers. Although there is considerable evidence for differences in the spatial connectivity, much less is known about the temporal dynamics of these brain networks in ASD. The aim of this study was to examine the EEG microstate architecture in children with ASD compared to TD at rest in two separate conditions - eyes-closed and eyes-open rest.

Resting-state EEG data was collected from 16 ASD between the ages of 8 - 14 years and 17 TD children matched on age, gender, and IQ in two conditions: eyes-open, eyes-closed using 128 channel electrode nets. EEG microstate analysis was performed using atomize and agglomerate hierarchical clustering method to isolate 4 template maps whose topographies corresponded to microstate classes A-D. Microstate parameters were quantified.

The duration of activation of the microstate C was increased, the frequency of occurrence of the microstate C was decreased, and the global field power (GFP) of microstate C was significantly decreased in ASD compared to TD in eyes-closed resting-state. We found no differences in EEG microstate parameters between the two groups in eyes-open resting-state except in GFP, where the GFPs of all microstates were significantly decreased in ASD compared to TD.

These results suggest a unique pattern of EEG microstate architecture in ASD relative to TD during resting states and also that EEG microstate parameters in ASD are susceptible to differences in resting state conditions.

Nguyen, Tin
Board 66, Session 2
PI: Cutting, Laurie

The Role of Home Environment in Brain Anatomy Differs with Age

Tin Q. Nguyen, Stephanie N. Del Tufo, Laurie E. Cutting

Early home environmental factors, such as socioeconomic status (SES) and home literacy environment (HLE), are well-established facilitators of childhood and adolescent development. While studies have related childhood SES with differences in brain anatomy, the contribution of HLE is less known. Different regions and features of brain anatomy exhibit distinct developmental trajectories. The links between childhood SES and HLE and brain anatomy may also differ across childhood and adolescence. Notably, HLE is suggested to play a potentially protective role for children and adolescents from lower-SES households. Yet, no studies have considered whether the relative contribution of HLE to brain anatomy may vary between and within lower- versus higher-SES groups across childhood and adolescence. In this study, we evaluated the role of home environment in brain anatomy in relation to age.

Analyses were conducted on 824 pediatric brain scans (ages 6-15). Using the double generalized additive mixed-effects regression strategy, we answered the primary question of the roles of home environmental factors (childhood SES and HLE) in brain anatomy in relation to age. Scanner effects, demographic information (sex, handedness, and race and ethnicity), and school and neighborhood environments were treated as subject-level covariates. First, we tested the covariation of age with childhood SES versus HLE, predicting differences in brain anatomy. As aforementioned, different regions and features of brain anatomy exhibit distinct developmental trajectories. A post-hoc examination was also conducted to assess the predictive effects of childhood SES versus HLE across specific age quantiles. Second, we evaluated the interaction between HLE and age between and within lower- versus higher-SES groups, predicting differences in brain anatomy.

When controlling for childhood SES, HLE still covaried with age, explaining unique variation in brain anatomy. When specific age quantiles, childhood SES explained variation in brain anatomy in childhood, while the predictive effect of HLE was significant in adolescence. Differences in brain anatomy were also predicted by the joint effect of childhood SES and HLE in relation to age. HLE was associated with differences in brain anatomy in adolescence especially within lower-SES group.

Our study highlights the dynamic relationship between home environmental factors and brain anatomy in relation to age. Our results for the association between SES and brain anatomy during childhood are consistent with prior reports. Unique to our study are the findings for the relation between HLE and brain anatomy in adolescence within lower-SES group. HLE may potentially mitigate the impacts of lower-SES on children and adolescent by tapping into brain development.

Patel, Kunj
Board 67, Session 1
PI: Corbett, Blythe

Significant Differences in Social Evaluative Stress Between Early Adolescents with Autism Spectrum Disorder and Typical Development

Kunj Patel, Aaron Pachol, Michael Kamel, Kaite Chance, Mary McGarr, Emma Gatlin, Rachael Muscatello, Blythe Corbett

Autism spectrum disorder (ASD) is characterized by deficits in several areas of social competence that include communication and interaction. The difficulties associated with the disorder have an impact on how individuals with ASD perceive and physiologically respond to various psychological stressors. Stress is primarily processed and regulated by the hypothalamic pituitary adrenal (HPA) axis, and the activation of this axis subsequently leads to the release of the cortisol hormone. Research has shown that the HPA axis is activated by social evaluative threat, which is a prototypical response to perceived negative evaluation. Previous research has shown that children (Lanni, Schupp, Simon & Corbett, 2011) and adolescents (Edmiston, Blain & Corbett, 2016) with ASD exhibit a blunted stress response to social evaluative threat. However, these were largely based on within-group analyses.

The Trier Social Stress Test (TSST) is an established psychosocial stressor intended to activate the HPA axis and elicit a stress response. The TSST is 20-minute task that includes a preparation period, followed by a speech, serial subtraction, and lastly a debriefing period. During the protocol, 6 salivary samples were collected during arrival, baseline, stress and recovery. The current study compared 156 youth between 10 to 13 years of age, 89 with ASD (11.29 years) and 67 with TD (11.61 years). Repeated measures analysis of covariance was used to compare the five cortisol samples collected during the TSST protocol while controlling for arrival cortisol level and age. Levene's test was also conducted in order to evaluate variability.

Results indicated significant between-group differences for the cortisol stress response $F(1,152) = 4.45$, $p = 0.04$, reflecting a significant rise in cortisol for TD youths in response to social evaluation, and a diminished response in youths with ASD. Levene's test of Equality of Error Variances indicated that there exists significant variability for the TSST cortisol stress and recovery levels ($p < 0.05$).

In a large sample of youths with and without ASD, the results replicate and extend previous research, in which youth with ASD exhibit a blunted stress response. The findings suggest that children with ASD do not perceive social evaluation in this context to be stressful. Moreover, notable variability in the stress response was observed in the sample, especially in the ASD group. Previous research in the lab has shown the influence of social perception (Corbett, Muscatello & Baldinger, 2019) as well as age and context (Corbett, Schupp, Simon, Ryan, & Mendoza, 2010) in determining the strength of the stress response to social evaluative threat.

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Perfitt, Tyler
Board 68, Session 2
PI: Colbran, Roger

Autism and ID-Linked Synaptic Proteins Modulate Signaling to the Nucleus and Activity-Dependent Gene Expression

Tyler L. Perfitt, Xiaohan Wang, Lan Hu, Roger J. Colbran

Precise regulation of neuronal gene transcription is essential for normal brain function. As one example, neuronal depolarization leads to phosphorylation of the nuclear transcription factor CREB (pCREB), a critical transcription factor in learning and memory, and the expression of immediate early genes such as c-Fos. Such activity-dependent gene expression is disrupted in many neurodevelopmental disorders, such as Autism Spectrum Disorder (ASD) and Intellectual disability (ID). These disorders often arise from mutations in membrane-associated synaptic proteins that interact with each other in large multi-protein complexes, such as CaMKII, Shank3, and L-Type Calcium Channels (LTCCs). However, the molecular basis for formation of these complexes and the roles of specific protein-protein interactions in activity-dependent gene expression are poorly understood. Therefore, we hypothesized that the loss of these signaling proteins, or mutations that disrupt their normal function or binding interactions, would disrupt signaling to increase pCREB signal upon depolarization and decrease c-Fos protein expression.

Using primary hippocampal neurons, we established a depolarization paradigm that increases levels of pCREB within 90 seconds, as measured by staining fixed neurons with antibodies that specifically detect pCREB. Moreover, returning the neurons to basal culture medium after this 90-second stimulation for 3 additional hours prior to fixation revealed robust expression of the c-Fos protein.

This depolarization paradigm significantly increases pCREB staining in the nucleus of excitatory neurons, and this increase is completely blocked by the LTCC blocker nimodipine. Knockdown of the expression of CaMKII or Shank3 using specific shRNAs reduces pCREB staining by 50% relative to control neurons, but the increases in pCREB staining can be rescued by expressing shRNA-resistant CaMKII-alpha or Shank3 proteins, respectively. However, the levels of pCREB cannot be rescued by mutant CaMKII proteins that are either kinase-dead or cannot bind to LTCCs, or by mutated Shank3 proteins that are unable to bind to either CaMKII or LTCCs. In parallel, we found that the increased c-Fos protein expression detected 3 hours after the 90 second depolarization is also completely blocked by nimodipine. Moreover, c-Fos expression is significantly reduced by knocking down the expression of endogenous Shank3 when compared to control neurons.

Our data show that each of the protein-protein interactions within this synaptic signaling complex is required for depolarization-induced phosphorylation of the CREB transcription factor in the nucleus. Moreover, the components of this complex are important for downstream expression of the c-Fos immediate early gene. Ongoing studies are probing other signaling pathways that can initiate calcium signaling to increase CREB phosphorylation, such as those initiated by Group I metabotropic glutamate receptors.

Pruett, Dillon
Board 69, Session 1
PI: Jones, Robin

Value-added predictors of changes in fluency in young children who stutter

Dillon G. Pruett, Tiffany G. Woynaroski, Tedra A. Walden, Robin M. Jones

Developmental stuttering is a speech disorder that typically begins around age 3 and is characterized by syllable repetitions and prolongations. Approximately 80% of children who stutter will recover. Identifying factors that predict stuttering recovery has the potential to inform pathogenesis and help parents and clinicians focus resources on children identified as highest risk for persistence. Multiple factors have been implicated in stuttering persistence including: age at stuttering onset, gender, family history of stuttering, speech sound production, linguistic measures, and temperament and emotion. Past research has almost exclusively focused on persistence and recovery as categorical outcomes. However, in practice, accurately categorizing individuals as persistent or recovered is difficult, especially in young children. One strength of the proposed study involves examining factors that contribute to the developmental trajectory of stuttering without relying on the categorical outcomes of persistent and recovered groups. This study investigates putative predictors accounting for variance in changes in speech fluency of children who stutter after controlling for intercorrelation among other predictors (i.e., "value added"). A diverse set of parent questionnaires, standardized speech-language assessments, and psychophysiological measures will be included as predictors of changes in frequency of stuttering. For speech fluency, our outcome measure is change in the frequency of stuttered disfluencies. The putative predictors are (1) age at stuttering onset, (2) gender, (3) family history of stuttering, (4) speech sound production, (5) expressive language, (6) receptive language, (7) emotional reactivity, (8) emotion regulation, and (9) physiological regulation.

206 children preschool-aged children participated in a longitudinal investigation of childhood stuttering conducted at Vanderbilt University. Participants and their parents visited Vanderbilt University every 7-10 months (based on availability). 138 participants completed at least one follow-up visit after an initial visit and were included in this study. Nine putative predictors were measured at Time 1. The dependent variable, percent stuttering-like disfluencies (%SLD), a measure of stuttering, was measured at each time point in the study.

Results are expected to reveal, upon centering time in study at Time 4, the model with fixed and random effects for the intercept and slope (i.e., the full simple linear model that considers individual variability in both the rate of change across time in the study and outcome at the end of the study) that was the best fit to the data for change in stuttering-like disfluencies. Or, in other words, which of the nine predictors best account for changes in fluency.

Discussion will focus on the clinical applications of value-added predictors in determining stuttering persistence.

Quinde, Jennifer
Board 70, Session 2
PI: Cascio, Carissa; Bodfish,Jim

Cognitive and Emotional Empathy in Autism: Implicit and Explicit Perpectives

Jennifer Quinde, Brynna Heflin, Lisa Mash, Carissa Cascio

Individuals with autism spectrum disorders (ASD) show varied responses in task- based self--ratings of empathy, including impaired cognitive empathy but intact emotional empathy. The role of emotional valence in self--rated empathy tasks is not well understood. Spontaneous facial mimicry (SFM) is a reflexive mirroring of emotional faces that reflects social reward, can be measured separately for positive and negative emotional valence, and may provide a bias-free index of emotional empathy. To date, no studies have used both self-ratings and SFM to assess empathy in individuals with ASD.

51 individuals (ASD = 25, typically developing (TD) = 26) performed the multifaceted empathy test (MET) consisting of 32 static images depicting people in emotionally charged conditions. Cognitive empathy was assessed by multiple choice emotion recognition, while emotional empathy was assessed by self-rating on a scale of 0--9. Separate mixed effects models were used for cognitive and emotional empathy scores to assess the influence of emotional valence of the stimuli and diagnostic group status. Participants' facial expressions were recorded while performing the task and analyzed with iMotion's FACET algorithm for emotion classification and scoring. Mean percent accuracy in emotion labeling (cognitive task), mean empathy scores (emotional empathy), median SFM across time, and correlations between facial expression emotion and empathy scores were compared between groups.

For cognitive empathy, there were significant main effects of diagnostic group ($p < .05$) and valence ($p=.001$), but no significant interaction between the two. Post--hoc comparisons revealed that the TD group was significantly more accurate than the ASD group ($p < .001$) and that accuracy was significantly lower for negative valence stimuli than for positive. There were no group differences in self-rated emotional empathy, consistent with previous findings. Facial expression analysis revealed no group differences in overall Joy or Sadness scores during cognitive or emotional empathy presses. Between group differences (TD > ASD, $p < .01$) were found in participants' Joy scores when responding to images with positive valence during both the cognitive and emotional presses. No group differences were found in participants' Sadness scores when responding to images with negative valence for either press. No correlations between SFM and empathy scores were significant.

These results replicate previous findings of impaired emotion recognition but intact self--ratings of empathy in individuals with ASD, but suggest the following new ideas: 1) emotional valence should be considered when assessing empathy, 2) spontaneous facial mimicry may be a more sensitive measure of emotional empathy and detected group differences for positive emotions, 3) Self- report and SFM may be indexing very different aspects of emotional empathy given their lack of correlation.

References:
(Dziobek et al., 2008),(Sims, Van Reekum, Johnstone, & Chakrabarti, 2012)

Raj, Sweeya
Board 71, Session 1
PI: Woynaroski, Tiffany G.

Parent-Child Engagement and Sensory Responsiveness in Infants at High-Risk for Autism Spectrum Disorder

Sweeya Raj, Jacob I. Feldman, Ashley E. Augustine, Sarah M. Bowman, Claire Daly, Kacie Dunham, Alexandra J. Golden, Pooja Santapuram, Evan Suzman, Shannon Crowley, Soo Yoon Kim, Kristen Bottema-Beutel, Neil Broderick, Ann Kirby, Bahar Keceli-Kaysili

Many children with autism spectrum disorder (ASD) demonstrate atypical patterns of responding to sensory stimuli (i.e., differences in sensory responsiveness). One such pattern is sensory seeking, which refers to behaviors that serve to intensify or extend a sensory experience (e.g., licking, smelling, sighting, or repeated touching or banging of objects). It has been proposed that differences in sensory responsiveness may emerge early in life and produce cascading effects on the development of higher-level skills in children with ASD. Recent work in our laboratories prospectively following infants at heightened familial risk for ASD based on their status as infant siblings of children diagnosed with the disorder (i.e., Sibs-ASD) has provided preliminary support for this theory of "cascading effects." Specifically, we found that early sensory seeking predicted future social deficits in Sibs-ASD. This effect appeared to be explained by reduced social orienting. We hypothesize, however, that the association between early sensory seeking and future social symptomatology may be better explained by the influence of sensory seeking on a child's tendency not just to orient towards, but rather to engage with and learn from, others in their environment. As a first step towards testing this hypothesis, the present study explores concurrent associations between sensory seeking and parent-child engagement in Sibs-ASD and infants at relatively lower, general population level risk for ASD (Sibs-TD).

Preliminary analyses were conducted on 20 infants and toddlers between the ages of 7 and 17 months (10 Sibs-ASD, 10 Sibs-TD). Groups were well matched on sex (5 males in each group) and mental age (Mage = 10.7mo for Sibs-TD and 11.6mo for Sibs-ASD). Sensory seeking was measured with the Sensory Experiences Questionnaires (SEQ). Additionally, seeking was measured using the Sensory Processing Assessment (SPA); these observational samples will be coded and available for inclusion in final analyses for the Gatlinburg Conference. Parent-child engagement scores were coded from two 15-minute parent child free-play (PCFP) videos. Each video was coded by two independent, blinded coders to derive indices of two types of engagement: total time spent in higher-order supported joint engagement (HSJE; wherein the caregiver influences child's play, and the child acknowledges the caregiver by engaging in reciprocal play) and total time spent in lower order supported joint engagement (LSJE; wherein the caregiver appears to influence child play, but the child does not actively acknowledge the caregiver by engaging in reciprocal play) across each PCFP. The total time spent in supported joint engagement (Total SJE) was also calculated as the sum of time spent in HSJE and LSJE. All metrics were averaged across coder and session to create aggregate engagement scores.

Preliminary results (based on parent reports of sensory differences only) show that sensory seeking is associated with HSJE across groups ($r = 0.33$), indicating that more sensory seeking behavior is associated with more time spent in HSJE, on average across Sibs-ASD and Sibs-TD groups. However, this correlation was moderated by group, such that more sensory seeking behaviors (to the extent they were displayed) were associated with more time spent in HSJE in the Sibs-TD group ($r = 0.57$) but not in the Sibs-ASD group ($r = 0.05$). The relation between seeking and total SJE was also moderated by group, such that more sensory seeking was associated with more time spent in SJE in the Sibs-TD group ($r = 0.58$), but greater sensory seeking was associated with less time spent in SJE in the Sibs-ASD group ($r = -0.37$). Final analyses, including results from observational measures of sensory seeking behavior, will be presented at the poster session.

Preliminary results indicate that sensory seeking may be linked with engagement, but that these associations likely vary according to risk group and may not always be in the anticipated direction. Implications for research, theory, and practice will be discussed.

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Roth, Marissa
Board 72, Session 2
PI: Humphreys, Kate

Breastfeeding Difficulties Predict Change in Mother-Infant Bonding from Birth to Age 6 Months

Marissa C. Roth, Kathryn L. Humphreys, Lucy S. King, Ian H. Gotlib, Thalia K. Robakis

A mother's emotional involvement with her infant facilitates the establishment of the infant's attachment toward the mother and forms the foundation of the child's early social-emotional development (Ainsworth, 1979; Bowlby, 1988). Given the positive impact of bonding on child development, it is important to identify predictors of initial levels of bonding, and to elucidate how the intensity of the mother-infant bond changes across the first months of life. Many mothers who intend to breastfeed but subsequently face difficulties struggle with their maternal identity and report feeling disconnected from their infant (Williamson et al., 2012). We investigated whether difficulties in breastfeeding in mothers who intended to breastfeed would be associated with both initial levels of bonding and trajectories of bonding levels across the first six months of life.

Each month for the first six months following birth, 121 mothers of newborn infants (age=23-45 years, M=32.3±4.8; 56.6% White/Caucasian, 23.0% Asian, 10.7% Hispanic, 9.0% Multiracial, 0.8% African American) completed the Mother-to-Infant Bonding Scale (MIBS) and reported whether breastfeeding was more difficult than they had anticipated (1=yes, 0=no). Mothers who attempted to breastfeed (107) reported on breastfeeding difficulty at the initial post-birth assessment, and all participants completed the MIBS at least once. We conducted linear mixed modeling to utilize the nested data structure and examined both intercept (initial levels) and slope (change in bonding) as a function of breastfeeding difficulty.

Forty-six percent of mothers reported initial difficulty breastfeeding (n = 54). Analyses yielded a main effect of postpartum month (β=.14, b=0.20, SE=0.04, t(425)=4.43, p<.001) and of breastfeeding difficulty (β=-.16, b= -0.32, SE=0.13, t(425)=-2.47, p=.014). The interaction of time and difficulty breastfeeding was marginally significant (β=.05, b=0.08, SE=0.13, t(425)=1.66, p=.098). To probe this interaction, we examined the simple effects of breastfeeding difficulty on bonding at 1 month postpartum relative to the 6 months postpartum. At 1 month postpartum, mothers who reported breastfeeding difficulty reported significantly lower bonding compared to mothers who did not report difficulty (b=-1.11, SE=.33, t(425)=-3.39, p<.001); at 6 months, however, this difference was no longer significant (b=-.34, SE=.36, t(425)=-.97, p=.33).

Mothers who reported difficulty breastfeeding in the first month also reported lower levels of initial bonding with their infants than did mothers who do not report difficulty breastfeeding. Importantly, however, bonding increased across the first 6 months of life, and differences between mothers with and without initial difficulties breastfeeding decreased over time. These results suggest that the initial effects of breastfeeding challenges lead to reduced bonding with one's infant, but that this decrease in bonding may be attenuated over time.

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Roth, Sydney
Board 73, Session 1
PI: Key, Alexandra

Brain-Based Markers of Cognition in Nonverbal Individuals with Angelman Syndrome

Sydney Roth, Dorita Jones, Alexandra Key

Angelman syndrome (AS) is a genetic disorder characterized by developmental delays, intellectual disabilities, minimal speech, hyperactivity, and motor deficits. These deficits hinder the use of standardized behavioral assessments in this population. Thus, the sensory and cognitive processes of individuals with AS have not been extensively investigated and current treatment targets mainly behavioral, physical, and communication difficulties. This study aims to better characterize the neurocognitive profile of individuals with AS using event-related potentials (ERPs) to look at auditory learning and memory in a passive listening environment.

Auditory ERP responses were acquired passively in 9 adolescents with AS, 28 developmentally typical infants, and 31 typical children matched by chronological age to the AS participants. Responses were recorded for the auditory incidental memory task for all three groups, in which nonsense words were presented and one was randomly selected to be repeated. AS individuals and typical children also completed a word recognition paradigm, in which words presumed to be known by 16 months of age were presented among nonsense words.

Adolescents with AS appear to have a recognition response to known words that occurs in the frontal region. Unlike typical children, a significant difference between the known and novel stimuli was not detected in the left temporal region. Similar to typical participants, individuals with AS displayed an auditory memory response reflected by more positive mean amplitudes in the parietal region for repeated nonwords.

These results demonstrate that some forms of auditory learning and memory are present in individuals with AS. Persons with AS demonstrate an observable memory response following repeated exposure to novel stimuli. However, they exhibit a frontal region response to known words different from the temporal response expected in typical populations, suggesting delayed or atypical maturation. The results obtained using the passive listening paradigms can help to characterize cognitive processes in AS and facilitate advancements in treatments that would effectively target the atypical neural processes.

Sachs, Lanier
Board 74, Session 2
PI: Cutting, Laurie

The Influence of Math Anxiety, Sex, and Reading Comprehension on Math Performance

Lanier P. Sachs, Sage E. Pickren, Stephanie N. Del Tufo, Laurie E. Cutting

Math anxiety is psychological and physiological anxiety that an individual experiences when encountering numerical and/or math-related situations (Suárez-Pellicioni et al., 2016). Even when controlling for trait anxiety and full-scale intelligence quotient, math anxiety predicts academic outcome. High levels of math anxiety have been negatively correlated with math performance across a wide range of ages. Math performance has been found to be associated with overall academic performance, sex differences, and availability of resources. What has yet to be fully understood is whether math anxiety differentially predicts two key components of math: numerical operations (e.g., addition/subtraction/multiplication) versus applied problem solving (i.e., math word problems) when also considering IQ, SES, sex differences, and reading comprehension. Reading comprehension is of particular interest as a predictor because it is a component of word problem solving, and reading comprehension is often reported to be higher in girls than boys.

Children (M Age = 8.45, SD=.36) who recently finished 2nd grade completed IQ, reading and math assessments, and a math anxiety questionnaire (SEMA; Wu et al., 2012) as part of a larger longitudinal study. Parents provided consent and completed the Hollingshead Socioeconomic Status (SES) measure. Two linear regression analyses were used to investigate the impact of IQ, sex, SES, reading comprehension, and the SEMA on math performance.

While both models were significant (numerical operations ($F_{5,134}=22.66$, $p<.001$, $R^2=.46$) and applied problem-solving ($F_{5,135}=13.66$, $p<.001$, $R^2=.34$)), we found that different variables predicted our two measures of math performance. Numerical operations (e.g., multiplication) was significantly predicted by SES ($b=.30$, $SE=.08$, $p<.001$), SEMA ($b=-.29$, $SE=.07$, $p<.001$), and reading comprehension ($b=.19$, $SE=.08$, $p<.05$). Applied problem-solving was significantly predicted by IQ ($b=.16$, $SE=.07$, $p<.05$), SES ($b=.23$, $SE=.06$, $p<.001$), sex ($b=-.32$, $SE=.12$, $p<.01$), and reading comprehension ($b=.42$, $SE=.07$, $p<.001$); these predictors remained significant even when calculation performance was entered as a predictor. No significant interactions with sex were found in any of the models.

After controlling for IQ and SES, math anxiety, sex, and reading comprehension performance were predictive of 2nd grade math performance; however, the predictors differed by type of math outcome. While SES and reading comprehension predicted both math outcomes, only math anxiety predicted numerical operations. Applied problem-solving items include pictures and/or words, which may alleviate higher levels of math anxiety by allowing students to tap into other supportive skills when encountering these types of problems, especially if they are strong at reading comprehension. The lack of interactions between sex and anxiety suggests that these are two separate components that contribute differentially to types of math outcomes.

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Saha, Neena
Board 75, Session 1
PI: Cutting, Laurie

An Examination of Whether Popular R-CBMs are Equated for Decodability

Neena M. Saha, Samantha Gesel, Laurie E. Cutting

Standardized Reading Curriculum Based Measures (R-CBMs) are widely used to monitor reading progress; yet, there are concerns as to how the passages are equated (e.g., Albano & Rodriguez, 2011; Miura Wayman, Wallace, Wiley, Tichá, & Espin, 2007). The current study therefore was conducted to examine whether R-CBM passages are equated on important word-level characteristics (e.g., digraphs, blends, and vowel sounds) listed in the first-grade Common Core State Standards (CCSS Initiative, Appendix A).

Four popular standardized, first-grade, R-CBM oral reading fluency passage sets were acquired: AIMSweb (version 1.0 and AIMSweb Plus), DIBELS (version 6, 8, & DIBELSNext), FastBridge, and easyCBM. Passages were scored using the Decoding System Measure (DSyM; Cutting, Saha, & Hasselbring, 2017), which was developed to measure decoding difficulty of texts (Saha, Bailey, DelTufo & Cutting, 2018). RDI graphical data analysis (box plots showing the raw data as well as descriptive and inferential statistics), were used to investigate the decodability of passages within and across the different R-CBMs.

Results indicate there was relatively large variability in decodability in passages within a publisher (with some passages more than 2 SD above and below the mean in the DIBELS 8 group). Furthermore, there was variability in the mean DSyM score across first-grade publishers: the 95% confidence intervals did not overlap, with easyCBM having the hardest mean difficulty and FastBridge having the lowest mean difficulty. There was an interesting trend in both AIMSweb and DIBELS: across time (versions), passage sets overall were progressively easier to decode (i.e., mean DSyM value decreased for each passage set), but variability across passages increased.

Additional analyses examining the exact word-level characteristics that yielded higher decodability indices are planned. Implications for passage equivalency and the use of R-CBMS for diagnostic purposes will be discussed.

Schwartzman, Jessica
Board 76, Session 2
PI: Corbett, Blythe A.

Unique perspectives: Understanding depression in early adolescents with and without Autism Spectrum Disorder through self- and parent-reports

Jessica M. Schwartzman, Blythe A. Corbett

Depressive symptoms are common in adolescence (1) and Autism Spectrum Disorder (ASD). Older adolescents with ASD endorse elevated severity as compared to typically-developing peers (2), but less is known about depression in early adolescence. Severity may vary by age in older adolescence (4), but the literature appears mixed for early adolescence (5,6). Additionally, differences in adolescent and parent perspectives have been documented (7,8). Therefore, it is essential to understand depression from both perspectives to improve conceptualization and intervention. The present study aims to examine depression in early adolescents with and without ASD, compare perspectives across adolescents and parents, and to understand patterns over age.

The total sample (N = 230) included early adolescents with ASD without intellectual disability (FSIQ>70; n = 133) and of typical development (TD; n = 97) who participated in the first year of a longitudinal study of pubertal development in ASD (PI: Corbett, MH111599). Participants were between 10:00-13:5 years old (M = 11.5, SD = 1.11). Depression was reported by early adolescents on the Children's Depression Inventory, 2nd edition (CDI-2) and by parents on domains of the Child Behavior Checklist (CBCL). Independent samples t-tests were employed to examine CDI scores between early adolescents with and without ASD, CBCL scores between parents, and differences in adolescent and parent perspectives. One-way ANOVAs were employed to examine differences in CDI and CBCL scores across ages.

Significant group differences emerged between early adolescents with and without ASD on the CDI for Total depression ($p<.01$), Emotional Problems ($p<.01$), and Functional Problems ($p<.01$) as those with ASD endorsed higher severity. Similarly, group differences emerged between parents on the CBCL in Internalizing Problems ($p<.01$), Depressed/Withdrawn subscale ($p<.01$), and Affective Problems ($p<.01$) as parents in the ASD group reported higher severity. Further analysis of perspectives across early adolescents and parents revealed significant differences within the ASD group only. Analyses of age revealed no group differences in CDI or CBCL scores in the total sample. However, closer examination of the ASD cohort revealed significant differences in CDI Emotional Problems across ages ($p<.05$) with elevations around 11 years old and gradual declines over age.

In this study, early adolescents with ASD endorsed greater severity of depression than their typically-developing peers, which was both statistically significant and clinically meaningful. This was supported by elevated ratings among parents in the ASD group on a similar index of depression. However, discrepancies in severity ratings between early adolescents and their parents highlights the need for multiple perspectives. Furthermore, the influence of age on depression among those with ASD may be an important factor in conceptualizing and treating depression in this group.

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Shavlik, Margaret
Board 77, Session 1
PI: Booth, Amy

Evaluating a Summer Reading Intervention Program in Central Texas

Margaret Shavlik, Amy Booth

More than 80% of children from lower SES families lose reading skills over the summer, in part because they lack access to resources with which to practice these skills (Read For Success, 2015). Research links the amount of reading materials at home to higher reading proficiency scores for children (Barton & Coley, 2007).

401 second-grade students (196 in the intervention group) were included in our analyses. Their teachers received training, books, and materials to scaffold advanced STEAM reading and vocabulary content in class during the months leading up to the summer break. At the end of Spring semester, students chose 10 books to keep. Students completed a "baseline" reading assessment (pre-intervention) in the Spring of 2nd grade, and an "outcome" reading assessment (post-intervention) in the Fall of 3rd grade. From these assessments, we also computed a "change score."

[1] Baseline reading scores in the intervention group were not significantly different from those of the comparison group ($t(399) = 1.02$, $p = .31$), while outcome reading scores for children in the intervention group were larger than those for the comparison group ($t(373) = 2.01$, $p = .046$, $d = .20$). [2] An independent-samples t-test (with unequal variance) confirmed that, on average, children in the intervention group had larger change scores than did those in the comparison group, $t(373) = 1.65$, $p = .05$ (1-tailed), $d = .17$. [3] After controlling for baseline reading levels, there was a significant effect of group (intervention versus comparison) on outcome reading score, $F(1, 398) = 6.25$, $p = .013$. [4] A chi-square test of independence confirmed that at the full-sample level, there was a relationship between group (intervention versus comparison) and reading trajectory, $X2$ ($N=401$) $= 13.62$, $p = .001$, $w = .18$. This trend was replicated for students scoring below average on their baseline reading assessments, and for students scoring more than one standard deviation below average on baseline reading assessments.

While the intervention was effective at the group level, its impact was most pronounced for students who were already falling behind their peers. At an average cost of only $50 per student, interventions such as these may be a more cost-effective and practical way of supporting at-risk children across the summer months than expensive camps with extensive staff, time, and transportation requirements

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Siemann, Justin
Board 78, Session 2
PI: McMahon, Douglas

Investigating the effects of photoperiod during sensitive periods in prenatal and postnatal development for the serotonin system

Justin K. Siemann, Douglas G. McMahon

Early life experiences during sensitive developmental periods have been linked to increased risk for neuropsychiatric disorders later in life. The serotonin system is implicated in mood disorders and is impacted by the duration of daylight or photoperiod. Human epidemiological work has now demonstrated that high magnitude photoperiodic changes during the second trimester of gestation result in a decreased risk for depression in the adult offspring. Recently, we found that, in mice, Long photoperiods program dorsal raphe (DRN) serotonin (5-HT) neuronal firing rate prenatally, resembling the firing rate of animals maintained under Long photoperiods throughout development. We also observed that Long summer-like photoperiod exposure during postnatal development results in elevated monoamine content along with reduced mood-related behavior compared to mice exposed to Short winter-like photoperiods. We are systematically investigating when during prenatal development Long photoperiods impact DRN 5-HT neuronal firing rate and the sensitive postnatal periods responsible for changes to midbrain monoamine signaling and mood-related behaviors.

For our prenatal experiments, we switched mice from Long to Short photoperiods at E14.5 as this is after 5-HT neuronal gestation, when 5-HT switches from a maternal to a fetal source, and represents the approximate equivalent of second trimester brain development in humans. Utilizing mult-electrode array recordings, we evaluated DRN 5-HT neuronal firing rate at P50, representing early adulthood in the mouse. For our postnatal experiments, we measured midbrain monoamine content in mice developed continuously under either Long or Short photoperiods at P8, P18, and P35, representing the approximate equivalent of third trimester, early childhood and early adolescent brain development in humans.

We found that mice exposed only to Long photoperiods before E14.5 demonstrated 5-HT neuronal firing rates (1.13 ± 0.12 Hz) similar to animals exposed to Long photoperiods during the entirety of prenatal development (1.18 ± 0.08 Hz) and mice maintained under Long photoperiods throughout prenatal and postnatal development (1.24 ± 0.10 Hz). For our postnatal experiments, we observed elevated levels of 5-HT ($p = 0.0001$), 5-HIAA ($p = 0.0001$), DA ($p = 0.0060$) and DOPAC ($p = 0.0120$) content for Long compared to Short photoperiod mice arising at P18 and P35.

We are continuing to systematically pinpoint the sensitive periods during prenatal and postnatal development impacted by photoperiod with the goal that this may lead to novel insights into the etiology and treatment options for mood disorders.

Smith, Nicholas
Board 79, Session 1
PI: Grueter, Brad

Hunger, via the arcuate nucleus neuropeptide BigLEN, suppresses excitatory transmission in a nucleus accumbens circuit that opposes feeding behavior

Nicholas K. Smith, Jared Plotkin, Brad A. Grueter

In order to ensure survival, animals must enact dynamic behavioral patterns dependent on their most pertinent needs. When energy stores are low, hunger alters animal behavior through a number of central circuit nodes that control feeding behavior. The arcuate nucleus of the hypothalamus acts as a key energy status sensor, compiling energy state information via a variety of sources. Arcuate nucleus neurons expressing Agouti-related peptide (AGRP) project across the brain and have been found to influence a growing number of behaviors via their canonical modulatory transmitters, AGRP and neuropeptide Y. However, despite the wide reach of these neurons, there is little work examining energy state dependent changes in basal forebrain structures.

Here, we find that BigLEN, a recently identified arcuate nucleus AGRP neuron neuropeptide, is able to act within the nucleus accumbens to suppress excitatory transmission.

Utilizing pharmacological tools, we link this action to the previously identified BigLEN receptor, GPR171. Antagonizing GPR171 in fasted animals results in a significant decrease in appetitive behaviors, including learned operant behaviors.

These results support a role for a relatively novel arcuate nucleus peptide in the higher order decisions an animal makes to seek food. Additionally, they point to a key modulatory role of energy state within the forebrain in the control of motivated behaviors.

Smith, Sydnie
Board 80, Session 2
PI: Hodapp, Robert

The Experiences, Level of Competence, and Comfort Level of Healthcare Professionals with Providing Treatment for Individuals with Disabilities

Sydnie E. Smith, Richard C. Urbano, Elisabeth M. Dykens, Robert M. Hodapp

Although most health professional do not have training in treating people with disabilities, small numbers do work with this population. We do not, however, yet know which disability conditions health professionals most often work with, nor which they feel most comfortable and competent to treat. By identifying specific levels of contact, competence, and comfort with persons of different disabilities, we can work to increase the numbers and expertise of disability-focused health professionals.

Respondents included 110 health professionals from nine different disciplines who, as some part of their professional practice, treat individuals with disabilities. Professions included Clinical Psychology, Dentistry, Family Medicine, Nursing, Nurse Practitioner, Pediatrics, Physician's Assistant, Psychiatry, and Social work, with all responses collected through an anonymous, web-based survey. We recruited from disability-health sub-disciplines, special interest groups, and organizations that represent disability-focused professionals. Respondents answered general questions regarding profession and training, pre- and post-school professional training, professional experiences, barriers and benefits to working with this population, and factors related to the decision to work with this population. Respondents were asked about the degree to which they have treated, were competent to treat, and felt comfortable in treating the following 10 disability conditions: Autism Spectrum Disorder, Deaf-Blindness, Deafness, Down syndrome, Other Genetic Syndromes, Intellectual Disability, Psychological Disorder/ Psychiatric Disorder, Speech and Language Disorder, Visual Impairment. Five-point scales ranged from never-to-often for experience and, for competence and comfort, from "not competent/not comfortable at all" to "extremely competent/ comfortable."

Respondents reported the highest amount of experience with individuals with Autism Spectrum Disorder ($M = 4.70$), the lowest with those with Deaf-Blindness and Deafness (2.58 & 2.89), $F(9, 94) = 35.69$, $p<.0001$. Competence with providing treatment was highest for individuals with Autism Spectrum Disorder and Intellectual Disabilities (4.14 & 4.13), lowest for Deaf-Blindness, Deafness, and Visual Impairment (2.46, 2.62, & 2.87), $F(9, 90) = 26.97$, $p<.0001$. Respondents also reported most comfort when treating individuals with Intellectual Disabilities (4.28), ASD (4.26), and Down syndrome (4.05); least comfort was reported for treating individuals with Deaf-Blindness and Deafness (2.73 & 2.83), $F(9, 93) = 20.50$, $p<.0001$.

We need to increase the number of health professionals who are experienced, comfortable, and competent to treat individuals with disabilities. It is also important to examine differences between health and mental health professionals and to determine the extent and type of training these professionals have-and need-to treat individuals with disabilities in a health capacity.

Spencer, Mercedes
Board 81, Session 1
PI: Cutting, Laurie

Investigating relations between executive function and reading comprehension performance: evidence from mediation models

Mercedes Spencer, Laurie E. Cutting

Reading comprehension (RC) is foundational to both academic and life outcomes (Fletcher, 2005; Hernandez, 2011). Yet, 32% of fourth graders continue to attain RC scores that are below the basic level (National Center for Education Statistics, 2017). Evidence suggests that decoding, or the ability to translate written into its spoken form (Ehri, 1991), and oral language are foundational for the RC process (Simple View; Hoover & Gough, 1990). However, more recent evidence points to additional mechanisms that may be responsible for individual differences in RC, such as executive function (EF; e.g., Cutting et al., 2009; Nouwens et al., 2016). Increasingly, studies have shown that EF contributes unique variance to RC over and above other well-established predictors (Sesma et al., 2009). EF deficits are also associated with RC weaknesses (Locascio et al., 2010). Further, given the evidence of sex differences in RC and word reading (Krafnick & Evans, 2018; Loveless, 2015), it is important to also examine whether these relations may differ across boys and girls.

The sample included 298 (girls N = 166; boys N = 132) English-speaking children (6.42 to 8.33 years). Measures included BRIEF Shift, Inhibit, and Working Memory and WJ Passage Comprehension and Word Attack. Univariate outliers were replaced with values at the high or low end of the range, respectively, and missing data was handled using maximum likelihood estimation. We tested hypothesized relations between EF, decoding, and RC using path analytic and latent variable mediation models; we used bootstrapping with 5,000 draws to obtain 95% confidence intervals.

For the full sample, EF was a direct and indirect predictor of RC. When boys and girls were modeled separately, however, this trend held only for the girls; for boys, the association between EF and RC was fully mediated by decoding.

When modeled separately, individual components of EF were differentially related to RC; however, models that included EF as a unitary construct also provided good fit to the data. In line with previous studies (e.g., Sesma et al., 2009), EF predicted unique variance in RC over and above decoding. Interestingly, EF was differentially associated with RC when boys and girls were modeled separately. In addition to further elucidating the specific nature of the relations between EF and RC, the findings suggest that sex may be an important consideration when targeting RC difficulties and that the assessment of EF may be a valuable addition to screening batteries aimed at identifying children who may be at risk for RC weaknesses.

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Su, Pumpki L.
Board 82, Session 2
PI: Bodfish, Jim

Measuring perception and processing of prosody in children: a feasibility study

Pumpki L. Su, Stephen Camarata, Duane Watson, Jim Bodfish

Spoken language conveys a wide range of information other than words or sentences, such as intonation, rhythm, stress. These features are collectively referred to as "prosody" and are an indispensable part of spoken language because it fulfills grammatical, semantic, and pragmatic functions. Atypical prosody has been frequently identified in individuals with ASD. These deficits tend to persist and affect long-term social communicative competence. Unfortunately, most research on prosody has primarily focused on expressive abilities. Receptive prosody remains poorly understood and no objective measure is available to assess receptive prosody in this population. This project aims to develop and test the feasibility of an objective measure of receptive prosody, specifically contrastive pitch accent (CPA), in typically developing (TD) children as a first step in accurately identifying prosodic deficits and evaluating how they relate to social-communication deficits in ASD more broadly.

We adapted the Visual World eye-tracking paradigm to assess participants' online processing of contrastive pitch accent. Twenty-two TD children between 8 and 14 watched a 15-minute video with 72 trials. On each trial, they were instructed to look for specific items on an image while listening to sentences with manipulated prosody so that the contrastive pitch accent was context-appropriate on half of the trials and context-inappropriate in the other half. Previous studies have shown that context-appropriate use of contrastive pitch accent accelerates participants' visual search (i.e. "facilitative effect") whereas context-inappropriate use of contrastive pitch accents delays one's search (i.e. "garden-path effect"). Participants' fixations to target area of interest were analyzed in generalized linear mixed effect models (GLMM) to assess their sensitivity to contrastive pitch accent cues.

TD children demonstrated knowledge of contrastive pitch accent by showing a robust garden-path effect in the context-inappropriate condition (i.e. slower and less looks to the target item). Statistical analyses showed that the odds of correct looks to the target were 2.13 times (95% CI: [1.31, 3.50]) less in the condition where the target word was preceded with an inappropriate contrastive pitch accent compared to a neutral condition with no contrastive pitch accent. However, we did not find a facilitative effect when context-appropriate contrastive pitch accent was used.

This study demonstrated the Visual World Paradigm is a feasible way of examining the processing of contrastive pitch accent. Given that we were able to systematically replicate only the garden path effect but not the facilitative effect, our results support limiting the use of this approach to analyses of the garden patch effect as a means of providing an objective and dimensional measure of prosody perception in children with ASD in future studies.

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Suárez Pellicioni, Macarena
Board 83, Session 1
PI: Booth, James

Fluency in symbolic arithmetic refines the approximate number system in parietal cortex

Macarena Suárez Pellicioni, James R. Booth

The objective of this study was to investigate, using a brain measure of approximate number system (ANS) acuity, whether the precision of the ANS is crucial for the development of symbolic numerical abilities (i.e., scaffolding hypothesis) and/or whether the experience with symbolic number processing refines the ANS (i.e., refinement hypothesis).

To this aim, 38 children solved a dot comparison task inside the scanner when they were approximately 10-years old (Time 1) and once again approximately 2 years later (Time 2). To study the scaffolding hypothesis, a regression analysis was carried out by entering ANS acuity at T1 as the predictor and symbolic math performance at T2 as the dependent measure. Symbolic math performance, visuospatial WM and full IQ (all at T1) were entered as covariates of no interest. In order to study the refinement hypothesis, the regression analysis included symbolic math performance at T1 as the predictor and ANS acuity at T2 as the dependent measure, while ANS acuity, visuospatial WM and full IQ (all at T1) were entered as covariates of no interest.

Our results supported the refinement hypothesis, by finding that the higher the initial level of symbolic math performance, the greater the intraparietal sulcus activation was at T2 (i.e., more precise representation of quantity).

To the best of our knowledge, our finding constitutes the first evidence showing that expertise in the manipulation of symbols, which is a cultural invention, has the power to refine the neural representation of quantity in the evolutionarily ancient, approximate system of quantity representation.

Suzman, Evan
Board 84, Session 2
PI: Woynaroski, Tiffany

Differences in Sensory Responsiveness Predict Poor Play Skills in Infants at High Risk for Autism

Evan Suzman, Jacob I. Feldman, Cara Damiano-Goodwin, Lisa Ibanez, Wendy L. Stone, Carissa J. Cascio, Tiffany G. Woynaroski

Children with autism spectrum disorder (ASD) often show differences in sensory responsiveness, or behavioral patterns of responding to sensory stimuli. These patterns can include hyporesponsiveness (i.e., reduced or absent responses to sensory stimuli), hyperresponsiveness (i.e., exaggerated responses to sensory stimuli), and sensory seeking (i.e., craving of certain sensory stimuli). It has been theorized that such differences in sensory responsiveness, especially early in life, may produce cascading effects on a child's development in a number of domains, by affecting his/her ability to engage with or learn from his/her environment. This theory is challenging to test, in large part because we cannot always reliably diagnose autism in the earliest stages of life (i.e., in infancy). As a potential solution to this problem, many researchers are prospectively following infants who are known to be at heightened risk for ASD based on their status as infant siblings of children with ASD (Sibs-ASD). In the present study, we use this approach to test whether early differences in sensory responsiveness may be producing cascading effects on play, an aspect of development that is critical for early engagement and learning and that is often impacted in children affected by ASD. We hypothesize that atypical sensory responsiveness (i.e., increased hyporesponsiveness, hyperresponsiveness, and/or sensory seeking) in infancy will predict future deficits in play skills in Sibs-ASD.

This study draws on data that was collected as part of a longitudinal correlational study that was carried out at Vanderbilt University and University of Washington. Participants were 20 infant Sibs-ASD (8 male; 12 female). Early sensory responsiveness was assessed with the Sensory Experiences Questionnaire (SEQ) when infants were 18 months old. Future play skills were assessed using the Vineland Adaptive Behavior Scales (VABS) when participants were 24 months and 36 months old. Bivariate correlational analyses were run to evaluate the direction and magnitude of associations of interest. SEQ hyporesponsiveness scores were log10 transformed to correct for a positive skew.

SEQ total scores at 18 months were negatively correlated with play skills at 24 months ($r = -0.49$), indicating that increased sensory features on the whole predicted poorer play skills in Sibs-ASD. Follow-up analyses indicated that all three patterns of sensory responsiveness were predictive of play at this timepoint (r values = -0.71, -0.57, and -0.43 for hyperresponsiveness, hyporesponsiveness, and sensory seeking, respectively). SEQ total scores at 18 months were not predictive of play at 36 months ($r = -0.21$). Only hyporesponsiveness at 18 months continued to significantly predict play skills at 36 months ($r = -0.47$; r values for hyperresponsiveness and sensory seeking = -0.36 and -0.04, respectively).

Results of this pilot study provide increased empirical support for the theory that early sensory differences may produce cascading effects on the development of skills such as play in children diagnosed with, or at heightened risk for, ASD. Atypical sensory responsiveness midway through the second year of life predicted more impoverished play six months later. These predictive links were present for all three patterns of sensory responsiveness, with moderate to large effect sizes. Associations were attenuated over a longer timeframe but remained statistically significant for hyporesponsiveness, suggesting that this pattern of sensory responsiveness may have the most lasting influence on play development. Findings are limited by the correlational nature of the design and by reliance on parent report to measure constructs of interest. Additional research, ideally incorporating observational measures of sensory responsiveness and play, is needed to determine whether the relations we have observed are causal in nature, and to evaluate whether any relation between sensory responsiveness and play may translate to effects on other "higher level" ASD and related symptoms. Future research may further explore the mechanisms by which early sensory differences are impacting play development.

We suspect that the associations we have observed may be explained by the effects of early sensory differences on parent-child engagement; we are presently working to test this theory in our laboratory. Implications for research, theory, and practice will be discussed.

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Taylor, Anne
Board 85, Session 1
PI: Grueter, Brad

Optogenetic stimulation of nucleus accumbens circuits elicits behavioral and synaptic plasticity

A. Taylor, K. Manz, J. Becker, B. Grueter

The nucleus accumbens (NAc) is important for integrating sensory information and coordinating motor output. The main neuronal cell type in the NAc are GABAergic medium spiny neurons (MSNs). Stimulation of either dopamine 1 (D1) receptor expressing or dopamine 2 (D2) receptor expressing MSNs result in activation of distinct pathways that differentially modulate behavior. Interneurons make up a minority of neurons in this region however they play a critical role in regulating principle cell firing. NAc MSNs receive excitatory glutamatergic inputs from many sources including the prefrontal cortex (PFC). Inhibition is mainly mediated by interneurons. Some of these cells are fast-spiking, parvalbumin expressing interneurons (PV-INs) which regulate MSN firing via a feedforward mechanism. In order to understand how NAc circuit function changes under pathological conditions such as drug addiction, it is critical to understand the nature of excitatory and inhibitory control exerted onto MSNs.

. In this study, we utilized optogenetics to investigate PFC to MSN and PV-IN to MSN synaptic plasticity as well as behavioral responding to PV-IN stimulation. We found that 1Hz and 30Hz stimulation of PFC terminals in the NAc induced long term depression (LTD) of optically evoked excitatory post synaptic currents.

1Hz and 30Hz stimulation of PV-INs caused LTD of optically evoked inhibitory post synaptic currents. In vivo, 1Hz stimulation of PV-INs caused place avoidance, whereas 30Hz stimulation induced place preference.

Investigation of the mechanisms underlying this plasticity will contribute to our understanding of how glutamatergic inputs and PV-INs shape NAc circuit function in both health and disease.

Teller, Laurel
Board 86, Session 2
PI: Schuele, C. Melanie

Strategies for Changing Preschool Teacher Complex Syntax Input

Laurel Teller, C. Melanie Schuele

Complex syntax (i.e., dependent clauses) is a preschool language skill that is critical to the development of academic language (e.g., Henrichs, 2010). Preschool teachers serve as a source of complex syntax input, but recommendations for increasing complex syntax input in ways that can be easily incorporated into the preschool classroom are lacking. Increased frequency of targeted grammatical structures in the input has previously led to improved child language outcomes (e.g., Fey, Cleave, Long, & Hughes, 1993). Thus, the purpose of our study is to investigate whether a simple training leads to increases in one category of complex syntax-complement clauses (i.e., full propositional complements, I wonder if we can put the monkey up in the tree, and WH complements, I wonder who is up in the tree).

Using a single case research design study we investigated the malleability of preschool teachers' production of complement clauses. We assessed whether there was a functional relation between a multimedia teacher training and teachers' production of four target complement clause verbs (CCV) with complement clauses in play interactions. We measured the impact of the teacher training using a multiple baseline across participants' design. The teacher training included (a) seven brief voice-over slide presentations that included videos of adult-children play interactions (b) worksheets integrated with the slide presentations and (c) written feedback after probe sessions. Target CCVs with complement clauses were tallied within 10-min probe sessions (teacher-children play interactions) across baseline, intervention, and maintenance phases. Teachers provided feedback about the utility of the training.

Visual analysis supported the conclusion of a functional relation between the teacher training and teacher production of target CCVs with complement clauses. The sustainability of these changes requires further investigation. Teachers saw value in producing CCVs in discussions related to preschool curricular standards (e.g., The Tennessee Early Learning Developmental Standards, 2018). Additionally, teachers observed the applicability of producing CCVs across classroom activities.

This study demonstrates the malleability of complement clauses in preschool teacher input, which informs the development of complex syntax interventions that can be easily implemented in practice-based settings. This study further supports the development of focused, multimedia trainings for language input strategies.

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Thomas, Jessica
Board 87, Session 1
PI: Colbran, Roger J

Similarities and distinctions in behavioral phenotypes of three CAMK2A mutant mouse lines.

Jessica R. Thomas, Keeley Spiess, Roger J. Colbran

It is well established that Ca2+/calmodulin dependent protein kinase II alpha (CaMKII alpha) is important for synaptic plasticity, learning and memory. Mutations in the CAMK2A gene, which encodes CaMKII alpha, have been linked to Autism Spectrum Disorder (ASD) and intellectual disability. Previous characterization of mice harboring an ASD-associated Glu183 to Val knock-in mutation in CaMKII alpha (E183V-KI), which reduces CaMKII alpha expression and activity, revealed an impairment in social motivation and repetitive behaviors, as well as hyperactivity.

To better understand behavioral roles of CaMKII alpha, we compared the phenotypes of mice with various CaMKII alpha genotypes (homozygous): E183V-KI; CaMKII alpha -null (KO); Thr286 to Ala knock-in (T286A-KI) mutation (prevents Thr286 autophosphorylation).

Compared to wild-type (WT) mice, all three genotypes displayed similar hyperactivity in a novel open field arena and spent less time in the center of the arena. Although open field behavior is consistent with increased anxiety, testing on an elevated plus or zero maze revealed that all three genotypes spent more time in the open domains compared to the closed relative to their WT controls, indicating decreased anxiety. Moreover, testing in a light-dark box revealed that none of the mouse lines displayed an anxiety phenotype. We interpret these data to indicate that these CaMKII alpha mutations do not affect anxiety per se, and that phenotypes in the open field arena and elevated mazes are driven by a heightened "escape" behavior, consistent with robust increases in jumping and rearing along the walls of the open field arena, as well as the overall hyperactivity. Despite these strong phenotypic similarities, testing in a 3-chamber arena revealed no deficits in social exploration in CaMKII alpha -KO mice, in contrast to E183V-KI mice (analyses of T286A-KI mice are ongoing). We also explored the impact of these CaMKII alpha mutations on tactile sensitivity. All three CaMKII alpha mutant mouse lines displayed increased threshold to respond in the Von-Frey filament test, compared to WT mice. Moreover, WT mice preferentially explored a textured object relative to a visually very similar but smooth object, whereas all three CaMKII alpha mutant mice failed to differentiate between these objects.

Together these data suggest that tactile sensation is impaired in these CaMKII alpha mutant mouse lines. In summary, our data demonstrate that CaMKII alpha has an important role in behavioral phenotypes associated with ASD.

Thompson, Emily
Board 88, Session 2
PI: Tharpe, Anne Marie

Evaluation of Unilateral Hearing Screening Failures

Emily Thompson, Alison Kemph, Adrienne Roman, Hayden Engstrom, Alyssa Fosnight, Anne Marie Tharpe

The Joint Committee on Infant Hearing (2007) recommends that newborn hearing screening (NHS) include the identification of unilateral as well as bilateral hearing loss. However, there is anecdotal evidence to suggest that it is not unusual for more concern to be placed on bilateral hearing screening failures than unilateral failures1-2. Given our current understanding of the psychoeducational risks associated with unilateral hearing loss in children, it was of interest to investigate unilateral failures to determine the likelihood of permanent hearing loss in one or both ears within one year of the initial screening.

Babies were screened utilizing the ALGO automated auditory brainstem response (A-ABR) system and were conducted by graduate students or technicians trained in the use of the equipment by Vanderbilt University Medical Center's (VUMC) newborn hearing screening coordinator, a licensed and certified audiologist. VUMC has a level IV neonatal intensive care unit (NICU) and admits approximately 1,300 newborns annually and the well-baby nursery admits approximately 4,500 newborns annually. Hearing screening and diagnostic data were retrieved retrospectively from a REDCap data repository from 2015 to 2018, encompassing approximately 8,000 screenings.

This project provides preliminary evidence that a small percentage of infants who fail their NHS in one ear are ultimately diagnosed with bilateral permanent hearing loss (~2%). Of note, diagnostic testing revealed a higher number of infants with bilateral sensorineural hearing loss (n=7) than permanent conductive hearing loss (n=3; due to etiologies such as atresia or other anatomical abnormalities).

However, as this project examined NHS results and diagnostic evaluation outcomes from the Well-Baby Nursery only, future investigation should include infants from the Neonatal Intensive Care Unit to determine if rates of conversion from unilateral failed screens to bilateral hearing loss are comparable in both cohorts.

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Torregrossa, Lénie
Board 89, Session 1
PI: Park, Sohee

Emotional Embodiment Experts: Enhanced Precision of Bodily Maps of Emotions in Athletes

Lénie J. Torregrossa, Eun Sol Chon, Matthew A. Snodgress, Lauri Nummenmaa, Sohee Park

The continuous integration of interoceptive and proprioceptive signals yields a stable representation of the body. Moreover, awareness of bodily sensations leads to the conscious experience of our affective states and helps us understand the emotional experiences of others. Therefore, increased bodily self-awareness can affect emotional experiences and improve social functioning. In addition to their exceptional bodily abilities, athletes learn strategies designed to enhance the mind-body connection. We hypothesized that trained proprioceptive and interoceptive experts (i.e., athletes) would have increased awareness of the bodily sensations of their emotions.

College athletes (ATH) and demographically-matched controls (CO) used a computerized visuospatial mapping tool (EmBODY) to report bodily activation and deactivation experienced in the context of 14 different emotions. Bodily sensation maps were generated and quantitatively compared between the two groups.

The topographical maps of emotions of ATH revealed more clearly defined regions of bodily sensations of emotions compared to those of CO. Quantitative analyses revealed that although ATH colored a similar number of pixels in the EmBODY task, they showed less dispersed bodily sensation of emotions.

ATH reported feeling emotions in more narrowly defined regions of the body. The enhanced precision of ATH's embodied emotions bears important clinical implications. Indeed, formal interoceptive and proprioceptive training might benefit individuals reporting anomalous embodied emotions. Additionally, the highly defined topographical maps generated by ATH could be used as a treatment tool for individuals experiencing difficulty recognizing their emotions.

Travers, Hilary
Board 90, Session 2
PI: Carter, Erik

What About the Peers? A Systematic Review of Peer-Mediated Interventions

Hilary E. Travers

Since the 1980s a number of peer-mediated interventions (PMIs) between peers with and without disabilities (e.g., Carter et al., 2016; Copeland et al., 2004) have been implemented to support students with developmental disabilities. Specifically, PMIs were developed with the intention of increasing academic success for students with disabilities in the general education classroom and/or increasing social interaction among students with and without disabilities. Yet despite the abundance of research documenting the benefits of these interventions and programs for students with disabilities (Carter et al., 2010), little work has been done to measure and understand the impact of these experience on the non-disabled peers.

An exhaustive review of the literature was conducted and 89 research studies were coded and analyzed with respect to the following methodological and outcome variables: participant characteristics (for both the students with and without disabilities), intervention setting, geographic location, study design, intervention components, peer training, and peer impact. Measurement of peer impact was limited to 62 studies, moreover, type of peer impact fell into 10 main categories: (1) social benefits (2) academic benefits, (3) skill development, (4) knowledge development (5) change in future intentions (6) change in views/perspectives about disability (7) change in self-perception (8) development of personal qualities/traits (9) general benefits, and (10) recommendation for other students to participate in PMIs with students with disabilities.

The findings of our synthesis indicate that middle and high school aged peers who participate in formal and sustained experiences alongside students with developmental disabilities are impacted in several significant ways that warrant the continued use of these interventions and programs.

As the use of PMI and other more broadly defined peer programs become more wide-spread, researchers and educators could better measure the impact on peers, in addition to the impact on student(s) with developmental disabilities, to enhance the utility of these planned experiences. We provide suggestions for ways to improve measurement.

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Walsh, Meagan
Board 91, Session 1
PI: Douglas Fuchs

Improving the Nonfiction Comprehension of Struggling Third Grade Readers

Meagan E. Walsh, Douglas Fuchs, Samuel A. Patton, III, Lynn S. Fuchs, Pamela Lehman

For 5 years, we have been working on developing a comprehensive intervention to improve the nonfiction comprehension of intermediate students (grades 3-5). The results for 4th and 5th grade students have been encouraging, but 3rd grade has proven more challenging. The purpose of this paper is to present the methods and results of the latest iteration of our intervention specifically targeting 3rd grade students and to discuss the potential implications.

78 students at risk for comprehension deficits were selected for this study from 14 schools in the Metro Nashville Public School district. Selected students were randomly assigned to treatment or BAU control. Students assigned to the treatment condition were then assigned to pairs. Tutored pairs received 42, 45-minute sessions of instruction with trained graduate students. Tutors used explicit instruction principals to teach students comprehension strategies. Students practiced these strategies on a variety of nonfiction texts. Instructional procedures were embedded in the program to promote transfer, improve engagement, and support positive behavior.

At pre- and post-, students were assessed on measures designed to assess various degrees of instructional transfer. Data for each outcome measure were analyzed using cross-classified hierarchical linear models. Hedge's g effect sizes were calculated using regression coefficients. Students in the treatment group significantly outperformed controls on measures of knowledge and strategy acquisition (g=2.58 and g=1.01). Results on a researcher created near-transfer measure (g=.37) and the expository passages from the Gates MacGinite form T (g=.46) approached significance. Unfortunately, treatment students did not outperform controls on a standardized far transfer measure of reading comprehension (Gates MacGinite, (full) Form S; g=-.09).

Results suggest that our instructional program has the ability to improve 3rd graders content knowledge, strategy mastery, and nonfiction text comprehension, but not overall comprehension ability. This highlights the need for a stronger emphasis on transfer instruction and continued program development.

Wang, Jin
Board 92, Session 2
PI: James R. Booth

Neural representations of phonology in temporal cortex scaffold longitudinal reading gains in 5- to 7- year-old children

Jin Wang, James R. Booth

It is essential in educational field to understand whether phonological processes are crucial for the development of reading skill (i.e. scaffolding hypothesis) and/or whether learning to read words fine-tunes phonology (i.e. refinement hypothesis). Unlike behavioral measurement, which is hard to dissociate multiple cognitive processes involved in a phonological awareness task, neuroimaging studies could provide a complementary measurement to probe the nature of different phonological processes by investigating different brain regions. The posterior superior temporal gyrus, STG, has been implicated in phonological representations, whereas the dorsal inferior frontal gyrus, IFG, has been implicated in access to those representations. Therefore, in this current study, We aimed at examine the scaffolding and refinement hypothesis using a brain measure of phonological processes, and specifically looked at how different grain sizes in these two brain regions implicated in phonological processing played a role in this bidirectional relation.

36 children completed a reading test outside the scanner and an auditory phonological task which included both small (i.e. onset) and large (i.e. rhyme) grain size conditions inside the scanner when they were 5.5-6.5 years old (Time 1) and once again approximately 1.5 years later (Time 2). To study the scaffolding hypothesis, a regression analysis was carried out by entering brain activation in either STG or IFG for either small (onset>perceptual) or large (rhyme>perceptual) grain size phonological processing at T1 as the predictors and reading skill at T2 as the dependent measure, with several covariates of no interest included. To study the refinement hypothesis, the regression analysis included reading skill at T1 as the predictor and brain activation in either STG or IFG for either small or large grain size phonological processing at T2 as the dependent measures, with several covariates of no interest included.

We found that only posterior STG, regardless of grain size, was predictive of reading gains. Parallel models with only behavioral accuracy were not significant. No refinement effects were found.

Taken together, our results suggest that the representational quality of phonology in temporal cortex is crucial for reading development. Moreover, our study provides neural evidence supporting the scaffolding hypothesis, suggesting that brain measures of phonology could be helpful in early identification of reading difficulties.

Whitten, Allison
Board 93, Session 1
PI: Morgan, Victoria L.

Relating Resting-State Functional Connectivity of the Hippocampus and Language Cortex to Language Abilities in Temporal Lobe Epilepsy

Allison Whitten, Monica L. Jacobs, Dario J. Englot, Victoria L. Morgan

The role of the hippocampus in memory function has been well-established, but recent studies have also highlighted the direct contributions of the hippocampus to language processing in healthy adults [1-2]. These novel findings suggest that the hippocampus and its connections to language regions may be related to language abilities in patients with hippocampal damage or impairment, like patients with temporal lobe epilepsy (TLE). The purpose of the present work was to investigate the relationship between functional connectivity of the bilateral hippocampi and cortical language areas to scores on neuropsychological language measures in patients with temporal lobe epilepsy.

Presurgical resting-state 3T fMRI data was acquired from 26 patients with right TLE (M: 39.8 years, SD: 10.8), 10 patients with left TLE (M: 36.2 years, SD: 15.7), and 42 healthy controls (M: 39.02 years, SD: 13.7). Functional connectivity (FC) was measured as the average connectivity between the hippocampus (right or left) to frontal and temporal language regions in the right and left hemispheres. The average connectivity values were then correlated to patient scores on measures related to language function, including a measure of Verbal IQ, a word generation task, and the Boston Naming Test.

There were no significant differences between groups in FC values between the hippocampus and language regions across both hemispheres. However, within the two patient groups, both right and left TLE patients showed significantly greater FC between the hippocampus and language regions ipsilateral to their seizure focus compared to the contralateral hemisphere ($p < 0.0001$). Pearson correlations between FC values and language measures revealed a significant positive correlation only in right TLE patients between Verbal IQ scores and connectivity of the left hippocampus to right hemisphere language regions ($r = 0.46$, $p < 0.05$). Follow-up analyses revealed this relationship was driven by connections between the left hippocampus to the right middle frontal gyrus and pars triangularis.

We found that presurgical TLE patients showed stronger functional connectivity between the hippocampus and language regions on the same side as their seizure focus. Furthermore, we found that higher verbal IQ abilities were associated with greater functional connectivity between the left hippocampus and language regions in the right hemisphere in right TLE patients, suggesting a compensatory mechanism in which greater connectivity to the unimpaired left hippocampus may improve overall language ability. These findings contribute novel insights into the relationship between the bilateral hippocampi and language functioning in TLE. Work is ongoing to extend these findings to postsurgical data in the same patients to determine whether reorganization of hippocampus-language functional connectivity patterns is related to language outcomes after surgery.

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Wilcox, Jordyn
Board 94, Session 2
PI: Harrison, Fiona

Chronic subcutaneous manganese suppresses motor performance decline in YAC128Q mice

Jordyn M. Wilcox, Anna C. Pfalzer, Timothy Halbesma, Preethi Umashanker, Kevin Yang, Michal Wegrzynowicz, Keith M. Erikson, Fiona E. Harrison, Aaron B. Bowman

Huntington's disease (HD) is an autosomal dominant inherited neurodegenerative disorder caused by an expanded CAG repeat in the Huntingtin (Htt) gene. Age of onset is inversely correlated with the number of CAG repeats, with > 60 CAG repeats being associated with juvenile onset. There is no cure and current treatments do not alter progression of the disease, but environmental factors can modify age of onset. Previous data have demonstrated mouse models of HD have reduced bioavailablility of manganese (Mn) in the striatum. Mn is an essential nutrient and co-factor for several enzymes throughout development and in adults although it is toxic in excess.

YAC128Q mice express Htt from a juvenile-onset HD patient with 128 CAG repeats. To determine if elevated systemic Mn could modify HD phenotypic onset and progression in YAC128Q mice, a chronic Mn exposure paradigm was implemented, administering either 0, 5, 15, or 50 mg/kg $MnCl_2•(H_2O)_4$ twice weekly, from 12 to 32 weeks of age. A battery of behavioral assessments was performed at 11 weeks, 22 weeks, and 30 weeks prior to euthanasia and tissue removal at 32 weeks of age. Striatal manganese concentrations were measured using graphite furnace atomic absorption spectroscopy (GFAAS).

At baseline YAC128 mice showed a small but significant deficit in motor coordination on the accelerating rotarod task compared to WT littermates. Performance declines in YAC128 mice were prevented in mice treated with 5 mg/kg Mn.

Low dose Mn prevented further decline in motor coordination deficits in YAC128 mice over an 18 week treatment paradigm. There were only minimal increases in striatal Mn levels at this lowest dose, suggesting accumulation did not occur to toxic levels. These findings warrant further investigation including earlier intervention and longer duration treatment with Mn supplementation as a therapeutic modifier of HD. Future studies will evaluate the underlying mechanism(s) of protection and evaluate the critical therapeutic time window for Mn supplementation.

Winalski, Laura
Board 95, Session 1
PI: Ess, Kevin

Identifying Mechanisms of mTORC1-Driven Tumor Susceptibility in the Developing Brain

Laura C. Winalski, Gabrielle V. Rushing, Asa A. Brockman, Grant Westlake, Madelyn K. Bollig, Serena R. Sweet, Kevin C. Ess, Jonathan M. Irish, Rebecca A. Ihrie

Patients with Tuberous Sclerosis (TSC) carry germline mutations that result in loss of control of the mechanistic target of rapamycin complex 1 (mTORC1), a central regulator of cell size, protein translation, and growth. These patients often develop benign brain tumors in the ventricular-subventricular zone (V-SVZ), a large neural stem cell niche. Recent studies of stem cells in normal V-SVZ have revealed highly variable transcriptional and functional capabilities, including activation of mTORC1. Further, distinct subgroups of stem cells in the niche are mitotically active during different time points throughout pre- and postnatal brain development. As brain tumors seen in TSC patients present early in life, central unanswered questions are whether pre- or postnatal neural stem cells are the cell of origin for these tumors, and at what developmental stage differing mTORC1 signaling activity emerges within the stem cell niche.

To map the emergence of differences in mTORC1 activity in normal and disease states, per-cell levels of mTORC1 activating signaling events can be quantified via imaging and flow cytometry analyses of brain tissue. Additionally, the same mTORC1-dependent signaling events can be quantified using cultured neural stem cells derived from pre- and postnatal mouse brain. To determine the time window in which tumor development can begin, an inducible mouse model of TSC will be used to temporally control the loss of mTORC1 regulation. To compare results across species and platforms, quantification of mTORC1-activated signaling events can also be analyzed in TSC patient-derived cell cultures.

As reported in Rushing et al. 2019, Life Science Alliance, beyond expression of stereotypic transcription factors, adult ventral neural stem/progenitor cells were consistently found to have higher levels of mTORC1 activity than their matched dorsal counterparts. These differences in mTORC1-dependent signaling events were detectable as early as postnatal day 2 and provide a rationale for investigating the embryonic time point at which these signaling differences - and consequential functional differences - first emerge.

I will discuss preliminary findings in developing brain using the methods detailed here. Results of this research will define possible windows of therapeutic intervention for patients with TSC by identifying the age and location where periventricular tumor cells of origin first exhibit elevated mTORC1 activity.

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Gabrielle V Rushing, Asa A Brockman, Madelyn K Bollig, Nalin Leelatian, Bret C Mobley, Jonathan M Irish, Kevin C Ess, Cary Fu, Rebecca A Ihrie
Life Science Alliance Mar 2019, 2 (2) e201800218; DOI: 10.26508/lsa.201800218

Yamasaki, Brianna
Board 96, Session 2
PI: Booth, James

Semantic and Phonological Neural Specialization Predicts Growth in Early Reading Skills

Brianna L. Yamasaki, James R. Booth

Contemporary developmental models argue that neural specialization underpins cognitive development (e.g., Johnson, 2011). That is, children initially rely on a distributed network of brain regions to perform a cognitive skill. However, over time and practice that network narrows, as specific regions begin to specialize, which ultimately facilitates skill development. Recent work has established that 5-to-6-year-old children already show neural specialization for oral language processing (e.g., Weiss, Cweigenberg, & Booth, 2018). While behavioral research has demonstrated that oral language skills support later reading development, limiting existing work has explored the neural basis of this relation. The aim of the current study was to address this gap by examining whether neural specialization for phonological and semantic processing, subcomponents of oral language, predict growth in reading skills.

The hypotheses and analytic approach for this study were pre-registered (see https://osf.io/ek8rc/). Data from twenty-four participants were included in this study. Reading skill was measured behaviorally when participants were 5-to-6-years-old (Time 1) and 7-to-8-years-old (Time 2). Participants additionally completed behavioral- and fMRI-based semantic and phonological tasks at Time 1. Four regression models were estimated in which reading growth (Time 2 - Time 1) was predicted from: (1) the intercept (Null-model), (2) performance on the semantic and phonological behavioral tasks (Behavior-model), (3) measures of semantic and phonological neural specialization (Brain-model), or (4) behavioral performance and neural specialization (Behavior-and-Brain-model).

Results from the primary analyses demonstrated little evidence that semantic and phonological processing reliably predicted reading growth. However, a secondary analysis was conducted in which the contrasts used to estimate neural specialization were adjusted. This secondary analysis revealed that only models including neural specialization significantly predicted reading growth (Brain-model: $R2 = 0.308$, $p = 0.021$; Behavior-model: $R2 = 0.076$, $p = 0.437$; Behavior-and-Brain-model: $R2 = 0.413$, $p = 0.031$). In addition, there was strong evidence that the Brain-model explained more variance than the Behavior-model (Bayes Factor = 32.32).

The results of this study demonstrate initial support for the hypothesis that early neural specialization supports later cognitive development. In particular, the secondary analysis revealed that neural specialization for semantic and phonological processing predicted growth in reading skill. However, given the limited sample size and the lack of supporting evidence in the primary analyses, future studies should aim to replicate this result to determine the robustness of this finding.

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Yeo, Darren
Board 97, Session 1
PI: Price, Gavin

A search for the representational content in the putative number form area

Darren J. Yeo, Courtney Pollack, Rebecca Merkley, Daniel Ansari, Gavin R. Price

A region in the posterior inferior temporal gyrus (pITG-numerals) is thought to show preference for processing Hindu-Arabic numerals relative to other symbols such as Roman letters. fMRI studies that compared passive viewing of numerals to other character types (e.g., letters and novel characters) have not found evidence of numeral preference in the pITG. Recent studies showed that the engagement of the pITG is highly modulated by attention and task contexts, which suggests that passive viewing paradigms may be sub-optimal for examining numeral specialization in the pITG. We hypothesized that the distributed patterns of neural activation as an index of neural representations (as opposed to average activation strength) in a candidate pITG-numerals evoked by task-irrelevant numerals, letters, and novel characters may reveal categorical distinctions. Here we examine whether the neural representations of task-irrelevant digits, letters, and novel characters in pITG-numerals are organized according to visual form and/or conceptual categories (e.g., familiar versus novel, numbers versus others).

We performed representational similarity analyses on three datasets that share the same task paradigm and stimulus sets (Ns = 19, 32, and 37). Specifically, we tested whether the neural representations of 36 digits, letters, and novel characters (scrambled versions of the digits and letters sets) in a candidate pITG-numerals in the right hemisphere were organized according to visual form and/or conceptual categories (i.e., familiar versus novel, alphanumeric versus novel, alphabet versus numbers versus novel, numbers versus others, and alphabet versus others). This candidate right pITG-numerals was derived from a meta-analysis of fMRI studies that showed greater average activation for numerals than for other symbol categories.

Small-scale frequentist and Bayesian meta-analyses of our dataset-specific findings suggest that the organization of neural representations in the right pITG-numerals is unlikely to be explained by differences in abstract shape, but can be explained by a digits versus letters distinction, or even a digits versus others distinction (i.e., numeral preference).

Taken together, the right pITG-numerals is likely to be part of a neural pathway biased for automatic predictive coding of objects with potential numerical relevance. Literacy and numeracy experiences may associate letters and digits with distinct processing goals (e.g., numerical relevance). For example, "4" recruits pITG-numerals because the brain predicts that "4" is likely to be numerically relevant, but not "A".

Zavalin, Kirill
Board 98, Session 2
PI: Lagrange, Andre; Delpire, Eric

Excitatory to Inhibitory Transition in GABAergic Currents As a Guide to Circuit Formation of Cortical Interneurons

Kirill Zavalin, Anjana Hassan, Zain Khera, Cary Fu, Eric Delpire, Andre H. Lagrange

Excitatory GABA is a crucial developmental cue that guides perinatal neuronal migration, synaptogenesis, and circuit formation. The switch from embryonic depolarizing GABA to mature hyperpolarizing responses is mainly determined by the onset of KCC2 expression. Previous work by other groups has found that prematurely upregulated KCC2 function produces dramatic abnormalities in brain development, especially in GABAergic cortical interneurons (INs). However, few studies address the repercussions of delayed onset of hyperpolarizing GABA. Here, we investigate how indefinitely-prolonged depolarizing GABA responses in INs adversely affect cortical circuit development using an IN-specific knockout (KO) mouse - DLX5:cre-IRES-eGFP; KCC2flox.

We hypothesize that GABAergic interneuron migration and inhibitory circuit formation is critically dependent on the timing of hyperpolarizing GABA onset. We expect an anachronistic excitable physiology and altered distribution/circuit integration in KCC2-/- KO INs.

KO mice exhibit abnormal neurological development, including: spontaneous seizures, a 45% faster onset of fluorothyl-induced seizures, reduced body weight, and late postnatal mortality, but normal gross and histological anatomy of organs, including feeding structures and the brain. We observe the earliest cortical KCC2 expression in layer 5 (L5) INs, as early as E16-18 in wild-type mice. We thus expected these cells to be the most affected by loss of KCC2, but instead found comparable densities of cells in both maturing (Dlx5:GFP+) and all INs (pan-IN marker) in L5 of KO and sibling. In addition, inhibitory synapses are roughly similar in quantity and GABAA receptor subtype composition.

We then postulated that the effects of KCC2 loss might be specific to IN subtypes, which in L5 consist mainly of somatostatin (SST) and parvalbumin (PV) INs with distinctly different circuit functions and developmental sequences. We found a 24% increase in L5 density of SST INs in KO, but no change in PV IN density. Accordingly, we found no change in frequency of L5 principal cell sIPSCs, which reflect somatic and proximal dendrite input of predominantly PV IN projections. Hence, while a timely KCC2 expression in INs is vital for cortical circuit functionality, our preliminary data suggest that only the L5 SST INs, but not the L5 PV INs, are affected in the KO. We are now investigating (1) the circuit-level repercussions of abnormal SST IN development in the KO, and (2) if an earlier IN developmental trajectory is particularly sensitive to KCC2 loss.

Zoltowski, Alisa
Board 99, Session 1
PI: Cascio, Carissa

Effects of sensory distractors on interoceptive processing in ASD

Alisa Zoltowski, Samona Davis, Michelle Failla, Lisa Mash, Brynna Heflin, Kimberly Schauder, Carissa Cascio

Our sense of our body's internal signals ("interoception") influences our emotional states, so it is a parsimonious target of study to understand both sensory and emotional processing in autism spectrum disorders (ASD). There is emerging evidence that individuals with ASD show nuanced strengths and weaknesses in this sensory system compared to typical development (TD), and these nuances have been linked to emotional outcomes such as anxiety. However, the few studies of this sensory system in ASD so far have mostly considered interoception in isolation from other senses. This study aims to investigate the extent to which individuals attend to interoceptive cues in the presence of competing, external sensory information, as we are always processing our internal signals in the context of ongoing sights, sounds, or touch. Though individuals with ASD are generally more distracted by competing sensory information, prior data from our lab looking at heartbeat counting over temporal intervals suggests that individuals' with ASD may show more "sticky" attention to their internal signals.1

N=45 participants (ASD: N=23, ages 8-43, TD: N=22, ages 6-53) completed a heartbeat counting task across each of four temporal intervals (25s, 35s, 45s, and 100s). Participants completed one block with distracting, vibrotactile stimulation of either "low" or "high" amplitude (randomized by participant) applied to their finger via a device plus one block without any vibrotactile input. Participant counts were compared to actual heartbeats, measured with a pulse oximeter.

Overall, the results showed high individual variability in heartbeat counting, such that baseline counting ability (with no distractor) was the only significant predictor of heartbeat counting with the distractor. However, there were preliminary differences in effect of distractor amplitude by diagnostic group, such that the TD group showed relatively worse performance during the high rather than low distractor (β=-3.9, n.s.), whereas the ASD group showed relatively worse performance during the low rather than high distractor (β=9.1, n.s.).

While this pattern of results is inconsistent with an overall group difference in tracking internal signals when distracted by other cues, they do suggest that the level that is most distracting may be different in ASD versus TD. The ASD group showed the greatest performance decrement in response to the low tactile distractor, whereas the TD group only showed somewhat of a decrement in response to the high tactile distractor. While this effect requires follow-up to confirm, a possible factor to consider may be the timing of the distractors relative to the individual's heartbeat, as the timing of multisensory inputs crucially affects their integration versus competition.

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Dear, Mary Lynn
Board 100, Session 2
PI: Malow, Beth

Learning Healthcare: Managing the Partnerships, Pathways, and Projects in Pragmatic Trials

Mary Lynn Dear, Reagan Buie, Estefania Gibson, Todd Rice, Christopher Lindsell, Jill Pulley, Cheryl Gatto

At Vanderbilt University Medical Center, our Learning Healthcare System (LHS) focuses on bringing clinical research and clinical operations together as collaborative partners. Evidence generated through carefully designed, rigorous study informs recommendations for best practices. At the same time, critical issues that arise in the delivery of patient care generate pressing questions to pursue. In launching the LHS Research Support Platform, the Vanderbilt Institute for Clinical and Translational Research (VICTR) has brought together a number of existing programs whose missions align with the LHS and has established the necessary structure to coordinate and accelerate activities. The structure is centered around the Project Management team. The team provides technical, procedural, and human infrastructure for organizing and supporting individual LHS projects to successful execution. We work with clinical, operations, research, and statistical experts to create the frontline team that drives the investigation. Capturing lessons from each new study, we are creating an environment for learning at the interface of research and practice. Moreover, we leverage our experience to facilitate the design, implementation and analysis of prospective, randomized, controlled, pragmatic clinical trials embedded within the context of routine care delivery. We promote the adoption of a healthcare culture that centers on learning from what we do and doing what we learn.

Dong, Hongwei
Board 101, Session 1
PI: Neul,Jeffery

Detection of EEG and ERP Phenotypes in a Rett Syndrome Mouse Model with R255X Mecp2 Mutation

Hongwei Dong, Jeffery. I. Neul

Mutations in the MECP2 gene cause the neurodevelopmental disorder Rett syndrome (RTT). Four of eight common diseases are caused by nonsense mutation which account for over 35% of all cases of RTT. In previous study, we characterized a mouse model containing a knock-in nonsense mutation (p.R255X) in the Mecp2 locus (Mecp2R255x). We found R255X mutant mice displayed similar behavioral phenotypes presented in Mecp2 null mice and the impairments were successfully rescued by genetically introducing an extra copy of MECP2. However, abnormal electroencephalographic (EEG) and event-related potential (ERP) phenotypes and how they change during development have not been investigated. Therefore, we recorded baseline and auditory evoked EEG in R255X mutant mice at different postnatal week in present study.

Female R255X mutant and their sibling wildtype mice were implanted EEG head mounts starting at 4 weeks old. After one-week recovery, animals were housed in transparent facilities for 24 hours EEG observation. Animals' activities were monitored using online camera and auditory related potential was evoked at the end of EEG recording. The recordings were repeated on each animal every four weeks. All data was obtained using Sirenia Software from Pinnacle Technologies, Inc and saved in the disk for offline analysis.

Our results showed that, at postnatal 20 weeks, R255X mutant mice had decreased strength in auditory evoked potential (AEP) and alpha brainwave (8-12Hz), but the differences were not seen when the animals were at postnatal 5 weeks. Specifically, AEP strength indicated a negative correlation with the severity of disease. Additionally, we characterized animal sleep rhythm and epileptiform discharge according to EEG phenotypes and video manifestation. We found R255X mutant mice displayed epileptiform discharges and prolonged waking time.

These results indicate that R255X Mecp2 nonsense mutant is enough to violate the daily rhythmic sleep pattern and induce epileptiform discharge in female mice. Its disruption on the age-dependent development of event-related responses may serve as a biomarker for RTT and treatment evaluation.

Malow, Beth
Board 102, Session 2
PI: Malow, Beth

ECHO Autism Transition: An Innovative Approach for Increasing Access to Healthcare for Adolescents and Young Adults with Autism Spectrum Disorder

BA Malow, G Stobbe, NC Cheak Zamora, A Curran, K Davis, A Hess, RL Loftin, MO Mazurek, M Mirza Agrawal, M Tapia, K Sohl

Dramatic increases in the prevalence of autism spectrum disorder (ASD) have been accompanied by a rising tide of adolescents with ASD who are entering adulthood. With well-documented shortages in the provider workforce, training of community healthcare providers to serve the unique needs of transition-age youth with ASD in geographic, racial, ethnic, and economically diverse communities requires novel approaches. Project Extension for Community Healthcare Outcomes (Project ECHO) framework is an approach that has proven successful in increasing the role and expertise of the practicing community-based primary care provider (PCP). Project ECHO uses secure multi-point videoconferencing technology to create a learning community, connecting PCPs in local communities ("spokes") to an interdisciplinary team of experts ("hub") through regular recurring sessions. During these sessions, learning is facilitated through brief evidence-based didactics, case-based learning (during which PCPs present their own cases for discussion and co-management), collaborative mentorship, and guided practice. We describe the development and implementation of an innovative approach to increasing access to healthcare for adolescents with ASD, entitled ECHO Autism Transition.

Twelve weekly 1-hour sessions were conducted, in which a series of didactic presentations were given by hub team members on topics related to transition-age years. Case presentations were delivered by spoke participants that allow for discussion between hub members and participants. Recommendations were discussed and formally given to the case presenter. Recommendations and resources were available online for participants to access at any time. Participants receive CME for participation.

Sixteen PCPs were recruited nationally and met weekly for the ECHO sessions. Didactic sessions included topics such as medical and psychiatric co-occurring conditions, behavior management in primary care, supporting families through transition, life skills development, supporting the self-advocate, guardianship, education, housing, and sexuality. Case presentations highlighted challenges facing adolescents and their families as they transition to adulthood. Total Self-Efficacy scores improved significantly from pre-to post-training ($p= .003$), as did scores in almost all subdomains, including Referral and Resources ($p= .033$), Healthcare Transition ($p= .003$), Managing Medical Comorbidities (, $p= .038$), and Managing Psychiatric Symptoms ($p= .038$).

Our pilot trial of ECHO Autism Transition was successful in improving self-efficacy among PCPs. A large proportion of participants also reported changes in their practice, including taking an interest in caring for additional patients with ASD and less professional isolation. ECHO Autism initiatives illustrate evidenced-based approaches in building workforce capacity and access to quality care in individuals with ASD.

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Kiser, Aislynn
Board 103, Session 1
PI: Kiser, Aislynn

Workforce Readiness and Preparation Program for High School Students with ASD

Katie Gregory, Kelly Luo, Aislynn Kiser, Pablo Juarez, Keivan Stassun

The Workforce Readiness and Preparation (WRaP) Online Course is designed to train facilitators to implement programs for individuals with autism spectrum disorder in order to improve workforce readiness skills. The online course, housed on TRIAD's online platform (triad.vkclearning.org), consists of brief online training modules with knowledge checks and supplemental documentation regarding implementation for future program development. WRaP, in partnership with The Treatment and Research Institute for Autism Spectrum Disorder (TRIAD), strives to increase quality employment opportunities through capacity building within local education agencies, employers, and vocational rehabilitation systems. This pre-employment program is a workforce preparation program using STEM (Science, Technology, Engineering, Mathematics) tools, encouraging innovation, leadership skills, and an entrepreneurial mindset. It offers challenges and opportunities for individuals with autism to explore the fields of technology by using LEGO MINDSTORM EV3 Educational Kits as a tool for accessing competencies relevant for the employment market with particular focus on STEM jobs. Through the WRaP Online Course, facilitators are able to receive training and materials exclusively online in order to implement a WRaP program within a local high school for individuals with ASD. Methods: The Workforce Readiness and Preparation (WRaP) program was piloted in July 2019 in New York, New York in collaboration with the ASD Nest Support Project at NYU Steinhardt. Four Nest high school educators with experience with transition-aged students completed the WRaP Online Training course prior to facilitating the program. Two additional consultants with the Nest Program (Co-Project Director and Instructional Support Specialist) completed the course and provided support to the facilitators throughout the four-week program. TRIAD consultants also provided support through weekly check-ins with facilitators, including three video conference calls and one two-day on-site visit. This pilot program served 13 students ranging in age from 15-19 years old. Facilitator feedback, online course evaluations, and student data were collected from this pilot program.

McDonald, T A
Board 104, Session 2
PI: T A M. McDonald

Autism Spectrum Identity and the "Lost Generation"

T A M. McDonald

The definition of autism spectrum conditions (ASC) expanded since its original inclusion in the DSM-III in 1980. These expansion in diagnostic criteria over time imply that an unknown number of individuals, termed the "Lost Generation" (Lai and Baron-Cohen, 2015), who are currently adults, were unidentified during childhood in the 1980's and 1990's as having an ASC. Some adults "self-diagnose" an ASC and little is known about this population. this submission compares adults diagnosed and self-diagnosed with an ASC on demographic characteristics and factor structure of the Autism Spectrum Identity Scale (ASIS).

A nationally distributed survey contained a questionnaire to assess how adults, either diagnosed (n = 893) or self-diagnosed (n = 172) with an ASC, vary in demographic variables (e.g., employment, medication use for comorbidities), factors of well-being, or in the autism identity. The validated four-factor structure of the ASIS was used to predict the factor structure of the ASIS scores for the self-diagnosed group. Chi Square analyses examined independence between diagnostic status on gender, term preference, education and employment status and medication use for comorbid conditions. A one-way ANOVA examined age differences across diagnostic status.

Results: The one-way ANOVA was significant for age and Chi Square analyses were significant for gender, employment, and term preference. Self-diagnosed individuals were older (M = 39, SD = 12.46) and more likely to be women (73%), employed (64%), and to prefer the term Asperger (61%) than those with an ASC diagnosis. Both groups were equally likely to have a diagnosis of anxiety, depression, bipolar disorder, ADHD, and OCD. Each factor from the ASIS four-factor model predicted a corresponding principle axis factor with promax rotation in the self-diagnosed population data with prediction values ranging from .91 to 1.00.

Discussion: This study provides initial validation of the ASIS to measure autism identity in self-diagnosed adults. Participants who self-diagnosed had the same structure of identity responses as the larger data set. It is possible this older and, mostly, female group represents a "lost generation" of undiagnosed adults with ASC who did not meet the criteria for classic autism (Lai & Baron-Cohen, 2015). Little is currently known about this self-identified, but undiagnosed, group of adults. Although access to diagnostic services has increased for children, these undiagnosed adults likely experience greater challenges related to assessment, diagnosis, and services, echoing the larger "services cliff" faced by adults diagnosed with an ASC. Future research should examine the accuracy of ASC self-diagnosis by adults.

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