Lifespan characterization of inter-network structural covariance: A big data, cross-sectional MRI study

Presenter: Katherine Aboud (katherine.e.swett@vanderbilt.edu)

Authors: Katherine Aboud, Yuankai Huo, Hakmook Kang, Ashley Ealey, Bennett Landman, Laurie Cutting

Introduction: Recent studies have characterized brain development in terms of morphological synchronization across brain regions. These structural covariance networks not only map onto functionally identified brain systems, but also correlate with a range of cognitive abilities across the lifespan; for instance, IQ has been found to correlate with structural covariance between frontal, temporal, and parietal regions. However, despite advances in within-network covariance examinations (e.g. covariance of regions within the language network), no studies to date have characterized inter-network structural covariance patterns (e.g. how language networks covary with visual networks). In the current study, we performed a cross-sectional analysis of volumetric network covariance in over 5000 subjects ranging in age from 7-90.

Methods: Whole brain segmentation (133 label) was conducted by a multi-atlas segmentation framework. Regions of interest were grouped into 15 networks, including primary sensory, language, memory, subcortical, and executive networks. The cross-age growth curves of each group were fit using a restricted cubic spline regression with bootstrap validation. Hierarchical clustering analysis was performed on the resulting network growth curves.

Results: All age groups demonstrated significant differences in inter-network parcellation (e.g. 'modularity'), and these differences were characterized by unique patterns of coordination between homotopic networks. Importantly, low SES populations exhibited significantly different network relationships in childhood (7-12 years) and older adulthood (55-75 years) than high SES counterparts. Specifically, children with low SES demonstrated lower volume in language-related areas at age 7, followed by a rapid 'catch-up' period until age 9. Older adults with low SES exhibited unified decline across all networks compared to more heterogeneous growth patterns in high SES older adults.

Discussion: This is the first study to characterize inter-network covariance trends across the lifespan. These findings provide a new framework in which to study brain development, aging, and pathology.
Characterizing Sleep in Adolescents and Adults with Autism Spectrum Disorders

Presenter: Megan Alder  (megan.l.alder@vanderbilt.edu)

Authors: Megan L. Alder, Beth A. Malow

Introduction: Only a few studies have compared sleep patterns in adolescents and adults with ASD and individuals of typical development (TD). We studied 28 adolescents/young adults with autism spectrum disorders (ASD) and 13 age/sex matched individuals of typical development (TD). A better definition of sleep patterns in this population, in combination with physiological measures, is important for the development of targeted interventions to improve sleep in this population. Age-matched individuals with typical development were included as a comparison group. Our hypotheses were that in comparison to those of typical development, individuals with ASD would have delayed bedtimes, prolonged sleep latencies (e.g., increased time to fall asleep), and abnormalities in endogenous salivary cortisol and melatonin.

Methods: Structured sleep histories, validated questionnaires, actigraphy, and endogenous salivary cortisol and melatonin were collected.

Results: Compared to those with TD, adolescents/young adults with ASD had longer sleep latencies and more difficulty going to bed and falling asleep, but normal cortisol and melatonin profiles. Sleep latency (SL) was longer and sleep efficiency (SE) was lower for the participants with ASD. Average participant scores indicated aspects of poor sleep hygiene in both groups. Across all participants, a longer sleep latency was associated with an earlier bedtime, although after adjusting for diagnosis (ASD vs. TD) and age, bedtime was no longer significant.

Discussion: To our knowledge, this study is the first to combine parent and child report of sleep with validated questionnaires, actigraphy, and measurements of salivary cortisol and melatonin. We had hypothesized that individuals with ASD would have longer sleep latencies, would go to bed later, and would have abnormalities in salivary melatonin and cortisol. In our work, we found that the first hypothesis was correct, but that the other two hypotheses were not correct. In comparison to those of typical development, individuals with ASD had prolonged sleep latencies. However, we also found that those with ASD also had more difficulty going to bed and falling asleep on a validated questionnaire compared to their TD counterparts. We conclude that sleep disturbance in ASD is multifactorial. Behavioral interventions may have promise in this population.
Exploring Why Broad Target Speech Recasts Intervention Improves Speech Comprehensibility in Children with Down Syndrome

Presenter: Anna Allen (anna.k.allen@vanderbilt.edu)
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Introduction: Individuals with Down syndrome (DS) exhibit substantial speech comprehensibility deficits.[1,2] For school-age children with DS with initially high verbal imitation skills, those randomly assigned to Broad Target Speech Recast (BTSR) intervention demonstrated greater speech comprehensibility gains than those who received an elicited-imitation intervention.[3] Results were consistent with speech recasts (i.e., accurate models of misarticulated words) being the active ingredient in BTSR. Speech recasts support the child's ability to compare his/her production with a correct model to improve words' 'sound templates.'[4,5] Because this internal comparison act cannot be observed directly, studying proportion of speech recasts imitated by participants (a proxy for a presumed process) might uncover why high imitators benefited most from BTSR. Imitating the recast could aid memory of the recasted utterance and comparison and may provide practice for speech accuracy. Children with high verbal imitation abilities may imitate recasts more than those with low verbal imitation abilities.

RQ1: Is there a positive association between initial imitation ability and the process variable? RQ2: Is there a positive association between the process variable and change in speech comprehensibility?

Methods: Extant data from 23 children with DS aged 5-12 years who received BTSR intervention were used.[3] Participants received 1-hour BTSR sessions twice weekly for 6 months. The process variable was calculated for one early and one late session per participant. Conversational speech comprehensibility was measured. Pearson product correlations were calculated between pre-intervention verbal imitation ability (Dynamic Assessment of Verbal Imitation[6]), average process variable score and change in speech comprehensibility.

Results: The association between initial verbal imitation ability and average process variable score was non-significant (r=.38, p=.08, bootstrap 95% CI [-.14, .61]). Associations between the average process variable and speech comprehensibility change were not significant (raw scores: r=.16, p=.47; residualized gain scores: r=.11, p=.61, respectively). A post hoc paired t-test indicated a decrease in the process variable from early (M=0.27, SD=0.15) to late (M=0.15, SD=0.15) sessions (t(22)=4.49, p<.001, ES=.73).

Discussion: Surprisingly, results do not support the hypothesis that participants with initially high verbal imitation skills were more likely to imitate speech recasts spontaneously, which might have resulted in improved speech comprehensibility during BTSR. The proportion of speech recasts imitated was not correlated with pre-intervention verbal imitation skills or speech comprehensibility changes. Findings add to evidence that at least some children with DS do not require speech accuracy training focused on elicited imitation to increase speech comprehensibility. Speech comprehensibility interventions for children with DS may draw upon implicit mechanisms similar to language interventions (i.e., mental comparisons). Continued research is required to identify the specific mechanism by which speech recasts facilitate speech comprehensibility.


Investigating the Temporal Dynamics of Word Processing Using Multiband fMRI

Presenter: Stephen Bailey  (stephen.k.bailey@vanderbilt.edu)

Authors: Stephen Bailey, Bennett Landman, Laurie Cutting

Introduction: Reading requires distant areas of the brain to rapidly coordinate, passing along information from visual regions to language processing regions that do not typically share information. Research using magnetoencephalography and electroencephalography suggests that this process occurs extremely rapidly, with the initial sweep of visual information occurring within 100ms, followed by feedback from various other cortical areas occurring between 200-400ms (Carreiras et al, 2014). However, these tools can only be generally descriptive about the areas of activation. fMRI, on the other hand, has very good spatial resolution but relatively slow temporal resolution (2-3s). Recent advances in parallel slice acquisition enable sub-second temporal resolution, opening up the possibility of studying network dynamics in tasks such as reading. Here, we sought to explore whether fMRI responses, resolved to a single second, could detect temporal differences in the BOLD responses of regions involved in word recognition and phonological processing.

Methods: We acquired 3-4 eight-minute runs of fMRI data from six subjects while they completed a rhyming task. Each fMRI volume was acquired in 600ms using multiband acquisition. The task involved differentiating between three stimulus types: rhyming, not-rhyming-but-similar-looking, and false fonts. Each stimulus set was presented every 20-30 seconds. Standard preprocessing in FSL was used to conduct data analysis. Response patterns at each voxel of the brain were modeled using finite impulse response basis functions, which allow parameter estimates to be freely estimated over each second of the response.

Results: Multiband fMRI was able to resolve significant BOLD response patterns in expected language areas, including the putative visual word form area, temporo-parietal junction and inferior frontal gyrus, within a window of 4-6 seconds around peak signal (5s post-stimulus). We were, however, unable to differentiate between signal onset in secondary visual processing areas (e.g. the visual word form area) and other important language areas. However, there was a clear temporal distinction between the peak signal in language nodes and deactivation within the default mode network (7s post-stimulus).

Discussion: These initial results suggest that multiband acquisition of fMRI data allows for increased sensitivity to task effects, due to its higher sampling rate. However, this increased speed of acquisition opens up the possibility for discovering larger network interactions in great detail, e.g. how the ventral attention network dynamically suppresses the default mode network during word recognition. Future studies will assess whether individual nodes can be identified which mediate this reconfiguration.

Foundations of Musical and Speech Rhythm - A Pilot Study

Presenter: Peter Bamikole (pbamikole15@email.mmc.edu)

Authors: Peter Bamikole, Aysu Erdemir, Reyna Gordon

Introduction: Gordon et al. (2015) found an association between two seemingly dissimilar tasks: rhythm perception and morpho-syntactic production. A follow-up study found that variance in musical rhythm perception predicts global grammatical performance, and is particularly associated with mastery of complex sentence structure (Gordon, Jacobs, Schuele & McAuley, 2015). Their finding raises more questions about the contributions of other processes to this association between rhythm and syntax. Processes like sensitivity to musical and speech rhythm (i.e. prosodic cues that mark syntactic elements), working memory, and more.

Methods: To tackle some of these questions, our pilot study tests the association between measures of musical and speech rhythm within two groups (children with language impairment, and with typical development). The two tests reported here, among the many included in our study visits, provide good assessments of musical and speech rhythm. For musical rhythm, the rhythm component of the Primary Measures of Music Aptitude (PMMA) assesses children's ability to make same/different judgments about short rhythmic phrases played to them. And for speech rhythm, the Tennessee Test of Rhythm and Intonation Patterns (T-TRIP) assesses children's facility with expressive prosody, by scoring their ability to perceive and produce sound patterns given to them.

Results: We expect a moderate correlation between musical and speech rhythm measures, providing evidence of a putative underlying mechanism by which musical and speech rhythm facilitate spoken grammar skills, as seen in Gordon, Jacobs, Schuele & McAuley's (2015) follow-up study.

Discussion: This result would be part of the groundwork to shape an emerging line of research concerning the role of rhythm in acquiring complex syntax.


Sing a song about sharing: Music making and preschoolers' sharing behavior

Presenter: Sara L. Beck  (sara.l.beck@vanderbilt.edu)

Authors: Sara L. Beck, John Rieser

Introduction: Educational children's media relies heavily upon musical sequences to convey prosocial messages about desirable behaviors, but little is known about the conditions under which children's social behavior is most likely to be influenced by engaging with music through movement or singing. Recent research has shown that engaging in joint music making can result in increased cooperative behavior among preschoolers (Kirschner & Tomasello, 2010) and that moving to a musical beat can foster increased prosocial behavior in infants as young as 14 months (Cirelli, Einarson, & Trainor, 2014). No studies to date have examined the impact of prosocial lyrics on children's behavior.

Methods: I am currently investigating 4 and 5-year-olds' sharing and helping behaviors following one of four experiences: engaging in joint singing and movement to a novel song with either prosocial or neutral lyrics, and engaging in joint non-musical play involving a novel rhyme with either prosocial or neutral content. The four conditions utilize identical props and matched interaction with the experimenter and a research assistant. I began by piloting only two conditions: music/prosocial lyrics and play/neutral lyrics.

Results: Children's sharing behavior was coded, and a t test showed that children in the music/prosocial condition shared more readily than those in the play/neutral condition (t(21)=-1.891, p=.05). Changes in children's affective state (indicated by each participant on a pictorial likert scale) did not account for the difference between the two groups, suggesting that the difference was not mediated by affect. Data collection is now underway for all four conditions, which will enable me to examine the unique contribution of prosocial lyrics and music making in facilitating prosocial behavior.

Discussion: I hypothesize that both music making conditions (neutral and prosocial lyrics) will result in greater willingness to share, and that prosocial lyrics paired with music will result in the greatest degree of sharing and helping. Research with adults has shown that song lyrics can alter subsequent behavior by making prosocial or aggressive thoughts and feelings more accessible (e.g. Greitemeyer, 2009; Greitemeyer, Hollingdale, & Traut-Mattausch, 2015). However, it is possible that in the context of this study, song lyrics may function similarly to 'normative preaching,' in which a nonparental adult states what should be done, but does not directly instruct the child - a type of instruction which has been shown to have no effect on children's sharing behavior (Bryan & Walbek, 1970). In that case, we may see no main effect of prosocial versus neutral song lyrics on children's social behavior.
Executive Function and Early Reading: Cortical Markers for Longitudinal Improvement

Presenter: Jonathan Scheff (jonathan.d.scheff@vanderbilt.edu)

Authors: Jonathan D. Scheff, Stephanie Del Tufo, Stephen Bailey, Miranda Richmond, Laurie E. Cutting

Introduction: This study aims to further explore the effect of executive function and word reading on the neural correlates of interpreting written language. Previous work has shown that executive functioning influences reading development (Cartwright, 2012; Cutting, Materek, Cole, Levine, & Mark, 2009) and, separately, that the inferior frontal gyrus (IFG) is a region of the brain that serves both executive functioning (Osaka et al., 2004) and reading—particularly compensation in dyslexic populations that demonstrate improvement in reading over the course of development (Hoeft et al., 2011).

Methods: Using longitudinal data from 63 children starting in first grade, we investigated if standardized behavioral measures of task-switching and single word reading would correlate with overlapping areas of fMRI activity during a written language task. Activity in the right IFG was associated with both of these cognitive abilities. Subsequently, we sought to compare how activity related to each function predicts longitudinal improvement in reading ability.
Auditory Working Memory across a Range of Language Skills: Neural Substrates and Behavioral Correlates

Presenter: Scott Blain  (scott.d.blain@vanderbilt.edu)

Authors: Scott D. Blain, Nori Jacoby, Reyna L. Gordon

Introduction: While language abilities are often studied in terms of higher-level skills including prosody, grammar, and complex syntax, lower-level processes such as auditory working memory may also play a role. Auditory working memory has been shown to correlate with language skills and may be impaired in those with deficits, such as children with language delay and specific language impairment (SLI). Further, the neural processes underlying auditory working memory show differences in children with SLI, compared to peers with typical language development (TD). While efforts have been made to study working memory in youth with language delays, many investigations have relied upon language-based stimuli, such as words or letters. Thus, the current study utilized a tone-based 1-back paradigm to assess auditory working memory in children with a variety of language abilities, as well as neural correlates and possible impact on language skills.

Methods: Participants included 3 children with SLI and 13 TD peers. Participants completed a standardized battery of grammar/language assessments, as well as a brief digit span task to measure working memory. Participants also completed an auditory 1-back task in which midi-tones were presented in succession and participants were asked to indicate when two notes of the same pitch played consecutively (a 'hit'). Electro-encephalography was used to record event-related potentials (ERPs), linked to the presentation of 'hits' and non-repeated tones.

Results: Participants with SLI were less accurate than TD peers in the 1-back task (t = -3.32, p = 0.005). Accuracy on the 1-back task showed non-significant positive associations with performance on the digit span task. Further, 1-back accuracy was positively correlated with various aspects of grammar as measured by the TOLD-P, SPELT, and TACL-4 (p < 0.05), even after controlling for age. ERP analysis revealed a positive voltage response approximately 300ms after stimulus presentation (P300s), greater in amplitude for the 'hit' condition. P300s were strongest in parietal regions. Positivity responses approximately 600ms after stimulus onset (P600s) were also present.

Discussion: Results of the current study add to a growing body of work demonstrating broader cognitive differences between children with typical vs. delayed language development. Furthermore, findings substantiate the hypothesis that auditory working memory may be an important mechanism in explaining higher-level language impairments as manifested in SLI. Additionally, ERP findings indicate neural responses associated with memory-related functions, helping validate the current 1-back task as a measure relevant to working memory for child participants. Further analyses will explore between-group differences in ERPs, as well as relation to language metrics and musical rhythm skills. In summary, auditory working memory may play a substantial role in language acquisition, as well as contributing to atypical language development.
Neural and Behavioral Metrics of Rhythm Processing in Relation to Individual Differences in Grammar

Presenter: Reyna Gordon (reyna.gordon@Vanderbilt.Edu)

Authors: Scott D. Blain, Natalie Wiens, Alexander Chern, Peter Bamikole, Magdalene Jacobs, C. Melanie Schuele, John R. Iversen, Reyna L. Gordon

Introduction: Our recent work shows that individual differences in rhythm predict grammar abilities in children. Research also shows that overlapping neural mechanisms may (at least in part) facilitate the processing of language and musical stimuli. Supplementing correlational evidence, manipulation of rhythmic context appears to influence performance on certain grammatical tasks. The current project seeks to extend research on the relation between rhythm, grammar, and underlying neural processes, by incorporating brain measures of rhythm perception and exploring rhythmic cues to complex sentences.

Methods: The project consists of two studies. In Study 1, participants (N=24) completed A) two measures of rhythm ability, including the Beat-Based Advantage task (BBA) and the Primary Measures of Music Aptitude (PMMA), B) The Structured Photographic Expressive Language Test (SPELT-3), a standardized test in which children are shown images and asked questions, using grammatical structures of varying complexity, and C) a dynamic attending task in which participants listen to a sequence of rhythmic woodblock beats while electro-encephalography (EEG) was used to record brain activity. In Study 2 (ongoing), participants complete the aforementioned tasks, as well as the ORCAS, a novel task examining understanding of complex syntax in relation to rhythmic cues.

Results: Preliminary data from Study 1 suggests that individual differences in EEG activity during listening to rhythmic sequences are associated with complex syntax abilities ($r = 0.64$, $p < 0.001$). Furthermore, stepwise regression revealed that a significant portion of variance in complex syntax ability was predicted by EEG gamma activity elicited during passive listening to rhythmic sequences, above and beyond the variance predicted using behavioral measures of rhythm alone ($\beta = 0.56$, $R^2 = 0.49$, $F = 8.90$, $p < 0.001$; $\Delta R^2 = 0.29$, $p < 0.01$). This relation remained true while controlling for age. Data collection for Study 2 is currently underway and will also be presented.

Discussion: Preliminary results from Study 1 suggest that neural activity during listening to rhythmic sequences may predict certain aspects of grammar, above and beyond individual differences in behavioral measures of rhythm ability. Follow-up analyses will incorporate independent components analysis of EEG data, in order to better elucidate the particular neural mechanisms underlying the links between rhythm and grammar. Study 2 will further these aims, incorporating more sophisticated measures to examine the influence of rhythmic regularity on grammatical performance. In conclusion, these new approaches will allow us to better understand the complex relation between rhythm, grammar, and underlying neural resources.
The Stuttering Stereotype: Negative Automatic Associations and Diminished Credibility

Presenter: Taylor Boothby (taylor.a.boothby@vanderbilt.edu)

Authors: Taylor Boothby, Tedra Walden

Introduction: Stuttering, a communication disorder involving involuntary, intermittent speech disfluencies, is one of the most common developmental disabilities. It affects 3-5% preschool-age children and 1% of adults worldwide. Stuttering typically begins in early childhood and often negatively impacts development. Children who stutter (CWS) are at risk for bullying, decreased communicative competence, poorer educational/vocational attainment, social functioning, and mental health. Negative attitudes toward people who stutter (PWS) have been reported in many populations. However, previous studies have examined only self-reported, explicit attitudes, which may not be truthful. This project, using two innovative methods, examines both explicit and implicit (subconscious, unreportable) attitudes toward stuttering to better understand what PWS face.

Methods: The computer-based Stuttering Implicit Association Test (IAT) measures strength of association between concepts (stuttering/fluent, positive/negative). Two categories are assigned to each of two response keys in trial blocks, then categorical exemplars are rapidly sorted. Compatible, more strongly-associated concepts are easier to pair together, resulting in faster responses (called the IAT effect). The fast-paced task resists self-presentation strategies, allowing assessment of implicit attitudes. Participants were 21 non-stuttering adults. The Credibility Task uses three video vignettes involving toy figurines. In each, a stuttering and a fluent character provide conflicting information about a hidden object's location. Participants decide whom to believe. They complete explicit scales for both speakers, rating bipolar adjectives (e.g. smart-dumb) on a 5-point scale. Participants were 19 3-7-year-old children, including 4 CWS.

Results: IAT: 20/21 adults showed negative implicit attitudes toward stuttering, and 1 was neutral. The mean D-score for all participants was 0.388, indicating a small-medium IAT effect. The mean difference in response latency between compatible and non-compatible pairings (stuttering-negative and stuttering-positive) was 252 milliseconds. Credibility Task: CWS showed no preference for either speaker, believing PWS in 50% (6/12) trials. CWNS preferred fluent information, believing the PWS in only 35.5% (16/45) trials. Children's mean explicit rating of PWS (3.0 on a 5-point scale) was significantly lower than their rating of the fluent speaker [3.6; t(17) = 2.994, p<0.01], indicating more negative attitudes toward PWS.

Discussion: The observed IAT effect indicates that most adults hold more negative implicit attitudes toward stuttered than fluent speech, and stuttering is more strongly-associated with negative attributes than positive. The Credibility Task reveals that CWNS perceive stuttered information to be less believable than fluent information. Stuttering may reduce credibility by interfering with cognitive fluency, because it is more difficult to process/understand. Together, these results indicate that negative attitudes toward stuttering operate on a deeper, more automatic level than was previously known, and may contribute to a negative stereotype that makes life more difficult for PWS.
Impaired autophagy in an HD STHdh cell line may contribute to defective Mn homeostasis via associated changes in PI3K signaling.

Presenter: Miles Bryan  (miles.r.bryan@vanderbilt.edu)

Authors: Miles Bryan, Michael Uhouse, Andrew Tidball, Terry Jo Bichell, Emma Bradley, Grace Tipps, Aaron Bowman

Introduction: Manganese, while toxic in excess, is an essential metal in almost all biological systems. Recently, we have shown that cellular models of Huntington's disease (HD) exhibit decreased Mn uptake that manifests as a Mn-selective deficit in ATM-dependent phosphorylation of p53. Interestingly, p53 has also been implicated in HD. In this study, we sought to see if other critical cell signaling proteins which have been more recently implicated in HD etiology (PI3K, AKT, mTOR) are similarly responsive to sub-toxic levels of Mn. We hypothesize that these pathways may contribute to neuronal Mn homeostasis, and HD associated alterations in these pathways contribute to deficits in Mn transport in this model.

Methods: Given the distinct similarities and connections between these pathways, we first screened several small molecule inhibitors (SMIs) of PI3K and PIKKs (phosphotidylinositol three-kinase-related kinases) to determine if any of these kinases can function to modulate Mn homeostasis.

Results: Our data suggest that Mn uptake can be drastically reduced (>50%) in STHdhQ7/Q7 and STHdhQ111/Q111 cells via selective inhibition of PI3K only and not ATM, DNApk, or mTOR. Given these findings, we then examined the responsiveness of these pathways to sub-toxic concentrations of Mn. We found that STHdhQ111/Q111 show diminished activation of these pathways in the presence of Mn. However, Mn-dependent activation of p53, AKT and S6 in HD STHdhQ111/Q111 cells can be restored to that seen in wild-type cells following exposure with Mn and 10uM KB-R7943, an inhibitor of NCX1/3, which can restore Mn uptake in this cell line. Considering that autophagy functions downstream of the PI3K/AKT/mTOR pathways, we investigated whether KB-R7943 acts through autophagy to increase Mn-uptake. Dual KB-R7943/Mn exposures increase expression of P62 and LC3-II/LC3-I expression, indicative of an increase in autophagy in both STHdhQ7/Q7 and STHdhQ111/Q111 cells and the striatum of the YAC128 mouse model.

Discussion: Consistent with our inhibition of Mn-uptake by PI3K inhibition, these findings could suggest that Mn uptake may be regulated via an autophagy-mediated route, controlled by upstream kinases including PI3K. Furthermore, mutant HTT's ability to inhibit autophagy could explain why both striatal cellular and mouse models exhibit a decrease in Mn-uptake. Taken together, these findings suggest a novel PI3K-mediated mechanism of neuronal Mn transport. In addition, further investigation of these findings suggests that PI3K is functioning through autophagy to modulate Mn homeostasis. This suggests that restoration of these homeostatic pathways could potentially alleviate Mn-responsive cell signaling defects common to most HD models. In future studies, we plan to examine these pathways in other cell models including patient hiPSC-derived striatal and cortical neuroprogenitors and neurons as well as HD mouse models.
Behavioral and neural patterns of vibrotactile stimulation and links to autism traits

Presenter: Lauren Bryant  (lauren.k.bryant@vanderbilt.edu)

Authors: Lauren K. Bryant, Li Min Chen, Arabinda Mishra, Carissa J. Cascio, Mark T. Wallace

Introduction: The sense of touch is understudied in autism spectrum disorders (ASD), despite its central role in early social development and strong links between aberrant tactile processing and clinical symptoms of autism (1). Much of what we do know about sensory processing in autism is derived from parent and self-report surveys, which are ecologically valid and insightful tools, but subjective in nature. Psychophysical methods allow researchers to quantitatively assess the relationship between physical stimuli and the perceptions they produce, an objective approach which could lend itself to improved treatment for sensory symptoms. Furthermore, the neural basis of such aberrations is not well understood. Atypical tactile responsiveness may arise from deviations in sensory cortical organization, as suggested by a previous magnetoencephalography (MEG) study (2). Yet, MEG lacks the precise millimeter spatial resolution afforded by high-field, 7-Tesla functional magnetic resonance imaging (7T fMRI) (3). Such resolution could reveal previously undetected relations between tactile perception and somatotopic organization.

Methods: We first examined vibrotactile detection ability at the left index finger tip in 24 neurotypical adults (10 male, mean age = 28 (4.24)) using a simple-choice detection paradigm, and then delivered high intensity (200 Hz, 400um) vibrotactile stimulation randomly to the left digits 2-4 during 7T fMRI (N = 16). Stimuli were delivered in a block design (20 secs stimulation/20 sec rest), repeated 5 times and alternating between 2 digits each run. Subtraction analyses involved comparisons between rest and stimulation periods, collapsing across runs to create activation maps for each digit. Additionally, each person received a battery of sensory and social communication self-report surveys (Social Responsiveness Scale-2: SRS-2, Adult/Adolescent Sensory Profile: SP, Broad Autism Phenotypes Questionnaire: BAPQ, Sensory Perception Quotient: SPQ) to explore the presence of autistic traits and altered sensory perception and their relationship with psychophysical variables.

Results: Preliminary fMRI results suggest the ability to replicate single digit separation in the somatosensory cortex using a novel method of vibrotactile stimulation. Emerging relations between psychophysical variables and sensory and social communication survey suggest that increased dynamic range of vibrotactile detection is negatively associated with reports of aloofness (BAPQ-Aloof) and the desire to socially interact (SRS-2: Social Motivation).

Discussion: In addition to quantifying inter-digit distance from our fMRI activation maps, ongoing work includes aggregating correlated items reasoned to measure the same construct (i.e., sensory hypo/hyper responsiveness, social interaction, communication) across self-report surveys and performing additional regression analyses with our psychophysical data. The ultimate goal of this research is to strengthen our understanding of how the brain processes tactile information and provide an empirical basis for advancing the treatment of sensory-based symptoms in autism.


Engaging Communities to Improve Employment Outcomes for Youth with Intellectual and Developmental Disabilities

Presenter: Jennifer Bumble  (jennifer.bumble@vanderbilt.edu)

Authors: Jennifer L. Bumble

Introduction: Through funding from The TennesseeWorks Partnership, a systems and policy change project funded through the Administration on Intellectual and Developmental Disabilities (AIDD), and support from the Vanderbilt Kennedy Center, I led a mixed-method longitudinal study to learn how seven geographically and economically diverse communities might implement community conversations to address employment barriers for transition-age youth with intellectual and developmental disabilities in their community.

Methods: Communities submitted mini-grant applications and were evaluated based on geographic and economic diversity, strength of their planning team, and potential for sustainable outcomes. Each community received a mini-grant, training, and resources to host two community conversation events and implement at least one idea generated at their initial conversation. Semi-structured interviews with each community planning team, surveys from attendees, observations of event organization and characteristics, and qualitative coding of the more than 2,500 ideas generated across community conversation events were analyzed to understand each community's perceptions on the efficacy and feasibility of the community conversation process as well as the impact and outcomes of the strategies they chose to implement.

Results: Through this mini-grant project, community planning teams developed the leadership skills to effectively plan and implement community-wide initiatives. They were trained in recruitment, engagement, data collection, data analysis, and sustainable action strategies. Each community hosted two successful community conversation events, and independently carried out at least one strategy generated by attendees at their first event (e.g., developed community-based training sites for youth with IDD, created parent and family advocacy groups, designed campaigns to recognize employers committed to hiring people with IDD, and formed advisory councils to strengthen community partnerships). In addition, community conversation attendees identified and took diverse action steps to overcome local employment challenges facing youth with IDD (e.g., talked to neighbors or family members about employment barriers in their community, educated employers on the importance of hiring people with IDD, hired individuals with disabilities in their own businesses). Data addressing the design, implementation, follow-up, and outcomes of these interventions will be presented, along with recommendations for research, policy, and practice.

Discussion: These promising findings are an indication of the high-impact of community conversations, the flexibility of the approach to fit community needs and culture, and their capacity to empower community members to drive change to overcome a range of barriers facing youth with IDD in their communities. Continued systems-level change and the emergence of strong community advocates as a direct result of the mini-grant project are expected over the next 1-5 years.
GABRB3(D120N), a Lennox-Gastaut Syndrome-associated mutation, induces behavioral abnormalities in both young and adult mice

Presenter: Mackenzie Catron  (mackenzie.catron@vanderbilt.edu)

Authors: Sherman Qu, Vaishali Janve, Ciria C. Hernandez, Robert L. Macdonald

Introduction: Lennox-Gastaut Syndrome (LGS) is an epileptic encephalopathy, a severe form of epilepsy, which is often intractable and characterized by early childhood onset (age 1-8), an abnormal electroencephalogram (EEG), and a broad range of seizure types. Additionally, LGS can persist into adulthood and is often accompanied by several comorbidities, including attention deficit hyperactive disorder, severe intellectual impairment, and other abnormal behaviors. A de novo mutation, GABRB3+/D120N, was identified in a patient with LGS. The D120N mutation is in the β3 subunit of the γ-aminobutyric acid type-A receptor (GABAAR), and is specifically located near the GABA binding pocket formed by this subunit.

Methods: After initial in vitro evidence that D120N impairs GABAAR function, we generated a knock-in mouse containing the mutation. We hypothesized that this animal would not only have a similar seizure phenotype to the patient condition, but that the animal would have similar behavioral abnormalities as can be seen in both LGS patients and in the D120N patient specifically. The work presented here is a suite of behavioral tests aiming to compare the D120N mouse and human LGS, having been performed at two ages: p49 and p200.

Results: These tests have revealed an array of abnormalities including anxiety, hyperactivity, abnormal sozialization, and deficits of cognitive ability in the D120N mice. A less severe phenotype at p49 (before sexual maturity) gives way to a more severe phenotype at p200 (full adulthood).

Discussion: We hope that sufficient parallels may be drawn between the D120N mouse and LGS such that this animal might serve as a model for this disorder, allowing us to further investigate mechanisms underlying the disorder and potentially identify novel or modified treatment options for patients with LGS.
MAG Lipase Inhibition Reduces EtOH-Abstinence Induced Depression

Presenter: Sam Centanni (samuel.centanni@vanderbilt.edu)

Authors: Samuel W. Centanni, Katherine M. Holleran, Sachin Patel, Danny G. Winder

Introduction: Alcohol use disorders (AUDs) are strongly associated with affective disturbances such as depression and anxiety. Alcoholics commonly cite stressors and negative affective states, such as depression and anxiety, as potent triggers of alcohol cravings and/or relapse. A better understanding of the brain circuitry driving AUDs and affective disturbances will help pave the way for the development of newer, more efficient treatments of alcohol abstinence-induced depressive symptoms. Converging evidence suggests that the transition from social use to negative reinforcement-driven alcohol seeking involves a set of brain structures collectively referred to as the extended amygdala. Specifically, the bed nucleus of the stria terminalis (BNST) is widely regarded as a critical node for stress-related affective dysfunction. The endogenous cannabinoid (eCB) system is intimately involved in mediating stress responses. Mounting evidence suggests decreased eCB signaling in the BNST contributes to the maintenance and/or severity of alcohol dependence.

Methods: Singly-housed female C57BL/6J mice were subjected to chronic drinking followed by forced abstinence (CDFA). We used this model in combination with several behavioral tests to measure depressive-like behaviors. We aimed to reverse CDFA-induced depression by pharmacologically enhancing endogenous levels of the eCB 2-AG with the MAG lipase inhibitor JZL-184. Furthermore, ex-vivo slice electrophysiological recordings were conducted in the BNST to determine the effect of CDFA on eCB signaling in the BNST.

Results: Depression-like behavior in the forced swim test (FST) is revealed only after a protracted (2 weeks), but not acute (24 hour), abstinence period. Further, once established, depressive behavior is long-lasting, as we observed a significantly enhanced latency to approach food even 35 days after ethanol withdrawal in the novelty-suppressed feeding test (NSFT). Here, we demonstrate that JZL-184 successfully reversed the EtOH-abstinence-induced latency to approach food seen in the NSFT. Additionally, co-administration of the CB1 receptor antagonist rimonabant with JZL-184 completely blocked this effect. Next, the physiological basis for this phenotype was examined using slice electrophysiology. AMPA-receptor mediated spontaneous excitatory postsynaptic currents (sEPSC) frequency was significantly increased in CDFA mice relative to control mice, suggesting CDFA-induced hyperexcitability of BNST neurons. Interestingly, slices from CDFA mice pre-incubated in JZL-184 exhibited sEPSC frequency comparable to control mice.

Discussion: CDFA produces a robust, persistent depression phenotype. JZL-184 successfully blocked CDFA-induced depression. Moreover, our data suggests that glutamatergic neurons in the BNST are eCB sensitive, and may represent a neural correlate for observed CDFA-induced depressive-like behavior. Collectively these data highlight an important role for BNST-eCB signaling in alleviating depressive-like symptoms during EtOH abstinence. Future studies will further explore the neurocircuitry underlying CDFA-induced depression by examining specific inputs to the BNST.
Influence of rhythm on grammatical performance in children with cochlear implants, developmental language disorders, and typical development

Presenter: Alexander Chern  (alexander.chern@vanderbilt.edu)

Authors: Alexander Chern, Barbara Tillmann, Reyna L. Gordon

Introduction: Rhythm is the way sound is arranged through patterns of time. Recent research has demonstrated relationships between music and language processing, notably for syntax. Children with cochlear implants are shown to perform worse than normal hearing peers in expressive language domains, and have also been shown to have deficits in music perception, notably pitch and timbre. Our study tests the influence of listening to rhythmically predictable or unpredictable musical sequences on how well children with cochlear implants (CI), specific language impairment (SLI), and typical development (TD) perform on grammatical tasks in English.

Methods: We have designed a study in which children listen to either rhythmically predictable or unpredictable musical sequences followed by blocks of grammatically correct and incorrect sentences. For each trial, they perform grammaticality judgment tasks, where they identify whether or not sentences are grammatically correct, as well as sentence repetition tasks, to assess complex syntax.

Results: Performance of all children (TD, SLI, and CI) in grammaticality judgment and complex syntax tasks are expected to improve after listening to rhythmically predictable musical sequences compared to rhythmically unpredictable musical sequences, in line with previous work by Przybylski et al (2013) on French-speaking children with TD and SLI.

Discussion: This ongoing work may have implications for elucidating mechanisms for auditory processing and in employing innovative, music-training elements during speech therapy for patients with developmental language disorders or cochlear implants.

Age and ocular pressure influence optic nerve astrocyte remodeling during experimental glaucoma

Presenter: Melissa Cooper (melissa.cooper@vanderbilt.edu)

Authors: Melissa L. Cooper, John W. Collyer, Karen W. Ho, Nick J. Ward, David J. Calkins

Introduction: Glaucoma is a highly prevalent, age-dependent neurodegenerative disease that targets the optic nerve, the retinal ganglion cell (RGC) projection to the brain. In glaucoma, RGC axonal survival is challenged by aging and intraocular pressure (IOP). We aim to understand how such stressors alter cellular interactions to influence glaucomatous progression. In the optic nerve, dynamic astrocyte processes provide support to the axons they surround. Here, we use the DBA/2J mouse model of chronic glaucoma and the inducible microbead occlusion mouse model to determine how age and elevated IOP alter astrocyte process distribution in the optic nerve. We also determine how loss of the transient receptor potential vanilloid 1 (TRPV1) calcium channel, an activator of stress-induced astrocyte remodeling, influences glial distribution.

Methods: Optic nerve cross-sections from DBA/2J mice aged 4-13 months with known IOP were analyzed for axon size, density, and astrocyte distribution using custom Matlab routines. We elevated IOP unilaterally in mice using microbead occlusion of aqueous flow and analyzed similarly. Contralateral eyes received an equivalent volume saline injection as an internal control. IOP was monitored for 5 weeks using Tono-Pen XL rebound tonometry. Animals were perfused transcardially with 4% paraformaldyde. We devised a metric of astrocyte morphology ('center of mass', CoM) to define the location along the nerve's radius for which 50% of the total glial area lies on either side.

Results: As the DBA/2J mouse progresses pathologically, glial area increases and the distribution is altered. Neither age (p=0.57) nor IOP (p=0.74) predicted total astrocyte coverage, which ranged from 10-50% of the cross-sectional nerve area. However, astrocyte processes distributed more evenly (determined by CoM) as coverage increased concurrent with axon loss (p<0.001). For C57 mice, the average microbead-induced IOP elevation was 30-35%. This resulted in a modest total astrocyte coverage of 15-25%. Here, lower glial coverage was associated with decreased axonal transport, a measure of RGC function. Additionally, increased coverage was associated with decreased CoM, indicating a bias towards the edge (p=0.02). Both correlations were absent in nerves from transgenic mice missing the transient receptor potential vanilloid-1 (TRPV1) channel with the same elevation in IOP (p=0.7; p=0.85).

Discussion: In nerves from DBA/2J mice, astrocyte process distribution is determined primarily by axonal properties rather than glaucomatous stressors directly. For C57 mice, modest IOP elevations have little influence on total astrocyte coverage of the nerve but do affect distribution. Previously, we determined that the TRPV1 cation channel contributes to astrocyte process motility after mechanical stress. Consistent with this, IOP elevation had no effect on astrocyte remodeling in nerves from Trpv1 -/- mice.

Cooper et al., 2015; Exp Eye Res; doi: 10.1016/j.exer.2015.11.016

Ho et al., 2014; Glia; doi: 10.1002/glia.22691

Calcium-binding proteins immunoreactivity in macaque V2 indicates differential population expression across cortical regions

**Presenter:** Jennifer Coppola  (jennifer.j.coppola@vanderbilt.edu)

**Authors:** Jennifer J. Coppola, Anita A. Disney

**Introduction:** Inhibitory interneurons of the primate cortex comprise heterogenous populations, with considerable structural and functional diversity. Traditionally, these populations were classified based on their morphologies. More recently, immunocytochemical and genetic markers have become a prevalent alternative for classification, with well-documented qualitative and quantitative data. In the present study, we use immunocytochemical markers to quantify the distribution and overlap of three neuronal classes in visual area V2. Expression of the calcium-binding proteins calbindin (CB), calretinin (CR) and parvalbumin (PV) by inhibitory interneurons has been found to define almost entirely non-overlapping classes of cells that, together, are believed to account for approximately 95% of the inhibitory neurons in the primary visual cortex (V1) of the macaque. Similarly, these proteins have been shown to represent distinct populations of neurons in the monkey prefrontal cortex (PFC).

**Methods:** In the present study, triple immunofluorescence labeling was used to identify neurons expressing CB, CR, and PV in V2 of three macaques. Laminar distribution and degree of co-labeling for each population were quantified. 1146 calcium-binding protein-immunoreactive neurons were counted in a total area of approximately 7.587mm².

**Results:** Our results indicate that these calcium-binding proteins represent non-overlapping populations in macaque V2; no neurons were found to be triple labeled, or to be dual labeled for CR/CB. Less than 1% of all cells were dual labeled for CB/PV (0.785%), and less than 1% were dual labeled for CR/PV (0.175%). Overall, we found PV-immunoreactive neurons to account for 52% of the calcium-binding protein-immunoreactive population, with CB-immunoreactive neurons accounting for 25%, and CR-immunoreactive neurons accounting for 23% of the same population.

**Discussion:** Previously in macaque V1, a significant majority of inhibitory neurons was found to be PV-immunoreactive. In the macaque PFC, however, these proportions shift such that CR-immunoreactive neurons are the largest population. Our data indicate that the expression of these three populations of calcium-binding protein-immunoreactive neurons in V2 is distinct from that found in V1 and in PFC, and support the use of CB, CR, and PV as immunocytochemical markers for non-overlapping neuronal classes.
Adaptive Behavior Impairments Vary with Depression Status in Adolescents and Young Adults with ASD

Presenter: Rachel Crist  (Rachel.N.Crist@Vanderbilt.edu)

Authors: Rachel N. Crist, Katherine Gotham

Introduction: Adaptive behavior is an important index of functioning in autism spectrum disorder (ASD), and has been shown to predict adult outcomes within this population. ASD is associated with high rates of impairment in adaptive behavior. Despite highly variable symptom expression and intellectual functioning within ASD, existing literature supports a general pattern in the adaptive behavior profiles of adults with ASD, with relative strengths in daily living skills and to a lesser extent communication, and relative weaknesses in socialization. Other clinical populations, such as adults with depression, tend to experience impaired adaptive functioning as well. Empirical evidence suggests high rates of psychiatric comorbidity in ASD across the lifespan, with depression a particularly common co-occurring condition for adults with ASD. Despite the known negative effects of ASD and depression singularly on adaptive behavior skills, the combined impact is unclear. This study aims to assess the relation between depression and adaptive behavior in adolescents and adults with ASD by comparing adaptive behavior profiles of those with and without co-occurring depression.

Methods: Participants included 50 adolescents and adults with ASD (16-35 years) and verbal IQ ≥ 70. ASD diagnosis was confirmed via parent completion of the Autism Diagnostic Interview-Revised (ADI-R), as well as administration of the Autism Diagnostic Observation Schedule (ADOS). Parents also completed the second edition of the Vineland Adaptive Behavior Scales (VABS-II) to assess participants’ adaptive functioning in the domains of Daily Living, Communication, and Socialization. Participants completed the Beck Depression Inventory, 2nd edition (BDI-II) to assess depressive symptoms.

Results: Age and verbal IQ were not significantly different between depressed (DEP) and non-depressed (ND) participants. Vineland composite adaptive behavior scores were found to be significantly lower among the depressed subsample (M=62.4, SD=12.8 vs. M=74.5, SD=13.1 in ND; F(2,46)=3.43, p=.041), as were the specific domain scores for Daily Living Skills (F(2,47)=5.94, p=.005) and Communication (F(2,46)=14.23, p=.000). Vineland Socialization domain scores were not significantly different between groups. We observed similar results when testing this dimensionally within the entire sample: BDI-II scores showed a significant negative correlation with both Daily Living (r=-.361, p=.010) and Communication (r=-.410, p=.003) domain scores, but were not significantly correlated with Socialization scores.

Discussion: These findings suggest that comorbid depression may exacerbate adaptive functioning impairments in adults with ASD. Furthermore, our results indicate that co-occurring depression is associated with diminished adaptive behavior skills in areas that otherwise tend to be relative strengths within ASD (Daily Living Skills and Communication), providing evidence for unique functional impairments related to this psychiatric comorbidity.


Infant Tool Use and Executive Function

Presenter: Ashley Detherage  (ashley.m.detherage@vanderbilt.edu)

Authors: Ashley Detherage, Amy Needham

Introduction: Tool use is a rapidly developing skill that provides infants with independence, more opportunities to engage socially, and the ability to explore the world around them (Lockman, 2000). Tool use can also provide us with interesting insight into how other skills, like executive function and social skills, are developing. This project aims to investigate the role of executive function on the development of infant tool use.

Methods: Infants between the ages of 14 and 18 months participated in a task requiring them to use a tool in a particular way (Barrett, Davis, and Needham, 2007). This task featured a box with a window through which colored lights were visible. When a tool is inserted in a small hole on the side of the box, the lights turn on (this is demonstrated by an experimenter). The small hole allowed the insertion of the handle, but not the bowl end, of the tool. Infants received two different tools to engage in this task on their own: a familiar tool, a spoon, and an unfamiliar tool similar in size and shape to the spoon. In one test trial, the presentation of the tool restricted infants' initial grasp of the tool: infants had to grasp the tool by the bowl end instead of the handle, which is their prepotent response at this age. In another test trial, the infants' initial grasp of the tool was not constrained. We compared behavioral data from these experimental trials with measures of parent-reported executive function using the Early Childhood Behavior Questionnaire (ECBQ) (Putnam, Garstein, & Rothbart, 2006).

Results: Our preliminary coding of the data show that, of the 28 infants that have participated so far, 15 infants solved the lightbox task during at least one of the test trials. Data collection and coding are ongoing; however, we expect to find that infants with higher Inhibitory Control (IC) scores as measured by the ECBQ will be more successful in completing the lightbox task than infants with lower IC scores. Additionally, we predict that infants will be more successful using the familiar tool to activate the lightbox when their initial grasp location is constrained.

Discussion: Infants in this study will likely show a wide range of behavior. However, we expect that this experiment will provide important insight into the development of tool use and executive function skills, which have been largely unexplored in infants younger than 18 months. Additionally, this project will demonstrate how two pathways-tool use and executive function-converge during an important phase of development.


Cortical Multisensory Circuits: Implications for Autism Spectrum Disorder

Presenter: Gabriella DiCarlo (gabriella.e.dicarlo@vanderbilt.edu)

Authors: Gabriella E. DiCarlo, Juliane Krueger, Mark T. Wallace

Introduction: Autism spectrum disorder (ASD) is a developmental disorder characterized by impairments in social communication and restricted, repetitive behaviors, interests, or activities. While there are no clinical biomarkers of ASD, nearly 30% of patients with ASD have elevated whole blood serotonin, implicating serotonergic dysregulation in the pathogenesis of this condition. Serotonin has been shown to be critical in key cortical developmental processes and in the formation of sensory processing networks. Alterations in serotonergic signaling have been shown to disrupt the formation and function of primary sensory cortices (somatosensory, auditory, and visual). It is not therefore surprising that the Diagnostic and Statistical Manual of Mental Disorders includes sensory processing abnormalities as a core symptom of ASD. Since an essential function of the nervous system is to integrate sensory information into a coherent percept, it is likely that disruptions in sensory processing that extend beyond unisensory processing alone may underlie the core deficits associated with ASD. This is supported by evidence indicating differences in connectivity between distant brain regions in children with ASD, as communication across cortical regions is necessarily required for the processing of information across sensory domains. Here we demonstrate the impact of a serotonin transporter mutation associated with ASD, SERT Gly56Ala (Ala56), on the pattern of thalamocortical and intercortical projections from and between primary visual cortex, primary auditory cortex, and area V2L (a multisensory region) in the mouse using neuroanatomical tract tracing.

Methods: Specifically, CTB-green was injected into the lateral region of V2L to visualize retrograde projections to this region in both wild type and Ala56 animals. Previous work has demonstrated projections from primary auditory and visual cortices to V2L in wild type animals, indicating a possible role for this region in multisensory integration.

Results: Previous work has demonstrated projections from primary auditory and visual cortices to V2L in wild type animals, indicating a possible role for this region in multisensory integration. As serotonergic innervation is critical to the formation of primary sensory maps and their function, we anticipate a reduction in the number and density of intercortical projections in Ala56 animals.

Discussion: This work has sought to determine the projection patterns into area V2L from primary visual and auditory cortical regions using anatomical methods in both wild-type animals and in a mouse model of ASD, the Ala56 mouse. The work is structured around the overarching hypothesis that serotonergic signaling dysregulation will result in marked decreases in the convergence of visual and auditory information into area V2L, and that these changes will alter multisensory function in ways that result in changes in sensory-driven behaviors and indices of social communication. The proposed line of research is directed toward providing a better understanding of the contributions of altered multisensory function to ASD.
Parent-Based Sleep Education in Autism: A Community-Academic Research Partnership

Presenter: Bethany Drury  (bethany.drury@vanderbilt.edu)

Authors: Bethany Drury

Introduction: Sleep disturbance affects 50-80% of children with autism spectrum disorder (ASD). Behavioral sleep education for children with sleep disturbance is currently provided largely within academic medical centers, which often include long waiting lists for this service. Our study aims to determine the feasibility of providing sleep education training to parents of children with ASD in a diverse community setting in relation to more traditional Vanderbilt-based studies.

Methods: The following elements comprised our study: (1) Recruitment and consent of participating families, as well as instruction in study procedures such as actigraphy (2) Collection of baseline data, (3) Therapist training and fidelity, (4) Delivery of sleep education to families, (5) Collection of intervention data.

Results: In contrast to Vanderbilt-based studies, we found that recruitment was easier for the community based study. Families expressed support for having study procedures done at their pediatrician office, and not having to drive to Vanderbilt. Initially, our community coordinator was consenting and instructing families in procedures such as actigraphy. Our community coordinator found it beneficial to have Vanderbilt personnel assist with consenting and instructing families and to focus more on recruitment and sleep education. We used on-line surveys through Research Electronic Data Capture (REDCap) to reduce family burden. Community therapists were trained by Vanderbilt personnel and reached excellent levels of fidelity. Families were very pleased with the program as evidenced by the following quote: 'From my perspective, she has been less stressed during the day. She still says she's tired, but not as much. Emotionally she's different, like happier. She still struggles, but I've noticed a change for the positive in her...'. Analysis of baseline and intervention data is in progress.

Discussion: This pilot study shows that sleep education can be extended to community practices, allowing families to receive behavioral sleep education in a familiar location with lower wait times. Partnering with community therapists to deliver such education to families provides an opportunity to broaden access to sleep therapeutics in the community, while forging collaborations between board-certified sleep medicine physicians and primary care providers. One community therapists commented on her involvement in the study by stating, 'Adequate sleep makes such a big difference in how the whole family functions. Now that I have been trained in sleep hygiene, this is an area that I regularly ask my families about, because now I have a way to help solve some of their sleep problems'.
Take a selfie!: Toddlers' understanding of the representational function of pictures

Presenter: Merna El-Rifai  (merna.el-rifai@vanderbilt.edu)

Authors: Merna El-Rifai, Rafat Hossain

Introduction: In 1994, DeLoache and Burns reported that 2-year-olds did not use a photo as a clue to find a hidden toy. Typically, children in the developed world saw pictures all around them. These pictures differed in their relation to reality: Family photos depicted familiar people at some point in the past (e.g., vacation photos from Disneyland). Pictures in books ranged from realistic to fantasy. Historically, picture-referent relations have not been simple to understand. However, very young children's exposure to pictures has changed recently. Today, most parents carry smartphones with cameras, using them to take frequent photos. Children can see a family 'selfie' photo on the screen as it is being taken and view it immediately afterward. Therefore, children today may have a different concept of how pictures relate to reality than children used to. As has been the case with experience with live video (e.g., Nielsen, Simcock, & Jenkins, 2008; Troseth, 2003; Troseth, Saylor, & Archer, 2006), new experience with pictures might change how children learn from the medium.

Methods: In the research to be presented, we examine 2-year-olds' use of photos in a DeLoache-style search task. In two conditions, a researcher shows children the place where 'Piglet' is hidden using small photos displayed either in frames (DeLoache & Burns, 1994; Troseth, 2003) or on an iPhone. In a third (training) condition, the researcher shows children how photos of the furniture can be taken on the iPhone. Then, during the hiding/search task, the researcher tells the child she will go hide Piglet, take a picture on the phone of where she hid him, and come back to show the child the picture.

Results: Data collection is ongoing. All potential results will update us about early symbolic development today. Possible outcomes: 1) A 2-year-olds successfully using photos for information about a real, current event would suggest that children's substantial experience with photos is advancing their early symbolic development. Alternatively: 2) toddlers may succeed in the iPhone version but not with photos in frames. Finally, 3) children may need the connection between a photo and reality to be pointed out. If children succeed in a condition, transfer tasks will probe the depth of their understanding; the need for more explicit training would indicate the kind of scaffolding that supports early pictorial competence.

Discussion: The current research suggests that, even with the exposure to picture-taking that is common for today's toddlers, thoughtful adult scaffolding is important to help these young users of media understand how images can communicate information relevant to real, current events. In future research, we will use transfer tasks to examine the depth of toddlers' understanding about images.


Intra-insular connectivity and somatosensory responsiveness in young children with ASD

Presenter: Michelle Failla  (michelle.failla@vanderbilt.edu)

Authors: Michelle D. Failla, Brittany R. Peters, Haleh Karbasforoushan, Jennifer H. Foss-Feig, Kimberly B. Schauder, Carissa J. Cascio

Introduction: The human somatosensory system comprises dissociable paths for discriminative and affective touch, reflected in separate peripheral afferent populations and distinct cortical targets. Differences in behavioral and neural responses to affective touch may have an important developmental role in early social experiences, which may be relevant for autism spectrum disorder (ASD). We examined structural integrity of two sensory-related white matter pathways: 1) thalmocortical (sensory thalamus to primary somatosensory cortex) and 2) intrainsular (posterior to anterior insula). The thalmocortical tract carries discriminative tactile information, while the intrainsular represents the cortical projection target of unmyelinated tactile afferents mediating affective touch (posterior insula) and integration of sensory and visceral inputs to interpret emotional salience of sensory stimuli (anterior insula). We hypothesized structural integrity in these pathways would mediate variability in behavioral responses to affective touch in young children with ASD.

Methods: Using diffusion tensor imaging and probabilistic tractography, we investigated the structural integrity of the thalmocortical and intrainsular tract by comparing fractional anisotropy, mean diffusivity, and tract volume in a group of young children with ASD and a group of typically developing (TD) peers. Within the ASD group, we also assessed association of tract integrity with a standardized observational assessment of both tactile discrimination and affective response to social touch.

Results: There were no group differences in white matter integrity in either tract investigated. Consistent with previous findings, the ASD group exhibited impairment in tactile discriminative ability and aberrant affective responses (both positive and negative in valence) to touch. In the ASD group, intra-insular tract integrity was associated with external touch localization. Associations between tactile seeking behavior, characterized by positive affective behavioral response and unusually intense interest in tactile stimuli, significantly differed by group. In the ASD group, increased intra-insular tract integrity was associated with more seeking behaviors while the opposite was true in the TD group. Reduced integrity in thalmocortical tracts was associated with increased tactile defensiveness across both groups.

Discussion: While there were no group differences in overall tract integrity, relationships between tract integrity and behavioral responses differed in the ASD group. These results are in line with previous findings that positive affective response to touch is mediated by somatosensory input to the posterior insular cortex. They further suggest that the neural substrate for propagation of this input to affective evaluation networks may be altered in ASD.
Animal-Assisted Interventions Enhance Quality of Life for Pediatric Cancer Patients

**Presenter:** Ashley Fallon (ashley.e.fallon@vanderbilt.edu)

**Authors:** David DeGrood, Megan Duffy, Aubrey Hord, Mary Jo Gilmer

**Introduction:** More than 40,000 children undergo cancer treatment in the United States every day and over 13,500 are diagnosed with cancer each year. Although survival rates have improved greatly, lingering psychological and behavioral effects may negatively impact cancer survivors and their families. Improving quality of life during treatment for childhood cancer patients and their families remains a concern. This longitudinal study 1) examines the physiological and psychological impact of canine interventions on children with cancer and their parents, and 2) establishes efficacy of animal-assisted interventions (AAI) in promoting positive quality of life outcomes among children recently diagnosed with cancer and their parents.

**Methods:** Baseline data were collected from children newly diagnosed with cancer (N=33), mothers (N=33), fathers (N=17), therapy dogs (N=3) and owners (N=3). Families were randomized to usual care or intervention groups. Each intervention consisted of an approximately 15 minute AAI session at the start of a weekly clinic visit. Researchers collected physiologic data (pulse, B/P, and cortisol level of dog’s saliva), psychological data (anxiety, quality of life, inventory of difficult events for parents), and a video-recording at each AAI session across 4 months.

**Results:** Children and parents in the intervention group reported less anxiety and enhanced quality of life when compared with families in the usual care group. These preliminary findings demonstrate a positive effect of AAI on self-reported quality of life of children who have recently received a cancer diagnosis and their parents.

**Discussion:** This study, funded by the American Humane Association, contributes to the state of science on palliative care. These findings validate the use of AAI as an ancillary service to support the psychosocial well-being of children when visiting the clinic for cancer treatment. This study links the positive quality of life outcomes with participation in AAI sessions and can be used to further inform best practice and encourage increased use of AAI with children with cancer.
Contributions of Morphological Knowledge and Vocabulary to Reading Comprehension

Presenter: Jacob Feldman (jacob.i.feldman@vanderbilt.edu)

Authors: Jacob I. Feldman, C. Melanie Schuele

Introduction: Morphological knowledge - 'knowledge of the internal, meaning-related structure of words' (McCutchen, Green & Abbott 2008, p. 289) - and vocabulary knowledge are argued to contribute to reading comprehension (Nagy, Carlisle, & Goodwin, 2014; Scarborough, 1990). There is a strong relation between morphological knowledge and vocabulary knowledge (McCutchen et al., 2008), which makes it difficult to examine their unique contributions to reading comprehension. A commonly used experimental measure of morphological knowledge is the Test of Morphological Structure (TMS; Carlisle, 2000), which consists of Derivation and Decomposition subtests. Carlisle (2000) found that the TMS was highly correlated with vocabulary in third graders ($r = 0.40$). Additionally, the TMS did not uniquely account for variance in reading comprehension in third grade but did account for 13.7% of the variance in fifth grade, though in those analyses study vocabulary and decoding abilities were not controlled (Carlisle, 2000). The purpose of the present study was to examine the unique and shared contributions of morphological knowledge and vocabulary to reading comprehension. It was hypothesized that vocabulary would uniquely account for more of the variance in reading comprehension than morphological knowledge.

Methods: Participants were 52 monolingual third graders (25 boys, 27 girls) aged 8;2 to 10;0 (Mage = 8;11) from four parochial schools in Nashville, TN. The children were drawn almost exclusively from families with college-educated parents. All participants were administered the following measures: the Peabody Picture Vocabulary Test-4 (PPVT-4; Dunn & Dunn, 2007), the Expressive One Word Vocabulary Test-4 (EOWPVT-4; Brownell, 2010), the Word Test 2-Elementary (WORD-2; Bowers, Huisingh, LoGiudice, & Orman, 2004), the Passage Comprehension (PC) and Word Identification (WID) subtests of the Woodcock Reading Mastery Tests, (WRMT-III; Woodcock, 2011), and the two subtests of the TMS.

Results: Multiple regression analyses were completed to examine the contribution of vocabulary knowledge and morphological knowledge to reading comprehension after controlling for participants’ age and word identification abilities. The full model accounted for about 49% of the variance in reading comprehension. Morphological knowledge was the only significant unique factor. Analyses indicate that vocabulary knowledge and morphological knowledge jointly account for a moderate proportion of the variance in reading comprehension (23.61%). The proportion of the variance uniquely attributed to the TMS (6.99%) is larger than that of vocabulary knowledge (2.46%).

Discussion: A multiple regression was conducted with age, word identification skills, morphological knowledge and vocabulary knowledge to account for variance in reading comprehension. The full model was significant, with morphological knowledge the only unique significant factor. It was hypothesized that vocabulary knowledge would account for a larger proportion of the variance than morphological knowledge. In this model, both the vocabulary knowledge composite and the morphological knowledge composite uniquely accounted for a small proportion of the variance, with the proportion uniquely attributed to morphological knowledge greater than that of vocabulary knowledge. The shared influence of morphological knowledge and vocabulary knowledge accounted for the largest proportion of variance.

References:
Control of BNST CRF neurons by norepinephrine and stress.

Presenter: Tracy Fetterly (tracy.l.fetterly@vanderbilt.edu)

Authors: Tracy L. Fetterly, Elias K. Awad, Yuval Silberman, Danny G Winder

Introduction: Stress has been implicated as a primary contributor to many disease states. Numerous studies suggest that stress can elevate norepinephrine (NE) levels to enhance corticotropin releasing factor (CRF) signaling and increase neuronal activity in the bed nucleus of the stria terminalis (BNST), a brain region critical to many behavioral and physiologic responses to stressors.

Methods: We are using both electrophysiological and immunohistochemical techniques to study the effects of stress and NE on BNST CRF neuron excitability and neurotransmission. We are able to specifically identify CRF neurons through the use of a CRF-tdtomato reporter mouse line (strain B6(Cg)-Crhtm1(cre)Zjh/J crossed with strain B6.Cg-Gt(Rosa)26Sor<tm14(CAG-tdTomato)Hze>/J).

Results: We have shown that NE can depolarize BNST CRF neurons, and that this depolarization is sensitive to a β-adrenergic receptor (AR) antagonist. Conversely, NE inhibits glutamatergic transmission onto BNST CRF neurons via an α-AR dependent mechanism, suggesting that AR subclasses may work to balance the excitability of BNST CRF neurons. In order to further understand NE regulation of glutamatergic transmission, we used an optogenetic mapping technique to identify glutamatergic afferents that synapse directly onto BNST CRF neurons. We used an AAV-CamKII-ChR2-YFP virus to express channelrhodopsin in brain regions known to send glutamatergic projections to the BNST and then monitored BNST CRF neurons for the presence of an optically-evoked excitatory post-synaptic current (oEPSC). We find that CRF neurons receive input from both the insular cortex and the parabrachial nucleus. Focusing on the insular cortex input, we found that the α2a-AR agonist guanfacine decreases oEPSC amplitude when stimulating the insular input specifically. To investigate the recruitment of these BNST CRF neurons by stress, we measured cFos expression following 1-hr restraint stress exposure. Restraint stress exposure increased cFos labeling in BNST CRF neurons and this increase was attenuated by either propranolol, a β-AR antagonist or guanfacine.

Discussion: Together, these results suggest a role for the insula to BNST CRF projection as an important site of stress actions and may underlie known actions of guanfacine, including its modulation of depressive phenotypes and body mass.
**Metabotropic glutamate receptor 7 as a therapeutic target in MECP2-related disorders**

**Presenter:** Nicole Fisher (nicole.m.fisher@vanderbilt.edu)


**Introduction:** Rett syndrome (RS) results from a mutation in the gene encoding Methyl-CpG-Binding Protein 2 (MeCP2), while an extra copy of the gene leads to MECP2 Duplication syndrome (MDS). These disorders share a significant number of symptoms (e.g., motor dysfunction, cognitive impairments, seizures), suggesting that certain pathways may be similarly disrupted between the two disorders and amenable to a common therapeutic strategy.

**Results:** We have found that GRM7, the gene encoding the metabotropic glutamate receptor 7 (mGlu7), is activated by MeCP2 binding to its promoter. mGlu7 is expressed presynaptically throughout the brain and regulates neurotransmitter release. We have observed dramatic reductions in mGlu7 expression in samples from Mecp2-deficient mice and importantly, in samples from RS patients. Furthermore, potentiation of mGlu7 activity with a positive allosteric modulator (PAM) ameliorates deficits in hippocampal long-term potentiation, contextual fear conditioning, and social recognition memory in Mecp2-deficient mice. This work was supported by grants from R21 MH102548, a Treatment Award from Autism Speaks, and rettsyndrome.org. We currently hypothesize that MeCP2 overexpression might drive increased mGlu7 protein levels in MeCP2-Tg1 mice, a model for MDS. While mGlu7 is indeed mildly overexpressed in the hippocampus of MeCP2-Tg1 mice, an mGlu7-selective negative allosteric modulator (NAM) has no effect on behavioral phenotypes. Interestingly, we have found that a PAM with activity at mGlu7 attenuates conditioned fear responses and normalizes anxiety-like behavior in symptomatic MeCP2-Tg1 mice. These findings suggest that potentiation of mGlu7 activity may have therapeutic potential in models of both RS and MDS. Intriguingly, we have recently observed that mice lacking mGlu7 exhibit fore- and hindlimb clasping phenotypes, along with spontaneous seizures, suggesting that impaired mGlu7 function may contribute to multiple symptoms observed in MeCP2-related disorders.
Analysis of the Minimum Data Set in a Long-Term Care Facility - Correlations with Spasticity Diagnosis

Presenter: William Steele Fisher  (william.s.fisher@vanderbilt.edu)

Authors: William Fisher, Taylor Hudson, Maxim Turchan, Chandler Gill, Amanda Currie, Anna Molinari, Fenna Phibbs, Christopher Tolleson, Mallory Hacker, David Charles

Introduction: Spasticity is a prevalent movement disorder in residents of long-term care facilities [1]. The prevalence of spasticity was evaluated in residents of a long-term care facility, and these patients were also regularly assessed using the Minimum Data Set (MDS), a standardized, comprehensive assessment of each resident's functional capabilities that assists staff in identifying health problems. An analysis was conducted to identify elements in the MDS that correlate with the presence of spasticity.

Methods: Residents of a long-term care facility who provided informed consent were eligible to participate in this IRB-approved study (IRB#090361, NCT01644123). Two neurologists conducted examinations for the presence of spasticity in 39 participants. MDS data was evaluated in patients with (n=12) and without (n=27) a spasticity. The significance of the relationship between spasticity and other factors was determined using chi-squared tests of contingency and Mann-Whitney U Tests.

Results: The areas of the MDS that were evaluated were stroke, epilepsy, depression, dementia, pain presence/intensity, urinary incontinence, bowel incontinence, age and activities of daily living. None of these factors were found to be significantly correlated with the presence of spasticity; however, there was a trend for an association of spasticity with history of stroke (p=0.08) and lower age (95% C.I.: Spasticity = 76.67 ± 2.94; Without spasticity = 79.79 ± 5.30; p=0.14).

Discussion: Since spasticity is prevalent in residents of long-term care facilities, it's important to explore its relationship with or impact on other health factors. Although none of the conditions investigated reached statistical significance, this MDS analysis did reveal a trend for an association of stroke and lower age with the prevalence of spasticity. A larger sample size is needed in order to make definitive correlations between the concurrence of these conditions and spasticity. Further investigation is needed and determining the relationship between spasticity and other conditions may improve care and quality of life for residents in long-term care facilities.

Language Brokering during Shared eBook Reading

Presenter: Israel Flores (israel.flores@vanderbilt.edu)

Authors: Israel Flores

Introduction: In sociocultural theories of cognitive development, the dominant form of information transmission is from a more skilled adult to a less skilled child (Vygotsky, 1978). Among immigrant communities in America, those roles can be reversed when young bilingual children are asked to serve as 'language brokers' between their non-English-speaking parents and English-speaking society (McQuillan & Tse, 1995). These child language brokers facilitate their parents' communication with English speaking adults (e.g., doctors, teachers, government agents) by interpreting and translating written English documents and spoken English. Parents include their child as an active participant in adult conversations and ask follow-up and clarification questions of the child to gain information. This inversion of typical adult-child roles may have implications for the academic achievement and cognitive development of English-learning bilinguals. To date, only a handful of studies have examined language brokering in children younger than 8 years (Perry, 2009; Lee, Hill-Bonnet, & Raley, 2011; Straits, 2010), so little is known about how this practice develops or its usefulness as an academic tool.

Methods: In the research to be presented, we probe whether language brokering can be repurposed to directly benefit 5- to 7-year-old bilinguals' vocabulary acquisition and story comprehension. Two conditions are used to examine the usefulness of language brokering as a learning tool. In the language brokering condition, a Spanish speaking researcher asks children to interpret a short story from English to Spanish and answer questions about the story. In a second, control, condition the Spanish speaking researcher simply listen to the story with the children, twice. Children complete the Bilingual Expressive One Word Picture Vocabulary test, story specific vocabulary assessments before and after the story, and a story comprehension measure.

Results: Data collection is ongoing and all potential results will provide us with new information about language brokering abilities in children under the age of 8, as well as its usefulness as a learning tool. We predict that children in the language brokering conditions will outperform children in the Spanish control group, who merely hear the story in English. Alternatively, complex task demands may limit what children can learn during language brokering, supporting a 'cognitive overload' explanation for bilingual children's academic struggles. If that is the case, group differences can provide evidence for future interventions.

Discussion: The current project aims to see if child skills around language brokering could be turned toward serving the child's language development. Thus, it is a strength-based approach that depends on parents and children's use of a common cultural practice to promote English language acquisition.


A role for NFκB in Schwann cell dedifferentiation associated with Charcot-Marie-Tooth disease

Presenter: Rose Folis  (rose.m.follis@vanderbilt.edu)

Authors: Rose Follis, Malathi Narayan, Sabina Dang, Jun Li, Bruce D. Carter

Introduction: Charcot-Marie-Tooth (CMT) disease is the most common inherited peripheral neuropathy, affecting 1 in 2500 people in the United States. Patients with CMT suffer from progressive axonal degeneration, often provoked by Schwann cell dedifferentiation and myelin degradation, resulting in sensory and motor deficits. Unfortunately, there is no treatment for CMT, making development of targeted drug therapies a priority.

Methods: A murine model of CMT1E, the Trembler-J (TrJ) line, carries a spontaneous point mutation in the gene encoding Peripheral Myelin Protein 22 (PMP22). The mutation causes severe motor and sensory deficits, as well as pathological Schwann cell demyelination. Additionally, TrJ Schwann cells have abnormal PMP22 retention in the Endoplasmic Reticulum (ER), and activation of ER stress pathway Ire1α. Moreover, we have found that TrJ mice display NFκB activation, a pathway downstream of Ire1α, in mature sciatic nerves.

Results: During myelin formation, NFκB acts as a transcriptional regulator in immature Schwann cells, but is suppressed in the mature, myelinated Schwann cells. Interestingly, when we induced aberrant activation of NFκB in normal adult sciatic nerves though adenoviral infection, there was an acute degradation of myelin. Therefore, we hypothesize that ER stress induces aberrant activation of NFκB through Ire1α pathway signaling, which, in turn, promotes alterations in Schwann cell differentiation, contributing to the loss of functional myelin observed in dys/demyelinating CMT.

Discussion: To test this hypothesis we will further elucidate the relationship between NFκB activation and Schwann cell dysmyelination by inducing NFκB activation in embryonic Schwann cells, using a targeted Desert Hedgehog (DHH) Cre transgenic model, and assessing the effects on myelin integrity and formation.
An International Case Study Illustrating Disability Inclusion in Action

Presenter: Anjali Forber-Pratt (anjali.forber.pratt@vanderbilt.edu)

Authors: Anjali J. Forber-Pratt, Dominique Lyew, Leah Samples

Introduction: Sharma and Das (2015) report that the majority of children with disabilities in India still remain out of school. Girls with disabilities face particular struggles to receive quality education in this context (Sahni & Sankar, 2012). India has been moving towards special and inclusive education with its mandate of Education for All (Singal, 2006b), however major challenges still include: training and supporting teachers in inclusive classrooms (Hettiarachchi & Das, 2014; Shah, Das, Desai, Tiwari, 2014), promoting true inclusivity in the classroom and ensuring effective student learning for all students (Singal, 2008). In addition, it has been found that teachers in the Indian school system can hold harmful views about the causes of disability (Singal, 2008). Two previous case studies aimed to provide a fuller picture of the state of special education in the Indian context (Barnes, Gibb, Ashbaker & Prater, 2014; Byrd, 2010), however, missing from these perspectives are also the student voices.

Methods: This case study involved one-on-one interviews, classroom observations, and document analysis. Semi-structured individual interviews with consented participants lasted between 60-90 minutes. Artifacts analyzed included blog posts, annual reports, photographs, news articles and brochures. 32 participants were interviewed and/or observed: 13 students (ages 3-16), 6 childcare workers, 7 teachers, 4 administrative staff (who held dual roles) and 2 board members.

Results: Results were grouped by the following themes: Peer supports Individual Learning Needs Other supports (Resources and Learning Pathways)

Discussion: The model of inclusive education used by Shishur Sevay is designed to impart knowledge and skills while also developing ways the children can communicate their feelings and needs. Having a foundation of inclusion that permeates social interactions, learning, living and recreation is part of what makes Shishur Sevay unique. They are an inclusive school in a part of the world where many may think would be impossible.


Overlooked and Underserved: Disability Status and Access to Public Benefits Among Homeless Families

Presenter: Zachary Glendening  (zachglendening@gmail.com)

Authors: Zachary S. Glendening, Erin J. McCauley

Introduction: Though homelessness and disability both receive considerable academic attention, the same cannot be said for their intersection. This study explored the prevalence and influence of disability status and SSI/SSDI benefit receipt among families experiencing homelessness. It also compared the influence of various housing interventions on SSI/SSDI receipt.

Methods: We used descriptive statistics to examine the prevalence of work-limiting disabilities among homeless family members and the extent to which homeless families reporting disabilities received SSI/SSDI. We used linear and logistic regression to examine (a) the extent to which disabilities influenced family course of homelessness and self-sufficiency; (b) the extent to which SSI/SSDI benefits influenced family course of homelessness and self-sufficiency; and (c) whether offers of permanent housing subsidies, temporary rapid re-housing subsidies, or project-based transitional housing affected SSI/SSDI receipt 20 months after shelter entry. This study used interview data from a 12-site, random assignment experiment called the Family Options Study.

Results: At shelter entry, 29% of respondents reported a disability in their family. Twenty percent of respondents reported a work-limiting disability in the family. At shelter entry, 24% of families reporting a disability received SSI/SSDI. This number increased to 32% at 20-month follow-up. Similarly, the proportion of those reporting work-limiting disabilities increased from 23% at shelter entry to 31% at follow-up. Disabilities significantly increased housing instability, food insecurity, and economic stress while decreasing work activity. Receipt of SSI/SSDI decreased returns to emergency shelter among families in this study. Benefits also slightly decreased work activity while increasing family income. Among respondents reporting an adult family member with a disability, permanent housing subsidies significantly improved access to SSI/SSDI.

Discussion: Given that 72% of respondent-identified family members with disabilities were under age 15, support for homeless families experiencing disabilities constitutes a child protection issue. Whereas nearly a third of homeless families reported a member experiencing disability, only a quarter of those families received SSI/SSDI at shelter entry. Though this number increased over time, most families remained unsupported at follow-up. Findings suggest that disabilities within homeless families reduce work activity, thereby disrupting physical and economic well-being. By increasing income, SSI/SSDI benefits appeared to improve the financial conditions and housing stability of families in this study. Furthermore, permanent housing subsidies appeared to increase SSI/SSDI receipt for homeless families reporting a disabled adult. Perhaps due to low sample sizes in housing intervention analyses, we found no other housing intervention effects. However, the overall strength and direction of permanent subsidy effects suggest that subsidies exert a stronger influence on SSI/SSDI receipt than our findings indicate.
Arginase-II protein expression changes with manganese exposure and genotype in Huntington's disease mouse models

**Presenter:** Timothy Halbesma  (t.halbesma@vanderbilt.edu)

**Authors:** T. Halbesma, T.J. Bichell, E.M. Bradley, K.G. Tipps, N. Fisher, V. Manglione, A.B. Bowman

**Introduction:** Trinucleotide CAG expansion in the Huntingtin (HTT) gene results in the translation of a harmful polyglutamine-expanded protein with toxic properties that cause Huntington's disease (HD). HD patients exhibit motor, cognitive, and psychological deficits with profound preferential neurodegeneration in the striatum. Altered metal homeostasis has been linked to neurodegenerative diseases. Expression of mutant HTT protein is associated with a deficit in striatal manganese (Mn) accumulation in the YAC128Q transgenic mouse model of HD. The urea cycle enzyme arginase-II (ARG2) requires Mn to stabilize the multiprotein complex and to hydrolyze arginine to urea and ornithine. Thus, impaired Mn handling may alter arginine metabolism in the HD brain.

**Methods:** We investigated the HD-ARG2-Mn interaction by treating YAC128Q mice with Mn. Male pre-symptomatic stage (12 week) mice were injected subcutaneously with 13.88 mg/kg Mn or vehicle on experimental days 0, 3 and 6. They were dissected on experimental day 7 for the striatum and other regions. B6CBA-R6/2 mice were also dissected and examined. These transgenic mice model a more advanced form of HD, developing severe symptoms as early as 15 weeks. Tissues from both strains were examined for ARG2 content by western blot.

**Results:** YAC128Q ARG2 protein expression in brain was significantly increased by subcutaneous exposure to Mn. ARG2 expression levels did not detectably differ between genotypes in YAC128Q mice. R6/2-model HD mice, which are at a later stage of degeneration, did however show a baseline decrease in ARG2 protein levels.

**Discussion:** ARG2 protein expression is Mn-responsive in a pre-symptomatic mouse model of HD and levels are deficient in the more advanced HD model. This, combined with a previously reported neuronal Mn-handling defect caused by HD, leads to the notion that Mn homeostasis is crucial in regulating cellular functions, and its dysfunction-presumably caused by mutant HTT-disrupts key pathways. Although there was no difference in ARG2 expression at baseline in the YAC128Q mice, the R6/2 mice showed a deficit in ARG2 in mutants compared to wild type. Our findings suggest Mn exposure may rescue a baseline deficit in ARG2 protein expression in HD mice at the symptomatic stage.
Uncovering the effects of agonism at postsynaptic α2A-adrenergic receptors on neuronal activity within the bed nucleus of the stria terminalis

Presenter: Nicholas Harris  (nicholas.a.harris@vanderbilt.edu)

Authors: Nicholas A. Harris, Austin T. Isaac, Michelle A. Xu, Stephanie A. Flavin, Robert T. Matthews, Danny G. Winder

Introduction: Stress is a major risk factor for relapse to drug-seeking behavior. The bed nucleus of the stria terminalis (BNST) receives an extensive noradrenergic input and has been shown to be critical in stress-induced relapse to drug-seeking behavior. In rodents, systemic or intra-BNST treatment with α2-adrenergic receptor agonists decreases stress-induced reinstatement behaviors. Clinical studies report that guanfacine, an α2A-AR agonist, curbs cravings for a variety of substances of abuse. We have previously shown that α2A-ARs are heavily expressed in the BNST, and that noradrenergic signaling in the region is dramatically altered in α2A-AR knockout mice. Data suggests that competing inhibitory and excitatory actions of this drug in the BNST could reflect carefully coordinated control of BNST activity. Our lab has shown inhibitory effects of guanfacine in the BNST on electrically evoked EPSCs and optically evoked EPSCs derived from parabrachial nucleus (PBN) afferents, consistent with canonical presynaptic Gαi signaling. In contrast, in a Thy1-COP4 transgenic mouse line, where ChR2 expression is drastically reduced in PBN afferents relative to others, bath application of guanfacine enhances optically evoked field potentials. In addition, systemic guanfacine is known to initiate c-fos expression in BNST neurons.

Methods: These findings led us to pursue mechanistic studies of this effect. To accomplish these, we combine RNA in situ hybridization experiments with immunohistochemistry and electrophysiological techniques.

Results: Using RNAscope in situ hybridization, we show that systemic guanfacine leads to 90% co-localization of c-fos with adra2a (α2A-AR) RNA, as compared to 10% co-localization after saline. Interestingly, ~50% of cells that express c-fos do not co-express adra2a RNA, suggesting potential involvement of an underlying BNST microcircuit in this effect. We hypothesize that this novel excitatory effect occurs via activation of postsynaptic α2A-ARs leading to decreased cAMP-dependent opening of hyperpolarization-activated cyclic nucleotide-gated nonselective cation (HCN) channels. This hypothesis is based on an observed Ih prevalence of 80% in c-fos+ cells after systemic guanfacine in a c-fos-eGFP mouse line, as well as enhanced excitatory field potential responses in Thy1-COP4 BNST slices after HCN inhibition by ZD7288. However, RNAscope experiments show little co-localization of adra2a and hcn1 RNA, suggesting either hcn2 involvement or independent mechanisms of activity enhancement. In addition, whole cell recordings show that guanfacine preincubation does not affect the amplitude of Ih in c-fos+ BNST neurons after systemic guanfacine.

Discussion: In conclusion, we have shown that postsynaptic α2A-ARs within the BNST elicit c-fos expression after intraperitoneal injections, suggesting excitatory action. Mechanistic studies suggest HCN channel involvement; however, HCN1 channels do not co-localize with α2A-AR receptors in BNST. Future studies will test the involvement of HCN2 channels and other candidates in guanfacine enhancement of BNST activity.
Endocannabinoid regulation of glutamatergic input onto central amygdalar CRF neurons.

Presenter: Nolan Hartley  (nolan.d.hartley@vanderbilt.edu)

Authors: Nolan D. Hartley, Alexis Jameson, Sachin Patel

Introduction: The central amygdala (CeA) is a limbic brain structure largely responsible for the generation of threat adaptive behaviors in response to highly salient stressors. Corticotropin releasing factor (CRF) signaling within the CeA has been shown to positively contribute to fear and anxiety phenotypes, and the use of knock in and transgenic reporter lines has allowed for reliable identification of CRF expressing (CRF+) neurons in this region. However, very little is known about how the activity of these neurons can regulate the expression of threat adaptive behaviors following stress exposure, and whether their activity is susceptible to endogenous feedback mechanisms aimed at decreasing stress-induced behavioral responses.

Methods: Here, we use optogenetic circuit mapping techniques, combining microscopy and whole-cell patch clamp electrophysiology to assess how specific ascending and descending glutamatergic inputs to the CeA regulate CRF+ neuronal activity. Using these techniques we probed each of these inputs for evidence of endocannabinoid (eCB)-mediated plasticity, a form of retrograde signaling resulting in suppression of neurotransmitter release.

Results: We report that CRF+ neurons receive the greatest input from descending cortical-like structures, over ascending inputs from the parabrachial nucleus, and that cannabinoid signaling capacity is greatest at these descending inputs. Furthermore, we identify forms of short-term and long-term eCB-mediated plasticity at specific inputs, suggesting that eCBs regulate CeA function via suppression of glutamate release onto CRF+ neurons.

Discussion: Therefore, we propose that eCB signaling in the CeA may serve as a homeostatic feedback mechanism, which is recruited following stress exposure to decrease excitatory drive onto CRF+ neurons. This form of signaling may ultimately normalize stress-induced behavioral responses.


**Loss of Jedi-1 results in increased proliferation of neural precursor cells**

**Presenter:** F. Edward Hickman  (francis.e.hickman@vanderbilt.edu)

**Authors:** F. Edward Hickman, Elizabeth Crummy, Rebecca Ihrie, Bruce D. Carter

We previously identified Jedi-1 as an engulfment receptor necessary for clearance of apoptotic sensory neurons in the dorsal root ganglia during normal development. Its role in the central nervous system, however, has not been investigated. In the perinatal (p6) mouse, we detected Jedi-1 mRNA expression primarily in endothelial cells, using a LacZ reporter mouse. However, we also found Jedi-1 expressed in neural precursor cells (NPCs) derived from the ventricular-subventricular zone (V-SVZ) of p6 mice. While neurogenesis in the developing mouse is complete by post-natal day 0 (p0), proliferation of stem cells continues in both the V-SVZ and subgranular zone of the dentate gyrus of the hippocampus (SGZ). Interestingly, NPCs derived from jedi-1-/- mice exhibited approximately a two-fold increase in proliferation relative to wild type, as observed by BrdU incorporation. Most proliferating cells were GFAP+ and Nestin+, common markers of early NPCs. As previously reported (Lu, 2011), we found NPCs have phagocytic ability, based on their ability to engulf carboxylated microspheres. Preliminary data indicate that jedi-1-/- NPCs do not have a deficit in engulfment capability, suggesting that Jedi-1 regulates proliferation of these cells through an alternate mechanism. Current experiments are aimed at assessing the regulation of NPC proliferation in vivo by Jedi-1.

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**Singing Away the Voices and Blues: Choral Intervention For AVH And Distress**

**Presenter:** Laura Hieber  (laura.l.hieber@vanderbilt.edu)

**Authors:** Laura Hieber Adery, Sohee Park

Widespread conceptions of individuals with schizophrenia (SZ) depict them as socially withdrawn by choice, as a result of anhedonia, or lack of desire for this interaction. Our previous work dispels this notion, revealing higher levels of loneliness in SZ than Healthy Controls. Increased loneliness is also found to correspond with increased debilitating symptoms overall in SZ. Thus, we next examine whether increasing social inclusion could be a highly beneficial treatment for increasing social accuracy and diminishing positive syndrome, as well as decreasing loneliness and distress in SZ. Given the multitude of demonstrated benefits of music, and in particular group musical experiences, and the overlapping neural recruitment between auditory hallucination (AVH) and melody production, we aim to determine the efficacy of a novel and naturalistic social intervention using group choral singing. We hypothesize that increased social stimulation inherent in the intervention, combined with benefits of choral singing, at neural and behavioral levels, will increase participant sense of well-being and reduce loneliness, potentially with decreased AVH experience. Preliminary findings will be highlighted from the study and pilot testing (n=6), conducted using measurements of cognitive capacity, perceptual acuity, pain sensitivity and self-report questionnaires to measure loneliness and social satisfaction in participants prior to and following an 8 week intervention phase.
Embodied Emotions in Schizophrenia

Presenter: Seok Jin Hong (seok.jin.hong@vanderbilt.edu)

Authors: Seok Jin Hong, Matthew A. Snodgress, Heathman S. Nichols, Lauri Nummenmaa, Enrico Glerean

Introduction: Schizophrenia is associated with abnormally experienced affect and bodily sensations. As such, individuals with schizophrenia (SZ) may experience the embodiment of affect differently than those within a normal population. In the current study, participants with SZ and healthy controls (HC) were asked to complete a self-report task about how they embody different emotions, a paradigm adopted from a prior Finnish study. We posited that the underlying phenomena giving rise to embodied emotions in HC should be more prominent than those of a SZ sample. Specifically, two separate principal components analyses (PCA) were conducted, one for each sample, in order to assess our hypothesis.

Methods: Ten participants with SZ and ten HC were asked to complete the emBODY task adopted from Nummenmaa et al. 2014. In the task, participants colored in maps of the human body in reference to emotion labels they were given. For example, after presenting the emotion label happiness, participants identified portions of the human body in which they personally feel happiness. Thirteen emotion labels were presented in addition to one neutral label. The embodiment patterns were analyzed with PCA to determine the size and number of underlying dimensions giving rise to our results.

Results: In accordance with our hypothesis, the pattern of principal components for HC differed significantly from that of the SZ sample. SZ participants showed more diffuse components with lesser magnitude than the HC sample. In addition, the amount of variance accounted for by these dimensions was significantly reduced for SZ, suggesting a relatively abnormal report of embodied emotion.

Discussion: A particular set of innate constructs should give rise to the report of embodied emotions. Our results imply that the complexity of this set is highly deviant from the normal population. This outcome has implications for studying the mind-body connection of SZ patients and how interoceptive awareness links onto psychotic symptomology. Further, understanding the underlying structure of reported embodied emotion in the healthy population holds potential for classifying sub categories of emotional abnormalities in SZ. While an important first step, our analysis was exploratory and limited by its small sample size. In future iterations of our study, we anticipate a) increasing our sample size and b) probing the contents of the underlying dimensions that give rise to embodied emotions.

Word learning in good and poor comprehenders: A distinct learning profile for children with S-RCD

Presenter: Neena Hudson  (neena.m.saha@vanderbilt.edu)

Authors: Neena M. Hudson, Nicole Landi, Laurie Cutting

Introduction: Vocabulary is a critical element of successful comprehension, however, few (if any) studies have investigated how children with differing reading ability learn words across contexts.

Methods: 87 4th-8th graders were divided into one of three groups based on reading ability: children with dyslexia (DYS), children with specific poor comprehension (S-RCD), and typically developing readers (TD). The word-learning paradigm presented words either in isolation or in context, with a test of meaning after each trial. Additionally, decoding of learned words was assessed in a test of rapid naming, and meaning was assessed in a sentences task.

Results: There were significant group differences in all three phases of the learning paradigm: overall percent correct $[F(2,77)=9.64, p < .001]$, mean reaction time on rapid naming $[F(2,81)=8.16, p = .001]$, and overall percent correct on sentences $[F(2,77)=8.03, p = .001]$. Post-hoc Tukey tests showed that TD performed significantly better than DYS & S-RCD on overall percent correct ($p < .001$) with no significant difference between S-RCD & DYS. During the rapid naming phase, S-RCD did not perform significantly worse than TD, whereas DYS was impaired ($p < .05$). Post-hoc tests of the sentences task showed that S-RCD and DYS performed significantly worse than TD ($p < .001$). Additionally, decoding errors were analyzed from the rapid naming trials of the learning paradigm to investigate whether S-RCD was as accurate (in addition to being as fast) as TD. Results of the ANOVA showed a significant between-group difference $[F(2,81)=94.082, p < .001]$, with post-hoc Tukey tests confirming that S-RCD & TD both showed significantly fewer errors than DYS ($p < .001$), and were not significantly different from each other.

Discussion: Children with S-RCD show a unique learning profile consistent with the literature that poor comprehenders may have a specific deficit of the semantic system that is dissociable from generally poor readers (DYS) and typical readers (TD). These results suggest that S-RCD is not simply a 'static' impairment, but affects the learning of new words, which has implications for educational practice.
The impact of 'neural noise' on abnormal perception and working memory in schizophrenia

Presenter: Megan Ichinose  (megan.ichinose@gmail.com)

Authors: Megan Ichinose, Woon Ju Park, Justin Hong, Duje Tadin, Sohee Park

Introduction: Working memory (WM) deficits are a core component of cognitive dysfunction in schizophrenia yet lack clear etiological explanation.[1] Much work points to schizophrenia-related difficulties in early WM stages of encoding perceptual information.[2,3] One hypothesis is that patients with schizophrenia (PSZ) create 'noisy' memory representations, leading to poor retrieval of the degraded perceptual signal.[4] Internal noise can be estimated by modelling performance on a visual discrimination task with the perceptual template model (PTM), which treats the perceptual system like a noisy amplifier to characterize relations between perceptual inputs and outputs.[5] Utilizing the PTM, this research will test whether PSZ exhibit higher internal noise during visual processing and whether this factor contributes to visual WM deficits.

Methods: PSZ and healthy controls (CON) completed a perceptual discrimination task which required deciding whether gratings were oriented to the left or right. Gratings varied on added external noise (static) and stimulus contrast. Internal noise was computed with the PTM as the contrast threshold at which accuracy was equally impacted by external noise and stimulus contrast. Participants also completed a visuospatial WM task, which required remembering grating orientations at various locations. Visual WM precision will be compared with internal noise metrics on the perceptual discrimination task.

Results: Hypotheses: PSZ will exhibit higher levels of internal noise on the perceptual discrimination task compared to CON. PSZ will also be less precise on the visual WM task. Greater internal noise should predict lower WM precision. Preliminary results are consistent with hypotheses: PSZ exhibit higher levels of internal noise than CON, requiring higher contrast at low levels of external noise to maintain accuracy. PSZ also demonstrate less precision in visual WM. Forthcoming data collection will determine relations between noise and visual WM.

Discussion: Preliminary findings suggest that PSZ experience higher levels of neural noise during visual perception. This work has implications for the NMDA-hypofunction model of schizophrenia, in which excitatory-inhibitory imbalance leads to noisier formation and maintenance of perceptual representations. Results have the potential to elucidate a common mechanism, neural noise, for perceptual and cognitive deficits in schizophrenia and inform cognitive targets for intervention.

Murray et al. (2014). Cerebral Cortex, 24(4), 859-872.
Spontaneous seizures in a genetic model of West Syndrome

Presenter: Laurel Jackson  (laurel.g.jackson@vanderbilt.edu)

Authors: Laurel G. Jackson, Shimian Qu, Robert L. Macdonald

Introduction: Epileptic encephalopathies are severe neurological disorders characterized by intractable seizures, cognitive deficits, and behavioral abnormalities. For example, West Syndrome patients experience infantile spasms that begin in the first year of life, and half of those patients have other seizure types including partial, myoclonic, tonic, and tonic-clonic seizures. The electroencephalogram (EEG) recordings from West Syndrome patients have a characteristic hypsarrhythmia pattern. Currently, there are no published models of genetic infantile spasms or West Syndrome. We have generated a mouse model expressing a West Syndrome-associated mutation in the GABA(A) receptor beta3 subunit GABRB3(N110D). We have previously shown by whole cell recordings in vitro that GABA(A) receptors containing GABRB3(N110D) have decreased amplitude and frequency; surface expression of mutant-containing receptors is similar to wild type receptors. This suggests that GABRB3(N110D) does not affect assembly and trafficking of GABA(A) receptor, but it impairs the receptor response to its agonist. In order to further investigate the effects of GABRB3(N110D), we have begun to characterize its effects in vivo. Validation of our knock-in mouse model will enable us to pursue studies into novel therapeutic avenues for West Syndrome.

Methods: In order to assess seizure phenotype, EEG headmounts (Pinnacle) were surgically secured to the skulls of wild type and Gabrb3(+/N110D) littermates. Using the Pinnacle system for video-synchronized EEGs, the mice were recorded for 24-hour periods. In addition, the mice were assessed for social interaction impairment and anxiety phenotypes using the three-chamber test and open field test, respectively. To test for differences in cognitive ability, the mice were tested in the Barnes Maze.

Results: Animals expressing GABRB3(N110D) have spontaneous seizures, including tonic-clonic, absence, myoclonic and tonic jerks, head and forelimb jerks followed by brief immobility. Using the Barnes Maze, no difference in learning and cognition was detected. The mutant mice exhibit behaviors suggesting impaired social interaction and anxiety phenotypes.

Discussion: The mutation GABRB3(N110D) was first identified in a patient with West Syndrome. After uncovering functional deficits associated with this mutation at the in vitro level, we have sought to understand the mechanism of its pathology by making a knock-in mouse model. Generation of a genetic model of West Syndrome has potential to reveal new therapeutic targets. While further studies are needed to complete the validation of this animal model, current results from the characterization of the Gabrb3(+/N110D) mice show a robust array of seizure phenotypes and behavioral data that align with the phenotype of West Syndrome.
Mechanisms of mGlu3-mediated synaptic plasticity in the prefrontal cortex

**Presenter:** Max Joffe  (max.joffe@vanderbilt.edu)

**Authors:** Max E. Joffe, Julie L. Engers, Craig W. Lindsley, P. Jeffrey Conn

**Introduction:** Dysregulation of synaptic plasticity is a key component underlying many psychiatric disease states. In particular, several poorly managed symptom clusters, i.e. deficits in cognition and motivation, are thought to be related to altered plasticity within of the prefrontal cortex (PFC). Recently, we demonstrated that metabotropic glutamate receptor subtype 3 (mGlu3) mediates long-term depression (LTD) of excitatory transmission in the mouse PFC and its function is required for a behavioral model of executive control. However, a mechanistic understanding of mGlu3-mediated plasticity is essential for the identification and evaluation of novel therapeutic uses.

**Methods:** To interrogate the mechanisms underlying mGlu3-mediated synaptic plasticity, we utilized whole-cell patch-clamp techniques to record excitatory postsynaptic currents (EPSCs) from layer 5 pyramidal neurons in the mouse PFC. We pharmacologically elicited mGlu3-dependent LTD with the mGlu2/3 agonist LY379268. Long-term potentiation (LTP) was generated by 2 Hz stimulation paired with depolarization. Input-specific glutamate release was evoked with 470 nm light stimulation 3-4 weeks after viral expression of channelrhodopsin-2 in PFC efferent regions.

**Results:** We corroborated previous findings by demonstrating that a selective negative allosteric modulator of mGlu3, VU0650786, blocked the induction of LTD induced by LY379268. Because mGlu3 is expressed presynaptically, postsynaptically, and on glia, we performed follow-up experiments to evaluate the functional site of action. Following mGlu3-LTD induction, we observed an increase in the coefficient of variation and a decrease in miniature EPSC frequency, suggesting reduced presynaptic release probability. Postsynaptic infusion of the calcium chelator EGTA also impaired mGlu3-LTD.

**Discussion:** In layer 5 of the PFC, the mechanism of mGlu3-LTD is consistent with production of a calcium-dependent retrograde messenger acting to decreases presynaptic release probability. We are continuing to explore the requisite signaling pathways to express mGlu3-LTD, including interactions with other metabotropic glutamate receptors and G protein-coupled receptors enriched on astrocytes and presynaptic terminals. A better understanding of how mGlu3 modulates PFC circuit function will be vital in the translation of novel mGlu3-directed therapeutics.
Differentiating Dialect from Disorder in a Child with Hearing Loss: A Case Study

Presenter: Kaitlyn Johnston  (kaitlyn.f.johnston@vanderbilt.edu)

Authors: Kaitlyn Johnston-Minchin, Caroline Remke, Jena McDaniel, C. Melanie Schuele

Introduction: Features of African American English (AAE) often overlap with speech and language features common in children with hearing loss, obscuring the difference between dialect and disorder. Children with hearing loss frequently exhibit distinctive speech and language features and errors (2,3,5). A child with hearing loss who uses a non-mainstream dialect also may present with dialect features that overlap with disordered features of Mainstream American English (MAE). Speech-language pathologists must differentiate dialects from disorders by understanding dialect features and being familiar with non-discriminatory assessment (1).

Methods: Issues of dialect, disorder, and hearing loss were examined in KW, an 8-year-old boy with asymmetrical mixed conductive-sensorineural hearing loss and a genetic syndrome who speaks AAE. KW has received speech-language intervention in school since first grade and at a hospital-associated clinic since second grade. This case evaluation considered KW’s performance between the age of 8;11 and 9;2. At this point, KW had improved his speech significantly, but observation revealed speech sound errors and grammatical performance that deviated from age expectations for child speakers of MAE. Two clinical questions were considered: 1. Are KW’s speech and language features that are not consistent with MAE age-expectations consistent with features of AAE or a non-mainstream dialect? 2. How might other factors change the assessment and treatment approach, particularly KW’s hearing loss, genetic syndrome, and family goals?

Results: KW (9;2) received a standard score of 84 on the Arizona Articulation Proficiency Scale-Third Edition, yet only a few errors are considered aberrant in both MAE and AAE. KW (9;2) received a composite standard score of 81 on the Clinical Evaluation of Language Fundamentals-Fifth Edition Metalinguistics. KW (8;11) was given the Developmental Evaluation of Language Variation - Screening Test, an assessment that identifies the degree to which a non-mainstream dialect is used and classifies language impairment vulnerability based on shared features of non-MAE dialects and MAE (4). KW was classified as a speaker with a non-mainstream dialect and at low risk for language impairment. These results suggested that features of KW’s dialect were obscuring his diagnosis, treatment, and prognosis by inaccurately magnifying his impairment.

Discussion: Initially, KW’s records appeared to indicate significant co-occurring speech and language disorders. Closer examination revealed that KW speaks a non-mainstream dialect with a few residual and nuanced errors that may be secondary to hearing loss. Speech and language treatment then focused on ‘errors’ that were inconsistent with both AAE and MAE and on areas of need for children with hearing loss. This case study underscores the need to thoughtfully evaluate the relation between dialect and disorder, particularly for children with hearing loss.


Lacking Toll-like receptor 4 leads to impaired drug reward learning and synaptic strength in the nucleus accumbens

Presenter: Daniel Kashima  (daniel.t.kashima@vanderbilt.edu)

Authors: Daniel T. Kashima, Brad A. Grueter

Introduction: Dysfunction of the reward system is implicated in neuropsychiatric conditions including autism, schizophrenia, and drug abuse. A key reward system structure is the nucleus accumbens (NAc), which integrates internal and external information to transform motivation to goal-directed actions. The primary neurons of the NAc are quiescent medium spiny neurons (MSN) that express either D1 or D2 dopamine receptors. The activity of these neuronal populations is dependent on excitatory drive and ultimately shown to have differing effects on reward behavior. Developmental perturbations or adult experiences including stress and drug exposure are known to alter excitatory synaptic function in the NAc with multiple neuron-mediated mechanisms being implicated. However, growing evidence suggests that the brain's innate immune system, including microglia, regulate circuit development and synapse function. Toll-like receptor 4 (TLR4), a pattern-recognition molecule expressed primarily on microglia, is involved in morphine- and cocaine-mediated reward learning. The contribution of TLR4 to NAc synaptic physiology has not been elucidated. We therefore determined the involvement of TLR4 on NAc-dependent learning and synaptic functions.

Methods: To examine the role of TLR4 in drug reward behavior and NAc synaptic physiology, we employed a combination of behavioral and ex vivo slice electrophysiology assays on wild type (WT) and TLR4 knockout (TLR4.KO) mice. We performed cocaine-induced locomotor sensitization and conditioned place preference (CPP) assays to test drug reward learning. We also performed open field and novel object recognition tests to control for basal locomotor activity, anxiety, and working memory. To examine synaptic function, we performed whole-cell voltage-clamp recordings in NAc MSNs from D1 dopamine receptor reporter mice +/- TLR4. Whole-cell recordings were assessed from naive and cocaine-treated animals.

Results: TLR4.KO animals exhibit significant attenuations in cocaine locomotor sensitization and low-dose cocaine CPP. Importantly, there were no differences in basal locomotor activity, anxiety, or working memory. Ex vivo slice electrophysiology revealed weaker synaptic strength in TLR4.KO animals as demonstrated by smaller AMPA/NMDA ratios in both D1 and D2 MSNs. There is a trend towards altered synaptic strength on D2 MSNs in TLR4.KO mice following drug exposure.

Discussion: Alterations of the reward system are a characteristic of many neuropsychiatric conditions. Despite the high prevalence and cost of such disorders, effective treatments are lacking in part due to an incomplete understanding of the underlying pathology. In our study, we used drug reward assays to study the NAc synaptic physiology and related behaviors in a TLR4 dependent manner. We found that TLR4 participates in reward behavior and shaping of NAc physiology. Future experiments will determine signaling mechanisms which may uncover novel therapeutic targets to mitigate neuropsychiatric conditions.
Examining Loss of Control in Emotional Eating

Presenter: Loran Kelly  (loran.kelly@vanderbilt.edu)

Authors: Loran Kelly, David Schlundt

Introduction: Emotional eating (EE) refers to a subclinical form of disordered eating behavior which involves eating in response to negative affect. Binge eating (BE) refers to a pattern of disordered eating which consists of episodes of uncontrollable overeating. A core feature of Binge Eating Disorder (BED), a new DSM-5 diagnosis, is loss of control (LOC), or the subjective sensation of being unable to stop eating. The current research examines LOC in a subclinical EE population using ecological momentary assessment (EMA). LOC has not been examined in EE or non-clinical samples. The current research question is whether LOC is present in a sample of non-treatment seeking adults, and aims to explore loss of control in an often overlooked population of non-treatment seeking adults.

Methods: Participants were recruited from the Patient Centered Outcome Research Initiative (PCORI) Clinical Data Research Network. PCORI is a prospective cohort study designed to create a network for hospitals and clinics to facilitate research. This network includes links to participants' electronic health records (EHS). The current study recruited participants through the PCORI network. A sample of 400 non-treatment seeking adults were enrolled in the current study. Participants were required to complete EMA monitoring for a period of 2 weeks. Participants were instructed to access the website after every meal or snack (event-driven monitoring). The EMA survey was brief and took no more than 5 minutes to complete. At the end of the 2-week period participants completed a follow-up questionnaire. Participants were instructed in the use of EMA materials. The online EMA training guide contains instructions to participants on how to access the internet on their cellular phones to complete a short questionnaire after a meal or snack.

Participants were also given detailed instructions regarding the DSM-5 definition of loss of control eating before beginning monitoring. These instructions were provided in order to enhance participants' understanding of what constitutes LOC.

Results: As predicted, results indicate that EE was significantly associated with LOC in this non treatment-seeking adult population. Participants reporting higher EE episodes (as determined via a median split) showed significantly higher LOC experiences than those reporting a lower frequency of EE episodes.

Discussion: The current study examined the relationship among LOC and EE. The existence of this relationship broadens our knowledge of EE and its relationship to BE, adding a new dimension to our understanding of their relationship. Examining this relationship may help advance understanding of EE behavior as a possible etiological factor for the onset or progression of eating pathology.


Derivational Morphology Knowledge of Children with Specific Language Impairment

Presenter: Hannah Krimm  (hannah.krimm@vanderbilt.edu)

Authors: Hannah Krimm, Krystal L. Werfel, C. Melanie Schuele

Introduction: It is well established that omission of inflectional (e.g., tense-marking) morphemes in obligatory contexts is a hallmark of young children with specific language impairment (SLI). Less is known about use of derivational morphemes by these children. Children with SLI make more errors on derivational morphology tasks than children with typical language, but the nature of these errors has not been investigated. Understanding derivational morphology knowledge of children with SLI will allow for greater specification of the disorder. The purpose of this study was to characterize the nature of derivational morphology knowledge in school-age children with SLI. We addressed the research questions: 1. Do children with SLI produce fewer invented derivatives than children with typical language? 2. Are there other ways in which children with SLI differ from children with typical language in derivational morphology knowledge?

Methods: The data for this study were extant data from a larger study on the speech, language, and literacy skills of children with SLI. Participants were children in second through fourth grade with SLI (n = 32; mean age = 112.02 months; sd = 12.44 months) and peers with typical language (n = 40; mean age = 104.85 months; sd = 11.86 months). Participants individually completed the derivation subtest of the Test of Morphological Structure (TMS; Carlisle, 2000). On the TMS, the examiner speaks a stem word followed by an incomplete sentence. The participant responds with a morphological derivative of the given stem to complete the sentence (e.g., farm. My uncle is a [farmer]). Non-target responses were coded to characterize presence of a derivational suffix, use of real words or invented derivatives, and syntactic appropriateness.

Results: Mixed-effects logistic regression was used to examine group differences in response type. Group was a significant predictor of omission of derivational suffixes (p < .001). Group was also a significant predictor of use of invented derivatives (p = .03). Children with SLI were more likely to omit derivational suffixes and less likely to produce invented derivatives than children with typical language.

Discussion: The response pattern demonstrated by children with SLI for derivational morphology mirrors the patterns seen with inflectional morphology. Children with SLI are more likely to omit inflectional suffixes and less likely to overgeneralize inflectional suffixes than children with typical language. The finding that children with SLI are more likely to omit derivational suffixes and less likely to use invented derivatives further illuminates the nature of grammatical impairment in children with SLI. Children with SLI are less able than peers with typical language to use derivational morphology generatively to complete linguistic tasks.

Conti-Ramsden, 2005
Rice, Wexler, & Cleave, 1995
Rice & Wexler, 1996
Marshall & van der Lely, 2007
Werfel, 2012
Oetting & Horohov, 1997
Changes in thalamocortical projection patterns in a mouse model of autism

Presenter: Juliane Krueger  (juliane.krueger@vanderbilt.edu)

Authors: Juliane Krueger, Cesar D.M. Vargas, Julia A. Mavity-Hudson, Michael J. Robson, Jeremy Veenstra-Vanderweele, Mark T. Wallace, Randy D. Blakely, Vivien A. Casagrande

Introduction: Autism Spectrum Disorder (ASD) is a heterogeneous disorder spanning a variety of symptoms involving sensory processing, repetitive behaviors, as well as, deficits in communication and social interactions. The neuromodulator serotonin (5-HT) is known to play an important role in normal brain development and has been implicated in perceptual and behavioral abnormalities in ASD. In fact, 5-HT has been considered a biomarker for ASD in about ~25-30% of all cases (Bennett et al, 1990; Veenstra-VanderWeele and Blakely, 2012).

Methods: Using a mouse model of ASD expressing a human coding variant in the 5-HT transporter (SERT, SLC6A4), the present study set out to characterize potential changes in cytoarchitecture and connectivity patterns of cortical sensory regions that might be linked to alterations in serotonin availability during development. The Gly56Ala substitution mutation at the N-terminus has been shown to produce a hyperactive SERT, clearing away more 5-HT than in the wild type form. With SERT being transiently expressed in thalamocortical axons during embryonic development, our initial analysis examines the anatomical effects of altered 5-HT clearance on the distribution of thalamocortical axons in the adult. Additionally since previous work showed that there is a greater concentration of SERT in projections deriving from unisensory thalamic nuclei than from multisensory nuclei (Lebrand et al., 1996), we expected that differential effects on thalamocortical development might be observable in different regions of cortex depending on their thalamic input source. Primary visual cortex (V1) and multisensory region V2L were subsequently selected for analysis.

Results: Utilizing the presence of vesicular glutamate transporter 2 (VGluT2) as a proxy to investigate thalamic projections to these areas, our data reveals a significant difference in the distribution of thalamocortical terminals in the adult knock in (KI) mice. KIs exhibited more broadly distributed VGluT2-positive terminals beyond layer IV in V1 but not in V2L compared to wildtype littermates (129S4/S6). Specifically, thalamic terminals appeared to encroach into supragranular layers suggestive of less precise targeting. Furthermore, since no differences were observed in V2L, alterations in 5-HT availability during development may preferentially impact unisensory regions, potentially leading to unisensory processing deficits. This change may have cascading effects shaping, for example, integration of visual sensory cues with other sensory signals further explaining some of the observable symptoms in ASD.


Associations between Reduced or Atypical Sensory Integration and Reduced or Atypical Sensory Responsiveness

Presenter: Wayne Kuang (wayne.kuang@vanderbilt.edu)

Authors: Wayne Kuang, Tiffany Woynaroski

Introduction: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impaired social interaction, verbal and non-verbal communication, and restricted and repetitive behavior, as well as atypical sensory function (American Psychiatric Association, 2013). Researchers have focused on different aspects of sensory function in children with ASD. More clinically-oriented researchers, namely occupational therapists (OTs), have focused on behavioral patterns of sensory responsiveness in children with ASD, whereas many sensory neuroscientists have focused on multisensory integration in this population (Cascio, Woynaroski, Baranek, and Wallace, 2016). There has been surprisingly little cross-talk between these groups, and thus we know little about how sensory responsiveness relates to multisensory integration in children with ASD. The present study will explore these associations in adolescents on the autism spectrum.

Methods: To answer our research questions, we drew on extant data from a previous study that examined multisensory integration in children with ASD as compared to typically developing peers. Results for between-group comparisons on low-level and high-level multisensory tasks have previously been published (Foss-Feig et al., 2010; Kwakye, Foss-Feig, Cascio, Stone, & Wallace, 2011; Woynaroski et al., 2013). As a part of this study, several parent report measures of sensory responsiveness were additionally collected, concurrent with psychophysical assessments of multisensory function. However, associations between multisensory integration and parent-reported sensory responsiveness have not been comprehensively examined for either children with ASD or their TD peers. This study is thus the first to explore these concurrent correlations within this study sample. Low- and high-level multisensory integration was measured using psychophysical illusions. Patterns of reduced (i.e., hypo) and other atypical (i.e., hyper, seeking) patterns of sensory responsiveness were measured via parent report measures that were developed for research and/or clinical purposes. These measures were all collected at the same time point (Baranek et al., 2013). Participants in this study included 18 children with ASD and 18 typically developing (TD) peers. Eligibility criteria for inclusion in the study were as follows: (a) chronological age between 8 and 17 years; (b) full scale and verbal IQ standard scores greater than or equal to 70 on the Weschler Abbreviated Scale of Intelligence (Wechsler 1999); (c) normal or corrected-to-normal hearing and vision per parent report; (d) completion of 80% of trials on multisensory speech perception tasks; and (e) susceptibility to the McGurk and Flash-beep illusions as demonstrated by report of at least one perceived integration on the each task (Woynaroski et al., 2013).


Using video prompting procedures to teach academics to students with autism in the general education classroom

**Presenter:** Emily Kuntz  (emily.kuntz@vanderbilt.edu)

**Authors:** Emily M. Kuntz, Victoria F. Knight

**Introduction:** Students with autism spectrum disorder (ASD) and intellectual disability (ID) often have difficulty completing multi-step tasks independently. Video prompting is effective for teaching a variety of chained tasks (e.g., social, functional), alleviating the need for teacher prompting. In addition, video prompting is a promising approach for increasing independence during class time, acquisition of new skills, and decreased need for adult prompting.

**Methods:** A multiple probe across three participants and three behaviors research design was used (Gast & Ledford, 2016). We relied heavily on stakeholder opinions in the development of the independent variable. The skills taught using video prompting were determined in collaboration with paraprofessionals, special educators, and general education content. All skills were taken from students' IEP and/or were being addressed in the general education setting. The dependent variable measured the percentage of independent, correct steps of a task analysis. Analysis of baseline conditions demonstrated a clear pattern of low-level responding, with increased levels and/or increasing trends in responding during intervention. The staggered introduction of skills and consistent probe conditions (e.g., same implementer, same setting) from baseline to intervention conditions strengthened the internal validity of the study. Variations in implementers, skills, and settings increased the generalizability of the study. Paraprofessionals and general education teachers completed social validity surveys indicating positive feedback with respect to cost, feasibility of implementation, and a lack of interfering with the general education classroom routines.

**Results:** All students increased their level and/or trend for each skill from baseline to intervention conditions. Two students met mastery with both skills. One student met mastery on one skill and made progress on second skill based on increased responding from baseline to intervention conditions as measured by the task analysis.

**Discussion:** Implications for future research and practice will be presented including limitations encountered.
Genetic Implications of Rhythm and Grammar Development

Presenter: Genevieve Kupsky (genevieve.g.kupsky@vanderbilt.edu)

Authors: Michaela Novakovic, Genevieve Kupsky, Ashley Hirsch, Nancy Cox, Reyna Gordon

Introduction: Recent literature suggests a connection between rhythm and grammar development, although the genetics driving this relationship are not yet known. Difficulties in timing skills and speech rhythm perception skills have emerged as a potential deficit in a specific language impairment (SLI). Recent genetic work has (separately) identified potential genotypes involved in grammar, timing skills, and spontaneous motor tempos (SMTs). The SMT is a pulse spontaneously generated by an internal clock or oscillator in the brain and seems to be required for movement along to a beat, but varies from person to person. Here, we hope to elucidate specific genotypes and genetic mechanisms that might contribute to an SLI phenotype and that can account for individual differences in rhythm and grammar skills.

Methods: We are investigating genotype-phenotype correlations in three ways. First, we are using the expression-based profiling tool, PrediXcan, to identify genes that are highly expressed in individuals with SLI. Second, we are using Vanderbilt’s database of linked medical records and genotypes, BioVU, to identify genotypes that occur more frequently in individuals with SLI. Third, complementary information on the role of these genetic mechanisms will be assessed by assessing the relationship between genotype, rhythm perception, and grammar skills in genotypes of children with and without SLI in our laboratory study. In this study, SMTs are measured by asking children to tap (on an iPad app) at a speed that ‘feels just right.’ Rhythm perception and grammar skills are assessed in a comprehensive test battery (described in other posters at this symposium).

Results: Data collection is underway. We expect that certain genotypes previously linked to poor grammar and timing skills will be significantly more prevalent in the SLI population of the BioVU records compared to our control population. In our genotyping of participants in our laboratory study, we expect increased frequency of genotypes linked to language disorders (identified from our work in language disorders from the BioVU and PrediXcan data) of children with weaker grammar and rhythm skills. We also predict that participants who exhibit a slower spontaneous motor tempo will have genotypes linked to an SLI diagnosis.

Discussion: The findings of this study may have important implications for diagnosis and treatment of language disorders and for understanding of genetic and neural mechanisms underlying language and rhythm development.
Development of a behavioral assay to measure stereotyped motor behavior in Drosophila

Presenter: Hannoori Lee  (han.noo.ri.lee@vanderbilt.edu)

Authors: Hannoori Lee, Robin L. Shafer, Aparna Shekar, Jenny Aguilar, Kathryn D. Slaboch, Jon Tapp, Aurelio Galli, James W. Bodfish

Introduction: Autism spectrum disorder (ASD) is a genetically diverse disorder characterized by social deficits and repetitive behaviors. Research has focused on molecular mechanisms and phenotypic consequences of genetic mutations associated with ASD using transgenic animal models. The fruit fly (Drosophila melanogaster) is beginning to be used to model genetic mutations associated with neurodevelopmental disorders including ASD due to its short gestation period and simple genome. Several assays exist to assess molecular mechanisms in drosophila. However, less work has focused on behavioral assays. No drosophila assay currently exists for stereotyped behavior - a common repetitive behavior in ASD that can be modeled across species. This study aims to develop a behavioral assay and coding scheme to measure stereotyped behavior in drosophila. We will test our assay and coding scheme by comparing wild type flies to transgenic flies expressing either a healthy or mutated copy of the human dopamine transporter (DAT) gene. The mutation is a recently discovered de novo mutation associated with ASD. Flies expressing mutant DAT have been used to study other molecular and behavioral aspects of ASD.

Methods: Eight male wild type flies and 18 male transgenic flies (9 with healthy and 9 with mutant human DAT) were tested individually in an enclosed arena that permitted locomotion but not flying. Flies were habituated to the arena prior to testing. The behavioral task lasted 5 seconds, and the fly's movements were recorded using a high-speed camera (1000 frames/second). During the first 2 seconds, the fly's baseline behavior was recorded. After 2 seconds, a wasp sound was presented, which is an ecologically relevant stimulus that is known to induce behavioral changes in flies. Since the wasp sound is a predatory signal, we expected it would lead to stress-induced stereotyped behavior upon presentation. To examine the behavioral response to the stimulus, videos were coded in Procoder software for (a) the one-second period immediately prior to stimulus onset (pre-stimulus), and (b) the one-second period immediately following stimulus onset (post-stimulus). The pre- and post-stimulus segments were divided into 150ms intervals for behavioral coding and were played back at 30 frames/second (150ms = 5 seconds of playback) for detailed behavior coding. A trained observer coded each interval as either locomotion, idle, stereotypy, or ambiguous. A randomly selected 25% of the videos were coded by an independent observer to calculate inter-rater reliability using MOOSES software. This poster will include data on inter-rater reliability of behavioral coding and the frequency of each behavior within and across groups as an assessment of the sensitivity of our assay and coding scheme for detecting stereotyped behavior.
Beat-based entrainment during infant-directed singing supports social engagement

Presenter: Miriam Lense (miriam.lense@vanderbilt.edu)

Authors: Miriam Lense, Warren Jones

Introduction: Social communication makes extensive use of predictable, rhythmic behaviors and individuals are acutely sensitive to the timing of these behaviors beginning in infancy. One example of such communication is infant-directed singing, a universal form of parent-child interaction that captures and maintains infants' attention and modulates their arousal levels. In the current study, we examined musical beat perception as a mechanism for the scaffolding of social attention and engagement. Specifically, as the eyes of a caregiver provide critical, meaningful social information (e.g., for directing attention or understanding emotions), we examined how attention to the eyes of others is modulated around the beat-based, rhythmic structure of infant directed singing.

Methods: Two-month and six-month old infants watched videos of actresses engaging them with infant-directed singing while eye-tracking data was collected. We measured if changes in looking to the eyes of the actress were time-locked to the beat of the singing. Beats of the singing were determined through vowel onsets and offsets of the beat-aligned syllables. We constructed crosscorrelograms and compared these distributions with chance rates of eye-looking using permutation testing.

Results: At both two- and six- months of age, infants demonstrated increased looking at the eyes of a singing actress that was time-locked to the musical beat: Looking to the eyes of the singer increased ~100 ms in anticipation of the beat and peaked around the beat. Increases in eye-looking around the beat were significantly greater in 6-month than 2-month old infants.

Discussion: These findings demonstrate how the rhythmic structure of musical interactions supports meaningful engagement with a social partner in infancy. The increased social, beat-based entrainment at 6-months of age compared with 2-months of age is consistent with increased sensitivity to rhythmic behaviors around this age (e.g., rhythmic hand banging and babbling), and also corresponds to a time of increased face-to-face experience with infant directed singing. Additionally, this research presents a novel method for examining entrainment to a musical beat in audiovisual stimuli that can be used with young children. Implications of this study for understanding the development of beat perception and sensitivity to social, rhythmic behaviors will be discussed.
Does It Make Sense? - Reading for Understanding

Presenter: Shih-Yuan Liang  (shih-yuan.liang@vanderbilt.edu)

Authors: Shih-Yuan Liang, C. Melanie Schuele

Introduction: It is well documented that children with specific language impairment (SLI) have substantial reading comprehension problems even after resolving decoding challenge. Inadequate comprehension-monitoring skills exhibited in children with SLI hinder the further development of self-regulated reading, which permits one to make self-corrections and repair comprehension breakdowns. Despite increasing emphasis on reading for understanding, research has shown that educators and parents use a limited repertoire to scaffold young struggling readers to correct their reading miscues, for instance, supplying the word. Such feedback invites minimal reflections on the text meaning as well as self-monitoring. The purpose of this study is to examine the treatment effect of building comprehension monitoring on the reading outcomes in school-age children with SLI. We address the research questions: 1. Do students with SLI produce more correction behaviors and fewer reading miscues after introducing the intervention? 2. Are there other factors that contribute to the malleability of students' reading behaviors?

Methods: This study employed a single subject, multiple-probe design. Participants were two first graders and one second grader referred by teachers at a charter school, East Nashville. They were students who failed the Spring benchmark reading assessment with various degrees of linguistic vulnerabilities. Participants received one-on-one reading tutoring for an average of 28 sessions across approximately 7 weeks. The probe assessments including an untimed passage-reading test and the DIBELS Oral Reading Fluency test were collected intermittently and on a weekly basis respectively. The untimed reading measure yields three dependent variables, which allowed us to track students' learning progress over time: (a) the proportion of correction behaviors to reading miscues (primary outcome variable), (b) % words read incorrectly, (c) % correction behaviors. In the intervention sessions, the experimenters modeled a single comprehension monitoring strategy. We provided explicit demonstration of how to track one's comprehension at the clausal level with guided and independent practice.

Results: Results indicate a functional relation between the comprehension monitoring training and reading correction behaviors, but no generalization to oral reading fluency. Two students demonstrated a growing trend in applying self-monitoring skills to correct their reading miscues and a downward trend of reading errors; one student demonstrated increased awareness of his reading miscues despite slower gains.

Discussion: Despite the presence of early decoding challenge, young struggling readers are able to learn to monitor their local understanding and to attempt to make self-correction when a reading miscue interrupts the construction of meaning from text. The malleability of self-regulated reading behaviors is dependent on students' linguistic strengths and co-occurring attention deficits. Suggestions for future research and implications for practice will be discussed.
Reading Instruction for Students with Disabilities: A Systematic Review

Presenter: Esther Lindstrom (esther.r.lindstrom@vanderbilt.edu)

Authors: Esther R. Lindstrom, Samantha A. Gesel, Christopher J. Lemons

Introduction: Reading ability increases success in school and beyond for students with and without disabilities. Despite substantial research on best practices for teaching reading to students with disabilities (e.g., RAND Reading Study Group, 2002; Snow, Burns, & Griffin, 1998), far fewer studies systematically examine the nature of reading instruction for students of this population. Experimental and observational studies, alike, tend to focus on students with high-incidence disabilities, thus inviting questions about instruction for students with other characteristics. This systematic review of observational studies examining reading instruction for students with disabilities synthesizes across disability categories and settings to depict the nature and quality of reading instruction since IDEA’s 1997 amendments, the NRP’s recommendations in 2000, and subsequent legislation (e.g., Reading First, No Child Left Behind, Race to the Top). Who is getting what kind of instruction? What has changed? What areas require more focus?

Methods: This is a systematic review of 16 studies between 1997-2016, following methodological guidelines by Cooper (2010) and Valentine and Cooper (2008). Included studies observed business-as-usual reading instruction for students with disabilities in public schools, reporting total minutes spent in various content areas (e.g., phonics, comprehension) and/or grouping (e.g., independent, teacher-led).

Results: Findings suggest increased explicit instruction in reading for students with disabilities since 1997, with instruction for high-incidence disabilities reflecting best practices more closely than for peers with cognitive or intellectual disabilities. Furthermore, trends indicate fewer evidence-based practices for students from districts with lower socioeconomic status. Results vary by region. More research is needed on instruction for students with severe disabilities, for whom tenets of such recommendations may also be applicable.

Discussion: Findings indicate some progress in a nationwide effort to improve reading instruction, but also highlight considerable gaps dividing research, policy, and practice. More high-quality observational studies are needed to better understand current reading instruction, especially for students with severe disabilities.
Microglial pruning of dendritic spines in the prefrontal cortex during adolescence

Presenter: Allyson Mallya (allyson.mallya@vanderbilt.edu)

Authors: Allyson P. Mallya, HuiDong Wang, Tuula Ritakari, Sahana N. Kalburgi, Daniel T. Kashima, Brad A. Grueter, Ariel Y. Deutch

Introduction: Excessive dendritic spine pruning in the prefrontal cortex (PFC) during adolescence has been suggested to lead to the cognitive symptoms of schizophrenia. Recent data point to microglial involvement in the sculpting of synapses and refinement of neuronal circuitry during early postnatal development. However, the role of microglia in the structural and functional maturation of the PFC, which is not complete until the early 20s, has not been examined. We therefore determined if microglia contribute to PFC PC spine elimination during the periadolescent period.

Methods: We determined if microglia engulf dendritic spines in the PFC. Immunohistochemical colocalization of microglia (defined by Iba1 expression) and dendritic spines (revealed by PSD-95) on PFC pyramidal cells (PCs) was determined at postnatal days 24 (a time of increasing PFC PC spine density), 30 (peak spine density), and 39 (decreasing spine number). As a prelude to future experiments that will assess the consequences of disrupting adolescent microglial pruning on adult PFC PC structure and function, we treated mice that express diphtheria toxin (DT) receptor in microglia with DT to establish the extent of PFC microglial depletion and the recovery rate of PFC microglia following DT administration.

Results: We observed a significant increase in Iba1 and PSD-95 colocalization in the PFC at P39 relative to earlier time points, suggesting microglia prune dendritic spines of PFC PCs during adolescence. Furthermore, our data suggest sexual dimorphism in the timing of microglial engulfment, with males but not females showing a non-significant (p=0.06) trend toward a significant increase in colocalization at P39. We observed a 90% decrease in the number of PFC microglia 2d after injecting DT to ablate microglia. There was significant recovery of PFC microglia by 4d after DT administration (34% depletion), with complete recovery seen 8d after DT treatment.

Discussion: Our data points to a critical role for microglia in the pruning of PFC PC dendritic spines during adolescence. This is substantially later than has been observed in other brain areas, consistent with the late maturation of the PFC. The potential sexual dimorphism in the timing of peak microglial engulfment would also be consistent with the observation that the age of diagnosis of schizophrenia occurs earlier in males than females. Our initial data suggest that DT can ablate microglia for a relatively short time period. We will exploit the short duration of microglial ablation in experiments that will assess in the adult the morphological and functional consequences of adolescent microglial ablation. Understanding developmental pruning processes may lead to the development of new microglial-based pharmacotherapies to mitigate structural and functional cortical changes in schizophrenia, including cognitive dysfunctions.
Endocannabinoid Modulation of Reciprocal Prelimbic Prefrontal Cortex Circuits

**Presenter:** David Marcus  (david.j.marcus@vanderbilt.edu)

**Authors:** David J. Marcus, Andre B. Haymer, Sachin Patel

**Introduction:** The prelimbic prefrontal cortex (pPFC) is a subregion of the medial prefrontal cortex (mPFC) that is involved in orchestrating anxiety and stress responses. Research has indicated that the activity of the mPFC and its ability to modulate responses to stressful situations is heavily influenced by local cannabinoid signaling. Local pharmacological activation of cannabinoid signaling in the mPFC induces an anxiolytic effect, while local inhibition of cannabinoid signaling prolongs corticosterone (CORT) secretion in response to acute stress and promotes an anxiogenic phenotype. Due to the primarily presynaptic localization of the cannabinoid receptor type 1 (CB1), the endocannabinoid system (ECS) may play a crucial role in gating excitatory glutamatergic inputs into the mPFC. In this study, we characterized how endocannabinoid signaling modulates glutamatergic inputs to the pPFC from two brain regions that have been implicated in the underlying pathophysiology of anxiety and stress disorders, the Basolateral Amygdala (BLA) and Mediodosal Thalamus (MDT).

**Methods:** The primary method used in this study is acute brain slice electrophysiology. With this method, we characterized glutamatergic inputs to the pPFC from the BLA and MDT by using an optogenetic projection targeting approach combined with retrograde labeling of pPFC cells using red retrobeads. These methods will allow us to characterize how endocannabinoid signaling modulates reciprocal glutamatergic pPFC circuits. One of the primary measures of endocannabinoid signaling we use is depolarization induced suppression of excitation (DSE), an endocannabinoid mediated form of transient synaptic depression.

**Results:** Neither retrobead positive nor retrobead negative cells in pPFC layer 6 receiving projections from the DMT express DSE. However, both retrobead positive and negative cells in layer 2 receiving inputs from the BLA exhibited DSE. Finally, only layer 5 retrobead positive cells receiving input from the BLA exhibited DSE. These distinct modes of endocannabinoid signaling may underlie the behavioral effects of both local mPFC and global cannabinoid agonist administration, and may be differentially modulated during periods of stress and anxiety.

**Discussion:** Clinical studies have documented that when marijuana users are asked why they use marijuana, some of the most common responses deal with its ability to alleviate symptoms of anxiety and its ability to help patients cope with stressful situations. However, how marijuana interacts with the endogenous cannabinoid system to elicit these effects is still poorly understood. In this study, we characterized how endocannabinoid signaling modulates glutamatergic circuits that have been implicated in affective disorders such as anxiety, post-traumatic stress disorder (PTSD) and depression. In the future, we hope to understand how traumatic stressors alter endocannabinoid signaling within these circuits and whether enhancing endocannabinoid signaling can confer resilience to stress.
Path Model of Expressive Vocabulary Skills in Initially Preverbal Preschoolers with Autism Spectrum Disorder

**Presenter:** Jena McDaniel  (jena.c.mcdaniel@vanderbilt.edu)

**Authors:** Jena McDaniel, Paul Yoder, Linda R. Watson

**Introduction:** To build a parsimonious model of language development in children with autism spectrum disorder (ASD), we developed a path model of predictors of expressive vocabulary skills in initially preverbal preschoolers with ASD. The number of expressive language predictors\[1,2\] can be reduced by statistically controlling for the intercorrelation among predictors without reducing the prediction’s accuracy. Remaining predictors are called value-added predictors. Additionally, investigating indirect and direct paths of association can increase the precision of thought regarding why associations between value-added predictors and the criterion variable occur. We extend the work of Yoder, Watson and Lambert\[3\] by asking two novel research questions related to the four value-added predictors of expressive language growth in preverbal preschoolers with ASD (i.e., intentional communication, diversity of key consonant used in communication [DKCC], responding to joint attention [RJA] and parent linguistic responses [PLR]).

1) Are associations between previously identified value-added predictors of expressive language growth and later expressive vocabulary mediated through later receptive vocabulary?

2) Is the association between early intentional communication and later expressive vocabulary mediated through DKCC?

**Methods:** Data were used from a longitudinal correlational study of speech development in 87 children with ASD who were 24 to 48 months and preverbal at study entry.\[3\] Data were collected across 4 time points spanning 16 months. The partial least squares path model included selected associations between the following constructs for the research questions: intentional communication, DKCC, RJA, PLR, early and later receptive vocabulary, and later expressive vocabulary. Aggregate measures were used for all constructs, except DKCC, to increase stability.\[4\] For a particularly stringent test of the value-added nature of the previously identified predictors, later receptive vocabulary was measured only 4 months prior to expressive vocabulary rather than 12 to 16 months for the other predictors.

**Results:** Intentional communication (β=.29, p<.01), DKCC (β=.37, p<.001) and PLR (β=.30, p<.01) accounted for unique variance in later expressive vocabulary even when controlling for more proximally measured (i.e., Time 3) receptive vocabulary. Unexpectedly, RJA did not (β=-.11, p<.16). None of the predicted indirect paths from the value-added predictors to expressive vocabulary through later receptive vocabulary were confirmed. These nonsignificant findings may be partially explained by the difficulty measuring certain constructs, particularly receptive vocabulary. DKCC mediated the tested association indicating that DKCC accounts for variance in the association between intentional communication and later expressive vocabulary.

**Discussion:** Findings suggest that intentional communication, DKCC, and PLR should be prioritized within research and clinical settings in an effort to maximize expressive language outcomes for children with ASD. Future internally valid treatment studies are required to confirm the relations found in this correlational analysis.


Teaching Financial Literacy Skills through Video Prompting to Students with Intellectual and Developmental Disabilities in a Postsecondary Education Program

Presenter: Maria Mello  (maria.p.mello@vanderbilt.edu)

Authors: Maria P. Mello, Cory Nichols

Introduction: Young adults with intellectual and developmental disabilities (IDD) have difficulty finding employment and becoming financially independent after completing high school. Postsecondary education (PSE) programs designed for young adults with disabilities equip students to continue learning independent living that are pertinent to a successful adult life (Hart et al., 2010). To support students to learn money management skills and to become more independent several studies have looked at using video modeling, task analyzing skills, and self-instructional tools (Hughes, Carter, & Wehman, 2012; Scott, Collins, Knight, & Kleinert, 2013).

Methods: In this study we used task analyzed video prompts on an IPad to teach practical financial literacy tasks. Financial literacy tasks were simulated during a weekly financial literacy class to teach the three financial skills (i.e., writing checks, depositing money, and money management). To assess skill acquisition we used a multiple probe across skills single case design for three students with IDD, ages 20-22, in PSE financial literacy class on a private university campus.

Results: We measured the percent of correct steps completed for each skill. All three students improved across all three skills in level from baseline to intervention. This study suggests a method for learning money management skills that can promote financial independence for students with IDD.

Discussion: Since paid employment rates for students with IDD are increasing, it is important that students understand how to manage their money. Thus, this study suggests an effective method that teachers, practitioners, and families can use to teach students with IDD financial literacy skills that promotes independence in money management. The use of technology is commonplace and socially acceptable method of support for students with IDD. Implications for the use of video modeling and technology to support students financial independence will be discussed.


**Does the dorsal medial visual area represent a unique target of the koniocellular pathway?**

**Presenter:** Brandon Moore  (brandon.moore@vanderbilt.edu)

**Authors:** Brandon Moore, Jamie Boyd, Ornob Roy, Julia Mavity-Hudson, Vivien Casagrande

**Introduction:** The primate visual system exhibits a well-studied division of labor whereby projections from the lateral geniculate nucleus (LGN) terminate in separate compartments of primary visual cortex (V1) with the parvocellular (P) pathway synapsing in the ventral tier of layer 4, the magnocellular (M) pathway terminating in the dorsal tier of layer 4, and the koniocellular (K) pathway synapsing in the cytochrome oxidase (CO) blobs of layer 3B. Even after V1, the M and P pathways appear to differentially extend to extrastriate visual areas with the P pathway targeting the second visual area (V2) and the M pathway predominately acting on the Middle Temporal (MT) visual area (Casagrande & Kaas, 1994). These differences offer clues concerning the role of different extrastriate areas. With this in mind and given that various hypotheses have been put forward about the role of the dorsal medial (DM) visual areas (Rosa et al., 2009), we asked whether the projections to DM, the likely homologue of area V3a or V6 in macaques, are from a specific layer of V1.

**Methods:** To reach this goal, we conducted a retrograde tracer study and examined the labeled cells in V1. Area DM was anatomically identified in a population of bush babies and pressure injections of cholera toxin subunit B conjugated to 7nm colloidal gold (CTB-Au) were made at a depth of 100μm. Each subject received multiple 1μL injections placed 500-700μm apart covering the entirety of DM in one hemisphere. After a 3 day survival period, the animals were perfused and posterior cortex was flattened into a block that was sectioned tangentially into 50μm sections. Tissue slides were imaged, posterized, and divided into blob and interblob regions (Shipp & Zeki, 1989). A computerized image quantification system was used to calculate the area of blob and interblob regions as well as to count the number of labeled cells occurring within these regions.

**Results:** Results show that the labeled cells tightly correlate with CO blobs throughout the entirety of V1.

**Discussion:** This finding suggests that DM may be driven by input from the K pathway - at least in bush babies. It is noteworthy that although CO blobs are often considered uniquely composed of color selective cells, bush babies only have a single cone type resulting in color blindness. The presence of blobs in these animals can be explained by the hypothesis put forward by Allman & Zucker (1990) who proposed that CO blobs take a more generalized role in processing surface features which include color, texture, and contrast. This suggests that the K pathway could serve as the first step in surface context information that eventually drives area DM. More analysis is needed to further elucidate the functional role of this extrastriate area.
Biased M1 PAMs Reveal Critical Role of Phospholipase D in M1-dependent Long Term Depression in the Prefrontal Cortex

Presenter: Sean Moran (sean.p.moran@vanderbilt.edu)

Authors: Sean P Moran, Ayan Ghoshal, Joy Marlo, Greg Digby, Hyekyung Plumley, Jonathon Dickerson, Jerri Rook, Zixiu Xiang, Craig Lindsley, P. Jeffrey Conn

Introduction: The M1 subtype muscarinic acetylcholine (ACh) receptor (mAChRs) has emerged as an exciting potential target for novel therapeutic agents for treatment of negative symptoms and cognitive disturbances in patients suffering from schizophrenia. Using these novel tools, we have previously provided compelling evidence that selective M1 PAMs have robust cognition-enhancing effects and have actions that predict reduction in negative symptoms in multiple rodent models relevant for schizophrenia. Of specific interest was the finding that M1 PAMs enhance a novel form of mAChR-induced long-term depression, termed mLTD, at the hippocampo-prefrontal cortex (PFC) synapse. Impaired mLTD at this synapse is disrupted in rodent models of schizophrenia and M1 PAMs can fully restore deficits of mLTD and accompanying behavioral deficits in these rodent models.

Mechanistically, it was assumed that M1 PAMs enhance mLTD and cognitive function through canonical activation of phospholipase C (PLC). However, our lab has shown that M1 activation can also lead to activation of phospholipase D (PLD) and that this is independent of PLC activation. While most M1 PAMs potentiate coupling of M1 to both PLC and PLD, we have reported M1 PAMs which display stimulus bias and potentiate M1 coupling to PLC, but not PLD. These findings are especially interesting in light of recent studies suggesting that PLD may be important in cognitive function. Thus, it is possible that different M1 PAMs could have fundamentally different effects on CNS function, depending on whether they potentiate coupling of M1 to both PLC and PLD or confer stimulus bias and only potentiate coupling of M1 to PLC but not PLD activation.

Methods: Extracellular field potential recordings were performed with adult male C57BL6/J mice using coronal slices (400 μm) containing prelimbic PFC. Paired-pulse field excitatory postsynaptic potentials were recorded from the layer V of the prelimbic PFC and evoked by paired electrical stimulus pulses of the superficial layers II-III, delivered through a concentric bipolar stimulating electrode.

Results: I present exciting new data using selective, isoform-specific PLD inhibitors which indicate that activation of PLD, specifically PLD1 is required for mLTD in the PFC. Furthermore, unlike unbiased M1 PAMs, such as VU0453595, the non PLD-coupling M1 PAM VU0405652 does not potentiate subthreshold carbachol-induced mLTD

Discussion: These data suggest that PLD plays a critical role in M1 PAM signaling in the prefrontal cortex. Developing an understanding of the signaling pathways that are most important for the efficacy of M1 PAMs will provide fundamental new insights into the roles of specific physiological effects on animal behavior and will help guide selection of drug candidates with the most appropriate profile for advancing to clinical testing.
Experiencing parasympathetic arousal, anxiety, and stress in children with ASD before and after a theatre-based, peer-mediated intervention

Presenter: Rachael Muscatello  (rachael.a.muscatello@vanderbilt.edu)

Authors: Rachael A. Muscatello, Blythe A. Corbett

Introduction: Many with ASD experience a variety of co-occurring symptoms, such as autonomic dysregulation, anxiety, and stress. Respiratory sinus arrhythmia (RSA) is an indicator of parasympathetic regulation and is theorized to serve as a marker of behavioral flexibility and adaptability. Dysregulation of this system may be related to anxiety and stress, especially in ASD populations. This study investigated associations between parasympathetic arousal, anxiety, and stress in children with ASD, as well as potential improvements following a theatre-based peer-mediated intervention.

Methods: The pilot investigation included two preliminary studies. In Study 1, twenty-one children with ASD, ages 8 to 16, participated in the Peer Interaction Paradigm (PIP). The 20 min PIP is comprised of four 5-min periods of independent (T1, T3) and cooperative play (T2, T4). RSA was collected throughout the playground interaction. Parent-reports of child stress and self-reported anxiety scores were collected. Study 2 utilized a pre/post model, with participants randomly assigned to either the experimental group (n=12) or the wait-list control (n=9). Between group differences were assessed following the 10-week theatre intervention. Statistical analyses included ANCOVA models for between-group differences and Pearson correlations to identify associations for autonomic arousal (RSA), anxiety (STAIC), and child stress (SSS). RSA reactivity was calculated as RSA during the playground subtracted from baseline.

Results: In Study 1, RSA reactivity for cooperative play (T4) was significantly positively associated with self-reported trait anxiety (r=0.46, p=0.04), and negatively associated at trend level with SSS (r=-0.42, p=0.06). In Study 2, there were no significant differences between groups in post RSA at baseline (F(1,16)=0.004, p>.05) or during cooperative play T4 (F(1,17)=0.13, p>.05). There were no significant group differences for post-intervention SSS (F(1,18)=0.11, p>.05) or trait anxiety (F(1,18)=0.46, p>.05).

Discussion: Results suggest that a blunted autonomic response to the social interaction is associated with more trait anxiety. In contrast, the opposite relation held true for stress, suggesting that those with greater stress had more negative RSA reactivity values, indicating a greater difference in task RSA relative to baseline. This decrease in RSA during a stressor is considered an adaptive 'mobilization' response, and thus for those with greater stress, the social interaction may be perceived as more threat-inducing. The positive association with anxiety suggests, however, that prolonged anxiety may blunt this adaptive response. Future studies to compare ASD and typically developing populations are required to draw larger conclusions. Study 2 results, though non-significant, may be impacted by the small sample size, as larger studies have shown between-group differences.
Diurnal and Stress Hormonal Profiles of Testosterone and Cortisol in Adolescents with Autism Spectrum Disorder (ASD) and Typical Development (TD)

**Presenter:** Ian Muse  (ian.muse@vanderbilt.edu)

**Authors:** Ian Muse, Blythe A. Corbett, Kale E. Edmiston, Rachael Muscatello

**Introduction:** Adolescence is a period of remarkable physiological, psychological, and social changes, which is evident in the regulation and responsivity of the hypothalamic-pituitary-adrenocortical (HPA) axis and the hypothalamic-pituitary gonadal (HPG) axis contributing to elevations in diurnal basal and stress cortisol (Cort) and Testosterone (T). The study investigated potential differences in Cort and T between youth with autism spectrum disorder (ASD) and typical development (TD), and associations between age, pubertal status and anxiety.

**Methods:** This pilot study included males between 13-to-17 years with ASD (N=24) or TD (N=14). Diurnal samples were collected over 3 days in the home, [Immediate Waking (MOR1), 30-min post-waking (MOR2) afternoon (AFT), evening (EVE)]. Stress samples were collected in response to the Trier Social Stress Test. Self- (STAIC) and parent-report of (CBCL-A) anxiety, and social functioning (SRS, SCQ) were collected. Repeated ANOVA models and correlations were conducted.

**Results:** There were no between-group differences based on age, pubertal status, or IQ. Using repeated measures, there were no significant between-group differences for MOR, AFT, or EVE samples. Pubertal status was correlated with T-MOR1 (r = .42), T-MOR2 (r=.41), T-EVE (r = .33), and anxiety. T and Cort were correlated in the AFT (r = .54) and EVE (r = .48), respectively. T stress samples were positively correlated with pubertal status, age, as well as self-report (STAIC) and parent-report (CBCL-A) of anxiety.

**Discussion:** Both groups exhibit a largely normal diurnal slope for both hormones. Pubertal status was associated with higher T in the morning, afternoon, and evening, but not cortisol. Groups differed in anxiety and social functioning, with the ASD group evidencing greater social difficulty and endorsement of anxiety symptoms. Adolescence is a potentially challenging time for many youth with ASD, and ostensibly the rise in pubertal development, age, and hormone expression coincides with greater reported anxiety.
Using pyPheWAS to Identify Comorbidities and Pre-diagnosis Features in Autism Spectrum Disorder

Presenter: Kunal Nabar  (kunal.p.nabar@vanderbilt.edu)

Authors: Kunal P. Nabar, Michelle D. Failla, Shikha Chaganti Carissa J. Cascio, Laurie Cutting, Bennett A. Landman

Introduction: Analysis of electronic medical records in a big data approach promises to aid understanding of complex medical phenomena. Using a process called PheWAS (phenome-wide association studies), de-identified electronic medical records can be mapped to specific disease or disorder cohorts based on International Classification of Disease, 9th edition (ICD9) codes. This big data approach provides rich datasets for examination of comorbidities within disease cohorts. This study examines comorbidities in individuals with autism spectrum disorder (ASD) compared to matched control patients to identify comorbidities and pre-diagnostic features.

Methods: Significant comorbidities and conditions in individuals with ASD were identified using pyPheWAS, a custom Python module designed for EMR-based PheWAS analysis. Complete ICD-9 histories were obtained for each patient from Vanderbilt University Medical Center. In pyPheWAS, individuals’ ICD-9 codes were mapped to PheWAS codes, and the incidence of each condition is determined relative to the control cohort. We compared 3231 individuals with ASD and 3231 matched controls. Pre-diagnostic features were examined in a censored cohort with EMR data from birth to 2 years (ASD, n=1329 with 1329 matching controls). Three regression methods were used to examine relative incidence of PheWAS codes in the ASD cohort compared to the control cohort: logarithmic, absence/presence; linear, count incidence; and duration, temporal length of the PheWAS code. pyPheWAS runs 1865 regressions (one for each PheWAS categorized condition) with each regression yielding a p-value indicating associations between the condition and ASD.

Results: In the large cohort, individuals with ASD were more likely to present with the following conditions: lack of normal physiological development (-log(p)=107.6), delayed milestones (-log(p)=44.4), perinatal jaundice (-log(p)=38.2), anxiety disorders (-log(p)=35.1), adjustment reaction (-log(p)=34.2), respiratory conditions of fetus and newborn (-log(p)=32.0), conduct disorders (-log(p)=31.0), among others. In the censored data, examining individuals with ASD prior to diagnosis (birth to age two), individuals who would eventually receive an ASD diagnosis presented with the following conditions prior to age two: perinatal jaundice (-log(p)=28.0), endocrine and metabolic disturbances of fetus/newborn (-log(p)=21.6), transitory tachypnea or apnea of newborn (-log(p)=14.2), fetal distress (-log(p)=12.1), among other conditions.

Discussion: The conditions we identified to be linked to ASD were related to delayed development, perinatal complications, and other anxiety or conduct disorders. Given the heterogeneity within ASD, big data approaches can help identify specific associated pathologies, leading to improved patient care. These models may even help identify risk profiles of ASD prior to the stable diagnosis age, leading to the possibility of earlier intervention. A potential next step would be exploring the use of different statistical models to calculate the associations, as well as analyzing the cohorts with respect to other demographic data.
Examination of Instructional Contexts in General Education Classrooms for Students with Persistent Problem Behavior

Presenter: Gretchen O’Henley (gretchen.j.ohenley@vanderbilt.edu)

Authors: Gretchen J. O’Henley, Emily S. Weaver, Blair P. Lloyd

Introduction: Evidence suggests that students with problem behavior benefit from small group instructional contexts, frequent teacher-delivered opportunities to respond (OTR), and careful monitoring of their academic responding (Baker, Clark, Maier, & Vigor, 2008; Simonsen, Fairbanks, Briesch, Myers, & Sugai, 2008). When these students with problem behavior are included in general education settings, how often do they contact these recommended practices? In this exploratory analysis, we examined the educational contexts of students with persistent problem behavior who were receiving academic instruction in a general education classroom. For these students, we explored the instructional contexts they experienced and how student and teacher behaviors varied across those contexts.

Methods: Participants were twelve elementary students who had been referred for functional behavior assessment and who received academic instruction in a general education classroom. For each student, we conducted five 30-minute observations in an academic setting in which teachers reported problem behavior most frequently occurred. Using the Multi-Option Observation System for Experimental Studies software (MOOSES; Tapp, Wehby, & Ellis, 1995), we collected timed-event frequency data on OTRs, student active responses, and low-risk problem behavior, as well as duration data on instructional context (i.e., large group, small group, one-on-one, independent work, and down time).

Results: For the majority of the participants, as well as on average across participants, large group instruction was the most common instructional context, followed by independent work, down time, small group, and one-on-one instruction. Across all participants, OTRs occurred at higher rates during large group instruction relative to independent work. However, students responded to a higher percentage of OTRs during independent work than large group instruction. Contexts associated with the highest rates of low-risk problem behavior varied across participants.

Discussion: Although our data are descriptive and represent a small sample of students, patterns we observed suggest that large group instruction and independent work are the most common instructional contexts that students who engage in persistent problem behavior encounter when included in general education classes. While OTRs occurred at the highest rates during large group instruction, more frequent monitoring of students’ active responses in this context may be needed to increase academic engagement for students with behavior problems. In addition, our data suggest that although OTRs are less frequent during independent work than large group instruction, student responses are more likely to follow OTRs during independent work than large group instruction. Providing more frequent OTRs during independent work to students who exhibit problem behavior may be another avenue to enhance academic engagement.


A Preliminary Correlational Analysis of Student Problem Behavior and Teacher Instructional Behavior in Elementary General Education Classrooms

**Presenter:** Naomi Parikh (naomi.parikh@vanderbilt.edu)

**Authors:** Naomi Parikh, Emily S. Weaver, Blair P. Lloyd

**Introduction:** Instructional environments for students with behavioral disorders in self-contained settings have been characterized by low rates of instructional interactions (e.g., Sutherland, Wehby, & Yoder, 2002; Wehby, Symons, Canale, & Go, 1998). Less is known, however, about instructional environments experienced by these students in general education settings. As part of a larger observational study, we evaluated correlations between frequencies of student problem behavior and teacher instructional behaviors. We hypothesized a negative correlation between average frequencies of problem behavior and opportunities to respond, and positive correlations between average frequencies of problem behavior and (a) instruction removal and (b) duration of down time.

**Methods:** Participants were 12 elementary students in general education classrooms who had been referred for functional behavior assessment. For each student, we conducted five 30-min observations during academic routines reported by teachers as most likely to evoke problem behavior. Using the Multi-Option Observation System for Experimental Studies software (MOOSES; Tapp, Wehby, & Ellis, 1992), we collected timed-event data on student problem behavior, teacher opportunities to respond, and instruction removal, as well as periods of down time with no instruction. We calculated pearson product-moment correlations between average frequencies of problem behavior and average frequencies or durations of each instructional behavior.

**Results:** Across participants, frequencies of opportunities to respond were high (M = 27.6; SD = 7.9) relative to student problem behavior (M = 8.9; SD = 5.1) and instruction removal (M = 5.8; SD = 3.6). The mean duration of down time was 2.8 min (SD = 2.1). Results of the correlational analysis indicated a near-zero correlation between student problem behavior and opportunities to respond (r = .002, p = .50). However, strong positive correlations were found between student problem behavior and instruction removal (r = .65; p = 0.01) and between student problem behavior and duration of down time (r = 0.62; p = 0.02).

**Discussion:** Although our data set represents a small sample of students, our results suggest that in general education classrooms, students with persistent problem behavior receive relatively frequent opportunities to respond regardless of how often they engage in problem behavior. However, increased frequency of problem behavior was associated with more frequent interruptions and delays to instruction. Given the descriptive nature of these data, we cannot conclude whether problem behavior is causing these interruptions to instruction or whether instructional routines with more interruptions or delays promote more frequent problem behavior. Sequential analyses are currently underway to evaluate moment-to-moment patterns between student and teacher behavior within each observation. Evaluating potential relationships between problem behavior and teacher instructional behaviors may inform strategies to support students with persistent problem behavior who receive instruction in general education settings.


Sutherland, K. S., Wehby, J. H., Yoder, P. J. (2002). Examination of the relationship between teacher praise and opportunities for students with EBD to respond to academic requests. Journal of Emotional and Behavioral Disorders. 10(1).
Investigating Cognitive Moderators of Reading Outcomes for Struggling Readers in Elementary Grades

Presenter: Sam Patton (sam.a.patton@gmail.com)

Authors: Samuel A. Patton III, Douglas Fuchs, Peng Peng, Lynn Fuchs, Loulee Yen Haga, Wen Zhang, Nicole Davis, Don Compton

Introduction: This study investigated several possible cognitive moderators - working memory (WM), short-term memory (STM), IQ, attention, and updating ability - in the context of a recent reading comprehension (RC) and WM intervention for struggling readers in third and fourth grades. Students assigned to one of the three treatment groups - RC alone, WM alone, and RC with embedded WM - outperformed their counterparts in the control group (Hedges' g 0.13-0.42) on three standardized RC measures that were collapsed into a single factor score. This investigation sought to provide a more nuanced interpretation of these findings by identifying which, if any, of the interventions proved more effective for students with higher or lower pretreatment levels of cognitive variables identified above.

Methods: The analyses were conducted on data collected as part of research conducted at the Center for Accelerating Academic Achievement of Students with Severe and Persistent Learning Difficulties at Vanderbilt. The study from which these data were collected occurred during the 2014-15 school year and included 116 3rd and 4th grade students from 48 classrooms in 11 Metro Nashville public schools. Students assigned to one of the three treatment groups received 42 25-minute sessions of 1:1 intervention three times per week for 14 weeks. Students in the RC alone and RC+WM groups received instruction in evidence-based reading comprehension strategies using informational texts grouped into thematic units. Students in the RC+WM group read the same texts and completed the same activities as their RC counterparts, but some activities were modified to emphasize processing and recall of relevant information to mirror 'traditional' WM tasks. Students in the WM group completed activities in three categories of working memory tasks (complex span, updating, and inhibition) linked to reading and comprehension; however, these students did not receive any reading instruction.

Results: For all analyses, student-level data were nested within schools and pretest RC performance was controlled for. No significant interactions were found between treatment group and any cognitive variable under consideration. Findings indicated that students with varying levels of WM, STM, IQ, attention, and updating ability did not differentially benefit among the assigned treatment groups.

Discussion: This investigation did not detect statistically significant cognitive moderators of performance across treatment groups. Possible explanations of this include (but are not limited to) an insufficient N per experimental group; weak strength of the interaction between these variables and experimental group; or a truly nonexistent relationship between the cognitive variables and experimental groups. It may also be the case that the efficacy of the interventions is robust for students with different levels of WM, STM, IQ, attention, and updating ability.
An Historical Comparison of Verbal Insults in Tween Television

Presenter: Hannah Peikes (Hannah.s.peikes@vanderbilt.edu)

Authors: Hannah Peikes, Colleen Russo, Geogene Troseth

Introduction: Verbal aggression on television has received relatively little scientific attention, yet televised insults occur often, particularly on 'tween' sitcoms. This content analysis replicates and extends the work by Russo et al. (in prep) which examined the frequency of verbal aggression in the most popular television programs for children during the 1990s (N=6) and the late 2000s (N=8), coding 10 episodes from each program. Results demonstrated that during this time, the amount of verbal aggression doubled (to nearly 20 utterances per episode in the late 2000s).

Methods: A total of 29 pilot episodes of all shows popular with children from 1990 - 2016 were coded for frequency of verbal insults (shows were selected based on Kids Choice Award nominations, consistent with the previous research). To further investigate this historical comparison, 40 episodes from the shows Boy Meets World (from the 1990s) and Girl Meets World (a spinoff from the 2010s) were analyzed. Two trained researchers completed the coding for both current analyses, with 25% overlap in coding to ensure inter-coder reliability.

Results: The analysis of the pilot episodes replicated the findings of Russo and colleagues, in that the number of verbal insults per episode on the television shows in the 2000s were double that of the 1990s (18.3 compared to 8.75, respectively). However, verbal insults on tween sitcoms have actually decreased in recent years—shows form the 2010s thus far prove to be more aligned with the 1990s shows with 11.5 insults per episode. Indeed, the in depth follow-up analysis revealed no significant difference in the number of verbal insults on Boy Meets World (11.3 per episode) compared to Girl Meets World (10.4 per episode).

Discussion: These results both replicate and expand upon that of Russo and colleagues. The continuation of her study shows that there was a peak in the amount of verbal insults in tween television shows between 2000 and 2009. This may be due to the fact that production companies are responding to the increase in childhood bullying, or that children and tweens of today not enjoying shows laden with insults and name calling. Our analysis of Boy Meets World and Girl Meets World further proves the findings of our analysis of the pilot episodes. According to series creator of both television shows, Michael Jacobs, "Girl Meets World" is a new show for a new generation that will be rooted in the same kind of honest, comedic storytelling about coming of age and the importance of family and friendship that made 'Boy Meets World' so popular.' (Huffingtonpost.com, 2013) Our results find this to be true. The findings of these two studies provide hope for the future of children and tween television and for a decrease in childhood bullying.

Characterizing a Direct Interaction between CaMKII and Shank3

Presenter: Tyler Perfitt  (tyler.perfitt@vanderbilt.edu)

Authors: Tyler L. Perfitt, Jason R. Stephenson, Xiaohan Wang, Kristie L. Rose, Christian R. Marks, Terunaga Nakagawa, Roger J. Colbran

Introduction: Shank3 is a postsynaptic scaffolding protein that is important for organizing neurotransmitter receptor signaling complexes at excitatory synapses. Mutations or deletions in the SHANK3 gene are associated with neuropsychiatric disorders, such as autism spectrum disorder (ASD). Shank3 contains several protein-protein interaction domains that link postsynaptic receptors to downstream signaling proteins and the actin cytoskeleton. Calcium/calmodulin-dependent protein kinase II (CaMKII) is a signaling protein that is activated by calcium influx through postsynaptic receptors, and recent proteomics data from our lab found that Shank3 is abundant in CaMKII immune complexes. Therefore, we hypothesized that CaMKII can directly bind to Shank3.

Methods: Immunoprecipitation assays were performed with a GFP antibody from HEK293 cells co-expressing GFP-Shank3 and CaMKII. GST-Shank3 fragments spanning the entire Shank3 protein were incubated with purified CaMKII for GST pull-down assays. Phosphorylation assays were performed using 32P-radiolabeled ATP, CaMKII and GST-Shank3.

Results: We identified a novel direct interaction between Shank3 and CaMKII. Shank3 associates with CaMKII immune complexes isolated from synaptic fractions of mouse forebrain and from co-transfected heterologous cells. Activated, T286 phosphorylated CaMKII can directly interact with a GST fusion protein containing residues 829-1130 of Shank3, and mutation of residues 949-951 (RRK) to alanine essentially abolishes binding in vitro and in heterologous cells. We also found that CaMKII phosphorylates Shank3 in vitro and identified multiple phosphorylation sites in the PDZ and SAM domains using a combination of phospho-proteomics analysis and site-directed mutagenesis.

Discussion: The phosphorylation or interaction with Shank3 may allow CaMKII to play an important role in functionally regulating Shank3. Ongoing studies are examining the impact of CaMKII on Shank3 localization in neurons, scaffolding interactions with other synaptic proteins, and on synaptic signaling to the nucleus.
Piloting a Rhythmic Speech Production Paradigm for Children and Potential Links to Language and Music Skills

**Presenter:** Rita Pfeiffer  (rita.pfeiffer@vanderbilt.edu)

**Authors:** Rita Pfeiffer, Alison Williams, Carolyn Shivers, Reyna Gordon

**Introduction:** A growing body of work points to a relationship between rhythm abilities and language skills, including grammar. Individual differences in sensitivity to rhythmic aspects of speech could be a mechanism underlying the association between musical rhythm and grammar skills found in our preliminary work. To assess this, we first modified a rhythmic speech production task and conducted a pilot study to determine whether typically developing six-year-olds would be able to do the following: 1) consistently say a given phrase with the same rhythm across multiple trials; 2) maintain a steady internal pacing; and, 3) synchronize their speech with an isochronous metronome.

**Methods:** We employed a modified version of the speech cycling task (Cummins and Port, 1998), in which participants speak short, metrically regular phrases along with an isochronous metronome. Twelve six-year-old children repeated a set of ten phrases (e.g., 'beg for a dime') with two patterns (whole note metronome: one click per cycle, and half-note metronome: two per cycle).

**Results:** Primary speech beats within each phrase were marked using an algorithm and analyzed in numerous ways: subdivision of beats within a phrase, the steadiness of pacing, and synchronization to the metronome. Preliminary findings show clear metrical organization of speech beats within each phrase. The metronome pattern (i.e., presence of a subdivided beat) significantly influenced children's ability to maintain a steady pace of speech and synchronize with the metronome, suggesting the importance of external rhythmic cues in scaffolding children's underlying synchronization.

**Discussion:** Pilot results show promise for future use of the paradigm to test an overlap of speech rhythm sensitivity, musical rhythm perception, and expressive grammar abilities. Ongoing work entails validating the speech cycling paradigm and enhancing its feasibility for assessment and intervention purposes.
The thermal effect in a mouse model of simple GABRG2 haploinsufficiency

Presenter: Sarah Poliquin  (sarah.e.poliquin@vanderbilt.edu)

Authors: Sarah Poliquin, Subhash Gutti, Huancheng Dong, Timothy Warner, Jing-Qiong Kang

Introduction: The inhibitory neurotransmitter GABA has several receptor isoforms in the mammalian nervous system, the predominant isoform being α1β2γ2. Mutations in the GABA receptor (GABAAR) can result in epilepsy because of reduced inhibitory GABAergic neurotransmission of the neurons. Of the many GABAAR subunits, the most epilepsy-causing mutations are in the γ2 subunit. These mutations include nonsense, missense, frameshift, deletion or insertion, and splice-site mutations. The resulting epilepsies range from relatively mild childhood febrile or absence seizures to the most severe form of epilepsy, Dravet syndrome. It is believed that the milder phenotypes are the result of haploinsufficiency due to the mutated GABRG2 gene while the more severe epilepsies are caused by toxic gain of function from the mutated gene.

Methods: In this study, γ2 knockout (KO) Gabrg2+/- mice were used to model haploinsufficiency. The mice were surgically implanted with a headmount electrode to record their EEG and EMG output. With the use of a heat lamp, the mice were heated until they reached a core body temperature of 42.5 °C to model a fever situation.

Results: When exposed to heat, wildtype littermate control mice began jumping at an average core body temperature of 40.36 °C while the KO mice began jumping at 39.67 °C. During the heat exposure, the KO mice had increased occurrence of spike-wave-discharges (SWDs) and myoclonic jerks. Additionally, the wildtype mice had only an average of 2 seizures (primarily myoclonic jerks, with some absence seizures) in a 30-minute post-heat observation period, compared to an average of 37.5 for the KO mice.

Discussion: Our findings support the hypothesis that GABRG2 haploinsufficiency lowers the temperature threshold for febrile seizures.
The functional neural overlap between arithmetic and phonological processing in children: A meta-analysis

Presenter: Courtney Pollack  (courtney.pollack@vanderbilt.edu)

Authors: Courtney Pollack, Nicole C. Ashby

Introduction: Mathematics and reading skills are interrelated. In particular, prior research has shown that phonological processing ability predicts arithmetic fact retrieval ability in children (e.g., De Smedt et al., 2010). At the brain level, arithmetic fact retrieval elicits brain activity in left lateralized frontal and temporoparietal brain regions that are implicated in phonological processing (e.g., Prado et al., 2011). However, whether common brain regions support both arithmetic and phonological processing is unclear.

Methods: In this study, we conducted a meta-analysis using Activation Likelihood Estimation (ALE) to examine the functional neural overlap between arithmetic and phonological processing in children. We hypothesized there would be clusters of overlapping activation in left frontal and temporoparietal regions.

Results: Results showed four clusters of concordant activation in frontal regions: right anterior insula, left precentral gyrus, left superior frontal gyrus, and left inferior frontal gyrus, and one cluster in temporo-occipital cortex in the left fusiform gyrus. Contrary to expectation, we found no clusters in temporoparietal cortex.

Discussion: Clusters in frontal areas may support attentional processes while the cluster in the fusiform gyrus may support symbolic processing of arithmetic problems and words. The present meta-analysis sheds light on brain regions that support both arithmetic and phonological processing, and lends additional support to the interconnectedness of mathematics and reading processes at the brain level.


Longitudinal study of respiratory sinus arrhythmia and developmental stuttering: Preliminary results

Presenter: Dillon Pruett  (dillon.g.pruett@vanderbilt.edu)

Authors: Dillon Pruett, Robin Jones, Tedra Walden

Introduction: Developmental stuttering is a speech disorder that typically begins in early childhood at approximately age three and is characterized by syllable and word repetitions and prolongations (Yairi & Ambrose, 2013). Despite a growing empirical knowledge base on factors that contribute to the development of stuttering, there is a need for a greater understanding of the precipitating and exacerbating factors of childhood stuttering. One theoretical account of childhood stuttering suggests that emotional reactivity, emotion regulation and their interaction are associated with the onset and the development of childhood stuttering (Walden & Conture et al., 2012). Respiratory sinus arrhythmia has been used in both biological and psychological studies in children and can be used as an index of emotion regulation (Porges, 2007). By using physiological correlates of autonomic processes, measures of RSA can provide information about internal temperamental and emotional states that can be difficult to assess exclusively via observation. The purpose of this study is to investigate potential longitudinal differences in respiratory sinus arrhythmia between preschool-age children who stutter and persist (CWSP), children who stutter and recover (CWSR), and children who do not stutter (CWNS).

Methods: Participants were 10 preschool-age children who stutter and persist (CWSP), 28 preschool-age children who stutter and recover (CWSR), and 27 children who do not stutter (CWNS). Participants were exposed to two emotion inducing video clips (negative and positive) with neutral clips used to establish pre- and post-arousal baselines. Video clips and baselines were followed by age appropriate speaking tasks. Respiratory sinus arrhythmia (RSA) - often used as an index of parasympathetic activity was measured while participants listened to and watched a video clip and also while performing a speaking task. Participants completed 3 to 5 visits over the course of 24 to 32 months.

Results: Results are expected to show that, at time point one, preschool-age children who stutter and persist and children who stutter and recover will exhibit lower RSA at baseline and higher RSA during speaking tasks compared to children who do not stutter. Final longitudinal results are in preparation.

Discussion: Findings will be taken to assess the role of emotion regulation, indexed physiologically by RSA, in the developmental trajectory of childhood stuttering.


Anger Appraisal Universality

Presenter: Weiqiang Qian (weiqiang.qian@vanderbilt.edu)

Authors: Weiqiang Qian, Craig A. Smith, Leslie Kirby

Introduction: Specific patterns of appraisals are tightly linked to the experience of specific emotions, but whether such patterns are universally related to these emotions has been subject to considerable debate. Some scholars have argued that appraisals of other accountability are not necessary for some people to experience anger. To address this issue, model based categorization methods were applied to a sample of 502 subjects with high anger ratings, selected from 1700 subjects aggregated across 18 studies. The goal was to extract classes of subjects with distinctive appraisal profiles for experiencing anger within a broad sampling of anger elicitation scenarios, which was assumed to approximate the range of possible situations that produce anger.

Methods: Subjects from the top quartile of anger rating were categorized with latent profile analysis (LPA) and multivariate finite normal mixture modeling (MFNM). Using appraisal ratings as observed variables, LPA and MFNM identify the latent groups of appraisal patterns that generate anger under the observed conditions. A modified likelihood ratio testing and several model fit indices were used for identifying the best models.

Results: The best model selected based on model fit indices yields a 3-class model for LPA: self-accountable, other-accountable, and a pattern with no obvious accountability appraisals, while MFNM yields a 2-class model including an other-accountable and a mildly self-accountable classes. By using anger rating as a predictor for classification, both the conditional 3-class LPA model and the conditional 2-class MFNM model confirm that the odds ratios of being classified into the no-accountability and self-accountable anger classes versus the other-accountable class are all significantly smaller than 1 for every unit increase in anger rating. These odd ratios mean that subjects with higher anger ratings are more likely to be placed in the other-accountable class than in other classes. Furthermore, for the 3-class LPA model, a reparameterization using the self-accountable class as the reference class shows that the odds ratio of being classified into the no-accountability versus the self-accountable anger classes is also significantly smaller than 1 for unit increase in anger rating.

Discussion: The no-accountability appraisal profile for anger, used by some scholars to argue against accountability appraisals being universal in inducing anger, is simply unable to produce strong anger. Self-accountable anger also seems to provide a less angry experience than does a strong other-accountability appraisal. However, compared to the no-accountable class, self-accountable class still allows for a more intense anger experience, and more importantly, self-accountable anger reflects a special types of anger. Self-directed anger has only started to receives attention in literature, so further analyses are needed to better understand this type of anger.
Parent Perceptions of Communication, Home Routines, and Intervention Goals

Presenter: Emily Dayle Quinn  (emily.d.quinn@vanderbilt.edu)

Authors: Emily D. Quinn, Sonya M. Kapoor, Ann P. Kaiser

Introduction: Including caregivers in language intervention facilitates generalization to daily contexts and represents recommended practice in early intervention. Caregiver-implemented language interventions involve a professional teaching caregivers how to use specific language support strategies to improve language development in their children. Even though the efficacy of caregiver-implemented interventions for young children with autism has been explored in the literature, research examining caregiver perspectives, especially parents with children who are minimally verbal is notably absent. Understanding parents' experiences and perceptions of (a) their child's communication, (b) speech-language language interventions, and (c) family routines will provide insight to improve existing caregiver implemented interventions for families of minimally verbal children with ASD. This project attempts to understand the perspective of caregivers of young minimally verbal children with ASD in the context of a larger randomized control trial of an intervention blending a naturalistic language intervention and Discrete Trial Training. Specifically, the project proposes the following broad research questions: (1) What perceptions do parents' of minimally verbal children with autism report regarding their children's communication skills? (2) What types of child, family, community, or environmental factors do parents identify as supporting or challenging participation in every day activities and family routines? (3) What are parents' expectations and goals for their child's participation in in speech-language intervention?

Methods: Study participants were 30 parents of young minimally verbal children with ASD. All participants were participating in a larger longitudinal study of a blended naturalistic language intervention. Parent's perceptions of their child's communication skills, family supports and challenges, and goals for speech language intervention were gathered using a semi-structured ethnographic interview, The Family Story. Interviews were digitally recorded and transcribed word for word. A Constant Comparative Analysis approach was used to compile all data related to child communication, daily supports and challenges, and goals for speech language intervention. Research assistants coded all transcripts using qualitative analysis software, Nivo11. After an iterative process including close coding and axial coding, a formal coding scheme was developed. The investigators extracted themes within each parents account and compared these themes identified in other parent's accounts. Relationships between themes were identified and confirmed.

Results: The final analysis will report themes that were predominant in the parents' accounts of their child's communication skills, supports and challenges within home routines, and communication goals. Select excerpts representative of these themes will be highlighted on the presentation poster, along with data display matrices.

Discussion: The results will have clinical implications for caregiver-implemented language interventions as clinicians form a more clear understanding of parent perceptions and goals for their child with ASD, as well as family supports and challenges.
In Vivo Efficacy of VU0431316, an mGlu5 Negative Allosteric Modulator, in the CK-p25 Mouse Model of Alzheimer’s Disease

Presenter: Deepa Rajan  (deepa.h.rajan@vanderbilt.edu)
Authors: Deepa H. Rajan, Jonathan W. Dickerson, Jerri M. Rook

Introduction: Alzheimer's disease (AD) is the prevalent form of dementia and features progressive neurodegeneration. AD presents excessive neuronal and synaptic loss, potentially the result of cell death due to excitotoxicity, and may be associated with the over-activation of N-methyl-D-aspartate (NMDA) receptors. Memantine, an NMDA inhibitor that is currently approved for AD treatment, offers little therapeutic efficacy, possibly due to its weak NMDA receptor activity. Metabotropic glutamate receptor 5 (mGlu5) regulates NMDA receptor activity, providing a novel mechanism to reduce NMDA receptor function and excitotoxicity in AD. Furthermore, the highly conserved allosteric site on mGlu5 facilitates greater binding specificity. Statement of Purpose: To test the hypothesis that potent mGlu5 negative allosteric modulator, VU0431316, will slow disease progression in the CK-p25 inducible mouse model of AD in the absence of unwanted adverse side effects.

Methods: Basal locomotor, rotor rod, marble-burying, fear-conditioning, and novel object recognition assays (assessing locomotion, motor coordination, anxiety, and learning and memory, respectively) were performed on CK-p25 mice. Mice were tested prior to the onset of AD pathology to determine baseline levels and were subsequently evaluated again after pronounced disease progression.

Results: In CK-p25 mice with advanced AD pathology, VU0431316 demonstrated anxiolytic and cognition-enhancing effects in the absence of impairment of locomotion and motor coordination. VU0431316 exhibited no effects on basal locomotion, motor coordination, anxiety, or cognition prior to induction of AD pathology.

Discussion: Preliminary data suggest that VU0431316 may possess disease-modifying efficacy in AD and shows substantial promise for slowing AD progression in animal models.
Latent transition assessment of late-emerging poor readers

Presenter: Miranda Richmond  (miranda.richmond@vanderbilt.edu)

Authors: Miranda C. Richmond, Stephen K. Bailey, Laurie Cutting

Introduction: Some children exhibit typical reading development in early primary school grades but later begin to struggle. This transition often occurs around fourth grade, when students transition from 'learning to read' in the classroom to 'reading to learn'. At this age, students must engage a wider array of cognitive processes, including those related to language comprehension and executive function, to perform well. Previous studies have suggested that up to 13% of children could be classified as 'late-emerging poor readers', about half of whom struggle primarily with comprehension and half of whom struggle with word reading skills or both (Catts, Compton, Tomblin and Bridges, 2012). In this study, we followed a group of first graders (N=140) longitudinally from first to third grade in an effort to identify children with possible late-emerging reading disorder (LERD).

Methods: Latent transition analysis was utilized to estimate the prevalence of good and poor readers at each time point, as well as their transition between those discrete groups. A two-class latent variable was estimated at each time point using categorical predictor variables delineating good and poor readers based on measures of word reading and reading comprehension. Measures were converted into z-scores and dichotomized so that scoring one standard deviation below the mean indicated poor reading. The transition of interest for the purpose of identifying LERD was end of first grade (V1) to end of third grade (V3).

Results: Overall at V1 and V3 a majority of subjects were defined as good readers (~83%) and the remaining subjects were defined as poor readers. Latent transition probabilities are expressed as the probability of being in one of the discrete classes at V3 based on classification at V1. Those subjects defined as poor readers at V1 had a high chance of remaining poor readers at V3 and little chance of transitioning to a good reader. Those defined as good readers at V1 were likely to remain good readers at V3, but a small group transitioned to being poor readers.

Discussion: Our results support the existence of a subset of readers who initially resemble typically developing readers but later exhibit reading difficulty compared to their peers. Future analyses including additional comprehension measures and executive functioning measures will seek to elucidate what the sources of late-emerging reading difficulty are and which might be evident in first grade.

Serotonin receptor 5-HT3A impacts autonomic neurogenesis and urinary bladder function

Presenter: Elaine Ritter  (elaine.ritter@vanderbilt.edu)

Authors: K. Elaine Ritter, Dennis P. Buehler, E. Michelle Southard-Smith

Introduction: The autonomic nervous system originates from the neural crest and is required for the proper function of all visceral organs, including the bladder and genitalia. Despite the wide prevalence of bladder dysfunction, few effective treatment options are available. Pelvic innervation regenerative strategies are promising, but surprisingly little is known about the molecular drivers of sacral autonomic neurogenesis.

Methods: We conducted a microarray analysis of sacral neural crest progenitors and differentiating autonomic pelvic ganglia. Upon identification of serotonin receptor 5-HT3A as a promising candidate, we used the Htr3a-EGFP transgenic reporter mouse line in conjunction with immunohistochemistry to characterize its expression over the course of fetal and postnatal development. Pharmacological assays on fetal pelvic ganglia explants were conducted to determine the role of 5-HT3A in autonomic neurogenesis. To determine the role of 5-HT3A in adult bladder function, we conducted physiological bladder assays with the Htr3a knockout mouse line.

Results: We observed robust expression of 5-HT3A in both sympathetic and parasympathetic autonomic pelvic ganglia neurons innervating the bladder that is maintained through fetal and postnatal development. Treatment of fetal pelvic ganglia explants with SR57227A, a potent 5-HT3A receptor agonist, resulted in dose-dependent blunting of neurite branching. Loss of 5-HT3A expression in mice results in aberrant proportions of autonomic lineages in pelvic ganglia and impaired urinary bladder function in adult animals.

Discussion: Our studies identify serotonin receptor 5-HT3A as a key player in the development of autonomic bladder innervation, with roles in both neuronal subtype differentiation and acquisition of normal neurite morphology. Function of this receptor is also necessary for normal urinary voiding in adult mice. Our findings reveal a novel role for this serotonin receptor in neural crest development and are relevant for elucidating underlying neurologic causes and treatments of urinary incontinence.
Neural Stem Cell Positional Identity Corresponds to Differential mTOR Activity in Subdomains of the Ventricular-Subventricular Zone

Presenter: Gabrielle Rushing (gabrielle.v.rushing@vanderbilt.edu)

Authors: Gabrielle V. Rushing, Nalin Leelatian, Amanda Jurewicz, Asa A. Brockman, Jonathan M. Irish, Rebecca A. Ihrie

Introduction: The ventricular-subventricular zone (V-SVZ) is the primary neurogenic niche in the postnatal brain, and is thought to be a site of origin for many brain tumors. Stem/progenitor cells (NPCs) in this niche have a positional identity: the cell's position predicts the types of progeny that will be generated, suggesting intrinsic differences between stem cell microdomains. However, it is not known whether the intrinsic patterning of NPCs corresponds to measurable proliferative signaling differences that may influence tumor development. We have developed phospho-specific flow cytometry assays in cultured NPCs to simultaneously measure the per-cell levels of multiple phospho-proteins relevant to mTOR pathway signaling, as this pathway is disrupted in many types of brain tumors. Flow cytometry and immunofluorescence data show that NPCs within the ventral subregion of the V-SVZ have elevated basal mTOR pathway activity as compared to their dorsal counterparts. As increased mTOR activity leads to increased cell size and protein translation, this raises the question of whether specific NPC subpopulations contribute differentially to the formation of brain tumors due to intrinsic differences in basal signaling.
Emerging role of GluN2D-containing NMDARs in modulating synaptic plasticity within the bed nucleus of the stria terminalis and anxiety/depressive-like behaviors.

Presenter: Gregory Salimando  (gregory.j.salimando@vanderbilt.edu)

Authors: Gregory J. Salimando, Tiffany A. Wills, Danny G. Winder

Introduction: The bed nucleus of the stria terminalis (BNST) plays an important role in regulating affective stimuli such as stress and anxiety that have been well-established as precipitating factors for major depressive disorder. Previously, our lab has shown that disrupting glutamatergic signaling in the BNST via the ablation or inhibition of N-methyl-d-aspartate receptors (NMDARs) containing the subunit GluN2B alters regional synaptic plasticity and produces an anti-depressant-like phenotype in mice. Using a proteomic strategy to analyze BNST tissues and identify GluN2B-associated proteins, we found that another NMDAR subunit, GluN2D, was co-expressed with GluN2B in synaptosomal fragments. The GluN2D subunit is known to possess slower deactivation kinetics and increased sensitivity to glutamate, suggesting that the presence of GluN2D-NMDARs in the BNST may play a unique role in mediating regional excitatory signaling.

Methods: Due to the previous role we established for GluN2B in NMDAR function and signaling, we investigated whether changes in GluN2D expression altered synaptic excitability in BNST. Additionally, because the BNST is a highly heterogeneous region, we sought to determine if the GluN2D subunit was expressed selectively in certain cell populations compared to others.

Results: We find that long term potentiation (a measure of synaptic strength/activation) in the BNST is significantly reduced during the early stages of induction in slices from GluN2D knockout animals compared to wildtype controls. Overall maintenance and duration of potentiated signals, however, is not altered in either condition. We next utilized RNAscope® fluorescent in situ hybridization to distinguish between different BNST cell populations, and find that GluN2D mRNA is highly co-localized with the stress hormone corticotropin releasing factor (CRF), with ~70% of CRF positive BNST neurons expressing GluN2D mRNA along with GluN2B mRNA. These data point to possible changes in the excitatory activity of neurons that participate in the regulation and interpretation of stressful stimuli, and may lead to alterations in behavioral response. We assessed baseline performance of GluN2D knockout mice in the elevated zero maze (EZM), open field (OF), light/dark box (L/D) and forced swim test (FST) and find that they exhibit phenotypic profiles across these tasks consistent with increased anxiety- and depressive-like behaviors.

Discussion: Taken together, these data suggest that GluN2D-containing NMDARs may participate in regulating depressive/anxiogenic behavioral outputs by altering excitatory signaling in a number of key brain regions and neuronal populations, with the BNST and CRFergic cells being prime candidates for further examination for the effects of targeted GluN2D loss/inhibition.


**Who Helps? Characteristics and Correlates of Informal Supporters to Adults with Intellectual and Development Disabilities**

**Presenter:** Kelli Sanderson (kelli.a.sanderson@vanderbilt.edu)

**Authors:** Kelli A. Sanderson, Meghan M. Burke, Richard C. Urbano, Katie Arnold, Robert M. Hodapp

**Introduction:** With diminishing funding for state agencies and long waiting lists for services, it is estimated that only 1 in 4 adults with intellectual and developmental disabilities (IDD) receive formal supports (i.e., paid supports). Instead, individuals and families are turning to informal, or natural (i.e., unpaid) supports. While much discussed, informal supports have been the focus of little research. This study was designed to examine informal supports in terms of: (1) Who provides informal supports to adults with disabilities and does the number of supporters differ across recreation, employment, and housing?; (2) For those supporters who are not family members, who are these people and are they connected to family supporters?; and (3) Which characteristics of the adult with IDD, parents, or siblings relate to the number of informal supporters in each area?

**Methods:** Siblings of 657 adults with IDD responded to a nationwide, web-based survey. Respondents were primarily female (86%) and middle-aged (X = 37.5 years), with individuals with disabilities predominantly male, middle-aged, and with intellectual disabilities and autism. Respondents reported on characteristics of their brother-sister with disabilities (gender; age; type of disability; residence); their parents (alive-deceased; age ; ability to care for individual with IDD); and sibling respondents' legal guardian status. Concerning the Work, Housing, and Leisure of the individual with IDD, respondents noted whether informal support was provided by the following individuals: sibling respondent; another sibling; parents; other family members; and non-family members.

**Results:** Although most adults with IDD received informal support, differences emerged across areas and supporters. Higher total numbers of supporters occurred in Leisure (X = 2.17) compared to Housing (1.69) or Work (1.43), F (2, 1312) = 80.09, p < .0001; conversely, higher percentages had no informal supporter listed in Work (27.9%) versus Housing (16.1%) or Leisure (11.6%). For all areas, the most common informal supporters were parents (from 53.6%-Work to 69.4%-Leisure); followed by sibling respondents (33.3%-Work to 65.3%-Leisure), and non-family supporters (22.7%-Housing to 39.0%-Leisure). The number and presence of informal supporters were related to family. When mothers were aged 70 or older (compared to younger), fewer informal supporters were listed for both Work and Leisure (not for Housing). Fewer informal Work or Leisure supporters also occurred when mothers had poorer health (p's < .001). Finally, family members-especially parents and sibling respondents-served as facilitators of non-family informal supporters. Across Work, Housing, and Leisure, rarely were any non-family supporters present when an individual with IDD had no family supporters (all p's < .002).

**Discussion:** Informal supports most often occurred in Leisure (versus Housing or Work) and were comprised of parents, respondents, and non-family members. As we strive to assist individuals with IDD and their families to access the supports they need, these findings have important implications for future research, practice, and policy.
Aided AAC Modeling for Children with Complex Communication Needs

Presenter: Elizabeth Biggs  (elizabeth.e.biggs@vanderbilt.edu)

Authors: Elizabeth E. Biggs

Introduction: All children need access to communication that empowers them to express their wants and needs, interact socially, participate in their environments, and share information about the world. Many children quickly develop communication using natural speech by being exposed to rich language models. However, for children with complex communication needs who use augmentative and alternative communication (AAC), linguistic input is more complicated because children may rarely see others communicate in this way. Aided AAC modeling (i.e., modeling use of an AAC device) may improve their linguistic input by demonstrating the device is an encouraged mode of communication and facilitating language mapping-helping children build connections between spoken words, graphic symbols, and their referents. This poster presents a systematic review of interventions using aided AAC modeling, addressing the following question: Are interventions involving aided AAC modeling effective in improving the expressive communication of children with complex communication needs?

Methods: Through a systematic search, 48 studies were identified (a) using experimental group or single-case design, (b) involving children (i.e., 21-years or younger) with congenital disabilities, (c) evaluating an intervention involving aided AAC modeling, and (d) measuring effects on expressive communication. Coding addressed three areas: descriptive information, methodological quality, and efficacy. Given concerns about non-overlap effect size metrics in single-case research, efficacy coding involved classifying dependent variables into broad categories of effectiveness using guidelines from the Council on Exceptional Children (2014).

Results: Forty-six studies used single-case design, involving a total of 144 participants meeting inclusion criteria; two group-design studies included 123 participants. Intervention approaches included: (a) focused interventions involving augmented input, (b) packaged interventions involving augmented input, (c) packaged interventions involving models as prompts, (d) packaged interventions involving models within instructional demonstrations, and (e) packaged interventions combining modeling approaches. Interventions had positive or strong positive effects on most dependent variables; mixed effects were demonstrated for 14.5% of variables (n = 8), most of which measured natural speech.

Discussion: Interventions involving aided AAC modeling positively impact children's communication. However, more research is needed investigating whether these interventions may also promote children's use of natural speech. Few studies measured dependent variables as potentially generalized behaviors, with most using context-bound assessment approaches. Although these measurement approaches limit evaluating of whether interventions equip children with highly generalized communication skills, there is evidence a variety of interventions involving aided AAC modeling support children's communication within particular contexts which provides opportunities to practice and build fluency with communication skills, encourages participation in inclusive environments, and promotes social interaction.

Developing a method to examine the role of sensorimotor mechanisms of stereotyped behavior in autism spectrum disorders

**Presenter:** Robin Shafer  (robin.l.shafer@vanderbilt.edu)

**Authors:** Robin L. Shafer, James W. Bodfish

**Introduction:** The emergence of motor stereotypy is indicative of neural pathology in several neurodevelopmental and neuropsychiatric disorders including autism spectrum disorders (ASD); however, it is also present early in normative development during the transition from simple, uncontrolled movements to complex, controlled movements. Unlike in ASD, stereotypy in healthy infants begins to decrease within the first year of life and is replaced with goal-directed motor behavior. Research in normative development demonstrates the importance of sensory feedback for the development of motor complexity - as children develop the ability to integrate sensory information from the environment with motor behavior, their behavior becomes less stereotyped and more complex, allowing them to interact adaptively in the environment. This is consistent with our understanding of sensorimotor integration in the brain. Prior studies from our group have found that individuals with ASD who have motor stereotypy also have reduced motor complexity, consistent with the notion that motor stereotypy is a manifestation of low motor complexity. Additionally, individuals with ASD often present with unusual sensory symptoms suggesting that sensory processing deficits may contribute to the development of stereotyped actions. To date, the contribution of motor and sensory factors to the development of stereotyped behavior has only been examined in isolation. There is a need for methods that assess the joint sensory and motor contributions to the emergence of the core features of ASD.

**Methods:** The purpose of this study is to develop a method for objectively measuring the role of sensory feedback on motor performance in ASD at the level of both brain and behavior. We are adapting methods from studies of normative motor development to assess the effect of sensory feedback on motor complexity in individuals with ASD and relate these metrics to concurrent neural activity. Our method involves the use of virtual reality gloves that monitor hand position in real time and provide sensory feedback in the form of vibro-tactile stimulation. Participants perform a task during which they use their index finger to track a moving stimulus on a screen. For half of the trials, participants receive online vibro-tactile feedback at the fingertip if they deviate from the stimulus, and in the other half of the trials, they do not receive vibro-tactile feedback. Performance is measured using indices of complexity of movement kinematics (via accelerometers embedded in the gloves) and neural complexity (via electroencephalography). Here, we present preliminary results from this novel approach focusing on (a) method feasibility and test-retest reliability and (b) the application of nonlinear dynamic analytic techniques to examine coupling of neural and behavioral output during this sensorimotor task.
**Missense mutations in the dopamine transporter network are associated with autism spectrum disorders**

**Presenter:** Aparna Shekar  (aparna.shekar@vanderbilt.edu)

**Authors:** Aparna Shekar, Nicholas G. Campbell, Andrea N. Belovich, James S. Sutcliffe, Heinrich J.G. Matthies, Kevin Erreger, Aurelio Galli

**Introduction:** Missense mutations are an important class of risk factors for autism spectrum disorder (ASD). Recently, whole exome sequencing of ASD families has identified novel missense mutations in the human dopamine (DA) transporter (hDAT) gene (SLC6A3), and one of its interacting partners syntaxin 1A (STX1A), resulting in aberrant transporter function. The hDAT is a presynaptic membrane protein that regulates dopaminergic tone in the central nervous system by mediating the high-affinity re-uptake of synaptically released DA, making it a crucial regulator of DA homeostasis. Here, we report the functional characterization of independent ASD-associated missense mutations in hDAT and STX1A.

**Methods:** We aim to create a novel platform of discoveries stemming from the structural and functional characterization of multiple new variants recently identified in individuals diagnosed with ASD. We engineered these ASD variants in hDAT to determine their putative structural and functional deficits in heterologous expression systems and primary neuronal cultures. We will compare the activities of wild type and variant hDAT by examining radioactive DAT-mediated [3H]DA uptake/function and DA affinity (Km), as well as by determining the maximal velocity of DA influx (Vmax). If changes in DAT transport capacity are observed, we will correlate these changes to either total or surface hDAT expression, using surface biotinylation. If the variants display normal surface expression, we will adopt amperometry (which measures DA fluxes by oxidation/reduction reactions) to define whether there exist any deficits in the reverse transport or 'efflux' properties of the transporter variant.

**Results:** We demonstrate that each mutation dramatically alters hDAT function, and they converge at the psychostimulant Amphetamine's ability to induce hDAT-mediated reverse transport of dopamine. While the hDAT T356M and A559V variations show anomalous dopamine efflux or a basal 'leak' phenotype, the hDAT R51W and STX1 R26Q variations show an alteration in amphetamine-induced efflux of dopamine.

**Discussion:** These results, when taken together with prior association of abnormal DAT function with ASD, may inform the link between hDAT dysfunction and the resulting impairment in DA neurotransmission with certain phenotypes associated with ASD. More importantly, this work adds to the growing body of literature implicating altered regulation of DA homeostasis/transport as a potential biological mechanism underlying liability to ASD.


**Increasing Access to Community Based-Care: The IDD Health Care Toolkit, Training Series and Telehealth Project**

**Presenter:** Janet Shouse  (janet.shouse@vanderbilt.edu)

**Authors:** Elise McMillan, Janet Shouse, Beth Malow, Tom Cheetham

**Introduction:** The Vanderbilt Kennedy University Center for Excellence in Developmental Disabilities (VKC UCEDD), in partnership with the Tennessee Department of Intellectual and Developmental Disabilities and TennCare, created two free, modular online training series focused on improving health care for adults with intellectual and developmental disabilities. Among the many health disparities that people with intellectual and developmental disabilities experience, research has found that often psychotropic medications are prescribed for people with IDD to try to address 'challenging behavior,' despite little evidence that such medications are effective in treating such behaviors. The hope is that by providing these training opportunities, inappropriate uses of psychotropic medications can be reduced, and individuals with IDD are able to receive the most appropriate physical and behavioral health care possible.

**Methods:** In 2014, the VKC UCEDD launched the IDD Toolkit, (www.iddtoolkit.org), an online resource for health care providers to better serve adults with IDD. The two training series are based on information in the Toolkit. One series targets health care professionals and offers free CME/CPD credits. The second training is intended for individuals with IDD, their families, and conservators and other caregivers, including direct support professionals.

**Results:** From Sept. 1, 2015, to June 30, 2016, 592 health care professionals have completed the eight modules of online training. For those receiving AMA or AAFP credit, 48% said they would change something in their practice as a result of having done the online training. Of those receiving APA credit, 92% said it would enhance their work, and 95.5% would recommend the training to others. For the family/caregiver training, 125 people have watched at least one module. Unfortunately, very few of the family members completed an evaluation. Of those who completed an evaluation, all agreed or strongly agreed that, as a result of this training, they had an increase in knowledge or skills.

**Discussion:** There is a huge need for additional training for primary care providers to have the knowledge, comfort level and skills to appropriately serve adults with developmental disabilities. The ‘commitment to change’ and the high recommendation levels attest to the value of this 90-minute online training.
Investigating a Critical Period Needed for Perinatal Photoperiod Effects on the Serotonergic System

**Presenter:** Justin Siemann  (justin.k.siemann@vanderbilt.edu)

**Authors:** Justin K. Siemann, Noah Green, Hideki Iwamoto and Douglas G. McMahon

**Introduction:** Globally, it is estimated that over 350 million individuals suffer from depression while 16 million Americans have reported experiencing at least one depressive episode. In addition, studies have shown seasonally varying risks for mood disorders with higher rates occurring during the fall or winter months when daylight is lowest in the year. The serotonergic system is known to be impacted by the duration of light exposure (i.e. photoperiod) and has been implicated in mood disorders, providing a promising new area of research. Thus, evaluating the mechanisms underlying the interaction between photoperiod and this system may provide understanding that is critical for developing insights into the etiology and novel treatment options. Recently, our lab has shown that mice exposed during development to long summer-like photoperiods of 16 hours of light and 8 hours of darkness each day (LD 16:8) demonstrate a greater neuronal firing rate of dorsal raphe serotonin neurons in isolated brain slices and higher levels of monoamines (i.e. serotonin and norepinephrine) in the midbrain along with more anxiolytic and anti-depressive behavioral effects compared to animals exposed to short winter-like LD 8:16 photoperiods or equinox LD 12:12 photoperiods. Based on these prior findings that used a developmental photoperiod from E0 to P30, we have now focused on when these photoperiod changes occur in development (i.e. the critical period), resulting in lasting changes in the serotonergic system.

**Methods:** From E0 to P0, C3Hf+/+ mice developed under either long or short photoperiods. At birth, animals were then switched to the opposite photoperiod and developed until adulthood (P50-P90). During adulthood, multielectrode array electrophysiological recordings were then performed on acute brain slices to evaluate the average firing rate of serotonin neurons in the dorsomedial region of the dorsal raphe nucleus.

**Results:** Specifically, we found that when animals were exposed only prenatally (E0-P0) to long photoperiods and then switched to a short photoperiod at birth, the average firing rate of dorsal raphe serotonin neurons measured in adulthood (P50-P90; 1.18 ± 0.076 Hz) resembled the firing rate for animals which continued to develop under a long photoperiod (1.24 ± 0.084 Hz). Interestingly, raphe neurons from animals that were prenatally exposed to a short photoperiod and then switched to a long photoperiod at birth, displayed an intermediate firing rate (0.99 ± 0.083 Hz) compared to those that were continuously exposed to either a long (1.24 ± 0.084 Hz) or short photoperiod (0.69 ± 0.024 Hz) throughout development.

**Discussion:** These findings demonstrate that photoperiodic programing of serotonin neurons can occur in utero, long photoperiods may be serving as an active agent and affecting the serotonergic system perinatally, and exposure to short photoperiods in utero may extend the critical period into the perinatal period. By evaluating a developmental critical period for the effects of photoperiod on the serotonin system, this may provide novel insights into therapeutic treatments for mood related disorders.
Neural Correlates of Sensory Hyporesponsiveness in Toddlers at High Risk for Autism Spectrum Disorder

Presenter: David Simon  (David.m.simon@vanderbilt.edu)

Authors: David M. Simon, Cara R. Damiano, Tiffany G Woynaroski, Lisa V. Ibañez, Michael Murias, Wendy L. Stone, Mark T. Wallace, Carissa J. Cascio

Introduction: Altered patterns of sensory responsiveness are a frequently reported feature of autism spectrum disorder (ASD), and are hypothesized to contribute to other core characteristics of the disorder. Younger siblings of individuals with ASD are at a greatly elevated risk of future diagnosis, and patterns of reduced sensory responsiveness emerge early in their development. Previous research has not characterized how patterns of neural activity in these high risk children relate to profiles of sensory responsiveness.

Methods: Younger siblings (n = 16) of children diagnosed with ASD participated in resting electroencephalography (EEG) at age 18 months. Data on toddlers' sensory responsiveness to daily environmental stimuli were obtained from concurrent parent report using the Sensory Experiences Questionnaire (SEQ). Correlation between parental report and patterns of oscillatory power, functional connectivity, and signal complexity were examined.

Results: High levels of reported sensory hyporesponsiveness were associated with alpha power asymmetry and increased left frontal theta power. Functional connectivity was increased to right frontal regions, decreased to left frontal regions, and broadly elevated in occipito-temporal regions in toddlers with high levels of reported hyporesponsiveness. Measures of EEG complexity indicated hyporesponsiveness was associated with less complex neural signals.

Discussion: Multiple complementary measures of neural activity corresponded with sensory hyporesponsiveness in toddlers at high risk for ASD. These findings suggest that concurrent measurement of neural signal features holds promise for facilitating early identification and targeted remediation in young children at risk for ASD.
The impact of temperament on children who stutter's vocabulary abilities

Presenter: Cara Singer  (cara.m.singer@vanderbilt.edu)

Authors: Cara M. Singer, Robin M. Jones, Tedra A. Walden

Introduction: The purpose of this study is to (a) assess the association of temperament and vocabulary ability in young children who stutter and children who do not stutter and (b) assess whether their joint impact predicts stuttering chronicity.

Methods: Participants, aged 3;0-4;11, were followed for 3-5 visits over a minimum of a two-year period and classified as children who stutter and are persisting (n=10), children who stutter and recovered (n=28), and children who do not stutter (n=27). All groups were matched for age and gender ratios. At the initial visit, participants completed the Peabody Picture Vocabulary Test, 4th edition, and Expressive Vocabulary Test, 2nd edition. Caregivers completed the Children's Behavior Questionnaire.

Results: Preliminary results indicate that higher negative affectivity is associated with lower receptive vocabulary and higher effortful control is associated with higher receptive vocabulary for all children. Neither temperament characteristic was associated with expressive vocabulary ability. Future results are expected to show that the joint impact of vocabulary and temperament predict stuttering chronicity.

Discussion: Probable explanations for the positive association of effortful control and receptive vocabulary and negative association of negative affectivity and receptive vocabulary will be discussed. Clinical implications will be detailed.
Developing an observational measure of the flexible use of pre-linguistic vocalizations in preverbal children with autism

**Presenter:** Kathryn Slaboch (kathryn.slaboch@vanderbilt.edu)

**Authors:** Kathryn D. Slaboch, Jim Bodfish, Tiffany G. Woynaroski, Paul Yoder

**Introduction:** Some children with ASD develop spoken language, but up to thirty percent of children persist in using minimal language despite early intervention. It is unknown why some children with ASD develop spoken language and some do not. Previous studies have suggested that children with ASD demonstrate differences in pre-linguistic skills, such as vocalizations, that are useful in predicting the extent to which they will develop spoken language abilities. A foundational pre-linguistic skill that has not been investigated in children with ASD who do not use words to communicate (i.e., preverbal children with ASD) is the ability to combine vocalizations with different affect types. Individuals with functional language are able to combine words with different types of affect to convey different messages to conversational partners. Findings from previous studies of typically developing infants suggest that this skill emerges as early as three months of age. The purpose of this study is to develop a method for measuring pre-linguistic vocalization functional flexibility (PVFF) in preverbal children with ASD.

**Methods:** This study will use an existing longitudinal data set from The Useful Speech Project (Yoder, Watson & Lambert., 2015; Woynaroski et al., 2016). The children with ASD in this study were between the ages of 20-48 months at baseline and were examined at five total measurement points separated by 4 month intervals. For the present study, multimedia recordings of each child as they participated in two different semi-structured assessments at time 2 will be used: Communication and Symbolic Behavior Scales and Early Symbolic Communication Scale. A partial-interval coding method is being used to code for the occurrence of vocalization and affect types. Vocalizations produced by children are classified in five categories based on pitch and phonation: squeal, vocant, growl, cry and laughter. Facial affect is categorized as positive, negative or neutral. A randomly selected 25% of all samples will be independently coded by a second trained observer to estimate interobserver reliability. PVFF will be operationalized using an operant contingency values (OCV) approach to quantify the degree of association between vocalization types and affect types. For this poster, we will present results based on these methods from a sample of 20 children with ASD who produced fewer than 20 word roots according to parent report and a semi-structured language sample. This poster will include data on the inter-rater reliability and stability (across assessment conditions) of the observational coding method, data on frequency of occurrence of the vocalization types and the affect types in this sample, and data from the OCV analyses used to quantify PVFF.

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Bodily maps of emotions in schizophrenia

Presenter: Matthew Snodgress (matthew.a.snodgress@vanderbilt.edu)

Authors: Matthew Snodgress, Heath Nichols, Lauri Nummenmaa, Enrico Glerean, Sohee Park

Introduction: Individual differences exist in how people perceive affective states manifested within their own bodies. When examining large samples, these differences conform to general patterns that have been independently cross-validated in healthy populations (Nummenmaa et al., 2014). For persons with schizophrenia (SZ) however, bodily perceptions are often distorted and highly idiosyncratic (Michael & Park, 2016), not complying with normal notions of space and even time. The present study sought to explore whether abnormal bodily perception for individuals with SZ extends into the affective realm by examining bodily maps of emotions, generated according to the methods described in Nummenmaa et al’s study (2014).

Methods: In this pilot study, 11 individuals with schizophrenia (SZ) and 11 demographically matched healthy controls (HCs) were recruited from the Nashville area. To generate bodily maps of emotion, participants were given an emotion word and blank outlines of the human body upon which they selected areas where they felt that particular emotion. 14 emotion words/categories were used (seven Ekman’s basic emotions (1992), six ‘complex’ emotions, and one neutral). Responses were organized into the following factors: (1) global embodiment, across all 14 emotion categories; (2) activation-deactivation, the former describing areas where participants felt activation and, the later showing areas where they felt deactivation; (3) regions of interest (ROI), such as the head or legs; and (4) specific emotion categories. To account for small sample size and heterogeneous variances, Fisher-Pitman permutation tests were used to assess mean group differences for these factors.

Results: For global bodily maps, SZ reported significantly less activation than HCs (Z = -6.49, p < 0.0001), an effect likely driven in part by a significant difference in deactivation scores (Z = -4.42, p < 0.0001). However, no difference was found in activation alone (Z = -0.564, p = 0.57). Among the five ROI-arms, legs, chest, head, and abdomen-differences were found in the chest and abdomen only (Z = -3.82, p < 0.01; Z = -4.64, p < 0.0001, respectively) where SZ reported less embodiment. Likewise, among the 14 emotion conditions, two were significant: fear (Z = -2.82, p < 0.05) and shame (Z = -3.23, p < 0.05) with SZ reporting less embodiment. All tests were corrected for multiple comparison with the sequential Bonferroni procedure (Holm, 1979).

Discussion: Given the preliminary nature of our study and the small sample size, our results were more robust than expected. General lack of embodiment in SZ relative to HCs, corresponds to part reports of elevated alexithymia in SZ-especially since negative emotion awareness is particularly reduced in alexithymic populations, and since SZ persons showed reduced embodiment only for two negative emotions (fear and shame). Further, the original study of healthy participants by Nummenmaa et al (2014) showed that bodily deactivation was reported only for depression and sadness. Visual inspection of individual SZ body maps showed broad abnormality for depression and sadness, particularly with increased activation occurring in the head (rather than deactivation in the limbs for large samples), though this result is tentative. To conclude, this pilot study showed significant differences between HCs and SZs in bodily maps of emotions, and indicate that a larger sample size should provide a clearer picture.

Metabotropic Glutamate Receptor 5 (mGlu5) mediates learning-induced metaplasticity in the hippocampus

Presenter: Branden Stansley (branden.j.stansley@vanderbilt.edu)

Authors: Branden J. Stansley, Rocco G. Gogliotti, Nicole M. Fisher, Craig Lindsley, P. Jeffrey Conn, Colleen M. Niswender

Introduction: Learning and memory processes are accompanied by a neural mechanism called synaptic plasticity, which is the activity-dependent modification in the strength of a synapse. A form of synaptic plasticity called long-term potentiation (LTP) in the hippocampus has been shown to be involved in fear learning. At the hippocampal CA1 synapse, the group I metabotropic glutamate receptor subtype 5 (mGlu5) has been shown to be involved in both synaptic plasticity and fear learning, and genetic reduction or pharmacological inhibition of mGlu5 results in impaired LTP at CA1, as well as a decrease in conditioned contextual fear responses (Lu et al., 1997). Interestingly, a delayed up-regulation of mGlu5 expression in the CA1 has been reported after a fear-conditioning paradigm (Riedel et al., 2000). Furthermore, paired-pulse low frequency (PP-LFS) induced long-term depression (LTD), which has been shown to be mGlu5-dependent at the CA1 synapse, has not been investigated after fear conditioning. Therefore, we hypothesized that the fear conditioning-induced upregulation of mGlu5 would lead to an enhancement of mGlu-dependent LTD at the hippocampal CA1 synapse.

Methods: 8-10 week old C57bl/6 male mice were used in all experiments. Mice underwent fear a two day fear conditioning paradigm and were sacrificed 1-week later for in-vitro acute slice electrophysiological studies. Field excitatory post synaptic potentials were recorded in hippocampal area CA1 by stimulating the axons of the schaffer collateral pathway.

Results: Fear conditioning resulted in an enhanced input-output function, without any changes in paired-pulse ratio; suggesting basal neuronal excitability is enhanced likely through a post-synaptic mechanism in area CA1. Additionally, contrary to our hypothesis, the PP-LFS protocol did not enhance LTD in slices prepared from conditioned mice, but instead resulted in a slow onset LTP. This dramatic switch in stimulation-response was blocked by the mGlu5 negative allosteric modulator (NAM) MTEP, suggesting this PP-LFS induced LTP is mGlu5 receptor dependent in slices from conditioned mice. The mGlu1 NAM VU0469650 failed to block PP-LFS-induced LTD in slices from conditioned mice. Furthermore, similar to classical high frequency-induced LTP, this PP-LFS-induced LTP caused by fear conditioning was NMDA receptor dependent, as the NMDA antagonist AP5 blocked PP-LFS-induced LTP. Finally, when MTEP was administered on training day, freezing behavior was significantly attenuated on test day. This also resulted in the blockade of PP-LFS-induced LTP 1 week later.

Discussion: These results demonstrate that fear learning can lead to a metaplasticity in the hippocampus CA1 region, which is mediated by mGlu5 receptor activity. This modification of synaptic plasticity provides insight into the molecular underpinnings of fear memory consolidation, and may provide therapeutic targets for learning and memory disorders such as post-traumatic stress disorder. Studies to determine the cellular pathways downstream of mGlu5 that are involved in this fear conditioning induced metaplasticity are planned.


A novel human CaMKIIα mutation disrupts dendritic morphology and synaptic transmission, and causes ASD-related behaviors

**Presenter:** Jason Stephenson  (jason.stephenson@vanderbilt.edu)

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**Introduction:** Characterizing the functional impact of novel mutations linked to autism spectrum disorders (ASDs) provides a deeper mechanistic understanding of the underlying pathophysiological mechanisms. Here we show that a de novo Glu183 to Val (E183V) mutation in the CaMKIIα catalytic domain, identified in a proband diagnosed with autism spectrum disorder (ASD), dramatically decreases both CaMKIIα substrate phosphorylation and regulatory autophosphorylation, and CaMKIIα binding to established ASD-linked proteins, such as Shank3, LTCCs and NMDA receptor subunits. Expression of the CaMKIIα-E183V mutant in neurons reduces CaMKIIα localization to dendritic spines, resulting in an increase of dendritic arborization and decreases in both dendritic spine density and excitatory synaptic transmission. Mice with a knock-in CaMKIIα-E183V mutation display aberrant behavioral phenotypes including hyperactivity, social interaction deficits and increased repetitive behaviors. Taken together, these data suggest that CaMKIIα plays a previously unappreciated role in ASD-related synaptic and behavioral phenotypes.
personalized storybooks enhance word learning in young children

Presenter: Pumpki Lei Su (lei.su@vanderbilt.edu)

Authors: Pumpki Lei Su, Casey Lew-Williams

Introduction: Shared storybook reading is a beneficial activity for children's language learning in many respects, promoting vocabulary growth (Kotaman, 2013; Sénéchal, 1997), grammatical development (Whitehurst et al., 1988), and emergent literacy (Justice & Kaderavek, 2002). Book-reading is a potentially powerful language intervention context for children developing language typically (Pakulski & Kaderavek, 2004), but previous research has shown that learning from shared storybooks is stunted when the child holds a negative attitude towards reading (Scarborough & Dobrich, 1994). Here, we examined a new way to address this limitation by embedding personalized, child-tailored features into storybooks as a means of enhancing children’s attention to and interest in book content and narrative. Previous studies have found that personalization in storybooks not only supports literacy (Bracken, 1982; DeMoulin, 2001), but also elicits higher rates of engagement and positive responses from children (Kucirkova et al., 2013). In examining the intersection of shared book-reading, personalization, and early word learning, we hypothesized that personalized storybooks would enhance young children's learning of new word/object mappings.

Methods: We tested young children’s abilities to learn novel words from storybooks that either did or did not contain each child’s personal photos and name. Participants were 36- to 54-month-old children from monolingual English-speaking families, who were randomly assigned to one of two experimental conditions. In the Personalized condition (n=18), children’s photos and names were collected from families and embedded into a custom storybook prior to their appointment. The plot of the book focused on a child going on an adventure in outer space and discovering new objects. Each parent collected photos of their child doing six specific actions (smiling, waving, cheering, pointing, reading, and sleeping), which were automatically extracted and integrated into a digital storybook. The book contained four exposures to each of four novel word/object pairs (target words: toma, pizer, hux, and koob; word/object pairs were counterbalanced between subjects). In the Non-personalized condition (n=19), children were read an identical storybook (same narrative, target words, and background illustrations), but with photos of a different, same-gender child as the protagonist. The same experimenter read to all children, and reliability analyses confirmed that her behavior and affect were consistent across conditions. On each of 24 test trials, participants viewed pairs of novel objects (e.g., the toma and pizer) and heard a sentence referring to one object (e.g., Where is the toma?), and completed a forced-choice word recognition task on a touchscreen monitor.

Results: Both groups demonstrated above-chance learning of target words, but children in the Personalized condition (M=.82, SD=13.36) showed a significantly higher accuracy rate than children in the Non-Personalized condition (M=.71, SD=12.90), F(1,35)=7.43, p<.01.

Discussion: The findings in this study suggest that embedding personal information into storybooks, such as a child’s own photos and name, can support young children's word learning by facilitating the initial encoding of novel words. Personalization of the sort tested here provides insights for educators, clinicians, and caregivers who strive to leverage young children's vocabulary growth, and more generally, to enhance motivation for learning.

Effects of Optimal Drug Therapy versus Deep Brain Stimulation on Employment in Early Stage Parkinson's Disease

Presenter: Christina Tamargo  (christina.l.tamargo@vanderbilt.edu)

Authors: Christina L. Tamargo, Mallory L. Hacker, Taylor Hudson, Maxim Turchan, Sarah H. Millan, David Charles

Introduction: Parkinson's disease (PD) progression is associated with increasing disability, often causing difficulty with work, early retirement, or unemployment. Many patients who remain employed report disease-related complications at work. As a result, most PD patients reduce work or stop working within the first three years following a PD diagnosis [1].

Methods: The deep brain stimulation (DBS) in early stage PD pilot trial was a five-year prospective, randomized trial completed at Vanderbilt University (NCT00282152, IDEG050016, IRB #040797). Early stage PD subjects (age 50-75, medication duration between 6 months and 4 years, without dyskinesias or other motor fluctuations) were randomized to receive optimal drug therapy (ODT) or subthalamic nucleus DBS plus ODT (DBS+ODT). After study completion, subjects and their spouses or caregivers were invited to participate in a retrospective phone survey. This survey examined a variety of work-related topics, including employment status, employment history, demands faced on the job, and ways PD affected the ability to work. Statistics were carried out using a Chi-square test. Results are presented for subjects who were employed upon enrollment in the pilot trial.

Results: Twenty-one subjects or spouses/caregivers completed the survey. Of these, 12 study participants were employed upon enrollment in the pilot trial (6 ODT, 6 DBS+ODT). Almost everyone in the DBS+ODT group (5/6) was no longer working, ceasing employment ~2.2 ± 2.3 years after enrolling in the study, versus 2 out of 6 in the ODT group (~2.5 ± 1.8 years after enrollment). None of the ODT subjects reported retiring on disability because of their PD, while a majority (4/6) of the DBS+ODT group did (p<0.05). Slowness equally affected both groups' ability to work, with all subjects reporting this as a hindrance. Finally, while no DBS+ODT subjects reported handwriting as the factor that most contributed to their inability to work, 3 out of 6 in the ODT group did (p<0.05).

Discussion: These findings suggest that DBS+ODT in early PD may adversely impact employment. Limitations of this study include its retrospective nature and the small number of respondents in each group. Additional study is needed to confirm these findings, and employment data will be prospectively collected in the FDA-approved, phase III, pivotal clinical trial of DBS in early PD.

Martikainen et al., Mov Disord. 2006;21(12):2187.
Psychological Effects of Self and Other-administered Body Centered Therapies (Body Psychotherapies).

Presenter: Mary Tarsha (mary.s.tarsha@vanderbilt.edu)

Authors: Mary S. Tarsha, Sohee Park

Introduction: This is the first review article of its kind to investigate the psychological and neurological effects of body-centered therapies on mental health and emotional well-being including both self and other-administered (receptive) therapies. The research reviewed includes studies that investigate effects of massage therapy, meditation, reflexology, acupuncture, functional relaxation, emotional freedom technique and dance therapy on conditions across the lifespan such as stress, PTSD and anxiety disorders, cancer, effects of aging, asthma, and prematurity in infants.

Methods: Articles were retrieved from proquest, Vanderbilt Peabody library and google scholar. Lack of empirical evidence and conflicting studies are noted.

Results: These studies combined suggest that massage therapy, meditation, dance and emotional freedom therapies reduce stress, depression, anxiety, migraines, improve autonomic and immune function in adults and increase weight-gain in infants.

Discussion: Mechanisms by which these therapies are effective include the bidirectional pathway between the brain and body-the body holds the potential to influence the brain. Integrating body-centered therapies in both clinical settings and as self-care is discussed.


**Weighting perception of ambiguous motion stimuli: The curious case of audition trumping vision**

**Presenter:** Antonia Thelen (thelen.antonia@gmail.com)

**Authors:** A. Thelen, M. Chadha, A.R. Nidiffer, R. Ramachandran, M.T. Wallace

**Introduction:** The ability to combine and integrate information from the different senses into a single coherent percept is an inherent ability of our nervous system. Moreover, this ability is crucial when available sensory information is degraded and/or ambiguous, and can confer powerful behavioral and perceptual benefits. While a large body of work has focused on static multisensory stimuli, less is known about the principles underlying the integration of dynamic (i.e. ethologically valid) stimuli.

**Methods:** To address this question at both the behavioral and neuronal levels, we employed dynamic motion stimuli (i.e. random dot kinematograms and auditory motion embedded in noise) in a two alternative forced choice task in which subjects had to judge the direction of motion. We manipulated both stimulus efficacy (i.e. motion coherence) and congruency between auditory and visual motion (i.e. leftward or rightward) stimuli on a trial-by-trial basis. Subjects performed the task while high-density EEG data were concurrently acquired.

**Results:** Preliminary findings revealed behavioral benefits under congruent multisensory presentation conditions as compared to either unisensory condition alone. These behavioral benefits were further increased as a function of motion coherence. Intriguingly, under incongruent pairing conditions, we found that subjects more heavily weighted auditory information. Moreover, auditory weights were further increased for pairings with high (60%), as opposed to low (6%) visual motion coherence. These findings seem to be inconsistent with prior findings, that suggest that subjects attribute higher perceptual weights to visual information in spatial tasks (i.e. Modality Appropriateness Hypothesis).

**Discussion:** Analyses of the scalp evoked responses focus on revealing the neuronal correlates in terms of response strength (Global Field Power) and neuronal generators (Topographic Dissimilarity) underlying the attribution of perceptual weights, and ultimately sensory-motor transformation. Moreover, we seek to identify the neuronal loci that are differentially recruited as a function of stimulus efficiency and behavioral choice. Some of the most informative analyses focus on trials in which the stimuli are identical but which the behavioral responses differ, thus providing insight into the network differences attributable to sensory statistics or perceptual choice. We expect to observe increased neuronal responses (e.g. GFP) in congruent trials underlying behavioral benefits. However, incongruent pairings, would result in the recruitment of differential neuronal networks, as a function of the perceptual weights attributed to either unisensory cue.
FM System Use in Home Setting: Impact on Language Environment and Child/Caregiver Communication

**Presenter:** Emily Thompson  (emily.c.thompson@vanderbilt.edu)

**Authors:** Emily C. Thompson

WITHDREW
The Role of the Engulfment Receptor Jedi1 in DRG development

Presenter: Alexandra Trevisan  (alexandra.j.trevisan@Vanderbilt.edu)

Authors: Alexandra J. Trevisan, Chelsea S. Sullivan, Francis E. Hickman, Mary Beth Bauer, Kevin Currie, Bruce Carter

Introduction: Chronic itch is a significant clinical problem that affects 20% of the U.S. population and results from a diverse array of pathophysiologies including somatosensory neuropathies. The dorsal root ganglia (DRG) contain the primary afferent sensory neurons that transmit somatosensory signals such as itch and pain from peripheral tissues to the spinal cord. An interconnected network of specialized glia termed satellite glial cells (SGCs) envelope individual DRG neuron cell bodies and critically regulate neuronal function. In several chronic pain models, SGCs have been shown to undergo 'gliosis' or activation as demonstrated by changes in morphology, proliferation, and gene expression. These activated SGCs contribute to chronic pain through several known mechanisms including increase in extracellular potassium, release of pro-inflammatory cytokines, and excretion of other small signaling molecules. Our lab previously discovered a novel function for SGCs as amateur phagocytes responsible for clearing apoptotic neurons during development using dissociated DRG neuron/glia co-cultures. We found that the type I transmembrane protein JEDI1 (PEAR1/MEGF12) was important for SGC-mediate phagocytosis. Jedi1 homologs in Drosophila and C. elegans have previously been characterized as engulfment receptors that initiate a phagocytic signaling cascade upon binding dead cell targets. To evaluate the function of Jedi1 in vivo, we generated global jedi1-/- mice. Our preliminary data shows that jedi1-/- mice exhibit excessive scratching behavior that manifests as open wounds in aged animals. Embryonic DRGs in jedi1-/- mice accumulate dead cells, suggesting a defect in neuronal apoptotic clearance as predicted by the function of Jedi1 as an engulfment receptor. The SGCs in jedi1-/- are hyperactivated in both adult DRG sections and in embryonic DRG cultures, especially upon induction of neuronal apoptosis by withdraw of the neurotrophin nerve growth factor (NGF). Because apoptotic cells that are not efficiently removed lose membrane integrity and undergo secondary necrosis, I hypothesize that the inability to phagocytose dead cells leads to SGC activation, presumably through factors release by necrotic cells. Additionally, electrophysiological data in early post-natal DRG neurons in the presence of glia shows that primary afferent neurons from jedi1-/- mice fire more action potentials compared to jedi1+/+ cells. I propose that SGC gliosis, rather than intrinsic differences in jedi1+/+ and -/- neurons, is the primary cause for itch sensitivity in these knock-out animals. These studies are the first to investigate how inability to properly phagocytose dead cells can cause activation of glia and whether gliosis can contribute to pruritus.

Methods: A global Jedi1 knock-out mouse was obtained from the KOMP consortium on a C57/BL6 background. LEFT: RT-PCR for JEDI1 and GAPDH transcripts are shown total brain RNA isolated from the brains of wild type (jedi1+/+) and knock-out (jedi1-/-) mice. The Jedi1 transcript is not detected in jedi1-/- mice. RIGHT: JEDI1 was immunoprecipitated (IP) from total brain lysates and immunoblotted with a different Jedi1 antibody. Jedi1 expression is low and not detected in the input lanes. By enriching for Jedi1 by IP, Jedi1 is detectable in jedi1+/+ but not jedi1-/- mice.

Results: 6-week old mice were habituated to individual housing for 4 days before recording them for 10 minutes. Videos were assessed by 2 independent observers for scratching behavior: hind-limb scratching and biting of hairy skin. Both bouts and time of these behaviors are shown.

Discussion: Global knock-out of Jedi1 in mice leads to chronic itch, resulting in open wounds due to excessive scratching behavior. The skin of Jedi1-knockout animals appears normal, suggesting that the itching sensation does not arise from a peripheral dermatomal abnormality. Itching in Jedi1-knockout animals does not seem to arise from an inflammatory phenotype because introduction of wild type BM does not rescue scratching in jedi1-/- animals, and -/- BM in a +/+ background does not induce scratching in these chimeras. Jedi1 knockout sensory neurons elicit more action potentials compared to wild type DRG neurons. Jedi1 knockout satellite glial cells (SGC) are hyperactivated compared to wild type SGCs.
The Potential Impact of Singing on Multisensory Integration in Children with Autism Spectrum Disorder: A Pilot Study

Presenter: Alex Tu (alexander.tu.1@vanderbilt.edu)

Authors: Alex Tu, Wayne Kuang, Julie Conrad, Lawand Yaseen, Pooja Santapuram, Jill G. Omer, Tiffany G. Woynaroski

Introduction: Past work in our laboratory has demonstrated that children with Autism Spectrum Disorder (ASD) show reduced or atypical multisensory integration of audiovisual speech stimuli when presented with a spoken 'McGurk' task (Stevenson, et al., 2014), in which the presentation of incongruent audiovisual speech tokens (e.g., a visual 'ga' and an auditory 'ba') result in the illusory percept that reflects a fusion of the two stimuli (e.g., 'da' or 'tha') (McGurk & MacDonald, 1976). We hypothesize that children with ASD may show enhanced multisensory integration for sung tokens, which offer more salient visual and auditory cues, in comparison to the spoken tokens that we have presented in prior research (Quinto, Thompson, Russo, & Trehub, 2010). If so, this supports the notion that music is a modality that may increase multisensory integration, and possibly even support language learning in children with ASD.

Methods: We will carry out a between-group experiment in children with ASD and TD children matched on chronological age, sex, and IQ. A comprehensive battery of cognitive and language measures will be used to characterize the sample. Handedness, neurological history of participant, and social-behavioral measures can also be accounted for using a variety of surveys. Participants will be presented auditory only, visual only, congruent 'ba', 'da', and 'ga' syllables, as well as incongruent auditory 'ba' dubbed onto visual 'ga' stimuli in 2 conditions (spoken syllables, sung in-tune syllables) presented in random order. After each presentation, the participant will be asked to report what syllable they perceived by pushing a button on a serial response box. We will assess auditory only, visual only, and congruent audiovisual accuracy, as well as magnitude of multisensory integration for incongruent stimuli in the spoken and sung conditions.

Results: Pilot data will be presented, as study is still ongoing.


The visual system of the northern elephant seal (Mirounga angustirostris)

Presenter: Emily Turner (emily.c.rockoff@vanderbilt.edu)

Authors: Emily C. Turner, Eva K. Sawyer, Jon H. Kaas

Introduction: Northern elephant seals (Mirounga angustirostris) are part of a diverse clade of carnivorous animals known as pinnipeds (seals, sea lions, and walruses). Pinnipeds are notable for their large, ape-sized brains, yet little is known about the central nervous system of these federally protected animals. The northern elephant seal spends most of its life at sea, but surfaces briefly on land each year to breed and birth; this unique coastal niche may be reflected in specific evolutionary adaptations to their sensory systems. Here we report on select parts of the visual pathway (optic nerve, lateral geniculate nucleus, and primary visual cortex) of the nervous system of the northern elephant seal.

Methods: Using stains for Nissl, cytochrome oxidase, and vesicular glutamate transporters in one elephant seal pup and the external anatomy of the brain of a second pup, we investigated the cytoarchitecture of the lateral geniculate nucleus and primary visual cortex. Similar to in rodents and primates, we find that these markers are useful for the identification of architectonic borders. Toluidine blue was used to visualize myelinated axons in the optic nerve of the northern elephant seal.

Results: We find that the lateral geniculate nucleus has distinct layers similar to that of closely related species. Primary visual cortex is located within the most posterior end of the highly gyrified cortex, and extends far anterior along the dorsal surface and medial wall. We found two distinct classes of myelinated fibers in the optic nerve, those with thick myelin sheaths (9%) and those with thin myelin sheaths (91%). Axons with thick myelin sheaths tended to be larger in diameter and clustered near each other in one small section on the edge of the optic nerve, while the rest of the optic nerve contained a more consistent distribution of many thinly myelinated axons mixed with fewer thickly myelinated axons.

Discussion: To our knowledge, this is the first comprehensive report on the visual anatomy of any pinniped. The results may be useful both in the veterinary setting and for other comparative studies related to the evolution of large brains.

Presenter: Kathryn Unruh (kathryn.e.unruh@vanderbilt.edu)

Authors: Kathryn E. Unruh, Jim W. Bodfish

Introduction: The Social Motivation Theory of Autism suggests that the social-specific reward deficits in autism spectrum disorder (ASD) result from a lack of motivation toward social information. While this theory has been influential in studying ASD-specific social deficits, few measures have been developed to directly quantify social motivation. Eye-tracking and pupillometry can be used to study attention in ASD. We have developed two novel tasks that incorporate these methods to quantify differential preference for and arousal to social and nonsocial stimuli.

Methods: Our preferential viewing (eye-tracking) task measures patterns of visual attention to social and nonsocial content. Face images are paired with an image of either a) high interest (HAI images; e.g. trains, electronics) or b) low interest (LAI images; e.g. clothing, furniture) to children with ASD. Our pupillometry task measures differential maintained attention (pupil dilation) over time to individual images (faces or HAI) presented sequentially. Participants included children diagnosed with ASD (N = 7, mean age = 39 mo) or typically developing (TYP; N = 42, mean age = 55 mo); groups were matched on IQ and gender. Gaze patterns were analyzed between array types (SOC + HAI and SOC + LAI). Pupil responses were analyzed between stimulus types (SOC and HAI) and across 5 epochs (1000 ms each).

Results: Preferential Viewing: Children with ASD exhibited longer latencies to first view social images than TYP, only when paired with an HAI nonsocial image (F = 4.3, p = .042). Children with ASD spent significantly more time looking to objects [F = 15.4, p = .005], while TYP showed a preference for faces (F = 20.1, p = .001). Pupil: A significant 3-way interaction revealed that pupil response to stimulus types differed as a function of age and time (F = 13.9, p = .013). Post-hoc paired-samples t-tests revealed greater pupil dilation to nonsocial images at each time period in older children (all ps < .05), but minimal differences between image type in younger children.

Discussion: Preferential viewing results suggest that our task is sensitive to group differences in social preference. Additionally, in ASD, social information processing deficits may be relative / context-dependent, rather than a fixed core feature of the disorder. In this model, social inattention may occur secondary to a positive attention bias to nonsocial information. Pupillary results suggest that our task may be sensitive to developmental differences in social and nonsocial information processing. The joint use of these tasks may provide a method to tease apart the differential approach patterns seen in ASD to social and nonsocial sources of information, while also examining differences in developmental trajectory.
Assessing Prosody-related Language Skills in Typical and Atypical Language Development

**Presenter:** Chloe Vaughan (chloe.m.vaughan@vanderbilt.edu)

**Authors:** Chloe M. Vaughan, Scott D. Blain, Katherine B. Jones, Uma Soman, Ashley B. Hirsch, J. Devin McAuley, Reyna L. Gordon

**Introduction:** Language learning relies on the ability to extract words from the complex speech signal, in part via expectations generated by preceding intonation and timing patterns; moreover, discrimination of prosodic patterns may contribute to higher-level language skills. Here we investigated prosody-related skills in children aged 5-7, with typical language and language impairment.

**Methods:** In Task 1, participants listened to an artificial language, and then identified whether sample words were present in the language and used a 6 point rating scale to indicate how confident they were that the sample word was present in the language. Sample words were either congruent with the prosody pattern in the artificial language, incongruent with the prosody pattern, or nonwords in the artificial language. In Task 2, a 'Prosody Matching' task, participants matched lowpass-filtered stimuli to non-filtered stimuli, discriminating between differing prosody in the sentences. Conditions for the stimuli included standard prosody, question intonation, broken intonation, and truncated phrases.

**Results:** Data collection and analysis is currently underway. We expect children with typical language development to be able to use upstream sentence prosody to facilitate word learning and recall for Task 1, and we also expect these participants to rate congruent words higher than incongruent words or nonwords. In the Prosody Matching task, we expect performance to be highest on the conditions asking participants to match the filtered stimuli to the truncated phrases. We expect performance on the other conditions to be higher in children with typical language development, compared to children with language delay/impairments. Furthermore, we expect performance to correlate with measures of musical rhythm discrimination, as well as higher-level language skills.

**Discussion:** Findings will be used to study individual differences in prosody skills and their relation to musical rhythm and grammar skills. Moreover, the role of these individual differences in prosody will be examined as a possible contributing mechanism to development delays in language. Finally, the paradigms tested will contribute to future investigations of prosody/speech rhythm, as related to broader musical and grammar abilities.
Volunteer Advocacy Project - Transition

Presenter: Sydney Waitz-Kudla (sydney.n.waitz-kudla@vanderbilt.edu)

Authors: Sydney N. Waitz-Kudla, Julie L. Taylor, Robert M. Hodapp, Meghan M. Burke, Carol Rabideau

Introduction: The transition from high school to adulthood is especially difficult for youth with autism spectrum disorder (ASD). They lose the familiar structure of school and entitlement to many federal services, but still often require assistance in employment and in activities of daily living. Additionally, the adult service system is much harder to navigate than school-based services, which makes it more difficult for parents to effectively acquire services for their son or daughter with ASD. Despite the significant challenges faced by youth with ASD, there have been few intervention studies to improve their transition outcomes. In the present study, we add to this literature by pilot testing a 12-week intervention (called the Volunteer Advocacy Project or VAP-T) to increase parents’ skills in advocating for adult services on behalf of their son or daughter with ASD during the transition to adulthood.

Methods: 45 parents of transition-aged youth with ASD were enrolled and randomized to either the treatment group (n = 22) or wait-list control group (n = 23); four families were lost to attrition, resulting in 20 treatment and 21 control group families. Data was collected prior to randomization and at post-test after the treatment group completed the VAP-T. Most (97.6%) parent participants were female and the majority were white (87.8%). Of the participants' sons/daughters with ASD, 31.7% left high school in May of 2016, 53.7% will leave high school in May of 2017, and 14.6% left high school between 2013 and 2015. Just over 31% percent of children (31.7%) had an intellectual disability. Our primary outcomes were parent-report (completed at baseline and post-test) and consisted of parent empowerment, parent skills and comfort in advocating for their children, and parent knowledge of the adult service system.

Results: Upon entry into the study, there were no statistically significant group differences in parents' knowledge about the adult services system, their skills and comfort in advocating for their son/daughter with ASD, nor in empowerment. After controlling for baseline scores, relative to the control group, parents in the intervention group knew more about the adult service system, F=17.41, p<.001, felt as though they were more comfortable and skilled in advocating for their son/daughter, F=15.02, p<.001, and felt more empowered, F=9.24, p<.01. Effect sizes for the group differences were large.

Discussion: Pilot results suggest that the VAP-T is efficacious in improving parents' knowledge about adult services, their comfort and skills in advocating for their children, and their empowerment. Six and twelve month follow-ups will examine whether these changes lead to improved transition outcomes for young adults with ASD.
A novel Calcium/calmodulin-dependent protein kinase II binding site in the L-type calcium channel N-terminal domain is required for nuclear signaling

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**Authors:** Xiaohan Wang, Tyler L. Perfitt, Christian R. Marks, Terunaga Nakagawa, David A. Jacobson, Roger J. Colbran

**Introduction:** Neuronal excitation-transcription coupling (E-T coupling) is critical for long-term memory formation. L-type voltage-gated calcium channels and the downstream calcium sensor Calcium/Calmodulin-dependent protein kinase II (CaMKII) play key roles in the E-T coupling process. How this process is initiated at the synapse remains unclear.

**Methods:** Purified, GST-tagged Cav1.3 intracellular domains were used to study the interaction between Cav1.3 and CaMKII. Rapamycin-induced dimerization was used to study the effect of vicinity on trans-holoenzyme phosphorylation. Primary hippocampal neurons were used to reveal the effect of Cav1.3/CaMKII interaction on nuclear signaling.

**Results:** We reported that the L-type calcium channel α subunit N-terminal domain and β subunit serve as multiple docking sites for CaMKII upon calcium influx. These docking sites provide vicinity for CaMKIIα/β and CaMKIIγ and allow CaMKIIα/β to phosphorylate CaMKIIγ in a trans-holoenzyme manner. CaMKII co-localize with L-type calcium channel in cultured hippocampal neurons, and the co-localization is disrupted by mutation/deletions in the calcium channel that block CaMKII binding. Disruption of the interaction between CaMKII and the calcium channel α subunit also blocks E-T coupling without affecting calcium influx in neurons.

**Discussion:** Our data suggest that the direct, activity-dependent interaction between CaMKII and the L-type calcium channel provides a starting point for the E-T coupling in neurons.
Comparing Structural and Pragmatic Language in Low and High-Functioning ASD

Presenter: Allison Whitten (allison.whitten@vanderbilt.edu)

Authors: Allison Whitten, Kathryn D'Ambrose Slaboch, Jim Bodfish

Introduction: Currently, the general consensus on language impairment in ASD is that while the social use of language, or pragmatic language, is universally impaired in ASD, evidence for structural deficits (e.g., syntax, phonology) has been inconsistent. However, most of the research on language impairment in autism has been restricted to high-functioning individuals with autism. Consequently, it is not known whether a comorbid intellectual disability further affects language impairment in low-functioning individuals, and thus may require more extensive interventions. Furthermore, studies that directly compare structural and pragmatic language are necessary to advance knowledge of the language phenotype within all of ASD. We aimed to compare both structural and pragmatic aspects of language across three groups: low functioning children with ASD (LFA), high functioning children with ASD (HFA), and an age-matched typically developing group (TD).

Methods: Using the Children's Communication Checklist-2 (CCC-2), we compared mean scores between LFA (n=15, Nonverbal IQ < 80, mean age = 12 years, range = 5 - 17 years), HFA (n=57, Nonverbal IQ > 80, mean age = 10 years, range = 6 - 17 years), and TD (n=52, mean age = 11 years, range = 6 - 17 years). We used one-way ANOVAs with planned post-hoc tests across 4 subscales measuring structural language (Speech, Syntax, Semantic, Coherence) and 4 subscales measuring pragmatic language (Initiation, Scripted Language, Context, Nonverbal Communication).

Results: There was a significant main effect of group for all four structural language subscales (F (2, 21) =Speech: 18.75, Syntax: 49.49, Semantic: 93.34, Coherence:101.80, all p < .001). Post hoc Tukey tests revealed the same pattern for all four structural subscales (p < .001), such that there were no significant differences between LFA and HFA, while both LFA and HFA groups scored significantly lower than TD. This same pattern was replicated across all four pragmatic subscales, with a main effect of group (F (2, 66) = Initiation: 61.32, Scripted Language: 64.58, F(2, 121) = Context: 175.04, Nonverbal Communication: 170.12, all p < .001). Again, post hoc Tukey tests showed no significant differences between LFA and HFA, with both LFA and HFA scoring significantly lower than TD. Pearson correlations between IQ and structural and pragmatic CCC-2 subscales found no significant associations, with one exception. The pragmatic subscale 'Context' was significantly associated with IQ within the LFA group only (r = 0.60, p < .05).

Discussion: We found evidence that the language deficits do not differ between LFA and HFA groups. Furthermore, our results suggest that structural features of language are impaired in ASD, as both LFA and HFA groups tended to score well below the TD group on all structural language subscales. In addition, our results suggest that future studies on language impairment in ASD should no longer exclude low functioning individuals, and examine both structural and pragmatic aspects of language; such research will be vital to improving language interventions in ASD, especially for children with ASD whose language deficits do not respond to intervention.
Do children with language impairment benefit from music and movement training?

**Presenter:** Natalie Wiens  (natalie.wiens@vanderbilt.edu)

**Authors:** Natalie Wiens, Emelyne Bingham, Apurva Jolepalem, Ashley Hirsch, Reyna Gordon

The link between rhythmic ability and language skills is increasingly well-documented. Specific language impairment (SLI) is characterized by deficits in grammar and recent studies have shown a connection between rhythmic ability and grammar skills among children with SLI. The aims of this research project are to examine the efficacy of music training (Suzuki violin lessons and group movement and music lessons) for improving grammar outcomes in children with SLI, ages 5.5-7, and to identify neural mechanisms underlying these changes. Later phases of research include a small scale intervention including 20 weeks of lessons vs. no-treatment controls and a randomized control trial comparing children receiving the music training to children in a control group that will receive an alternate activity. We present findings from the feasibility pilot of 12 weeks of lessons: we examine how best to capture musical and linguistic progress of children throughout the treatment and we propose a behavioral coding system to establish treatment fidelity of the music training.
Eight-Year Growth in Math Skills and Its Relationship to Nonsymbolic and Symbolic Number Processing

Presenter: Eric D. Wilkey  (eric.d.wilkey@vanderbilt.edu)
Authors: Eric D. Wilkey, Dale C. Farran, Kerry G. Hofer, Gavin R. Price

Introduction: A growing body of research seeks to understand the relation between numerical magnitude processing skills, as indexed by nonsymbolic (e.g. groups of objects) and symbolic (e.g. Arabic digits) magnitude comparison tasks, and math performance. Nonsymbolic comparison tasks are thought to index the precision of representation within neural systems supporting the perception of numerical magnitude. However, the mechanisms indexed by the symbolic comparison task are more opaque, ranging from efficiency of the mapping of symbolic numerals onto their nonsymbolic counterpart to efficiency of a completely independent number system. A number of studies have shown an independent relation between nonsymbolic processing and math competence, and at least an equal number have shown an independent relation between symbolic processing and math, with no clear explanation for the varied results. To our knowledge, no studies have investigated the relation between concomitant symbolic and nonsymbolic poor performance and math development. Specifically, do individuals with low performance on both the symbolic and nonsymbolic comparison task display different behavioral profiles than those performing poorly on just one of the tasks?

Methods: To answer this question, we related symbolic and nonsymbolic number comparison performance in a longitudinal sample of 446 students to growth in math performance from Pre-K to 6th grade, 6th grade math skills, working memory, and inhibitory control. The sample was divided into four groups: (1) students with above average performance in both nonsymbolic and symbolic tasks (n= 163), (2) below average nonsymbolic, above average symbolic (n = 116), (3) above average nonsymbolic, below average symbolic (n = 76), (4) and below average in both (n = 91).

Results: Results indicate the low symbolic group had less growth in math performance and poorer concurrent math skills than groups with higher symbolic performance. Further, the group of individuals with low performance on both the nonsymbolic and symbolic comparison tasks performed significantly worse than all other groups in concurrent math skills, working memory, and inhibitory control.

Discussion: These results suggest that concomitant low performance on symbolic and nonsymbolic magnitude processing tasks is associated with lower math skills than poor performance on either task alone.
An epilepsy mutation gabrg2(w461x) has no dominant negative suppression on the partnering subunits

Presenter: Lan Xiao  (lan.xiao@vanderbilt.edu)

Authors: Lan Xiao, Qi Zhang, Wangzhen Shen, Vinodh Narayanan, Keri Ramsy, Jing-Qiong Kang, Robert L Macdonald

Introduction: There are many mutations in GABAA receptor subunit genes that are associated with epilepsy. Among all GABAA receptor genes, mutations in GABRG2 are most frequently associated with epilepsy with phenotype ranging from simple childhood absence epilepsy or febrile seizures to generalized epilepsy with febrile seizures plus (GEFS+) to the most severe Dravet syndrome. We have extensively characterized the GABRG2(Q390X) mutation associated with GEFS+/Dravet syndrome and conclude that the epilepsy phenotype could be modified by the amount of the mutant protein. The more steady state of the trafficking deficient mutant protein would exacerbate the epilepsy phenotype. In this study, we report a novel e mutation GABRG2(W461X) that is associated with epilepsy in humans.

Methods: We have used flow cytometry, immunocytochemistry as well as surface biotinylation to determine the surface and the total receptor subunit expression. We used whole cell patch clamp to determine the GABA evoked receptor current amplitude.

Results: We have demonstrated that the mutation resulted in rapid degradation and produced no to minimal amount of the mutant γ2 subunits. Importantly, the mutant γ2(W461X) subunits had no suppression on the wild-type partnering subunits like α1 and β2 subunits and the wild-type subunit expression was similar to the hemizygous condition. This is different than the mutant γ2(Q390X) subunits which impose strong dominant negative suppression on the wild-type partnering subunits. Therefore, Gabrg2+/− heterozygous knockout would be a good model to further study the pathophysiology of the mutation during development.
Early Sensory Hyporesponsivity Predicts Later Deficits in Language Understanding in Infants at High Risk for Autism Spectrum Disorder

Presenter: Lawand Yaseen  (lawand.m.yaseen@vanderbilt.edu)

Authors: Tiffany Woynaroski, Cara Damiano, Carissa Cascio, Wendy Stone, Lisa Ibanez, Sarah Bowman, Abigail Morgan, Lawand Yaseen (School of Science and Math at Vanderbilt)

Introduction: Individuals with autism spectrum disorder (ASD) often show atypical responses to sensory stimuli, even as early as infancy. A pattern of hyporesponsivity (characterized by absent or reduced responding to sensory stimuli) in particular seems most prevalent in, and specific to, ASD. It has been proposed that reduced responsivity to sensory stimuli early in life may produce cascading effects on higher level abilities, such as spoken language, in individuals with ASD. Past work has found that sensory hyporesponsivity covaries with concurrent spoken language in preschool and school-age children with ASD. However, to date no study has evaluated whether hyporesponsivity in infancy predicts future spoken language in children with ASD. A primary obstacle to this work is our inability to diagnose ASD in infancy. One way to overcome this challenge is to prospectively study infants who are known to be at high risk for ASD, such as infant siblings of children diagnosed with ASD (Sibs-ASD).

Methods: Sensory hyporesponsivity of 14 Sibs-ASD, as well as 18 Sibs-TD was assessed at 18 months using the Sensory Experiences Questionnaire. Language use and understanding was assessed at 24 months using the Vineland Adaptive Behavior Scales. An independent samples t-test was used to evaluate mean differences in early hyporesponsivity between Sibs-ASD and Sibs-TD, and bivariate correlational analyses were used to examine predictive associations between early hyporesponsivity and later language abilities for Sibs-ASD and Sibs-TD.

Results: We found several anticipated effects, including a trend towards higher hyporesponsivity-reduced responding to sensory stimuli-at 18 months in the Sibs-ASD group relative to the Sibs-TD group (d = .64). Hyporesponsivity at 18 months was strongly predictive of language understanding at 24 months in the Sibs-ASD group (r = -.82), but not the Sibs-TD group. Associations between early hyporesponsivity and later language use were non-significant.

Discussion: Results provide increased empirical support for the proposal that early sensory differences may produce cascading effects on higher-level abilities, such as spoken language, in children diagnosed with, or at high risk for, ASD. Findings specifically suggest that sensory hyporesponsivity may be a valuable predictor of later deficits in language understanding in ASD. Implications for practice and needs for future research will be discussed.


The role of numerical estimation flexibility in mathematical competence

Presenter: Darren Yeo (darren.j.yeo@vanderbilt.edu)

Authors: Darren J. Yeo, Eric D. Wilkey, Gavin R. Price

Introduction: A growing number of studies have used nonsymbolic (i.e., arrays of dots) estimation tasks to examine individual differences in the mapping of exact, symbolic numerals to approximate, nonsymbolic magnitudes. While various studies have found significant relationships between the accuracy, variability or linearity of verbal estimates and math competence in children and adults, results have thus far been mixed. Moreover, estimation performance has been found to be highly susceptible to calibration when an anchor numerosity is provided, and little is known about how the flexibility of one's estimations induced by calibration is related to math competence. The current study thus explores the role of estimation flexibility in math competence.

Methods: To this end, adults first completed a nonsymbolic, free estimation task, and then repeated the task with the same stimuli, but were given a misleading upper bound that was twice as large as the largest actual numerosity. Changes in estimation accuracy, variability, and linearity between the free and calibrated estimation conditions were measured.

Results: Consistent with some extant findings, variability, but not accuracy and linearity, of free estimation is associated with math competence. Crucially, the effect of calibration on one's linearity, but not accuracy and variability, of estimation is associated with math competence.

Discussion: These findings suggest that higher math competence is partly accounted for by the ability to implement a symbolic structure more readily and effectively to nonsymbolic numerical magnitudes, and the reliability in mapping exact, symbolic numerals to specific nonsymbolic magnitudes. Notably, the findings suggest a possible mechanism for the widely observed logarithmic-to-linear shift in numerosity estimation with development in numerical experience and mathematical competence.
Cortical Associates of Emotional Reactivity and Regulation in Children Who Do and Do Not Stutter

Presenter: Hatun Zengin-Bolatkale (hatun.zengin@vanderbilt.edu)

Authors: H. Zengin-Bolatkale, E. Conture, S. Key, T. Walden, R. Jones

Introduction: There is increasing evidence suggesting a significant association between emotion and stuttering. Yet, much remains to be known about this association. Evidence for this association has been obtained using methods such as caregiver reports, behavioral observations, and psychophysiological measures (e.g., skin conductance). Certainly, findings based on these methodologies have significantly contributed to our understanding of the association between emotion and childhood processes. However, there are salient aspects of emotion processing that occur in the order of milliseconds, events too rapid to be easily detected by the three methodologies mentioned above. To date, no previous study has employed measures of cortical associates of emotional reactivity and regulation in young children who stutter. Therefore, we presently have limited understanding of the cortical indices of emotion processing in young children who stutter. Thus, it was the purpose of the present study to employ scalp recorded event related potentials (ERPs, specifically the late positive potential (LPP)) to assess emotional reactivity and regulation in young children who stutter and their normally fluent peers while they viewed emotionally salient pictures and listened to short reappraisal stories about them.

Methods: Participants were 17 children who stutter and 19 children who do not stutter (between 4 years 0 months to 6 years 11 months). The dependent measures were (1) mean amplitude of late positive potential (LPP, an evoked response potential (ERP) sensitive to emotional stimuli) during passive (i.e., no response required) picture viewing and directed reappraisal tasks as well as (2) emotional reactivity and regulation related scores on caregiver reports of children’s temperament (Children’s Behavior Questionnaire, CBQ).

Results: Findings indicated that young CWS, when compared to their CWNS peers, exhibited: (a) no significant differences in LPP amplitudes to the pleasant pictures, (b) significantly greater LPP amplitudes to the unpleasant pictures (c) no significant differences in the positive and neutral reappraisal of negative pictures. Further, there were significant correlations between only CWS’s cortical measures of emotional reactivity and aspects of their temperament, as well as only CWS exhibiting significant correlations between CWS’s cortical measures of emotion regulation and temperamentally related measures of emotion regulation.

Discussion: This was the first study to investigate cortical associates of emotional reactivity and regulation in young children who stutter. Results were taken to suggest that CWS, when compared to CWNS, are more emotionally reactive to negatively-valenced stimuli (as indicated by cortical measures of emotional reactivity) and that CWS’s emotional reactivity and regulation (as indexed by cortical measures of emotional reactivity and regulation) are correlated with their caregiver reports of emotional reactivity and regulation, while such correlations were not observed for CWNS.


A double deletion of GABRA1 and GABRG2 in an individual with refractory epilepsy

Presenter: Qi Zhang  (qi.zhang.1@vanderbilt.edu)

Authors: Qi Zhang, Cynthia Forster-Gibson, Lan Xiao, Huancheng Dong, Martin Gallagher, Jing-Qiong Kang

Introduction: Mutations in GABAA receptor subunit genes are frequently associated with epilepsy and different mutations in different GABAA receptor subunit genes are associated with different epilepsy syndromes. Particularly, mutations in GABRA1 have been associated with childhood absence seizures to juvenile myoclonic seizures while the mutations in GABRG2 have been associated with a spectrum of seizures ranging from mild childhood absence or febrile seizures to generalized epilepsy with febrile seizures plus (GEFS+) to Dravet syndrome.

Methods: In this study, we report an individual with heterozygous loss of GABRA1 and GABRG2. This individual began to have febrile seizures at the age of 9 months, with evolution to include non-febrile seizures, grand mal seizures, complex partial seizures and possible occipital seizures. The seizures have been medically refractory. He was diagnosed with optic atrophy around age 4 and is legally blind.

Results: We have expressed the recombinant human GABAA receptors with conditions mimicking the wild-type, hemizygous of GABRA1 or GABRG2 or the double deletion of GABRA1 and GABRG2, we have found that the GABA evoked currents were smaller in the GABRA1 or GABRG2 deletion alone or double deletion of GABRA1 or GABRG2, the total and surface expression of α1 and γ2 subunits were reduced in GABRA1 or GABRG2 hemizygous or double deletion condition.

Discussion: We also generated Gabra1+/-/Gabrg2+/- double knockout by breeding Gabra1+/- with Gabrg2+/- in C57BL/6J background. We are currently characterizing the seizure and eye phenotype of Gabra1+/-/Gabrg2+/- double knockout mice.
The Impact of Prior Postural Experience on Chinese and American Infants' Object Exploration Behaviors

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Introduction: A sitting position confers infants several advantages that enable them to engage in more frequent and advanced reaching behaviors (Carvalho, Tudella, & Savelsbergh, 2007). While in a sitting position, infants plan and execute more upper-body movements with fewer gravitational constraints as compared to when infants are in either supine or prone positions (Soska, Galeon, & Adolph, 2012). They also engage in more frequent multimodal exploration of objects while sitting, utilizing not only manual, but also visual and oral exploration concurrently (Soska & Adolph, 2014). However, for young infants who have not gained the ability to sit independently, sitting is by no means a common experience (Bayley, 1969) and infants' postural experiences are largely determined by their parents' child-rearing practices (Lobo & Galloway, 2012). Many cross-cultural studies have demonstrated the influence of cultures on parental caregiving practices and infants' motor development trajectories (Kaplan & Dove, 1987; Hopkins & Westra, 1989; Karasik, Tamis-LeMonda, Adolph, & Bornstein, 2015). Specifically, parents from certain cultures use more restrictive child-rearing practices that confine their babies' motor development (Mei, 1994; Lin & Fu, 1990). In the current study, we investigate how differences between Chinese and American parents' child-rearing practices will influence Chinese and American infants' prior experiences with different body orientations.

Methods: Twenty Chinese babies and 20 American babies were recruited from Beijing, China and Nashville, TN, respectively. All participants were between 2.5- to 3.5-month old and were unable to sit independently. During the study, all infants were presented with three toys (rattle, ball, key ring) in sitting, lying and reclining positions. The toys were linked to a baby gym and hung within infants' reach. Both parental report data and behavioral data were collected, coded, and analyzed.

Results: We hypothesize that infants' level of familiarity with certain postures will be associated with differing amounts of exploration behaviors in those positions. We also predict that different parenting practices will impact infants' prior experience with different postural positions in terms of infants' familiarity with and level of exposure to those positions.

Discussion: The results from the current study aim to demonstrate how prior experience with different body orientations, on top of infants' chronological age, is an important constraint that should be taken into consideration when investigating infants' reaching development.
Using Visual Activity Schedules for Children with Persistent Problem Behavior

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Introduction: Approximately 5 million children birth to six years of age are at risk or currently exhibit problem behavior (Powell et al., 2007). Although problem behavior occurs at an alarming rate in preschool, teachers may be unable to identify specific, individualized interventions to support children exhibiting problem behavior in classrooms (Snell et al., 2012). Visual activity schedules (VAS) have been well documented for improving engagement, transition, and recreation behaviors with children with autism spectrum disorder (ASD) and intellectual disabilities (ID; Koyama & Wang, 2011; Lequia et al., 2012; Wong et al., 2014). However, children exhibiting problem behavior in inclusive preschool settings do not necessarily have an ASD or ID diagnosis. The current study provides the first evidence of an evaluation of the use of VAS in a preschool setting for children at-risk for social delays due to persistent problem behavior. The study also evaluates the use of a systematic prompting procedure, constant time delay (CTD), to teach three children with persistent problem behavior to use VAS.

Methods: Participants included three children with persistent challenging behavior and two comparison peers reported to have average engagement in classroom activities. Teachers selected activities each child did not complete (when typical classroom contingencies were used) as intervention targets. VAS intervention occurred during typical activities alongside peers in an inclusive preschool classroom (i.e., art, blocks, sign in routine). Visual schedules included a picture of each step required to complete the activity. Children were taught to use the visual schedule by the researcher using CTD procedures. Engagement and problem behavior were measured in the context of A-B-A-B withdrawal designs.

Results: Children learned to independently use the VAS through CTD procedures. All children's levels of engagement and problem behavior matched levels similar to typical peers in intervention conditions (approximately 95-100% session engaged; 0-1 instances of problem behavior). However, children did not generalize schedule use to novel contexts when schedules were available but not directly taught.

Discussion: Results suggested that CTD+VAS may be a feasible individualized intervention to increase engagement in young children at-risk for social delays exhibiting persistent problem behavior. Children's engagement improved to match the engagement of typical peers in the classroom and problem behavior decreased to near zero levels when children were given a schedule during typical classroom activities, suggesting a low-cost intervention can substantially improve children's problem behavior in inclusive preschool classrooms. Additional research is needed to investigate how teachers can use VAS across multiple classroom activities and routines to improve the behavior of children at risk for social delays and improve long-term outcomes.


Connecting the dots: Examining the role of preschoolers' number ability and interest in parent-child number exploration during card game play

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Introduction: Children develop math knowledge at an early age, and display variation in this development during the preschool years (Starkey, Klein, & Wakeley, 2004). Math is strongly based in number, requiring familiarity with number words, Arabic numerals, and importantly, cardinal (Wynn, 1990) and numeral knowledge (Purpura et al., 2013), which is the understanding that number words and numerals represent specific non-symbolic quantities. Adults' number talk about visible non-symbolic quantities positively contributes to children's abilities to make these connections (Gunderson & Levine, 2011; Mix et al., 2012), but little is known about the contexts in which this exploration occurs. The current study examined how parent-child dyads explore the connections between non-symbolic and symbolic quantities during a card game with increases in child age, and child factors that moderate these relations.

Methods: Ninety-four 3- and 4-year-old children and their parents (60% mothers) were recruited from a children's museum in a mid-Atlantic city. Parents filled out a survey while children's numerical knowledge was assessed. Parents and preschoolers were then videotaped playing a modified version of the card game War. Behavioral coding of the recordings assessed dyads' exploration of non-symbolic arrays, symbolic number names and numerals, and the connections between them, as well as children's interest in the game.

Results: Results showed that dyads explicitly explored quantities on about half (45%) of the cards played, doing so symbolically (number words or numerals) on about a third of those cards (30%), and discussing the connections between symbolic and non-symbolic quantity information on 15% of the cards. Three-year-olds explored quantities explicitly more often than 4-year-olds t(92) = 2.17, p < .03, though number knowledge and children's interest separately moderated these relations. Specifically, children with low number skills showed a positive association between age and symbolic quantity comparison, but in higher ability children, this association was negative. For children with high interest in the game, age and quantity exploration were significantly negatively related, but low interest kids showed no increase in explicit math exploration across age groups.

Discussion: Findings suggest the importance of examining child factors such as interest and ability in understanding variation in the quality of number exploration of parents and preschoolers during number game play. Early number talk and explicit exploration may actually be most prevalent in dyads with high ability 3-year-olds and low ability 4-year-olds, when they are developmentally ready to work through these concepts. In contrast, highly able 4-year-olds did the least amount of explicit number exploration, likely because they could use mental math. Additionally, low interest kids in both age groups explicitly explored very minimal amounts of number concepts.