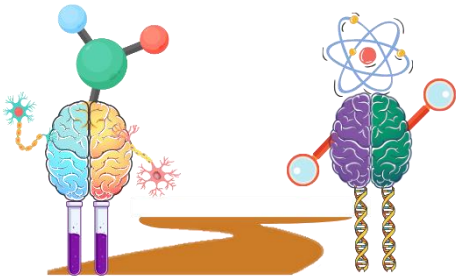
Kennedy Krieger Institute



Paving the way for research innovation

The Gary W. Goldstein Research Symposium and Trainee Poster Day

April 16, 2024

Schedule:

8:50am – **Opening/Welcome**

9am - **Trainee Rapid Fire Session**

Savannah Tate “Exploratory assessment of diurnal bruxism in autism"

Lukman Ismaila “Impact of Spinal Cord Injury (SCI) level on Cortical Reorganization”

Benjamin Schindel “The Impact of the COVID-19 Pandemic on Suicide Risk Screenings within Pediatric Neurodevelopmental and Related Clinics”

Allison Kalinousky “Investigating long term potentiation in Kabuki syndrome”

Dawn Lammert “Neurotransmitter homeostasis and anapleurosis in neonatal brain injury”

Shreya Sriram “Risk Factors and Prevalence of Vestibular and Auditory Dysfunction in a Pediatric Sickle Cell Disease Population”

10am - **Break**

10:15am – **Mentor Keynote Speaker - Douglas N. Robinson, PhD -** "Mentees - a Privilege, not a Right"

11am - **Poster Session I**

12pm – **Lunch**

12:15pm **- 2020 Goldstein Innovation Awardee: Luke Kalb - "**Evaluation of a Parent-Mediated Mental Health Crisis Prevention Program in Autistic Youth: A Randomized Clinical Trial"

12:45pm **- 2024 Goldstein Innovation Grant Awardees Announced**

1pm - **Poster Session II**

2pm - **Faculty and Staff Talks Session I**

Paul Salib “Coping with pain: Thought patterns and interference with daily activities in communicative adults with cerebral palsy”

Aliyah Allick “Global White Matter Changes and Associations with Cognition in Pediatric Sickle Cell Disease”

Daniel Lidstone “HaptiKart: A Novel Videogame for Assessing Proprioception vs. Visual Bias in Children with Autism”

2:50pm - **Break**

3:05pm - **Faculty and Staff Talks Session II**

Chase Solomon "R183Q GNAQ Sturge-Weber syndrome Leptomeningeal and Cerebrovascular Developmental Mouse Model"

Bayley Lindsay "Delivery of DARS2-AAV9 as a Potential Therapeutic Approach for Leukoencephalopathy with Brainstem and Spinal Cord Involvement and Lactate Elevation"

3:35pm - **Closing**

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Morning Session Posters

11am-12pm

Title: Comparative studies on the optimal liposome fusion protocol for preparing hybrid extracellular vesicles for drug delivery and imaging

Authors: Safiya Aafreen, PhD; Wenshen Wang; Aline M. Thomas; Guanshu Liu

Presenter: Safiya Aafreen, PhD, Trainee

Mentor: Guanshu Liu, Professor

Abstract:
The integrity of the blood-brain barrier (BBB) is pivotal in maintaining central nervous system (CNS) health, with its compromise being implicated in various neurological diseases. Extracellular vesicles (EVs) have emerged as promising carriers for drug delivery across the BBB due to their inherent ability to traverse it. Among EV loading methods, membrane fusion with liposomes has shown efficacy, yet systematic comparisons of fusion techniques remain scarce. Here, we present the first analytical study comparing three fusion methods—freeze-thawing, extrusion, and PEG-mediated fusion—for loading therapeutic cargo into EVs. Our findings reveal PEG-mediated fusion as the most efficient method, yielding high cargo uptake and gene transduction rates. Notably, in vivo MRI tracking in a murine model of multiple sclerosis (MS) demonstrated successful delivery of hybrid EVs across the BBB. Moreover, PEG-mediated fusion preserved EV membrane integrity and homing capabilities. The versatility of this method allows for loading various drugs or genes into EVs secreted from different cell types. Our study pioneers the application of hybrid EVs for MS treatment and imaging, showcasing their potential in traversing the BBB. These findings underscore the promise of PEG-mediated fusion in engineering customizable EV-based therapies for CNS disorders.

Title: Global White Matter Changes and Associations with Cognition in Pediatric Sickle Cell Disease

Authors: Aliyah Allick, BS; Emily Rao, MD, MA, MS; James F. Casella, MD; Keith Slifer, PhD; Alicia Cannon, PhD; Hangyi Jiang, PhD; Eric Chin, MD; Eboni Lance, MD, PhD

Presenter: Aliyah Allick, BS, Staff/Faculty

Mentor: Eboni Lance, MD, PhD

Abstract:
Introduction: Sickle cell disease (SCD) is a hemoglobinopathy affecting multiple organs, including the brain. Neurocognitive deficits occur regardless of brain injury status. Prior studies identified underlying white matter microstructural changes associated with cognitive measures using diffusion tensor imaging (DTI) metrics in SCD populations. The goals of this study are to 1) define differences in global white matter microstructure between SCD and control participants and 2) determine characteristics of pediatric participants with SCD and abnormal DTI metrics.

Methods: Thirty-eight participants (28 SCD, 10 control) between 8-12 years-old without prior brain injury were enrolled in a prospective longitudinal study including brain MRIs and neuropsychological testing. Thirty-five participants who had usable DTI imaging and neuropsychological testing at study entry were included.

Results: Diffuse differences in white matter microstructure were explored using 19 bilateral regions of interest. We computed global mean diffusivity (MD) and fractional anisotropy (FA) scores using ANOVA loadings and 95% prediction intervals by age using control participants. We identified SCD participants with global scores outside of the 95% prediction interval and compared their characteristics. SCD diagnosis, age, and group x age interactions significantly impacted our MD model (p<0.001). Only age significantly impacted our FA model (p<0.001). Four children with SCD had global DTI metrics outside of the 95% prediction intervals. All participants had abnormal MRIs and 3 participants had abnormal full scale IQs scores.

Conclusion: We identified differences in global white matter microstructural indices between SCD and control participants with blunting of expected decreases in mean diffusivity with age.

Title: Metabolics of a Novel Asymmetric Walking Paradigm Using a Single Belt Treadmill

Authors: Caitlin L. Banks, PhD; Brooke L. Hall, B.A.; Junyao Li, B.S.; Jan Stenum, PhD; Ryan T. Roemmich, PhD

Presenter: Caitlin Banks, PhD, Trainee

Mentor: Ryan T. Roemmich, PhD

Abstract:
Millions of people walk with asymmetric gait patterns due to a variety of neurologic and orthopedic conditions. Unfortunately, most rehabilitation approaches may restore symmetric walking require specialized equipment that is unavailable in most clinics. Our lab developed a novel dynamic treadmill controller than can be used to selectively modify gait asymmetry using only a single-belt treadmill. Our hypothesis was that the metabolic power needed with the dynamic controller would be less than that required for fast walking, suggesting that this strategy could be used to target gait asymmetry in patients who may not be able to tolerate fast walking. Eleven healthy young adults walked on an instrumented treadmill. The dynamic treadmill controller alternated the treadmill between 0.75 m/s and 1.50 m/s for 50% of each gait cycle, with a metronome playing to target stepping along with the speed changes. We sampled oxygen consumption and carbon dioxide production to calculate net metabolic power during each walking bout. We showed that net power varied significantly by condition. Net power for the dynamic treadmill condition represented a metabolic intermediate between normal walking at the fast and slow speeds. These findings and our previous work synergistically demonstrate this technique's potential for delivering asymmetric gait training at a reduced metabolic demand relative to fast walking. These results in healthy individuals add insight that therapeutic use of this controller may be ideal for those individuals who cannot tolerate fast walking, a popular rehabilitation strategy for individuals with better cardiovascular fitness.

Title: Unlocking the neural basis for reading fluency in neurodevelopmental disorders: The role of sensory integration and executive functions in reading fluency

Authors: Alyssa DeRonda, M.S.; Jenny Fotang, M.A.; Natalie Alessi, M.S.; Keri S. Rosch, Ph.D.; Tzipi Horowitz-Kraus, Ph.D.

Presenter: Alyssa DeRonda, MS, Trainee

Mentor: Keri S. Rosch, Ph.D.; Tzipi Horowitz-Kraus, Ph.D.

Abstract:
Reading fluency (RF) is the ability to read quickly and accurately. Executive functions (EF) are critical for RF, but neglected in dyslexia models, some of which theorize a lack of synchronization between sensory (auditory-visual) networks. Recently, we demonstrated that lower RF is related to lower auditory-visual functional connectivity (FC) and, importantly, poorer EF, raising questions about the relationship between EF, sensory network engagement, and RF, and whether these relationships differ across clinical groups. Participants included 8-12-year-old English-speaking children with dyslexia (n=83), ADHD (n=25), ASD (n=23), and typical readers (TR; n=95). Participants completed behavioral measures of RF (TOWRE-2 Sight Word Efficiency) and EF (WISC-V digit-span and coding). A subsample (dyslexia [n=18], ADHD [n=19], ASD [n=14], TR [n=33]) completed a brain scan. Sensory and EF network FC was compared across four groups using an analysis of variance (ANOVA). Relationships between EF and RF were also examined with correlations. Results suggest significantly lower RF ($F(3,222)=54.121$, $p<.001$, $\eta 2=.422$) and EF (digit-span: $F(3,211)=8.563$, $p<.001$, $\eta 2=.109$), coding: $F(3,215)=6.773$, $p<.001$, $\eta 2=.086$)) in the clinical groups compared to TR. Significant positive correlations were observed between RF and EF across groups (digit-span: $r=.37$, $p<.001$; coding: $r=.32$, $p<.001$). Clinical groups showed significantly reduced FC within the EF (CO: $F(3,80)=9.798$, $p<.001$, $\eta 2=.269$; FP: $F(3,80)=3.406$, $p<.05$, $\eta 2=.133$) and sensory networks (visual-auditory: $F(3,80)=5.591$, $p<.01$, $\eta 2=.173$) compared to TR. These results suggest that RF, EF, and sensory networks are affected in dyslexia, ADHD, and ASD. An important next question is whether and how EF differentially contributes to RF across clinical groups.

Title: Adapting a virtual, group, Cognitive Behavior Therapy (CBT) intervention for youth with autism and trauma exposure: Results of a pilot study

Authors: Lauren Duvall, BS; Hanna Kent, BS; Nikeea Copeland-Linder, PhD; Deepa Menon, MD; Tracee Hutt-Brown, LCSW-C; Kathryn Van Eck, PhD

Presenter: Lauren Duvall, BS, Staff/Faculty

Mentor: Kathryn Van Eck, PhD

Abstract:
Limited research exists on interventions for individuals with autism who have had traumatic experiences. Cognitive Behavioral Intervention for Trauma in Schools (CBITS) is a group-based intervention that has demonstrated reduced depression, anxiety, and post-traumatic stress (PTS) symptoms for typically developing youth. More research is needed to identify its effectiveness for youth with autism who have experienced trauma (Jaycox et al., 2018). The current study aimed to assess differences in parent and child reported PTS, anxiety, and depressive symptoms of youth with autism before and after a pilot study of an adapted version of CBITS. 12 participants (6 parents,6 youth – 11-17 years old) enrolled in this quasi-experimental pragmatic pre-post intervention. Youth with autism were recruited from service waitlists and provider referrals and had received an autism diagnosis thorough psychiatric evaluation. Inclusion criteria also included parent report of two depression or anxiety symptoms and sufficient language skills. Participants completed parent- and child-reported measures with strong psychometric properties that assessed PTS, anxiety, and depression symptoms. Analyses used descriptive statistics and paired samples t-tests. Findings demonstrated that youth experienced significantly fewer depression symptoms and fewer anxiety and PTS symptoms. Results provided preliminary evidence that this group-based intervention may prove beneficial for youth with autism with trauma exposure who experience PTS, anxiety, and depression symptoms. Limitations of this study included a small sample size and the lack of a control group. Future research should assess which youth with autism may benefit most from this intervention and under what conditions this intervention is most effective.

Title: Child and Parent Rated Anxiety in Epilepsy: Interim Results from a Clinical Trial of Pharmaceutical Grade Cannabidiol

Authors: Deniz Ertenu, MA; Karen Chen, MD; Catherine Eliades, BS, CCRC; Jay A. Salpekar, MD

Presenter: Deniz Ertenu, MA, Staff/Faculty

Mentor: NA

Abstract:
Abstract Background: The concordance between child self-reports and parent proxy-reports is crucial for understanding QoL outcomes in children, particularly with complex neuropsychiatric illnesses like epilepsy. Objectives: Examining the concordance between child self-reports and parent proxy-reports in assessing quality of life (QoL) and psychological outcomes in children with epilepsy.

Methods: This is a 16-week open label flexible dose clinical trial of pharmaceutical grade cannabidiol (Epidiolex®) for the treatment of epilepsy and anxiety. Child and parent behavioral measures were obtained with the GAD 7, SCARED, and QoL scales at baseline, weeks 8 and 16. Child and parent ratings were compared in 9 subjects completed to date (66.7% F; mean age = 12.3)

Results: While there is notable concordance in QoL assessments, variations emerge in the GAD 7 and SCARED scales. The QoL scale shows increased parent-child concordance at week 16 ($r = 0.551$, $p = 0.124$), while the GAD 7 scale demonstrates fluctuating concordance; agreement at week 8 ($r = 0.871$, $p = 0.024$) diminishes by week 16 ($r = -0.155$, $p = 0.769$). The SCARED scale shows variable parent-child agreement; moderate at baseline ($r = 0.386$, $p = 0.449$) and low at Week 8 ($r = 0.096$, $p = 0.857$).

Conclusion: Discrepancies were noted where parents underestimate or overestimate their child's well-being. These variations align with existing literature, reinforcing unique dynamics in parent-child perceptions of well-being regarding neuropsychiatric illness. Findings highlight the importance of considering both child and parent reports when treating psychiatric conditions in children with epilepsy.

Title: Introducing the Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT)

Authors: Naomi Franklin, BS; Eric Chin, MD; Erika Augustine, MD, MS; Ellen Mowry, MD, MCR

Presenter: Naomi Franklin, BS, Staff/Faculty

Mentor: Erika Augustine, MD, MS

Abstract:
Background/Objectives: Clinical trials and biomarker development are particularly challenging for uncommon/rare neurological diseases. NeuroNEXT is a National Institute of Neurological Disorders and Stroke-funded multi-center network focused on conducting Phase 2-3 clinical trials for neurological diseases. Kennedy Krieger Institute and The Johns Hopkins Hospital joined NeuroNEXT as a joint hub in 2023. Our poster will introduce NeuroNEXT to Kennedy Krieger Institute investigators and trainees and highlight associated research and training opportunities. Description: We will introduce Research Day attendees to the structure of NeuroNEXT (at a national level as well as at the institutional implementation level), to the breadth of ongoing and completed NeuroNEXT studies, and to current network priorities. For investigators, we will review the unique iterative review process for NeuroNEXT project applications and highlight infrastructure available for developing, leading, and conducting projects. We will also review opportunities for committee participation and for secondary research building upon ongoing and completed studies. For learners (from pre-doctoral to junior faculty levels), we will highlight NeuroNEXT-based training resources including an annual supported NeuroNEXT fellowship, networking meetings, and network-based didactic series. Significance: Collaborative multi-site studies have proven essential for studying uncommon/rare neurological diseases, and NeuroNEXT is a flagship effort by NINDS to promote such studies. By introducing Research Day attendees of all levels to local and national NeuroNEXT offerings, we hope to foster network engagement and ultimately to improve treatment for individuals with neurological diseases.

Title: The Effects of Electrical Stimulation in Children with Spina Bifida: A Case Series

Authors: Sabrina Harrison, DPT

Presenter: Sabrina Harrison, DPT, Trainee

Mentor: Elena Bradley PT, DPT, PCS

Abstract:
Objectives: Functional Electrical Stimulation (FES) is standard of care for individuals with spinal cord injury. New studies are investigating the effects of altering excitability over multiple spinal segments through Transcutaneous Spinal Cord Stimulation (tSCS). There is limited evidence supporting the benefits of electrical stimulation in children with spina bifida. The purpose of this study is to investigate the safety and feasibility of these modalities for this population.

Methods: Patient A (18 months) and Patient B (10 years) with spina bifida received 3 hours of weekly physical therapy for 7-8 weeks. tSCS and/or FES was utilized for 30 minutes each session. Patient A baseline assessment consisted of observation, parent report, Battelle Developmental Inventory, and progress towards goals. For Patient B, sensation and manual muscle testing, parent report, progress towards goals, 2 Minute Walk Test, and 10 Meter Walk Test. Reassessments occurred every 4 weeks and at discharge. Interventions for Patient A included developmental skills and gait training. For Patient B: gait training, supported standing, and lower extremity strengthening.

Results: Neither patient experienced adverse effects. Patient A demonstrated increased limb movement, improved coordination, and motor control. Total distance ambulated increased, although assistance level varied. Patient B demonstrated improvements in 2 Minute Walk Test score, 10 Meter Walk Test score, and sensation. There was no change with manual muscle testing, but improvements in step length and lower extremity posture may indicate functional strength gains.

Conclusions: tSCS shows promise as an adjunct intervention to improve functional outcomes in children with spina bifida.

Title: AAV9 mediated Dars2 gene therapy prevents neurodegeneration in two mouse models of LBSL

Authors: Garofolo Ines, BS

Presenter: Garofolo Ines, BS, Staff/Faculty

Mentor: NA

Abstract:
Leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (LBSL) is a rare white matter disease caused by mutations in the mitochondrial aspartyl-tRNA synthetase (mt-AspRS, or DARS2) gene, which is important for the synthesis of proteins in mitochondria. Abnormalities within cerebral white matter, brainstem, and spinal cord are observed in all patients' MRI; however, a large phenotypic spectrum exists. Previously, we have shown that Dars2 deletion from CamkII alpha excitatory neurons results in a severe and slowly progressive phenotype emerging at 22 weeks old, consisting of significant cortical atrophy and ventricular enlargement (Nemeth et al., 2019). More recently, we have generated mice with Dars2 deletions in Advillin-expressing cells, or sensory neurons of the dorsal root ganglia. Dars2/Advillin deletion mice display severe ataxic behavior starting at as young as p14, eventually leading to death by 6 weeks. As LBSL patients primarily experience symptoms associated with ataxia, disordered gait, and white matter abnormalities, these models provide a representation of disease phenotype for the further study of disease mechanism, cell-type specific effects, and therapeutic efficacy. Our current focus in therapeutic testing within these mouse models is via treatment with an Adeno-Associated Viral (AAV) vector, serotype 9, containing a human DARS2 plasmid. Our hope is to improve the biochemical and phenotypic deficiencies in our models by way of intracerebroventricular (ICV) or intrathecal (IT) injection of the AAV9 vector.

Title: Models to Facilitate Culturally Responsive Patient and Family CenteredCare within Audiology Practices

Authors: Kathryne Knepp, BS

Presenter: Kathryne Knepp, BS, Trainee

Mentor: Holly Duncan, Au.D., CCC-A; Sarah Ellis, Au.D., CCC-A; Amy Gaskin, Au.D., CCC-A

Abstract:
An audiologists most important work is centered around patient and family centered care. There are many subsets and models that a provider can implement to provide effective patient/family centered care (P/FCC) and accommodate to patients' needs, such as trauma informed care, neurodiverse care, and the Patients/Families as Hosts model. Trauma informed care (TIC) is the act of accounting for a patient's life as a whole to provide appropriate and effective care. A provider can implement TIC into their practice by knowing the signs and symptoms of trauma, understanding the impact of trauma, implementing knowledge of trauma into workplace trainings, and by providing a safe and empathetic area where patients' who have experienced trauma can feel empowered. Neurodiverse care/neurodiversity affirming care is the act of providing safe and effective care to patients who are neurodiverse. Neurodiversity is an umbrella term that emphasizes the range of differences that an individual's brain can function. There are many ways a provider can implement neurodiverse care, such as, reducing sensory stimuli (e.g., dimming overhead lights), using clear and common communication, practice active listening, and acknowledging that all behavior is communication. The Patients as Hosts/Families as Hosts model is a model of P/FCC that highlights that patients/families invite you into their lives and offer to host you as a provider. As providers, it is essential that we meet patients where they are, and tailor their care accordingly. P/FCC is something to highlight in our everyday practice. To treat everyone as individuals is to provide P/FCC.

Title: Web-based caregiver-reported survey of seizures in Juvenile-onset Huntington's Disease

Authors: Dawn Lammert, MD, PhD; Sanaya Shenoy, MSPH; Carl Stafstrom, MD, PhD; Heather Riordan MD

Presenter: Dawn Lammert, MD, PhD, Trainee

Mentor: Heather Riordan, MD; Carl Stafstrom, MD, PhD

Abstract:
Juvenile-onset Huntington's Disease (HD) presents unique challenges for diagnosis and treatment. Adult-onset HD is characterized by mood and behavioral changes, followed by abnormal movements, most notably chorea. However, juvenile-onset HD, defined as symptoms beginning 20 years of age or younger, often looks much different, with decreasing school performance, attention difficulties, oral motor dysfunction, gait instability, and parkinsonism. Unlike adult-onset disease, patients with JoHD uniquely are affected by seizures. Approximately 15% have seizures as a presenting symptom, and up to 50% of JoHD patients are eventually affected by epilepsy. Over the last 10 years, there has been an increase in anti-seizure medications and improvements in electroencephalography (EEG), with an increased use of continuous video EEG monitoring. The latter can help differentiate disorders of movement and sleep from seizure. However, to-date, there is a paucity of understanding of the current provider practices of caring for patients with JoHD affected by seizures. We undertook an anonymous, web-based caregiver-reported survey distributed through Help4HD's social media platforms to better understand current medication and EEG utilization, and which providers are predominantly caring for this ultra-rare patient population (e.g. adult movement, general neurologist, pediatrician, pediatric neurologist, epileptologist). Preliminary results are presented. Survey recruitment is currently ongoing.

Title: Step Up or Step Back: Longitudinal Associations between Peer Victimization and Youth's Aggression and Internalizing Symptoms as Moderated by Overprotective/Intrusive Parenting

Authors: Maria C. Lent, MA; Casey Buck, MA; Dianna Murray-Close, PhD

Presenter: Maria Lent, MA, Trainee

Mentor: Dianna Murray-Close, PhD

Abstract:
Peer victimization is a pervasive childhood experience with adverse implications for youth's academic, physical health, and mental health outcomes. Specifically, victimization is associated with physical (e.g., hitting) and relational (e.g., purposeful exclusion) aggression and internalizing symptoms (e.g., worry, sadness). Associations may vary based on the form (i.e., relational or physical) of the victimization, child gender, and/or parental overprotection/intrusion. This study investigated the role of physical and relational peer victimization and overprotective/intrusive parenting in preadolescents' physical and relational aggression and internalizing symptoms. Data were collected using a community sample of 236 eight- to twelve-year-old children (53.8% female; Mage = 10.14 years, SDage = 0.68 years) across one calendar year. Physical victimization was marginally, positively associated with physical aggression for girls experiencing high levels of overprotective/intrusive parenting. No associations were found for physical victimization and relational aggression or internalizing symptoms. Relational victimization was positively associated with internalizing problems for girls experiencing high levels and boys experiencing low levels of overprotective/intrusive parenting. Children, broadly, who were more relationally victimized were more likely to be physically aggressive, and boys, specifically, were more likely to be relationally aggressive. Relational victimization was also positively associated with relational aggression for girls experiencing high levels of overprotective/intrusive parenting and negatively associated for girls experiencing low levels of overprotective/intrusive parenting. Findings contribute to a growing literature on the importance of parents' response to victimization for later outcomes and suggest possible differences in adaptive parenting practices for boys and girls.

Title: Delivery of DARS2-AAV9 as a Potential Therapeutic Approach for Leukoencephalopathy with Brainstem and Spinal Cord Involvement and Lactate Elevation

Authors: Bayley Lindsay, Brett Ratajczak

Presenter: Bayley Lindsay, Staff/Faculty

Mentor: NA

Abstract:
Leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (LBSL) is a rare neurological disorder caused by mutations in the DARS2 gene, which encodes for mitochondrial aspartyl-tRNA synthetase. This study aimed to restore the production of DARS2 transcripts and functional protein in LBSL patient derived neurons through treatment with Adeno-Associated Viral vectors (AAV9). LBSL patient induced pluripotent stem cells (iPSCs) were differentiated into mature motor neurons and treated with the DARS2- AAV9 vector on in vitro Day 11. Ten days after exposure, DARS2 expression (qRT-PCR), neuronal arborization (high content imaging), mitochondrial energetics (Agilent Seahorse Mito Stress Test), and lactate levels (colorimetric assay) were measured. Expression of unmutated DARS2 transcripts increased in a dose-dependent fashion, suggesting functional protein production. DARS2 gene expression was increased in parallel to increased neuronal arborization as measured by high content imaging. On Day 21, mitochondrial analysis revealed increases to oxygen consumption and max capacity without affecting cell viability. Lactate release from neurons decreased in a dose-dependent manner suggesting reduced mitochondrial stress. Together these data suggest that gene delivery is sufficient to induce functional changes to neuronal health. While further testing is needed to confirm these findings, it is promising that gene delivery increases normal DARS2 protein production, reducing the phenotypic burden in vitro. Additional studies are underway to investigate the effect of AAV9 treatment on electrophysical activity and the effect of AAV9 in vivo. To date, studies suggest gene therapies may be a viable treatment for mitigating disease progression in mitochondrial tRNA synthetase disorders.

Title: Enhancing Support for Spanish-Speaking Caregivers: Evaluating the Impact of a Telehealth Support Group

Authors: Elias S. Loria Garro, M.Ed.; Nitza Torres González, B.A.; Jessica Mercado Anazagasty, PhD.; Breya Whitefield, M.A., BCBA; Sydney Puga, M.A., RBT; Marian Galan-Torres, PhD.

Presenter: Elias S. Loria Garro, M.Ed., Trainee

Mentor: Mariangely Galan-Torres, PhD.

Abstract:
Research has documented the unique challenges faced by caregivers of neurodiverse children. More specifically, caregivers from linguistically diverse backgrounds must navigate linguistic and cultural barriers that frequently impede access to reliable support systems. Support groups may offer a platform to connect, share experiences, and increase access to resources and information, helping caregivers navigate the complexities of raising a neurodiverse child (Mandell & Salzer, 2007). This study investigated the efficacy of a telehealth parent support group tailored for Spanish-speaking caregivers. Sixteen Spanish-speaking parents participated in weekly group sessions. The telehealth support group addressed behavioral strategies, parental stress and anxiety through a mindfulness and acceptance and commitment therapy (ACT) lens. Each of these families received behavioral services concurrent to the scheduled telehealth group sessions. Efficacy of the telehealth support group was measured by analyzing changes in the Behavior Rating Scale (BRS) scores reported by parents during their participation in group treatment. Clinical and practical implications will be discussed.

Title: Paternal, Maternal, and Familial Factors as Predictors of Sturge-Weber Syndrome Neurological Outcome

Authors: Kieran D. McKenney, B.A; Andrew T. Zabel, Ph.D.; Jayda M. Harris; Anne M. Comi, M.D.

Presenter: Kieran McKenney, BA, Staff/Faculty

Mentor: Anne M. Comi, M.D.

Abstract:
Few studies have investigated the impact of prenatal factors on Sturge Weber Syndrome (SWS). Thus, the aim of the present study is to identify potential risk factors influencing SWS and neurological outcome in individuals with SWS and Port-wine birthmarks (PWB) from paternal, maternal, and familial factors. Higher paternal age at conception was associated with a range of cognitive dysfunctions in offspring with SWS brain involvement. Indeed, paternal age was associated with low IQ (n=25, p=.004), strokes or stroke-like episodes (SLEs) (n=34, p=.030), gross and/or fine motor delay (n=34, p=.036), delays in ability to perform activities of daily living (n=30, p=.012), and delayed learning compared to peers (n=31, p=.027). Furthermore, paternal age was correlated with worse cognitive outcome, as measured by cognitive Neuroscore (rs=.575, p<.001, n=32). When maternal thyroid disease and hypertension were present during pregnancy, offspring were more likely to experience low IQ (n=30, p=.041) and the regression of any abilities (n=37, p=.045), respectively. Logistic regression confirmed the association between paternal age and severe cognitive Neuroscore (β=.580, p=.033, OR: 1.79 95% CI: [1.05, 3.04]), even when controlling for the effects of seizures and strokes or SLEs. Prenatal factors were associated with neurological symptoms in subjects with SWS. Older paternal age, in particular, may predict worse neurocognitive outcome. Further research is needed in larger cohorts to determine the value of the identified prenatal factors as prognostic tools. Likewise, animal models may be used to determine the impact of prenatal factors on the severity of outcome.

Title: Lifespan in the Neuronal Ceroid Lipofuscinoses (NCLs)

Authors: Nadia Moore; Heather Adams; Jennifer Vermilion; Amy Vierhile; Jonathan W. Mink; Erika F. Augustine

Presenter: Nadia Moore, Staff/Faculty

Mentor: Erika Augustine

Abstract:
The neuronal ceroid lipofuscinoses (NCLs) are a group of neuronal lysosomal storage disorders characterized by neurodegeneration, epilepsy, progressive loss of visual, cognitive, and motor function, and shortened lifespan. However, specific published data on lifespan in the NCLs are limited. Such information could inform more accurate anticipatory guidance for families, clinical trial design and would enable evaluation of the impact of approved therapies. We aim to determine the average lifespan of individuals impacted by an NCL diagnosis, based on NCL type, sex, and age at symptom onset. We separately analyzed data from two sources: Batten Disease Support and Research Association (BDSRA) and University of Rochester Batten Center's (URBC) natural history database and contact registry. Data extracted from the BDSRA source included 534 individuals. We utilized parent reported NCL diagnosis, age at death and sex from the BDSRA. Data extracted from the URBC registry source included 111 individuals. We utilized genetically confirmed NCL diagnosis, age at death, sex, NCL phenotype, and age at first parent-reported cardinal symptom from the URBC. These data were summarized with descriptive statistics, additionally we compared age at death based on 1) diagnostic group and 2) sex by diagnostic group. We assessed the correlation between age at parent-reported symptom onset and age at death. Among the data samples, individuals with CLN3 disease experienced the longest lifespan. Across all NCLs, there is strong correlation between age at symptom onset and lifespan. Statistically significant differences in lifespan between males and females were not detected.

Title: Genetic Variants lead to Psychosis/Catatonia: A Case for Neuronal Hyperexcitability

Authors: Jonathan Muniz, MD; Gurpreet Singh Walia; Pratik Agrawal; Monah Salehi, MD; Marco Grados, MD, MPH

Presenter: Jonathan Muniz, MD, Trainee

Mentor: Marco Grados, MD; Maria del Carmen Lopez-Arvizu, MD

Abstract:
Introduction: Catatonia is a complex neuropsychiatric syndrome characterized by motor and behavioral abnormalities including mutism, negativism, echopraxia, stereotypy, withdrawal, and autonomic abnormalities. It is symptomatic of neuropsychiatric conditions such as acute mania, psychosis, or organic brain disorders (autoimmune encephalitis, tumors). Three individuals with catatonia who were hospitalized in a child psychiatry inpatient unit for treatment of psychosis were found to harbor neuropsychiatric genetic variants on genomic testing. The genetic variants implicated pointed to neuronal hyperexcitability as a possible common mechanism in clinical psychosis/catatonia.

Methods: A retrospective chart review was conducted to ascertain pediatric patients who were hospitalized for psychiatric inpatient treatment in an urban academic medical center for psychosis, catatonia. Known or newly identified genetic variants which were plausibly causal of the psychosis/catatonia syndrome were identified in the retrospective review.

Results: Three patients were identified who met criteria for psychosis/catatonia, received ECT treatment and who harbored genetic variants which were plausibly linked causally to their psychiatric illness.

Conclusion: Psychosis and resultant catatonic syndromes are a final common pathway of profound dysregulation of neuronal function in key neurocircuitry, usually affecting dopamine-mediated mesolimbic pathways (psychosis) and broader brain regions (neuronal hyperexcitability and catatonia). Catatonia is not a common phenomenon in psychosis and can have significant morbidity and mortality, usually signaling a profound deficit in neuronal homeostasis resulting in neuronal hyperexcitability and neurotoxicity. In this report, three individuals with psychosis/catatonia harbored genetic variants which are plausibly directly linked to neuronal hyperexcitability (KCNQ1, ADCY8; due to prolonged repolarization) or psychosis-high risk neurodevelopmental changes (CNTN4/GPR29/LYPD1). Linking hyperexcitability to neuronal function, in the third instance, GPR39 duplication may have also resulted in dysregulation of the developmental GABA switch process early in life, predisposing to neuronal hyperexcitability. Further research into the genetic and molecular mechanisms underlying catatonia is warranted.

Title: Sleep Deprivation and Rest Activity Rhythm in SynGAP-1

Authors: Het Patel, BS

Presenter: Het Patel, BS, Trainee

Mentor: Dr. Constance Smith-Hicks, MD, PhD

Abstract:
SYNGAP1 is a neurodevelopmental disorder characterized by moderate to severe intellectual disability. It accounts for 1-2% of all individuals with intellectual disability, with an incidence rate of 1-4 per 10,000 individuals. Symptoms also include epilepsy, sleep and circadian rhythm disturbances, autism spectrum disorder, and behavioral disorders, resulting from pathogenic variants in the SYNGAP1 gene. Sleep difficulties manifest with problems initiating and maintaining sleep. Sleep disruption significantly impacts cognition, epilepsy, and behavior, all of which are present in individuals with SYNGAP1-ID. The SYNGAP1 gene is expressed in the Suprachiasmatic Nucleus (SCN) and regulates circadian rhythm. The SCN is vital for neurodevelopment, sleep, myelination, seizures, and network connectivity. We studied the effects of sleep deprivation (SD) on rest-activity rhythms (RAR) and behavior in SynGAP1 +/- rodent model. With RAR we have explored difference in behavior related to sleep homeostasis, sleep pressure, and response to sleep deprivation. At baseline, SynGAP1 +/- mice had higher levels of activity in the dark phase. Following sleep deprivation, their activity levels in the dark phase decreased, while there were no significant changes in the WT activity levels. Chronic SD in SynGAP1 mice leads to decreased activity in the rest phase and rebound in activity phase in contrast to the pattern in WT mice. Future direction includes further exploration on homeostatic sleep pressure (Process S) being dysregulated in SYNGAP1/SynGAP1.

Title: Made to Measure: A Needs Assessment Approach to Tailor Healthcare Transition Programs for Individuals with Cerebral Palsy

Authors: Sanaya Shenoy, MSPH; Deborah Sahlin, RN; Paul J. Salib, BS; Melanie Pinkett-Davis, PhD; Theodore A. Zabel, PhD; Eric M. Chin, MD; Deanna Johnson, MS; Heather Riordan, MD

Presenter: Sanaya Shenoy, MSPH, Staff/Faculty

Mentor: Heather Riordan, MD; Deanna Johnson, MS; Eric M. Chin, MD

Abstract:
Healthcare transition (HCT) can be complicated and multi-dimensional for individuals with cerebral palsy (CP). Existing programs are not specific to this population and inadequately account for their diverse physical and psychosocial needs. Outside clinical settings, Person-Centered Planning (PCP) is frequently used to establish individual life goals and is often a prerequisite for requesting disability aid. We present our plan for the clinical application of the PCP framework to elicit patient/caregiver needs while preparing for adulthood. Based on lived experience and literature review, we created a simplified PCP questionnaire that assesses needs across four domains: 1) Physical/Mental wellbeing, i.e., medical management, healthy living 2) Vocational wellbeing, i.e., employment, education, volunteering 3) Financial wellbeing, i.e., budgeting, disability aid 4) Community participation. Patients aged 12-23 years and/or their caregivers will indicate the level of needed support in each domain and rate the domain's importance. Demographics, self/caregiver reported scores of function and cognition, barriers faced during HCT, and patient perspectives on adulthood will also be collected. To our knowledge, this project represents a novel adaptation of the PCP to assess unmet needs beyond medical management which contribute to holistic wellbeing. We aim to use this tool to personalize HCT planning across widely varying populations based on each individual's unique characteristics. We also hope to use aggregate data to inform Institute-wide HCT planning initiatives. Both aims will empower patients and families by incorporating their input to fine-tune their HCTs and the broader HCT infrastructure.

Title: Down Syndrome Regression Disorder, Catatonia, and Moyamoya Syndrome - Is there a connection?

Authors: William Silver, DO; Aaron Hauptman, MD; Clay Smith, MD; George Capone, MD; Kyung Eun Paik, MD

Presenter: William Silver, DO, Trainee

Mentor: Aaron Hauptman, MD

Abstract:
Abstract Background: Down Syndrome Regression Disorder (DSRD) is a rare, idiopathic, neuropsychiatric syndrome in individuals with Down syndrome (DS) with heterogeneous presentation. Affected individuals may experience loss of previously acquired social, cognitive, adaptive skills and new neuropsychiatric symptoms. Catatonia has been described in some patients with DSRD. Catatonia has also been reported in individuals with Moyamoya Syndrome (MMS), which is a chronic, progressive cerebrovascular disease caused by the idiopathic narrowing of proximal intracranial arteries leading to the development of friable collateral circulation. Autoimmunity is hypothesized to play a role in MMS and in DSRD, but to date there is no established causal relationship between MMS and DSRD. Our case will be the first to report DSRD with catatonia in an adult with DS who was found to have MMS.

Case History: An 18-old male with DS who was social, independent in activities of daily living, and verbally communicative presented with subacute onset of confusion, apathy, decreased eye contact and oral intake, social withdrawal, stupor, posturing, and negativism. Evaluation discovered new diagnosis of MMS with resultant chronic ischemia in the left frontal cortex, right parietal cortex, and supratentorial white matter. Bilateral encephalo-duro-arterio-syangiosis of MMS did not improve his mental status. Catatonia improved mildly with diazepam. Conclusions: This is the first case described of DSRD with catatonia in an individual with DS and MMS. This case exemplifies the importance of comprehensive work up to identify potentially treatable causes of regression, and raises the question of a potential connection between DSRD and MMS.

Title: Differential developmental contributions of limbic and motor connectivity underlying neuromotor abnormalities in preschool-age children with and without ADHD: a longitudinal study

Authors: Daniel Simmonds, MD, PhD; Deana Crocetti; Stewart H. Mostofsky, MD; Lisa Jacobson, PhD; Keri Rosch, PhD

Presenter: Daniel Simmonds, MD, PhD, Trainee

Mentor: Stewart H. Mostofsky, MD

Abstract:
Objective: Attention-deficit/hyperactivity disorder (ADHD) is primarily characterized by symptoms of hyperactivity and inattention, but is also highly associated with subtle neuromotor abnormalities, whose neural underpinnings are not well understood. In this study, we employ a longitudinal approach to examine development of structural connectivity in children with and without ADHD and its association with neuromotor abnormalities.

Methods: This study employed linear mixed-effects models to characterize developmental changes in structural connectivity using diffusion tensor imaging (DTI), and how these are associated with ADHD-related differences in neuromotor function (measured by the PANESS instrument). The longitudinal study included 127 preschool-age children (ages 4-7 at study onset) with an initial diagnosis of ADHD (n=72, 29 girls) or typically developing (TD) controls (n=55, 23 girls). There were 376 time points with 208 usable DTI scans across 94 subjects. Data were analyzed with a standardized approach (see Simmonds et al., 2014 for details).

Results: Developmental increases in fractional anisotropy (FA, higher values reflect greater integrity of white matter microstructure) were seen broadly across the brain. Analyses revealed significant interaction of age, diagnosis, and neuromotor abnormalities. In limbic circuitry (cingulum), developmental increases in FA were associated with less neuromotor dysfunction in ADHD group, and greater dysfunction in TD group. In contrast, in motor circuitry (internal capsule), the opposite pattern was seen.

Conclusions: These findings suggest differences in the development of motor circuitry in preschool-age children with ADHD. Dissociation in the development of motor and limbic circuitry suggests that the limbic system may be compensating for suboptimal motor systems.

Title: Using Functional Communication and Competing Stimuli to Gradually Increase the Distance of Transitions in the Treatment of Tangibly Maintained Elopement

Authors: Savannah A. Tate, PhD, BCBA

Presenter: Savannah Tate, PhD, BCBA, Trainee

Mentor: Michelle Frank-Crawford, PhD, BCBA-D

Abstract:
Behavioral interventions are highly efficacious in reducing elopement. However, few studies explicitly examine elopement during transitions, and they typically do not include criteria for distance traveled without elopement. We report on a successful treatment consisting of functional communication to "go see" places and things during transitions along with competing stimuli during reinforcer delays for a young boy whose elopement occurred during transitions and was maintained by positive reinforcement in the form of access to tangibles. During generalization, we also gradually increased the distance of the transitions.

Afternoon Session Posters

12pm-1pm

Title: Ultra-High Field (7T) Imaging of the Cerebellar Dentate Nucleus in Children with Autism and with ADHD

Authors: Maansi Barnwal; Laura C. Rice, PhD; Micah Plotkin, BS; Beatrice Ojuri, BS; Dylan Parodi; James Pekar, PhD; Catherine Stoodley, PhD; Xu Li, PhD; Deana Crocetti, MS; Stewart H. Mostofsky, MD

Presenter: Maansi Barnwal, Trainee

Mentor: Laura C. Rice, PhD

Abstract:
Hypothesis/Objective: The present study applies recently-developed methods for imaging the cerebellar dentate in children with autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD). We hypothesized that children with ASD and ADHD would show smaller dentate volumes compared to typically-developing (TD) children.

Methods: Children ages 8-12years completed MRI scanning, including ASD (n=3), ADHD (n=2) and TD (n=3). Quantitative susceptibility maps were used to delineate dentate structure with manual segmentation applied to total dentate volume (TDV) as well as dorsal and ventral subregion volumes, with effects of diagnosis examined using linear regression, covarying for total intracranial volume (TIV).

Results: There were no group differences in age; TIV was marginally greater for ADHD (p=.09). ADHD and ASD showed marginally greater TDV compared to TD (ADHD>TD: p=.08; ASD>TD: p=.18); there were no significant differences between TD and ASD. Examination of ratios of dorsal and ventral volumes to TDV revealed that ASD showed smaller dorsal and larger ventral ratios compared to TD and ADHD (ASDvsTD: p=.03; ASDvsADHD: p=.06); there were no significant differences between TD and ADHD.

Conclusions and Implications: Our study is the first to implement innovative 7T MRI methods to investigate dentate structure in children with ASD and ADHD. We found a unique effect of ASD on dentate subregion volumes, with smaller dorsal volumes (crucial to motor control) and larger ventral volumes (crucial to cognitive control) compared to both TD children and children with ADHD. Future studies will expand upon sample sizes and also investigate effects of diagnosis on dentate functional connectivity.

Title: Treatment of Epilepsy and Comorbid Anxiety: Interim Results from a Clinical Trial of Cannabidiol (EAPE)

Authors: Karen Chen, MD; Catherine Eliades, BS, CCRC; Jay A. Salpekar, MD

Presenter: Karen Chen, MD, Staff/Faculty

Mentor: Jay A. Salpekar, MD

Abstract:
Anxiety and mood disorders are highly prevalent in epilepsy, yet few studies have evaluated a comorbid treatment response. Epidiolex®, a pharmaceutical grade cannabidiol, is FDA-approved for the treatment of complex epilepsy syndromes and may be efficacious for a wide variety of seizure types. In addition, Epidiolex® may serve a "dual role" in treating both seizure disorders and mood and anxiety disorders. This open label, adjunctive, flexible dose study is actively recruiting and to date has reached approximately 70% of the intended recruitment goal, prompting interim analyses to identify trends. The aim of this clinical trial is to evaluate whether Epidiolex® may offer broad improvements in seizure control as well as comorbid neuropsychiatric symptoms in pediatric populations. This study recruits participants ages 6-17, with active epilepsy requiring medication treatment, and with impairing anxiety symptoms. Titration occurred from 5 mg/kg/day to a target dose of 20 mg/kg/day over a 4-week period, but flexible dosing was allowed to more closely mimic clinical practice. Ratings from 20 completers will be used to assess primary outcome measures such as changes from baseline to end-of-study (EOS) scores in anxiety, as measured by Clinical Global Impression Improvement (CGI-I) ratings, where ratings of a 1 or 2 on a 7-point scale will be considered positive responses. 13 participants have been enrolled at the time of abstract submission (mean age = 12.5 years; 61.5% female). Nine participants completed the study, and three terminated early. Of the 13 enrolled, all have presented with baseline CGI-Severity ratings of markedly ill (5) or higher in the overall (mean = 5.4, SD = 0.5) and anxiety (mean = 5.3, SD = 0.5) subcategories. Across the nine completers, the mean CGI-I scores at EOS were 1.7 (SD = 0.9) and 1.6 (SD = 0.9) for the overall and anxiety subcategories, respectively; seven completers (77.8%) demonstrated a final score of 1 or 2 indicative of a robustly positive response. In addition, most completers (88.9%) have shown improvement in anxiety from baseline to EOS visits on parent-reported anxiety measures such as the Screen for Child Anxiety Related Emotional Disorders with a mean decrease of 13.6 points across completers. Overall, interim data suggest that Epidiolex® notably improves both seizure control and anxiety symptoms simultaneously and represents a potentially effective treatment option for anxiety comorbid with pediatric epilepsy.

Title: Burnout in Pediatric Physical therapy: Facilitating Attuned Interactions (FAN) and Moving Toward Solutions

Authors: Brittany Hornby, PT, DPT; Elena Bradley, PT, DPT; Tarra Dendinger, MS, PT; Heather McLean, MPT, PT; Stephanie Tabrisky, MS, PT

Presenter: Tarra Dendinger, MS, PT, Staff/Faculty

Mentor: NA

Abstract:
Healthcare providers are experiencing increasing stress, "burnout," and fatigue. Predictors of burnout include excessive workload, high administrative burden, negative professional relationships and values, and an organizational culture that does not value work-life integration. In both the inpatient and outpatient locations in our department, staff members reported causes of stress including care management, caseload, colleagues and the way they are tasked to do things. The objectives of our poster are to: highlight proposed evidence-based solutions to burnout, describe how Facilitating Attuned Interactions (FAN) training within the Physical Therapy Department (PTD) has assisted with decreasing burnout, and present future measures to combat burnout using Six Sigma's DMAIC model, a five-phase progress improvement method (Define, Measure, Analyze, Improve, and Control). FAN training offered PTs a beneficial communication toll to provide more empathetic, collaborative care. While FAN training is a resource to address parts of the multifaceted problem of burnout, other approaches are needed to ensure the well-being of PTs. Future interventions to address and prevent provider burnout include: a department retreat, an Institute-wide employee engagement survey and provision of additional time on a regular basis to assist with completion of administrative tasks.

Title: Biochemical characterization of a novel mouse model for Adult Refsum Disease (ARD)

Authors: Wedad Fallatah; Shaghayegh Zokaei; Paul A. Watkins; Joseph G. Hacia; Ann Moser; William G. Wong; Joseph Scafidi

Presenter: Wedad Fallatah, Trainee

Mentor: Joseph Scafidi

Abstract:
An audiologists most important work is centered around patient and family centered care. There are many subsets and models that a provider can implement to provide effective patient/family centered care (P/FCC) and accommodate to patients' needs, such as trauma informed care, neurodiverse care, and the Patients/Families as Hosts model. Trauma informed care (TIC) is the act of accounting for a patient's life as a whole to provide appropriate and effective care. A provider can implement TIC into their practice by knowing the signs and symptoms of trauma, understanding the impact of trauma, implementing knowledge of trauma into workplace trainings, and by providing a safe and empathetic area where patients' who have experienced trauma can feel empowered. Neurodiverse care/neurodiversity affirming care is the act of providing safe and effective care to patients who are neurodiverse. Neurodiversity is an umbrella term that emphasizes the range of differences that an individual's brain can function. There are many ways a provider can implement neurodiverse care, such as, reducing sensory stimuli (e.g., dimming overhead lights), using clear and common communication, practice active listening, and acknowledging that all behavior is communication. The Patients as Hosts/Families as Hosts model is a model of P/FCC that highlights that patients/families invite you into their lives and offer to host you as a provider. As providers, it is essential that we meet patients where they are, and tailor their care accordingly. P/FCC is something to highlight in our everyday practice. To treat everyone as individuals is to provide P/FCC.

Title: Faith Community Learning Collaborative for Faith Leaders: an inclusive faith support ambassador program

Authors: Diogo Fortes

Presenter: Diogo Fortes, Trainee

Mentor: Mirian E. Ofonedu, Ph.D., MSW, LCSW-C

Abstract:
Faith communities play a key role in shaping an individual's environment, acting as important sources of social and moral support. However, individuals with I/DD and their families often feel excluded from faith-based spaces: fear of judgement and lack of accommodations often result in their absence from such spaces, furthering social isolation. As respected community agents, faith leaders are uniquely poised to shape attitudes of their congregations and denounce discrimination. However, despite being motivated to create disability-inclusive religious spaces, many feel uncertain and underqualified in doing so. Using an inclusive faith support training curriculum that draws from the Six P's to Inclusive Practice framework, the Faith Community Learning Collaborative (FCLC) is an ambassador program that aims to provide faith leaders with the tools to assess, plan, and implement inclusive practices. FCLC consists of a two-day training, followed by continued technical assistance, and the opportunity to apply for grants to fund small-scale community projects. In the pilot phase, 13 faith leaders were recruited, representing Christian (n=10) and Jewish (n=3) denominations varying in size from small (<100 members) to mega-sized (>2,000 members). Preliminary results (based on pre- and post-training survey responses) suggest high levels of satisfaction with the curriculum, and improved self-reported ability to promote inclusionary practices in their community. To better monitor effectiveness, we will continue follow-up of our pilot cohort and recruit additional FCLC cohorts. Dissemination of inclusive practices in faith spaces represents an underexplored, yet vital step in ensuring that individuals with I/DD meaningfully participate in their communities.

Title: Comparing the Efficacy and Social Validity of Two Re-presentation Formats for Expulsion

Authors: Brianna M. Groch, BA; Sarah D. Haney McDevitt, PhD, BCBA

Presenter: Brianna M. Groch, BA, Staff/Faculty

Mentor: Sarah D. Haney McDevitt, PhD, BCBA

Abstract:
Previous research has identified re-presentation an effective treatment for expulsion (i.e., spitting out food/liquid) when used alone or in combination with other treatments (e.g., chin prompt; escape extinction; Coe et al., 1997; Girolami et al., 2007; Ibañez et al., 2021; Sevin et al., 2002). Researchers have described re-presentation as being implemented in two distinct formats: re-presenting the expelled bite/drink or re-presenting a new bite/drink of the same food/liquid that was expelled. However, the re-presentation format may vary across clinicians and contexts. For example, clinicians may present a new bite/drink only under certain conditions such as following expulsion onto the floor or other unsanitary surface; Ibañez et al., 2021; Shalev et al., 2018). There is no existing literature that explores which re-presentation format is more effective at decreasing expulsions. In the current study, we used a multielement and reversal design to compare the efficacy of both re-presentation formats. Caregivers completed a satisfaction questionnaire measuring the acceptability of each re-presentation format. Results revealed that both re-presentation formats were similarly effective at reducing expulsion. Additionally, caregivers preferred the re-presentation format with a new bite of food. We discuss the application of these results to the treatment of expulsion for children with feeding disorders.

Title: Studying The Effects of Enterovirus D68 Infection On The Neuromuscular Junction And Motor Neuron Toxicity Using Novel Co-culture Methodologies

Authors: Michael Imai, ScM

Presenter: Michael Imai, ScM, Trainee

Mentor: Matthew Elrick, MD, PhD

Abstract:
Acute flaccid myelitis (AFM) is a polio-like pediatric neuromuscular condition characterized by muscle weakness and atrophy and is most often caused by enterovirus D68 (EV-D68). We currently do not understand the mechanisms behind how EV-D68 causes neurotoxicity in motor neurons, which causes AFM. Clinical observations, such as spontaneous recovery and similarity to enterovirus A71 (which rarely causes AFM) suggest that neuronal death is preceded by a period of reversible axonal dysfunction as opposed to longer nascent recovery periods following peripheral nerve Wallerian degeneration. This period of reversible dysfunction also suggests that studying the neuromuscular junction would provide vital insights into the physiological and structural alterations in the early stages of EV-D68 infected motor neurons. Using induced pluripotent stem cell (iPSCs) derived motor neurons and skeletal muscle, microfluidic co-culture devices, and microelectrode arrays, we have developed novel techniques to study the effects of EV-D68 infection on the neuromuscular junction to better mimic in vivo disease. We will further discuss how this model can be utilized to evaluate the function, morphology, and physiology of axons, the neuromuscular junction, and muscle in the immediate phases after EV-D68 infection.

Title: Unraveling the Neural Threads: Exploring the Impact of Violence Exposure on Early Adolescent Brain Connectivity

Authors: Emma Jagasia, PhD, MSN, MPH, RN

Presenter: Emma Jagasia PhD, MSN, MPH, RN, Trainee

Mentor: Mary Beth Nebel, PhD

Abstract:
Exposure to violence poses significant risks to emotional, physical, and psychological development, with over one billion children globally exposed yearly. Despite high rates of violence exposure among US youth, little attention has been paid to its developmental consequences in early adolescence. The purpose of this study is to examine the effects of violence exposure on neurobehavioral development and the role of environmental factors for youth ages 9-10 enrolled in the Adolescent Brain Cognitive Development (ABCD) Study over a four-year period (age 13-14 at end). Utilizing a longitudinal design approach, the specific aims are to: Aim 1: Examine the association of individual characteristics and cumulative violence with intrinsic functional connectivity (rsFC) at year 4, controlling for baseline FC. Regression is being employed to analyze associations between violence exposure measured by the juvenile victimization questionnaire (JVQ) and functional connectivity of specified regions of interests (ROI). Aim 2: Evaluate whether intrinsic functional connectivity mediates the association between violence exposure and psychopathology. Aim 3: Evaluate if environmental factors (caregiver support, peer support) are protective of violence exposure and intrinsic functional connectivity. This presentation will highlight preliminary analysis and findings from Aim 1, focusing on the associations between violence exposure and intrinsic functionally connectivity. Total sample size is inclusive of 2640 youth participants with three years of data.

Title: The neuropsychiatric phenotype and psychiatric symptom management of a child with a rare triplication of the 22q11.2 chromosomal region

Authors: Hala Katato, DO; Aaron Hauptman, MD

Presenter: Hala Katato, DO, Trainee

Mentor: Aaron Hauptman, MD

Abstract:
Background: Features of 22q11.2 deletion syndrome, formerly known as DiGeorge or Velocardiofacial syndrome, are well-described in the literature and include facial dysmorphia, cardiac anomalies, thymic hypoplasia, hypoparathyroidism, cognitive deficits, neuropsychiatric symptoms (psychosis, autism, etc.) and other comorbidities. 22q11.2 duplication syndrome is described, but with varying phenotype (e.g., developmental delays, behavioral challenges, hypotonia, etc.). Little is known or reported about neuropsychiatric symptoms in individuals with triplications in this chromosomal region. We describe a rare case of a child with 22q11.2 triplication who experienced significant neuropsychiatric comorbidities which were successfully managed with low-dose fluoxetine and lisdexamphetamine.

Case History: A 9-year-old African American boy with developmental history of speech and language delay initiated psychiatric care at age 5 for aggression, inattention, hyperactivity, anxiety and behavioral rigidity. He was later diagnosed with autism spectrum disorder, attention-deficit hyperactivity syndrome, combined type, Tourette syndrome and an incidental finding of benign familial neutropenia. On genetic testing, he was found to have a 403 kb distal triplication on 22q11.23, involving three genes BCR, IGLL1 and DRICH1. Neuropsychiatric symptoms responded well to fluoxetine 4 mg and lisdexamphetamine 30 mg.

Conclusions: To our knowledge, there are only 4 case reports in the literature detailing the clinical features in 22q11.2 triplication, and our case is the first individual with this neuropsychiatric profile and without facial dysmorphic features. This case is also the first to address the treatment and resolution of the associated neuropsychiatric symptoms. Subsequent reports on this triplication are essential in characterizing the phenotype of this rare genetic syndrome.

Title: Cognition and Learning Disabilities in Cerebral Palsy, a Single Center Neuropsychological Overview

Authors: Brooke Kimbrell, MD, MSE; Lisa Jacobson, PhD, NCSP, ABPP; Eric Chin, MD

Presenter: Brooke Kimbrell, MD, MSE, Trainee

Mentor: Eric Chin, MD

Abstract:
Population cohort studies indicate that 50% of people with cerebral palsy (CP) have intellectual disability (ID), but rates of cognitive impairment are unevenly distributed by motor impairment severity and comorbid epilepsy (Reid 2018). The rates of specific learning disabilities (SLD) in CP have not been described, although studies show poor academic performance in research participants (Wotherspoon 2023, Micheletti 2023). Difficulties with attention, memory, and executive function are frequently reported by caregivers of children with CP, with ADHD rates of 30% in a study excluding people without ID (Pahlman 2020). This study describes the cohort characteristics of 137 people aged 6-21years with CP who underwent Neuropsychological evaluation at KKI between 2019 and 2023. Rates of ID, learning disabilities, and ADHD are reported for the subgroup with full scale intelligence quotient as measured by the Weschsler Intelligence Scales for Children 5th Ed. This overview compares the clinical referral population to prior studies and informs the rates of clinical diagnoses provided by neuropsychological assessment.

Title: Autism-Associated Difficulties with Visual Tracking is Associated with Increasing Stimulus Speed

Authors: Daniel E. Lidstone, PhD; Natalie Alessi, MS; Stewart H. Mostofsky, MD

Presenter: Daniel Lidstone, PhD, Staff/Faculty

Mentor: NA

Abstract:
Background: This trans-diagnostic study examines tracking accuracy between static vs. dynamic and fast vs. slow visual stimuli to identify mechanisms underpinning autism-associated differences in visual-motor integration (VMI).

Methods: Forty-six typically developing (TD) individuals (mean age 13.6 ± 6.0 years), 16 with ASD (mean age 16.0 ± 6.9 years), and 9 with attention deficit hyperactivity disorder (ADHD) (mean age 11.3 ± 2.5 years) participated. Participants performed tasks involving tracking static (15% maximal voluntary isometric precision-grip forces - MVIP) and dynamic targets (0-25% MVIP). Dynamic targets included slow ramp, fast ramp, and oscillating wave stimuli. Tracking accuracy was measured using the relative root mean square error (rRMSE). Statistical analyses examined the effects of diagnosis, speed, age, and their interactions on tracking accuracy.

Results: Three-way interactions (Group x Speed x Age) were significant for ASD vs. TD for static vs. fast ($p = 0.01$) and showed a trend for static vs. wave ($p = 0.05$), indicating younger children with ASD had poorer tracking of dynamic stimuli. In the comparison of slow vs. fast, a significant two-way interaction (Group x Speed) was observed for ASD vs. TD ($p = 0.02$), where ASD participants had greater difficulty tracking fast targets. Differences in fast vs. slow tracking accuracy correlated with ASD symptom severity (ADOS-2) ($r2 = 0.52$, $p = 0.01$).

Conclusion: ASD diagnosis is linked to differences in tracking dynamic visual stimuli. Future studies should explore whether interventions involving gradual speed adjustments could benefit individuals with ASD in improving skills reliant upon dynamic VMI.

Title: Neuropsychological Functioning of Pediatric Patients with Long COVID

Authors: Jessica C. Luedke, MA; Gray Vargas, PhD; Dasal Tenzin Jashar, PhD; Laura A. Malone, MD, PhD; Amanda Morrow, MD; Rowena Ng, PhD

Presenter: Jessica Luedke, MA, Trainee

Mentor: Rowena Ng, PhD

Abstract:
Objective: To determine the neurocognitive profile for youth with long COVID presenting with cognitive concerns.

Method: This study is a case series of 54 pediatric patients (65% female, Mage = 13.48, SD = 3.10, 5-19) with long COVID who were referred for neuropsychological testing from a post-COVID-19 multidisciplinary clinic. The outcomes of interest were neuropsychological test scores and parent ratings of mood, attention, and executive functioning. The percentage of patients with neuropsychological test scores below the 9th percentile (below average range) and those with at-risk or clinically significant scores (T-scores > 59) on parent-informant inventories were computed.

Results: A portion of children with long COVID showed weaknesses in sustained attention (29%) and divided attention (35%). This portion of patients did not differ when comparing patients with and without pre-existing attention and mood concerns. A high percentage of parents reported at-risk to clinically significant concerns for cognitive regulation (53%), depression (95%), anxiety (85%), and inattention (66%) on standardized questionnaires.

Conclusions: The present case series showed that approximately a third of children with long COVID demonstrate objective weaknesses on sustained and divided attention tasks but were largely intact in other domains of neuropsychological functioning. Importantly, children with long COVID had similar difficulties in attention, regardless of pre-existing attention or mood concerns. Parents reported high rates of mood, anxiety, and executive functioning difficulties which likely impact daily functioning. Attention and emotional regulation should be closely monitored and treated as necessary in pediatric patients with long COVID to aid functional recovery.

Title: The Neurobiological Mechanisms and Cognitive Effects of Zatolmilast (BPN14770)

Authors: Maria B. Halaguena, B.S.; Lexie M. Mathis, M.A.; Dejan B. Budimirovic, M.D.

Presenter: Lexie Mathis, MA, Staff/Faculty

Mentor: Dejan B. Budimirovic, M.D.

Abstract:
Efforts continue to develop treatments for core cognitive deficits in people with neurodevelopmental disabilities such as fragile X syndrome (FXS). Zatolmilast, or BPN14770, is a phosphodiesterase 4D (PDE4D) inhibitor which has shown preliminary efficacy in Phase 2 clinical trials. Zatolmilast is currently undergoing large scale Phase 3 clinical trials in FXS (NCT05163808, NCT05358886, NCT05367960). Here, we review literature exploring the neurobiological targets of zatolmilast. The loss of function or reduced expression of the Fragile X Messenger Ribonucleoprotein 1 (FMR1) gene in individuals with FXS results in diminished levels of cyclic adenosine monophosphate (cAMP). Normally, cAMP is hydrolyzed by the PDE4D enzyme to form adenosine monophosphate (AMP). Zatolmilast inhibits the PDE4D enzyme and increases the availability of cAMP as a secondary messenger for long-term potentiation in neurons, which is of relevance for learning and memory. The aforementioned clinical trials aim to determine whether zatolmilast is effective for extended durations. Additional research is needed to examine efficacy across sexes. If this drug proves to be effective, it would be a breakthrough treatment for individuals with intellectual disabilities, such as those with FXS. This progress may also be useful for other conditions involving cognitive impairments with similar neuropathological processes.

Title: Edited MRS of the Infant Brain on 28 Scanners

Authors: Saipavitra Murali-Manohar; Helge J. Zöllner; Christopher W. Davies-Jenkins; Aaron T. Gudmundson; Steve C.N. Hui; Yulu Song; Borjan Gagoski; M. Dylan Tisdall; Muhammad G. Saleh; Kimberly B. Weldon; Jens T. Rosenberg; Ralph Noeske; William T. Clarke; Georg Oeltzschner; Jessica L. Wisnowski; Richard A.E. Edden

Presenter: Saipavitra Murali Manohar, Trainee

Mentor: Richard A. E. Edden

Abstract:
Motivation: The Healthy Brain and Child Development (HBCD) study is a longitudinal, multi-vendor, multi-site study of early brain development, which will enroll ~7,500 infants. It is the largest ever study to incorporate MRS. In this abstract, we present in vivo data demonstrating MRS performance across vendor and site.

Goal(s): The goal of this abstract is to present HBCD MRS pilot data, and identify any vendor and site differences in MRS data quality and measured metabolite concentrations.

Approach: HBCD pilot MRS data were successfully acquired on 28 scanners, and analyzed using Osprey 2.5.0, to examine vendor and site differences.

Results: ANOVA results show minimal vendor and site differences which is encouraging for such a large-scale multi-site, multi-vendor study.

Title: Initial Use of the Coma Recovery Scale for Pediatrics (CRS-P) in Young Children with Disorders of Consciousness

Authors: Morgan Nitta, PhD; Tyler Busch, BS; Stacy Suskauer, MD; Beth Slomine, PhD

Presenter: Morgan Nitta, PhD, Trainee

Mentor: Beth Slomine, PhD

Abstract:
Objective Disorders of Consciousness (DoC), including vegetative state/unresponsive wakefulness syndrome (VS/URS) and minimally conscious state (MCS-/+), can occur following severe traumatic or acquired brain injury (ABI). Accurate assessment of DoC upon admission to inpatient rehabilitation is important for clinical decision-making and prognostication yet is challenging in young children. Previous work in young children with DoC revealed that visual and motor signs of emerging consciousness are observed more frequently than language-based features, and emergence from MCS (eMCS) is detected more frequently based on motor skills (functional object use) rather than language skills (answering yes/no questions accurately). We previously adapted the Coma Recovery Scale-Revised (CRS-R), the gold standard for assessing DoC in adults, to develop a tool for DoC assessment in young children. The Coma Recovery Scale for Pediatrics (CRS-P) has been preliminarily validated in a cohort of typically developing young children. Here, we describe initial use of the CRS-P in young children with DoC. Participants and Methods: Starting in 3/2020, we clinically administered the CRS-P to children <6 years of age admitted to inpatient rehabilitation with DoC following ABI. This sample includes children admitted between 3/2020 and 4/2022 with an admission CRS-P. The CRS-P includes 6 subscales (auditory, visual, motor, oromotor/verbal, communication, arousal). Total scores range from 0-23 with higher scores indicating greater responsivity. Admission CRS-P total and subscale scores, admission DoC state based on the CRS-P, discharge DoC state, and first sign of eMCS (obtained from behavioral observations documented within neuropsychology notes and/or CRS-P assessment) were gathered via retrospective chart review. Results Nine patients were included (Female=33%; Age range=8 months-5 years). Length of rehabilitation admission ranged from 29-101 days. Etiology of ABI was primarily non-traumatic (88.9%). Total CRS-P scores at admission ranged from 4-17. Percentage of patients with admission subscales scores at the floor varied: auditory=43%, visual=71%, motor=0%, oromotor/verbal=0%, arousal=14%, communication=100%. Admission DoC state included VS/UWS (n=7) and MCS+ (n=2). Of the 7 patients admitted in VS/UWS, 3 (42.8%) emerged from MCS, 2 (28.6%) progressed to MCS-, and 2 (28.6%) remained in VS/UWS at discharge. Both patients admitted in MCS+ were eMCS by discharge. For all 5 patients who emerged, the first sign of eMCS was functional object use (3/5 were first observed to show spontaneous play, the modified CRS-P criteria for this item). The youngest patient to show eMCS was 15 months old. Conclusions. Across this initial clinical sample, the CRS-P was used to categorize children into all stages of DoC during inpatient rehabilitation. At admission, only 2 of 7 patients demonstrated any visual responding (e.g., visual startle); thus, CRS-P visual items representing signs of consciousness (e.g., fixation, tracking) were not reliable early indicators of consciousness. Functional object use, including spontaneous play, was consistently the first sign of eMCS, reaffirming the importance of motor assessment in very young children and highlighting risks of DoC assessment in children with the most severe motor impairment, particularly those who also have visual impairment. A larger sample of young children in DoC is needed to further evaluate the psychometric properties of the CRS-P.

Title: Characterizing Heterogeneity in ADHD: Cluster-based Profiles of Motivation and Executive Control in Relation to Clinical Presentation

Authors: Isabella Palumbo, M.A.; Natalie Alessi; Keri Rosch, Ph.D.

Presenter: Isabella Palumbo, MA, Trainee

Mentor: Keri Shiels Rosch, PhD

Abstract:
Accentuating the contribution of neurobiological trait processes to psychopathology has advanced our understanding of etiological mechanisms that contribute to transdiagnostic risk and heterogeneity within existing diagnostic groups. In ADHD specifically, individual differences in trait-based motivation (i.e., sensitivity to reward [SR] and punishment [SP]) and regulatory mechanisms (i.e., executive control [EC]) may reflect within-group heterogeneity relevant for treatment response. The present study thus aimed to apply a trait-based, neurobiological lens to understand individual differences within ADHD. Temperamental profiles were derived using k-means clustering among a sample of 303 youth (ages 8-17), either with a diagnosis of ADHD or typically-developing (TD) controls, based on parent report of SR, SP, and EC. Results revealed three subgroups with varying tri-dimensional profiles: (1) average SR/SP and EC, (2) high SP/poor EC, and (3) high SR/poor EC. Cluster 1 primarily consisted of TD children, and children with ADHD were primarily included in Clusters 2 and 3. Furthermore, Cluster 3 included a higher rate of children with externalizing disorders and symptom severity relative to Cluster 2, while children with comorbid anxiety disorders were equally represented in both groups. Examination of task-based assessments of SR/SP and EC among the subgroups revealed that Cluster 2 and 3 did not differ in motivational responding, but Cluster 3 showed greater variability in EC than Cluster 2. Collectively, these findings suggest the presence of clinically-relevant heterogeneity within the ADHD cluster groups that are driven by trait-based motivational and regulatory processes and contribute to variability in comorbidity, clinical outcome, and response to intervention.

Title: Fighting the Good Fight: Addressing Racial and Systemic Trauma with Black Parents of Neurodiverse Children

Authors: Jennifer Shepard Payne, PhD, LCSW-C; Erika Sims, MA

Presenter: Jennifer Payne, PhD, LCSW-C, Staff/Faculty

Mentor: NA

Abstract:
African Americans have the highest rates of trauma in the United States. Thus, trauma may play a part in the lives of many African Americans, which is especially difficult to navigate while parenting children with special needs. Acceptance and Commitment Therapy (ACT) is a viable intervention to be used with African Americans. ACT shows potential in treating Black trauma because: 1) It is a non-pathologizing approach. 2) It promotes that suffering is part of the human condition (not a diagnosable condition). 3) It normalizes avoidance yet helps individuals move toward value-driven living. These attributes of ACT are noted in prior research as appealing to Blacks. This presenter created a Culturally Tailored form of ACT (POOF) for African American trauma. Culturally Tailored ACT provides: • The use of culturally relevant metaphors • Experiential exercises • Faith-based mindfulness and/or religious references • Reality-based, role plays • Addresses racism/ discrimination, barriers to treatment, and stigma/cultural views about mental health treatment POOF is a 10-week group that is structured this way: Week 1: An Introduction through Suffering Week 2: It Is What It Is Week 3: Freedom to Let Go Week 4: In the Here and Now Week 5: I Am More than My Experiences Week 6-7: Living Life Like It's Golden Week 8-9: Getting It Done Week 10: Going from Here This poster will present program evaluation feedback about a POOF group which was conducted with ten African American parents of neurodiverse children at the Center for Child and Family Traumatic Stress at Kennedy Krieger (Summer 2023).

Title: Coping with pain: Thought patterns and interference with daily activities in communicative adults with cerebral palsy

Authors: Paul J. Salib, BS; Sanaya Shenoy, MSPH; Heather Riordan, MD; Alexander Hoon, MD; Lauren Jantzie, PhD; Claudia Campbell, PhD; Shenandoah Robinson, MD; Eric M. Chin MD

Presenter: Paul Salib, BS, Staff/Faculty

Mentor: Eric Chin, MD

Abstract:
Chronic pain interferes with daily activities for many adults with cerebral palsy (CP). In other clinical populations with chronic pain, maladaptive patterns of behaviors/thoughts about pain frequently compound pain-related impairment. We examined associations between pain interference and maladaptive behavior/thought patterns in adults with CP. We hypothesized that maladaptive pain-related behavior/thought patterns would be associated with higher levels of pain interference in communicative adults with CP. Volunteers completed standardized questionnaires via in-person interview or online survey. Participants with CP (n=31) had an established diagnosis and endorsed ability to answer questionnaires independently. Typically-developed (TD; n=37) adults endorsed no neurological/developmental diagnoses. We assessed group-level differences using a two-tailed t-test. We tested our hypothesis by examining Pearson correlation coefficients between pain interference and explanatory variables against a null hypothesis of no association. Study groups were similar in age (CP:mean 34±SD 12; TD:39±16;p=0.12), but not sex (CP: 14 male, 17 female; TD: 5 male, 32 female). Adults with CP, compared to TD adults: experienced more pain interference (CP:51.3±9.9;TD: 45.1±6.7;p< 0.01), catastrophized to a higher degree (CP:12.3±11.7;TD: 4.4±7.1;p< 0.01), and scored higher for anxiety/depression (CP:2.68±1.9;TD: 1.17±2;p< 0.05). For adults with CP: pain interference was positively correlated with catastrophizing (r=0.6; 95%CI [0.25,0.81]; p< 0.01) and negatively correlated with wellness-focused coping (r=-0.57[-0.82, -0.14], p< 0.05). Pain interference was positively correlated with anxiety/depression (r=0.45; 95%CI [0.1,0.7]; p< 0.05). Communicative adults with CP exhibited elevated pain interference. Pain interference was associated with maladaptive behavior/thought patterns and anxious/depressed symptoms. Pain catastrophizing may be a key target for individualizing behavioral pain treatments.

Title: Improving reading fluency via the utilization of executive functions networks in children with ADHD and dyslexia: an fMRI study

Authors: M. Ramona Sanghvi, M.P.S.; Masa Khashab; Keri Rosch, Ph.D.; Sanad Ghanaiem; Rola Farah; Tzipi Horowitz-Kraus, Ph.D.

Presenter: Ramona Sanghvi, M.P.S., Trainee

Mentor: Tzipi Horowitz-Kraus, Ph.D.

Abstract:
While attention-deficit/hyperactivity disorder (ADHD) and dyslexia/reading difficulty (RD) are discrete conditions in the DSM, symptoms of RD are observed in 40% of the ADHD population. This phenomenon may be explained by the fact that in addition to the primary deficit in phonological processing and reading fluency (RF) in those with RD it is also characterized by executive dysfunction, whereas the latter is primarily associated with ADHD. Individuals with RD-only may show differing rates of executive dysfunction from those with RD and comorbid ADHD. This study examines a reading fluency intervention that also targets executive functioning (EF) skills to determine the clinical utility of the intervention on reading difficulty among English-speaking children 8-12 years old. Participants were split into three groups, RD+ADHD (n=19) and RD-only (n=18) and typically developing children (n=18), matched for age and nonverbal IQ. Each completed behavioral testing and a fMRI resting-state scan before and after the 8-week intervention to determine effects on EFRF, and EF networks, such as fronto-parietal (FP) and dorsal attention networks (DAN). A 3-group x 2-time repeated measures (RM) ANOVA was conducted for behavioral and brain measures. Regression analysis was used in prediction models that connect behavioral and neurobiological changes. Children with RD+ADHD experienced greater improvement in reading fluency and executive dysfunction than those with RD only. The RD+ADHD group saw a significant decrease in functional connectivity in FP and DAN. The results provide evidence that connects EF to reading fluency in support of precision education approaches for children with different profiles of reading/EF.

Title: Age of Autism Spectrum Disorder Diagnosis in a Nationally Representative Sample

Authors: Benjamin Joffe Schindel, MD, MPH; Paul H Lipkin, MD

Presenter: Benjamin Schindel, MD, MPH, Trainee

Mentor: Paul H Lipkin, MD

Abstract:
1 in 36 eight-year-olds in the United States has been diagnosed with autism spectrum disorder (ASD). An emphasis on ASD diagnosis and intervention in early childhood has received substantial attention through early identification initiatives, but many individuals with ASD will not reach clinically detectable thresholds until well into school ages or adolescence. The objective of this study was to examine the ages of ASD diagnosis and factors associated with later diagnoses. We used nationally representative data from the 2016-2019 National Survey of Children's Health (NSCH) to determine the age at which children were diagnosed with ASD. From a total sample of 114,476 individuals from ages 3 to 17 years, 3231 individuals (2.8%) were included in analysis. The median age at ASD diagnosis was 5 years old with little variability for all respondents who were 8 years or older at the time of survey completion. 50.6% were diagnosed in early childhood (0-5 years old) while only 19.1% were diagnosed in adolescence (12-17 years old). Early childhood age at diagnosis was associated with male sex, Black and non-Hispanic race/ethnicity, and English-speaking households. In younger children, primary care providers were more likely to diagnose ASD, while medical specialists, non-school psychologists, and psychiatrists diagnosed ASD more often in adolescents. Groups with ASD diagnoses at younger ages may have more missed diagnoses in older ages, fewer interventions, and greater risk for potentially modifiable negative health and socioeconomic outcomes.

Title: Perceptions of Providers on the Administration and Management of Intrathecal Baclofen Pumps in the United States

Authors: Sanaya Shenoy, MSPH; Saurav Chakraborty; Colleen Lenz, MS; Shenandoah Robinson, MD; Heather Riordan, MD

Presenter: Sanaya Shenoy, MSPH, Staff/Faculty

Mentor: Heather Riordan, MD

Abstract:
Intrathecal baclofen (ITB) has been used to alleviate spasticity in children aged >4 years for over 25 years. However, the medical community still relies on anecdotal experience for the administration of ITB. We present preliminary evidence on the perspectives of ITB pump practitioners and areas of variability and/or commonality. We designed a questionnaire for providers in the Pediatric ITB Network to indicate their perspective on catheter tip location, dose of ITB, malfunction management, follow-up care and effect on dystonia. The Network includes 100+ ITB pump practitioners across the United States. Data collection is ongoing and will be concluded by March 2024. We have received 26 responses from 20+ institutions representing 15 states. Early findings are consistent with existing literature, indicating intra-institution and inter-institution practice variation. Level of agreement among providers varies by the area of ITB management. For instance, >80% respondents found ITB bolus and pump x-ray series beneficial to manage suspected withdrawal but had diverse views on dosage modification in case of withdrawal. Regarding location of catheter tip placement, there was agreement on cervical placement for severe dystonia, but mixed responses for spastic quadriplegia and diplegia. The effect of ITB on dystonia was indeterminate, with >60% providers indicating ITB being 'sometimes' useful regardless of dystonia type. To our knowledge, this is a novel effort to document varying perspectives among pump practitioners. Understanding practice patterns is a critical step towards establishing standardized and evidence-based guidelines for ITB pump management and therefore, monitoring and improving patient outcomes for spasticity.

Title: Identifying Multiple Sclerosis Lesion Subtypes with Distinct Microstructural Features using Advanced Microstructural MRI and Unsupervised Machine Learning

Authors: Hyeong-Geol Shin; Blake E. Dewey; Jan Brabec; Jinwei Zhang; Omar Ezzedin; Kaitlyn Ecoff; Anna Kim; Alexandra Ramirez; Anna DuVal; Kathryn Fitzgerald; Linda Knutsson; Filip Szczepankiewicz; Jerry Prince; Shiv Saidha; Peter A. Calabresi; Peter van Zijl; Xu Li

Presenter: Hyeong-Geol Shin, Trainee

Mentor: Peter van Zijl

Abstract:
Conventional MRI methods struggle to capture heterogeneous histopathological subtypes within multiple sclerosis (MS) lesions, mainly due to a lack of microstructural specificity. In this study, we aim to unveil distinct subtypes of microstructural alteration MS lesions using advanced multi-contrast microstructural MRI, including tensor-encoded diffusion MRI and chi-separation, in order to to increase sensitivity to individual microstructure. To characterize underlying lesion subtypes with distinct microstructural alteration, a unsupervised machine learning-based clustering algorithm, k-means algorithm, was applied to multi-contrast microstructural MRI quantities, including parameters from diffusometry (μFA [axonal integrity marker], mean diffusivity), susceptometry (quantitative susceptibility mapping, χdia [demyelination marker] χpara [marker for iron-laden microglia]), and relaxometry (R2*, R2, T1). Five MRI-driven lesion subtypes were identified with with unique microstructural property combinations (Type 1: hyper-paramagnetic, Type2: loss in both myelin and axon, Type3: loss in axon, Type4: loss in myelin, Type 5: normal appearing peri-lesional), revealing potential histopathological features of MS lesions. Lesion subtypes with microstructural features histo-pathologically relevant to disease progression (e.g., iron accumulation [Type1], severe tissue damage [Type2]) showed enhanced sensitivities to clinical outcomes (EDSS, T25-FW, 9-HPT, SDMT, and LC-VA), compared to the other subtypes (Type3-5) and whole white matter lesion. In conclusion, this study identified MS lesion subtypes with unique microstructural changes that correlated with worse clinical scores in a manner that was expected based on previous studies using theses MR approaches individually (e.g, iron accumulation or extensive axonal/myelin damage).

Title: MRI and MPI of iPSC derived EVs in a mouse model of myocardial infarction

Authors: Wenshen Wang, PhD

Presenter: Wenshen Wang, PhD, Trainee

Mentor: Guanshu Liu, PhD

Abstract:
Leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (LBSL) is a rare neurological disorder caused by mutations in the DARS2 gene, which encodes for mitochondrial aspartyl-tRNA synthetase. This study aimed to restore the production of DARS2 transcripts and functional protein in LBSL patient derived neurons through treatment with Adeno-Associated Viral vectors (AAV9). LBSL patient induced pluripotent stem cells (iPSCs) were differentiated into mature motor neurons and treated with the DARS2- AAV9 vector on in vitro Day 11. Ten days after exposure, DARS2 expression (qRT-PCR), neuronal arborization (high content imaging), mitochondrial energetics (Agilent Seahorse Mito Stress Test), and lactate levels (colorimetric assay) were measured. Expression of unmutated DARS2 transcripts increased in a dose-dependent fashion, suggesting functional protein production. DARS2 gene expression was increased in parallel to increased neuronal arborization as measured by high content imaging. On Day 21, mitochondrial analysis revealed increases to oxygen consumption and max capacity without affecting cell viability. Lactate release from neurons decreased in a dose-dependent manner suggesting reduced mitochondrial stress. Together these data suggest that gene delivery is sufficient to induce functional changes to neuronal health. While further testing is needed to confirm these findings, it is promising that gene delivery increases normal DARS2 protein production, reducing the phenotypic burden in vitro. Additional studies are underway to investigate the effect of AAV9 treatment on electrophysical activity and the effect of AAV9 in vivo. To date, studies suggest gene therapies may be a viable treatment for mitigating disease progression in mitochondrial tRNA synthetase disorders.

Title: Strategies to Improve Accessibility in Clinical Research: Participant Reimbursement and Travel Coordination

Authors: Amber Quinlan, BA; Emily Wirt, BS; Jen Bodensteiner, BA, MA; Hana Kim, BA, BS, MS; Erika Augustine, MD, MS

Presenter: Emily Wirt, BS, Staff/Faculty

Mentor: Erika Augustine, MD, MS

Abstract:
To collect accurate and generalizable data in clinical research, it is essential that samples are representative of the entire population, including groups that have previously been underrepresented in research. Historically, barriers have prevented ethical research involvement for women, people in minoritized groups, incarcerated populations, and those of lower socioeconomic status. Participation in studies involves routine visits to study sites, which can be challenging for those who live far from sites, do not have reliable transportation, must take time off work, arrange childcare, or have other challenges. Reimbursement of research participants and coordination of travel arrangements are among strategies used to improve accessibility. In Kennedy Krieger Institute's Clinical Trials Unit (CTU), investigators and research coordinators play a major role in recruitment and retention processes, including reimbursement and travel coordination, to minimize barriers for patients and their families to participate in research. Studies across the CTU have a variety of reimbursement schemes that differ in what is specifically covered. Of 41 trials within the CTU, 43.9% of them offer a stipend for completing research visits, which range from $30 to $650. Most studies that offer stipends provide $30-$50 per onsite visit. 58.5% of trials provide reimbursement of travel expenses, but 29.2% of those studies lump travel costs within the stipend. Of note, only 2 of the 24 studies that cover travel offer pre-booking and travel coordination. Only one study provided reimbursement for childcare services. While there are processes in place to increase involvement of underrepresented individuals in clinical research, gaps persist.

Trainee Talks Sessions

Title: Impact of Spinal Cord Injury (SCI) level on Cortical Reorganization

Authors: Lukman E. Ismaila, PhD

Presenter: Lukman Ismaila, PhD, Trainee

Mentor: Ann S. Choe, PhD

Abstract:
This study addresses the critical need for early detection of response to therapeutic interventions in individuals with chronic Spinal Cord Injury (SCI) by leveraging resting-state functional MRI (rs-fMRI) as a sensitive imaging biomarker to detect early functional network changes. Currently, functional electrical stimulation (FES) therapy relies on the International Standard of Neurological Classification for Spinal Cord Injury (ISNCSCI) scoring system, which lacks sensitivity in assessing the degree of functional loss. To fill this gap, this research employs rs-fMRI to detect subtle yet crucial early changes in brain function during therapeutic interventions. Neurological recovery in SCI patients is closely associated with cortical reorganization, which can be investigated using graph theory analysis of inter-regional functional connectivity derived from rs-fMRI data. Previous research has indicated changes in mesoscale graph measures across functional networks in individuals with chronic SCI, suggesting compensatory adaptations due to disrupted spinal cord-brain communication. Notably, within the somatomotor network, a pattern of segregation corresponding to upper and lower body representations, as well as orofacial regions, was observed. The study aims to investigate cortical reorganization patterns in chronic SCI patients, specifically differentiating between cervical and thoracic injuries. Employing graph theory analysis of functional connectivity, data from 32 chronic SCI patients and 32 healthy controls were analyzed, revealing significant alterations in somatomotor and visual networks in the SCI cohort. We observed that individuals with thoracic injuries exhibited more pronounced functional segregation within the somatomotor network. These findings have important implications for clinicians, researchers, and rehabilitation specialists, providing insights into tailored interventions and raising new questions about optimizing SCI recovery strategies. This study aims to provide understanding to plastic cortical changes after SCI, offering a new clinical tool and imaging biomarker for therapeutic intervention assessment, thus significantly enhancing approaches to managing chronic SCI patients.

Title: Investigating long term potentiation in Kabuki syndrome

Authors: Allison Kalinousky, BS

Presenter: Allison Kalinousky, BS, Trainee

Mentor: NA

Abstract:
Kabuki syndrome (KS) is a Mendelian disorder of the epigenetic machinery (MDEM) caused by loss of function variants in either of the two genes: KMT2D, resulting in KS type 1 (KS1) or KDM6A, resulting in KS type 2 (KS2). Both genes are involved in the regulation of histone methylation. Clinically, individuals with KS are characterized as having mild to moderate intellectual disability, distinct facial features, postnatal growth deficiency, and skeletal anomalies. Previously, we have found that a mouse model of KS1 has hippocampal memory defects and decreased adult neurogenesis. This hippocampal memory defect was subsequently confirmed in individuals with KS through cognitive testing, which revealed measurable impairment of visuospatial memory and reasoning tasks.
Long term potentiation (LTP) is the rapid strengthening of synapses in the neural network, and is thought to be the mechanism underlying learning and memory. LTP has an early phase (E-LTP), which begins immediately after the LTP inducing stimulus and depends on short-term kinase activity, and a late phase (L-LTP), which involves the activation of transcription factors and protein synthesis. As individuals with KS have issues with visuospatial memory, we suspect that they will have impaired LTP. Using the KS1 mouse model, we found KS1 mice have increased E-LTP but decreased L-LTP compared to wildtype littermates.
To test whether individuals with KS have impaired LTP, we developed an auditory EEG paradigm. This paradigm consists of beeps at a regular interval for a period of time, then beeps at a random interval, then back to the regular interval to see if the brain is “learning” this pattern. We generate event-related potentials (ERPs) from these EEGs, and compare those to age and sex matched controls. With more investigation, ERPs can potentially be used as a biomarker to test whether LTP is rescued in clinical trials of KS.

Title: Neurotransmitter homeostasis and anapleurosis in neonatal brain injury

Authors: Dawn B. Lammert, MD, PhD; Regina Fernandez, PhD; Susanna Scafidi, MD; Joseph Scafidi, DO, MS

Presenter: Dawn Lammert, MD, PhD, Trainee

Mentor: Joseph Scafidi, DO, MS

Abstract:
Infants born very and extremely premature have immature breathing patterns that lead to episodes of apnea and bradycardia, referred to as apnea of prematurity. This hypo-oxygenation and subsequent re-oxygenation from critical care interventions (e.g. supplemental oxygen, mechanical ventilation) are associated with brain injury. Long term, these infants are at risk of cognitive and behavioral problems, cerebral palsy, and epilepsy. Oxidative metabolism through the tricarboxylic acid cycle (TCA) is important not only to produce energy but also neurotransmitters. Using a clinically relevant mouse model of apnea of prematurity, we tested the hypothesis that perturbations of the TCA cycle would disrupt neurotransmitter homeostasis, particularly the Glutamate-GABA-Glutamine cycle, which derives directly from α-ketoglutarate in the TCA cycle. Using microwave beam irradiation paired with capillary electrophoresis-Fourier transform mass spectrometry, we analyzed metabolites from mouse hippocampi subjected to intermittent hypoxia and found that, surprisingly, directly after injury and 6 days after injury, the levels of Glu, GABA, and Gln were unchanged. These neurotransmitter levels were unaltered despite the decrease in pyruvate carboxylase protein expression and enzyme function. Pyruvate carboxylase is an enzyme expressed exclusively by astrocytes and needed for anapleurosis - the introduction of new carbons to the TCA cycle. Taken together, these findings suggest that Glu-GABA-Gln cycling is preferentially preserved after intermittent hypoxia at the expense of other anabolic functions of the TCA cycle (e.g. purine and pyrimidine synthesis, energy production, and lipogenesis). Understanding these dynamic changes will help identify therapeutic targets to prevent brain injury in very preterm infants.

Title: The Impact of the COVID-19 Pandemic on Suicide Risk Screenings within Pediatric Neurodevelopmental and Related Clinics

Authors: Benjamin Schindel, MD, MPH

Presenter: Benjamin Schindel, MD, MPH, Trainee

Mentor: NA

Abstract:
In 2017, our healthcare organization implemented universal suicide risk screening in outpatient clinics for all patients aged 8 years or older presenting for treatment of neurodevelopmental and related disorders (NRD). Utilizing results of the Ask Suicide-Screening Questions (ASQ) tool, we analyzed factors that influenced suicide risk screening as well as suicide risk in children with NRD who presented for initial treatment in medical clinics before and after the onset of the COVID-19 pandemic. Screenings were performed as part of routine triage for onsite visits by a registered nurse in our clinics for psychiatry, neurology, genetics, developmental pediatrics, neuromotor, rehabilitation, and autism spectrum and related disorders. Patients or caregivers could respond to the ASQ questions or decline participation. A retrospective medical record review was conducted on all initial visits for patients aged 8-17 years who presented for outpatient care from July 2019 to April 2023. Descriptive statistics were performed on results of ASQ, clinic attendance, and comparison of positive ASQ screening (a “yes” response to any question) frequency from before (July 2019-February 2020) and after (July 2022-February 2023) the onset of the COVID-19 pandemic. There were 5362 eligible children who presented for an initial visit, with 3326 eligible pre-pandemic and 2036 post-pandemic. A total of 3236 children between the ages of 8 and 17 underwent initial screenings, with 1851 completed pre-pandemic and 1385 post-pandemic. Significantly more screenings were declined prior to the pandemic than after (44.3% vs. 32%, respectively), p<.001. The prevalence of positive screens was 10% or greater in psychiatry (15.5%), autism spectrum and related disorders (13.1%), neurology (10.5%), and rehabilitation (10.3%) clinics. In contrast, developmental pediatrics (5.6%), genetics (4.0%), and neuromotor (3.0%) clinics exhibited comparatively lower prevalence rates. Although not statistically significant, we observed an overall increase in rates of positive suicide risk screening after compared with before the pandemic (7.1% vs 5.7%, respectively), p=.104. Qualitatively, rates of positive screens decreased by 3.5% for neurology, while rates slightly increased for genetics (+0.3%), behavior and development (+1.3%), neuromotor (+3.3%), and rehabilitation (+1.1%) clinics. Given rates of positive screenings across clinics, this study supports continued universal suicide risk screening of children with NRD. Patients were more likely to participate in suicide risk screening after the onset of the pandemic than before, perhaps due to increased focus on mental health. Our data suggested a trend toward increased positive suicide risk screenings, although it is unclear if this trend reflects changes in mental health risk factors related to the pandemic or if it reflects risk factors related to clinical populations. Deeper analysis of individual clinical groups may help to illuminate risk factors.

Title: Risk Factors and Prevalence of Vestibular and Auditory Dysfunction in a Pediatric Sickle Cell Disease Population

Authors: Shreya Sriram

Presenter: Shreya Sriram, Trainee

Mentor: NA

Abstract:
INTRODUCTION: Sickle Cell Disease (SCD) affects approximately 100,000 Americans and impacts multiple organ systems. Children with SCD have an increased risk of hearing loss (HL), but risk for developing vestibular dysfunction is still unknown. Furthermore, there is a lack of research to support regular auditory and vestibular screening throughout childhood for those with SCD. This study aims to clarify the prevalence of hearing loss and vestibular dysfunction in children with SCD and identify novel risk factors in developing these deficits.

METHODS: We reviewed 270 charts of children with SCD for hematologic, audiometric, and treatment data. All patients presented to the Johns Hopkins Kennedy Krieger Institute between January 2000 and September 2016. HL was defined as pure tone average (PTA) >15 dB hearing level, and vestibular dysfunction (VD) as at least 1 episode of vertigo with presentation to the clinic or emergency department. Multivariate logistic regression was performed to identify predictors of HL and VD, adjusting for covariates based on significance (p<0.05) in bivariate analyses.

RESULTS: Median age was 15 years (range 7-23); 50% were female, 94% were Black. Genotype breakdown was 63% SS, 25% SC, 10% SB+, and 2% SB0. Eighty-six percent of children who underwent audiometric testing were identified as having HL (n=80 children, 30%). VD was identified in 71 children (26%). History of stroke (OR 2.62, p=0.019) and gentamicin use (OR 6.13, p=0.014) were independently associated with HL. Older age (OR 1.01, p<0.001) and history of OSA (OR 3.28, p=0.007) were independently associated with VD. Older children with HL (OR 1.02, p=0.011) with OSA (OR 7.38, p=0.009) were independently associated with developing VD. Receiving chelation (OR 4.0, p=0.030) or using gentamicin (OR 12.7, p=0.029) were independently associated with developing HL for children with VD. Older age (OR 1.02, p=0.011) and OSA (OR 7.38, p=0.009) were independently associated with developing VD in children with HL. The incidence of dizziness and HL in our cohort was significantly higher than the national averages for both adults and children (p<0.001).

CONCLUSION: Vestibular and auditory symptoms are common in pediatric patients with SCD. Novel risk factors, including older age, medication/treatment history, and comorbid conditions, may help identify at-risk patients earlier in life and improve understanding of inner ear disorders in SCD.

Title: Exploratory assessment of diurnal bruxism in autism

Authors: Savannah Tate, PhD, BCBA

Presenter: Savannah Tate, PhD, BCBA, Trainee

Mentor: NA

Abstract:
Diurnal bruxism, defined as audible grinding of teeth while awake, has several harmful side effects including abnormal tooth wear, loss of teeth, and tongue indentations. These issues often result in dental work, which may pose a challenge for individuals with autism spectrum disorder (ASD). Research indicates that 10.3%-60% of individuals with ASD engage in diurnal bruxism. Thus, it may be important to identify environmental variables that are related or unrelated to the occurrence of diurnal bruxism. We conducted a descriptive analysis of diurnal bruxism and used calculations similar to risk ratios to identify environmental variables associated with differential levels of engagement in bruxism. Eight autistic children in early intervention settings participated. The children participated in observations that lasted between 15-30 minutes, and were conducted at least twice weekly for a minimum of one month. Based on our modified risk ratio calculations, we identified correlations associated with higher and lower relative rates of bruxism for all individuals. Ear plugging, attention, contexts with demands, other topographies of problem behavior, and prompts were correlated with higher rates of bruxism across many participants.