

2026 PEDIATRIC NEUROSCIENCES RESEARCH SYMPOSIUM

**Accelerating Neuroscience through
Synergistic Collaborations**



ABSTRACT BOOK

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Children's Healthcare of Atlanta Support Center

Presented by:

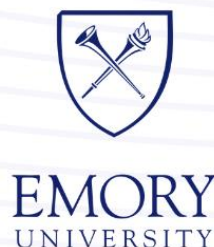


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Poster Finalist Abstracts

Medulloblastoma Spatial Transcriptomics Reveals Tumor Microenvironment Heterogeneity with High-Density Progenitor Cell Regions Correlating with High-risk Disease

Presenting Author: Franklin Chien, Emory University School of Medicine

Poster Number: 1

Co-Authors: Franklin Chien, Marina E. Michaud, Mojtaba Bakhtiari, Chanel Schroff, Matija Snuderl, Jose E. Velazquez Vega, Tobey J. MacDonald, Manoj K. Bhasin

Background: No curative options are available for medulloblastoma (MB) in the relapse setting. The tumor microenvironment (TME) influences progression and therapy response, presenting a promising target for therapeutic advances. Prior single-cell analyses have characterized the cellular components of the TME but lack spatial context. We hypothesize that spatial architecture, beyond cell composition, influences tumor progression and treatment outcomes. **Methods:** We performed spatial transcriptomic sequencing on 18 pediatric MB samples obtained at diagnosis, including two matched diagnosis-relapse pairs. Samples at diagnosis were stratified into high- and standard-risk groups. Spatial data was analyzed for spatial proximity to other cell types, cell-cell communication networks, and expression of cell-cycle dormancy signatures. Findings were validated using immunohistochemistry in the same cohort. **Results:** Our analyses revealed inter- and intra-tumoral heterogeneity within the TME, comprised of tumor-associated astrocytes (TAAs), macrophages (TAMs), stromal components, and distinct subpopulations of MB cells at different stages of neuronal differentiation and cell-cycle progression. We identified dense regions of quiescent progenitor-like MB cells enriched in patients with high-risk (HR) features and an increase in TAAs, TAMs, and dysregulated vascular endothelium following relapse. **Conclusions:** Our study presents novel insights into the spatial architecture and cellular landscape of the MB-TME, highlighting differential spatial patterns correlating with HR features. Future studies should evaluate their role in relapse and therapy resistance and may lead to uncovering novel therapeutic targets

Shifts Toward Normative Brain Coherence Patterns and Concurrent Functional Change in the Context of Individualized Neurodevelopmental Intervention: A Case Series Using Quantitative EEG

Presenting Author: Holly Haynes, Pillar Research Institute, The Jacob's Ladder Group; Fresno Pacific University

Poster Number: 2

Co-Authors: HAYNES, HOLLY; Gonzalez, Julian; O'Dell, Amy; George, Bagie; Gaynor, Jayden

Background. Quantitative electroencephalography (qEEG) offers non-invasive measures of brain connectivity that can inform individualized intervention planning for children with neurodevelopmental differences (Turner, 2021; Keizer, 2021). However, few studies examine whether coherence changes observed following intervention co-occur with functional gains in neurological organization, academic performance, or behavioral regulation. We hypothesized that children receiving personalized neurodevelopmental intervention would demonstrate movement toward normative coherence of qEEG

coherence alongside concurrent functional improvement, regardless of diagnostic category.

Methods. Twenty-seven clients (13 female, 14 male) with paired qEEG assessments were drawn from a larger outcomes evaluation of an individualized neurodevelopmental program spanning three diagnostic categories: Autism Spectrum Disorder ($n = 14$), Emotional/Behavioral/Relational challenges ($n = 4$), and Other Neurodevelopmental Disorders ($n = 9$). Assessments used sLORETA-linked-ear coherence mapping compared with a normative database. The 10 most deviant hyper-coherence and 10 most deviant hypo-coherence connections (based on absolute z-score magnitude) were identified at baseline and tracked at follow-up. Change was calculated as a reduction in absolute z-score deviation from the normative mean. Functional outcomes were assessed concurrently using the Primitive Reflex Assessment, the Wide Range Achievement Test, 4th Edition, and internally developed channel-mastery assessments. Co-occurrence of neurophysiological and functional improvement was examined descriptively.

Results. All 27 clients demonstrated movement toward normative coherence (mean $\Delta|z|=2.57$, $SD=0.88$), $t(26)=14.81$, $p<.001$, $d=2.90$; Wilcoxon $W=0$, $p<.001$. At the connection level, 530 of 540 connections (98.1%) shifted toward normative values. Hypocoherent connections showed larger gains than hypercoherent connections ($z=2.90$ vs. $z=2.23$). Improvements were consistent across diagnostic groups (ASD: $p<.001$; EBR: $p=.002$; Other: $p<.001$), with no between-group differences, $F(2,24)=0.89$, $p=.42$. Both female and male clients improved (both $p<.001$). Among clients with functional data, 75% improved in primitive reflex integration and 81% showed improvement on at least one WRAT4 subtest.

Conclusion. This case series documents consistent normalization of brain coherence alongside concurrent functional improvement across diagnostically diverse pediatric clients. Co-occurrence of neurophysiological and functional change across unique coherence profiles suggests that multi-level assessment may offer a more complete picture of developmental change than either brain-based or behavioral measures alone. These descriptive findings warrant replication with larger samples

Epigenetic C-Reactive Protein and Corticolimbic Gray Matter Volume in Youth at Clinical High Risk for Psychosis

Presenting Author: Benson Ku, Emory University

Poster Number: 3

Co-Authors: KU, BENSON; Xu, Ying; Goldsmith, David R.; Sawyers, Chelsea; Addington, Jean; Bearden, Carrie E.; Cadenhead, Kristin S.; Cannon, Tyrone D.; Carrion, Ricardo E.; Keshavan, Matcheri S.; Mathalon, Daniel H.; Stone, William S.; Woods, Scott W.; Walker, Elaine F.; Perkins, Diana O.; and Bozack, Anne K.

Background: Psychotic disorders typically emerge during adolescence and young adulthood, making early identification of youth at clinical high risk for psychosis (CHR-P) a priority for pediatric mental health and early intervention. Immune dysregulation and elevated inflammatory markers precede and contribute to psychosis onset, and structural alterations in corticolimbic regions are well documented. C-reactive protein (CRP) has been linked to reduced gray matter volume (GMV) in the prefrontal cortex, anterior cingulate cortex, and hippocampus. Epigenetic CRP, a DNA methylation-based proxy of cumulative inflammatory burden, may index chronic immune dysregulation more effectively than a single plasma measurement, yet whether it relates to brain structure in CHR-P youth is unknown.

Methods: We examined associations between epigenetic and plasma CRP, regional GMV, and positive

symptom severity in 165 youth (108 CHR-P, 57 healthy comparisons; mean age 19, range 12–30; 67% female) from the North American Prodrome Longitudinal Study Phase 2. Epigenetic CRP was derived from the Illumina 450k array; plasma CRP was quantified via multiplex immunoassay. GMVs of the prefrontal cortex, anterior cingulate cortex, and hippocampus were extracted from 3-Tesla MRI; positive symptoms were assessed with the Scale of Prodromal Symptoms. Structural equation modeling tested the hypothesized pathways. Results: Epigenetic and plasma CRP were only weakly correlated ($r = 0.19$). Higher epigenetic CRP was associated with lower GMV in several corticolimbic regions, including the left caudal anterior cingulate cortex (cACC; $\beta = -0.08$; 95% CI -0.13 to -0.01 ; $p = 0.011$), and lower cACC volume was associated with greater positive symptom severity ($\beta = -0.26$; 95% CI -0.43 to -0.15 ; $p = 0.001$). The cACC emerged as a point of convergence, where both inflammation-associated and symptom-associated volume differences localized. Plasma CRP showed no significant associations with any brain measure. Conclusions: To our knowledge, this is the first study to show that epigenetic CRP is associated with corticolimbic structural differences in CHR-P youth during a critical neurodevelopmental window. Epigenetic CRP may serve as a more sensitive marker of neurostructural alterations than plasma CRP, with potential to improve early risk stratification. Longitudinal pediatric studies are needed to determine whether epigenetic inflammatory markers can identify youth at greatest risk for psychosis conversion.

Tailored Thalamic Stimulation During sEEG to Guide Neuromodulation

Presenting Author: Kishore Vedala, Emory University

Poster Number: 4

Co-Authors: VEDALA, KISHORE; Lin, Jenny; Zhang, Guojun; Laxpati, Nealen

BACKGROUND: We present a case of a 9 year-old female with right-sided periventricular leukomalacia and porencephaly, intractable focal epilepsy, and epileptic encephalopathy with spike-wave activation in sleep (EE-SWAS) who was admitted for stereo-EEG (sEEG). Presurgical evaluation suggested a wide but primarily unilateral hemisphere epileptogenic network. In anticipation of considering neuromodulation modalities, thalamic electrodes were implanted in the right anterior (ANT) and centromedian (CM) nuclei. sEEG monitoring showed frequent electrographic seizures during wakefulness and continuous spike-wave discharges during sleep. We therefore developed a tailored protocol of thalamic stimulation with the goal of aborting seizures to determine the optimal nucleus and stimulation paradigm.

METHODS: We used two neurostimulation strategies: (1) “open-loop” high frequency stimulation during periods of continuous spike-wave discharges (i.e. ESES) in sleep, and (2) “closed-loop” high frequency responsive stimulation to electrographic seizures or runs of prolonged diffuse discharges, where stimulation was delivered at bedside immediately upon onset. Though there are no set guidelines for thalamic stimulation during sEEG, we used available literature to guide stimulation parameters. The “open-loop” strategy utilized stimulation for 1 min intervals followed by an interceding 1 min “off” period. The “closed-loop” strategy utilized stimulation delivered at the onset of a run of interictal discharges. Stimulation was attempted with each strategy on each thalamic nucleus. **RESULTS:** The “open-loop” stimulation did not result in a significant reduction of epileptiform discharges. In contrast, the “closed-loop” stimulation resulted in near-immediate abortion of electrographic seizures in 67%

(4/6) of the stimulations in the CM nucleus but only 20% (2/10) of the stimulations in the ANT. This data was used to guide the decision to place RNS electrodes in the right CM nucleus along with an additional electrode in the right SMA. Following implantation and initiating stimulation, the patient experienced significant improvement, from a reported pre-implantation frequency of daily to weekly seizures to no definite seizures reported in 12 months since RNS implantation. **CONCLUSIONS:** This case study supports the utilization of thalamic stimulation during SEEG to guide neuromodulation modality and thalamic nuclei selection for electrode implantation. Further responsive stimulation studies in a systematic approach would help validate the findings in this case.

A Novel EEG-Driven Framework for Objective Assessment of Motor Planning in Childhood Apraxia of Speech

Presenting Author: Noor Alzraikat, Emory University

Poster Number: 5

Co-Authors: ALZRAIKAT, NOOR; Key, Alexandra P.; Maziashvili, Giorgi; Brane, Natalie; McElhanon, Barbara; Niehaus, Carley; Jones, Rheinallt M.; Wynn, Bridget; Scahill, Lawrence; Morris, Claudia R.

Background: Childhood apraxia of speech (CAS) is a neurological motor planning speech disorder of unknown etiology. It is often underdiagnosed, delaying intervention during critical periods of speech and language development. CAS affects approximately 1–2 per 1,000 children. The burden of CAS is amplified by its overlap with autism spectrum disorder (ASD), with 63% of children with ASD reported to exhibit CAS. Management relies on speech therapy with variable outcomes, and no FDA-approved pharmacologic treatments exist. Because early identification is critical, electroencephalography (EEG) may offer an objective tool to identify motor planning deficits. We evaluated the feasibility and preliminary utility of EEG to identify reduced neural markers of speech integration with articulatory movements in children with CAS. **Methods:** This interim-analysis included 17 children aged 3–6years with CAS (n=4) and age-matched neurotypical controls (n=13), enrolled in an ongoing pilot case-control study. 128-channel EEG was recorded during: (1) audiovisual speech perception (AVS) task where consonant-vowel stimuli were presented in auditory-only, visual-only, and combined audiovisual conditions, and (2) speech production (SP) task (nonword repetition), involving watching a puppet produce novel 2-and 3-syllable words and repeating each word following a visual “go” cue, allowing isolation of the motor preparation period before speech. **Results:** Groups were comparable in age (CAS:4.5±1.0 vs controls:4.8±1.4 years) and sex (male: 75% vs 85%). In the AVS task, the CAS group demonstrated enhanced multisensory response consistent with the lack of predictive auditory-visual associations when viewing moving faces. Controls showed reduced P300 amplitude for audiovisual compared to visual-only stimuli, reflecting multisensory facilitation. During the SP task, controls demonstrated the expected right frontal Contingent Negative Variation (CNV) response for all stimuli beginning ~400 ms after motor preparation onset (mean slope=-0.578). The CAS group exhibited a reduced CNV in the 2-syllable condition (slope=-0.217) and no CNV in the 3-syllable condition (slope=0.369). **Conclusion:** Children with CAS may demonstrate altered neural signatures of audiovisual integration and motor preparation. Findings are preliminary but provide neurophysiological evidence supporting impaired motor planning and multisensory processing. If confirmed in larger studies, EEG

may provide an objective tool to characterize neural signatures of speech perception and production in CAS.

Targeting of the YAP/TAZ-TEAD axis Restricts Intra-tumoral Heterogeneity in Pediatric High-Grade Glioma

Presenting Author: Jorge Luis Jimenez Macias, Emory University

Poster Number: 6

Co-Authors: Jimenez-Macias, Jorge Luis; Oh, Se-Yeong; Yin, Kevin; Hu, Zhengang; Sele, Nisan; Boon, Nikki; Sign, Anson; Sloan, Steven A.; and Read, Renee D.

Background: Pediatric high-grade gliomas (pHGGs) are invasive and fast-growing brain malignancies. They account for up to 40% of all brain tumor-related deaths in childhood. Genetic alterations that characterize these gliomas include H3 onco-histone mutations and genetic alterations in receptor-tyrosine kinases (RTKs), including amplification, mutation, and gene fusions in RTKs. However, direct targeting with tyrosine kinase inhibitors (TKIs) has shown at best partial responses in patients due to the molecular heterogeneity within these tumors. Thus, alternative therapeutic approaches to treat pHGGs are urgently needed. The YAP/TAZ transcription factors, which cooperate with TEAD co-factors to promote target gene expression, orchestrate stem-cell fate decisions, and stimulate proliferation downstream of RTK signaling during neural development. Our data showed that YAP expression is upregulated in RTK mutant and H3 mutant pHGGs. **Hypothesis:** We hypothesize that targeting the YAP/TAZ-TEAD pathway will have anti-oncogenic effects in pHGGs. **Methods:** We utilized RTK-aberrant patient-derived pHGG cells and we established an in vitro human brain organoid-pHGG assembloid in which these pHGG cells are engrafted to iPSC-derived human brain cortical organoids. We tested genetic depletion (via iRNA) and pharmacological depletion of the YAP/TAZ-TEAD pathway (via Verteporfin (VP), a YAP/TAZ-TEAD inhibitor). We screened anti-oncogenic responses via imaging and single-cell RNAseq. **Results:** Our data shows that depletion of YAP via RNAi inhibited pHGG stem cell-like self-renewal capacities and induced apoptosis, recapitulating its developmental roles. VP mimicked the effects seen by YAP genetic depletion. To further characterize the pre-clinical potential of YAP/TAZ targeting in clinically relevant models of pHGG, we tested VP in the brain organoid-pHGG assembloids. Engrafted pHGG cells showed cytoplasmic and nuclear YAP expression, were actively proliferating, and presented transcriptional heterogeneity comparable to pHGG patient tumor specimens. Treatment of these brain organoid-pHGG assembloids with long-term VP constrained transcriptional heterogeneity and cell-to-cell communication among tumor cells, but yielded VP-persisters pHGG cells. **Conclusion:** Our current work seeks to investigate how long-term YAP-TEAD inhibition affects transcriptional reprogramming of pHGGs. We aim to uncover new mechanisms underlying tumor progression and cellular interactions within the tumor microenvironment that drive drug resistant persister cells. Our work may lead to the development of new therapeutic strategies for pHGG.

EP2 Receptor Antagonism Preserves Inhibitory Interneurons and Reduces Long-Term Seizure Burden After Status Epilepticus in an Adolescence Seizure Mouse Model

Presenting Author: Hao Xing, Emory University

Poster Number: 7*Co-Authors: Hao Xing, Wenyi Wang, Thota Ganesh*

Background: Epilepsy in infancy and childhood is a major neurological disorder associated with recurrent seizures, neuro-inflammation, and long-term neurodevelopmental consequences. Status epilepticus (SE) can initiate persistent epileptogenesis, and inflammatory signaling has been implicated in both acute injury and later seizure recurrence in developing brains. Here we evaluated the novel selective EP2 receptor antagonist BPN37440 in a mouse model of pilocarpine-induced SE. Our data show that BPN37440 reduces long-term spontaneous recurrent seizure (SRS) burden and preserves parvalbumin+ interneuron density, supporting EP2 antagonism as a potential strategy for preventing chronic epilepsy after early-life neuro-inflammatory injury. Methods: Terbutaline and methylscopolamine were i.p. injected into 6-8 weeks old C57BL/6 male mice. 30 minutes later, pilocarpine HCl (280 mg/kg) was i.p. injected to induce SE for 1 hour, followed by diazepam (10 mg/kg) to interrupt SE. Mice were randomized to two groups and treated with either BPN37440 (10 mg/kg) or vehicle (10% DMSO, 50% PEG400 and 40% Water) at 4, 8, and 19 hours post-SE. After 4 weeks post-SE, a customized 3D-printed headcap was implanted on tested mice skull. Free moving mice were recorded EEG to detect SRS for 10 weeks starting at the 5th week post-SE. Results: Acute BPN37440 administration significantly reduced the accumulation of SRS burden over the 5–16 week recording period ($p = 0.0006$, Kolmogorov-Smirnov test; $n = 8$ mice/group). In terms of gliosis, BPN37440 treatment significantly decreased the Iba1+ covered area in both the CA1 and parietal cortex regions ($p = 0.0131$, $p = 0.0026$, respectively) and also significantly reduced the Gfap+ covered area in these same regions ($p = 0.0401$, $p < 0.0001$, respectively; unpaired t-test). Compared with the vehicle group, BPN37440-treated mice also showed a higher density of PV+ interneurons in the brain after pilocarpine-induced long-term SRS ($p = 0.0044$, $p = 0.0377$ for CA3 and parietal cortex regions, respectively; unpaired t-test, $n = 8$ mice/group, 3 replicant staining from each mouse). Conclusion: These findings support a mechanistic link between suppression of neuro-inflammation, preservation of inhibitory interneurons, and reduced long-term seizure burden after SE. EP2 receptor antagonism may represent a promising disease-modifying approach for preventing chronic seizure recurrence after early neuro-inflammatory brain injury.

Behavioral Regression and Language Dysfunction in Pediatric Post-COVID-19 Encephalitis: A Case ReportPresenting Author: Hung Bui, Medical College of GeorgiaPoster Number: 8*Co-Authors: Mai, Sarah; Bui, Hung; Roberts, Danice*

Background: Post-infectious encephalitis is a rare but increasingly recognized neurologic complication of SARS-CoV-2 infection in children. While motor deficits such as gait instability and ataxia are well-defined symptoms of pediatric post-COVID-19 encephalitis, altered mental status (AMS) including personality changes, behavioral regression and progressive language impairment is underrecognized and may delay diagnosis because AMS often present differently in young children than in adults. We describe a pediatric case of post-COVID-19 encephalitis to highlight these atypical clinical features and their

diagnostic implications. **Methods:** We reviewed the clinical course, diagnostic evaluation, neuroimaging, treatment, and clinical outcome of a previously healthy child diagnosed with post-infectious COVID-19 encephalitis. **Results:** A previously healthy, developmentally appropriate, and energetic 3-year-old girl with fever tested positive for SARS-CoV-2. Five days after fever onset, despite fever resolution, she presented with lethargy, frequent falls, dysmetria, and impaired fine motor coordination. Initial laboratory evaluation was unremarkable, and she was treated supportively before discharge. By outpatient follow-up on day 10, her neurologic symptoms progressed to decreased social interaction, inappropriate laughing episodes, expressive aphasia, and near-complete loss of speech, prompting hospital admission. Cerebrospinal fluid analysis demonstrated pleocytosis, while repeat SARS-CoV-2 PCR, viral studies, and electroencephalography were unremarkable. Brain MRI revealed an ill-defined T2/FLAIR hyperintensity involving the right lentiform nucleus. The delayed onset after acute infection, negative repeat infectious evaluation, inflammatory CSF findings, and characteristic neuroimaging supported a diagnosis of post-infectious immune-mediated COVID-19 encephalitis. Treatment with high-dose intravenous methylprednisolone followed by an oral corticosteroid taper resulted in rapid neurologic improvement and discharge within several days. **Conclusion:** This case demonstrates that AMS in pediatric post-COVID-19 encephalitis may present with both motor deficits and subtle neurobehavioral changes. Progressive language regression, expressive aphasia, diminished interaction, and inappropriate affect may be early manifestations of immune-mediated encephalitis rather than isolated developmental or behavioral abnormalities. Recognition of these age-specific presentations, together with timely neuroimaging and cerebrospinal fluid evaluation, can facilitate earlier diagnosis, prompt immunotherapy, and favorable neurologic outcomes. This case further emphasizes the need for heightened clinical suspicion of post-infectious encephalitis in children who develop new behavioral or language changes with motor disturbances following recent SARS-CoV-2 infection.

Robust Neonatal Brain Segmentation in the Privacy and Convenience of the Browser

Presenting Author: Armina Fani, TReNDS Center, Georgia State University

Poster Number: 9

Co-Authors: FANI, ARMINA; Le, Isabelle; Shultz, Sarah; Calhoun, Vince; and Plis, Sergey

Background: Accurate segmentation of neonatal brain MRI is critical for studying early neurodevelopment, yet existing tools are often computationally demanding, difficult to install, or too slow for clinical and research workflows. We hypothesized that a deep learning segmentation model trained exclusively on synthetic data, combined with lightweight browser-based deployment, could achieve robust, accurate neonatal brain parcellation across diverse datasets while increasing accessibility to state-of-the-art tools. **Methods:** We developed a set of 3D deep learning segmentation models for neonatal brain imaging, trained exclusively on synthetic data to maximize generalizability and eliminate dependence on large labeled clinical datasets. Multi-modal compatibility was achieved through aggressive domain randomization during training, enabling robust performance across T1-weighted, T2-weighted, and other acquisition protocols in infants aged 0-9 months. The model architecture was optimized for lightweight inference without sacrificing segmentation fidelity. The final model is deployed

on BrainChop, a browser-based neuroimaging platform requiring no installation, no upload of data to external servers, and no specialized hardware. A command-line version with one-step installation is also available for integration into automated pipelines. Results: Preliminary validation demonstrated that our model produced anatomically faithful parcellations across real neonatal MRI data, performing competitively with state-of-the-art methods. Inference completed in under 15 seconds within a standard web browser. Conclusion: This work presents a freely accessible, installation-free, privacy-preserving tool for neonatal brain segmentation capable of robust parcellation across MRI modalities and ages. By leveraging synthetic training data and in-browser inference via BrainChop, this model lowers barriers to neonatal neuroimaging analysis for researchers and clinicians.

Developing Patient-Derived Pediatric Brain Tumor Organoid Models for Functional Therapeutic Testing

Presenting Author: Jonathan French, Emory University

Poster Number: 10

Co-Authors: FRENCH, JONATHAN; KIM, DANIEL; Cordero, Charlie; Tikunov, Andrey; MacDonald, Tobey; Gershon, Timothy; and Junqueira Alves, Chrystian

Background: Patient-derived pediatric brain tumor organoids enable direct studies of pediatric brain tumors by presenting human brain tumors in an experimentally tractable system while retaining cellular heterogeneity. These organoids also retain features of the tumor microenvironment that are often lost in conventional cell lines and patient-derived xenograft models. We sought to establish a workflow for generating three-dimensional models from freshly resected pediatric brain tumors and to determine whether these models could support studies of tumor invasion and cellular immunotherapy. Methods: Fresh neurosurgical specimens from the CHOA/IFF Biorepository were dissociated and seeded at high density in media with appropriate growth factors in ultra-low-attachment 96-well U-bottom plates. Tumor cells formed spheroids that we subsequently embedded in Matrigel and maintained in low-attachment plates on an orbital shaker. We co-cultured these tumor spheroids with human iPSC-derived brain organoids to image tumor invasion into tumor–neural assembloids using confocal microscopy. For cell therapy studies, we generated from Smo-mutant, mouse medulloblastomas and added mouse CAR T cells targeting the B7-H3 antigen then used time-lapse imaging to measure organoid growth. Results: Organoids grew from freshly resected pediatric brain tumor specimens, and matured into three-dimensional structures suitable for longitudinal imaging and therapeutic testing. When cocultured with human neural organoids, the tumor spheroids formed assembloids and exhibited invasive behavior readily visualized by confocal microscopy. In a complementary mouse tumor-organoid model, B7-H3-targeted CAR T cells accumulated within and around the organoids and significantly reduced tumor dispersion compared with unmodified control T cells. Together, these findings establish brain tumor organoid models as versatile platforms for quantifying tumor growth, invasion, immune-cell infiltration, and therapeutic response. Conclusions: Patient-derived pediatric brain tumor samples grow as organoids and can fuse into human neural organoids, generating experimentally tractable models. Coupling these patient-derived models with live-cell imaging and CAR T cell assays provides a foundation for studying tumor–brain interactions and evaluating therapeutic responses in clinically relevant systems.

Infants With and Without Later Autism Diagnosis Attend Equally to Caregiver Positive Affect in the First Six Postnatal Months

Presenting Author: Peyton Narr, Emory University School of Medicine

Poster Number: 11

Co-Authors: NARR, PEYTON; Miliaki, Maira; Douglas-Brown, J. Dylan; Kushner, Elizabeth; Walum, Hasse; Shultz, Sarah; Jones, Warren; and Ford, Aiden

Background: Social smiles, which emerge around 2 months in response to caregivers' social-communicative behaviors, become increasingly coordinated with infants' attention to the eyes and faces of others over the first 6 postnatal months. Exchanges of infant and caregiver signaling behaviors form the foundation of reciprocal social interaction. Although atypical social responsiveness is a core feature of autism, and differences in infant eye gaze have been documented as early as two postnatal months; early-coordination between these behaviors remains unexplored in autism. This study examines caregiver smiling and infant gaze allocation in infants later diagnosed with autism (AUT) and typically-developing (TD) infants. **Hypothesis:** Infants in the AUT group will show reduced eye-directed attention during caregiver smiling compared with TD infants, and these group differences will increase with age. **Methods:** Infants completed longitudinal recordings of screen-mediated infant-caregiver interactions with concurrent eye-tracking from 2-6 months. N=50 infant-caregiver dyads contributed n=67 sessions. The first 30-seconds of interaction were coded for caregiver smiling ($\kappa_{\text{caregiver}} = 0.76$), and infant fixations to their caregivers' eyes were quantified. A generalized additive model (GAM) with a beta response distribution was used to examine infant eye-directed attention during caregiver smiles from 2-6 months between diagnostic groups. **Results:** Infant attention to caregiver eyes was significantly non-zero from 2-6 months (intercept = -0.874, $z = -3.919$, $p < .001$). Additionally, the amount of time infants spent attending to the eyes of their caregivers during smiles did not change from 2-6 months in either TD (edf = 1, $x^2 = 1.27$, $p = .259$) or AUT (edf = 1, $x^2 = 0.85$, $p = .358$) infants and did not differ in overall magnitude between diagnostic groups ($\beta = 0.005$, $p = .984$). Overall, the model accounted for a small proportion of variance in visual attention (3.79%). **Conclusion:** Infants across both groups spent ~25% of the time attending to their caregivers' eyes during smiles. This suggests that infant-directed smiling may be an effective cue for eliciting infant attention to eyes, regardless of neurodevelopmental outcome, offering a promising behavioral target for caregiver-mediated early interventions. Ongoing work aims to increase sample size to examine these developmental patterns across a larger cohort.

Modeling PLXNB2-Associated Neurodevelopmental Disease Using Patient-Derived Cerebral Organoids

Presenting Author: Charlie Cordero, Emory University

Poster Number: 12

Co-Authors: CORDERO, CARLOS; Kalayci Tuğba; Smith, Claire; and Junqueira Alves, Chrystian

Hypothesis/Background: Plexins are mechanosensitive transmembrane receptors that translate extracellular semaphorin signals into cytoskeletal remodeling and changes in cellular behavior. Semaphorin–plexin signaling regulates axon guidance, neuronal migration, cell–cell interactions, and tissue organization throughout nervous-system development. Variants affecting Plexin-A and Plexin-B

receptors have been associated with autism spectrum disorder, intellectual disability, and epilepsy. More recently, biallelic PLXNB2 variants were shown to cause a multisystem developmental syndrome with prominent neurological manifestations. Despite these genetic associations, how Plexin-B2 dysfunction alters human brain development remains poorly understood. Our previous studies identified Plexin-B2 as a regulator of cortical actin tension that maintains neural progenitor identity and prevents premature differentiation. We hypothesized that disruption of either the extracellular or intracellular Ras-GAP domain of Plexin-B2 compromises this developmental checkpoint, accelerating neurogenesis and impairing the structural and functional maturation of human cerebral organoids. Methods: Patient fibroblasts carrying the homozygous PLXNB2 p.Leu293Pro Sema-domain variant were reprogrammed into hiPSCs and validated for pluripotency. CRISPR/Cas9-generated PLXNB2 knockout hESCs served as a loss-of-function reference and were rescued with wild-type Plexin-B2 or constructs disrupting the Ras-GAP (mGAP), Rho-binding (mRBD), VTDL (Δ VTDL), or extracellular (Δ ECTO) domains. Cells were differentiated into neural cultures and cerebral organoids. SOX2/TUJ1 expression, neurite outgrowth, and day-42 ventricular-like organization were evaluated. Organoid network activity was assessed using Axion 3DMap microelectrode arrays. Results: PLXNB2 loss accelerated neuronal differentiation and increased TUJ1-positive neurite outgrowth, whereas wild-type Plexin-B2 restored progenitor maintenance. The mRBD and Δ VTDL constructs produced near-wild-type phenotypes, while mGAP and Δ ECTO failed to rescue the knockout. Day-42 knockout, mGAP, and Δ ECTO organoids displayed disrupted ventricular-like architecture. Patient-derived p.Leu293Pro cultures similarly showed increased neurite outgrowth and fewer organized ventricular-like structures. Preliminary 3DMap recordings detected spontaneous activity and suggested altered spike organization and network bursting in patient-derived organoids, although additional recordings are required. Conclusion: These findings identify the extracellular and Ras-GAP domains as essential regulators of Plexin-B2-dependent neural progenitor maintenance. Our laboratory is establishing a patient-derived iPSC biobank and cerebral organoid modeling platform to investigate how disrupted Plexin signaling contributes to neurological dysfunction and abnormal human brain development.

Using a Bayesian Network to Quantify Effects of Diagnosis and Developmental Outcome Scores in Visual Learning

Presenting Author: Marina Nakayama, Emory University

Poster Number: 13

Co-Authors: NAKAYAMA, MARINA; Jones, Warren; Shultz, Sarah; and Gibeily, Caius

Background: Eye-tracking provides a measure of social visual engagement and offers insights into early social learning and development. However, quantifying individual heterogeneity in visual learning is difficult given complexity of relationships between data types. Bayesian networks could characterize how sequences of what children attend to are structured by developmental ability and autism diagnosis. We examined the feasibility of this by evaluating whether learned network structures in the model accurately recover both established and novel group differences. Methods: Eye-tracking data were collected from toddlers aged 20-30 months who were typically-developing (TD; n=131) or received an autism diagnosis (AUT; n=169), via longitudinal studies of infant social development at the Marcus

Autism Center. Toddlers viewed video scenes depicting naturalistic peer interactions. Age-equivalent scores in visual reception, receptive and expressive language from the Mullen Scales of Early Learning were determined for each child and discretized into four ordinal levels. For each scene, Bayesian networks were jointly fitted on viewing sequences, Mullen scores, and diagnostic groups using AIC-penalized structure learning over 5000 bootstrap samples. Edge retention was determined by Fisher's C statistic, ensuring only edges with significant mutual information were preserved. Jensen-Shannon distance (JSD; bounded [0,1], most to least similar) and conditional probability distributions were computed to examine whether the network quantified diagnostic differences in viewing and developmental ability. Results: Of 205 candidate edges, 61 were retained. Retained edges exhibited substantially greater normalized mutual information than non-retained edges (median NMI: 0.095-0.114 vs 0.018-0.043), confirming the thresholding procedure preserved informative direct relationships. Median JSD between TD and AUT viewing sequences were 0.046, 0.069, 0.190 for each scene, indicating scene-dependent divergence in visual engagement. When conditioned on diagnosis, the probability of the two lowest Mullen score categories was approximately 10–20% for the TD group compared with 80–90% for the AUT group, consistent with known group differences in developmental delay. Conclusion: These results demonstrate that Bayesian networks can be leveraged to interrogate differences in sequential looking behavior by diagnosis and developmental ability. These methods offer a framework for future work examining the relationship between clinical intervention and outcome measures to evaluate effectiveness of interventions promoting developmental skill acquisition.

Gut Microbiome Metagenomic Profiles and Associated with Psychoneurological Symptoms in Children with Solid Tumors Undergoing Chemotherapy

Presenting Author: Sofia Oliver, Georgia Institute of Technology

Poster Number: 14

Co-Authors: OLIVER, SOFIA B.; Sutton, Kathryn S.; Hatt, Janet K.; Bruner, Debra W.; Konstantinidis, Konstantinos T.; and Bai, Jinbing

Hypothesis and Background: Children with cancer receiving chemotherapy often experience co-occurring psychoneurological symptoms (PNS) including pain, fatigue, anxiety, depressive symptoms, and cognitive dysfunction¹. The occurrence of these symptoms may be linked to the disruption of the gut microbiome through the microbiome-gut-brain axis². Chemotherapy reduces gut microbial diversity which can lead to a dysregulation of microbiome-mediated signaling processes³. However, the connection between gut microbiome signaling and PNS is not well investigated in cancer, particularly in pediatric cancer. Microbial genera have been identified to be associated with PNS pathways⁴, but a more precise characterization using shotgun metagenomic sequencing is necessary. This study aimed to determine whether gut microbiome composition differed significantly between children with cancer and age-, sex- and race-matched healthy controls based on genus-level taxonomic assignments from 16S rRNA gene sequencing. We further used metagenomic sequencing of selected samples to identify species-level microbial features associated with PNS. Methods: 41 children with cancer and 39 healthy controls were analyzed. Stool samples were collected for sequencing and Pediatric PROMIS scales were used to assess PNS at pre-cycle 2 chemotherapy and completion of chemotherapy. The 16S rRNA amplicons were classified

into amplicon sequence variants (ASVs) using QIIME2. ASVs rarely provide species-level resolution; shotgun metagenome sequencing was performed to distinguish between highly related ASVs. Quality-filtered metagenomic reads were binned into metagenome-assembled genomes (MAGs), and taxonomically classified. Results: In healthy controls, the genera *Dorea*, *Ruminococcus*, *Fusicatenibacter*, and *Anaerostipes* were significantly enriched, whereas in cancer samples, these were significantly depleted. Furthermore, in healthy controls, there was negligible relative abundance of *Klebsiella*, *Enterococcus*, *Escherichia-Shigella*, and *Ruminococcus*, but these were present in cancer samples; however, ASV species assignment was inconclusive. Metagenomic species-level identification revealed pathogenic *K.pneumoniae* and *K.variicola*; *E.faecium* and *E.raffinosis*, which both naturally harbor antimicrobial resistance genes; and *R.torques* and *R.gnavus* which are associated with gut inflammation when overgrown⁵. Conclusion: These findings support gut dysbiosis during chemotherapy and identified pathogens and overgrown species present in the cancer microbiome. Developing a microbiome profile can aid PNS management plans in the clinical practice, direct probiotic treatments to restore the microbiome and potentially reduce PNS in children with cancer receiving chemotherapy.

Postnatal ZIKA Infection Alters Development of Temporal Lobe Structures in Rhesus Macaques

Presenting Author: Ruy Tobar Mosqueira, Emory University

Poster Number: 15

Co-Authors: Tobar Mosqueira, Ruy Amaru; Kovacs-Balint, Zsofia; Suthar, Methul; Lebovic, Rachel; Wang, Andrew; Acevedo-Polo, Jose; Gowda, Nayana; Chahroudi, Ann; Styner, Martin; Vlasova, Roza; Raper, Jessica; and Sanchez, Mar M.

ZIKA is a neurotrophic virus (ZIKV) that can cause congenital defects (e.g. microcephaly, malformed brain development) following fetal exposure. However, infants and toddlers are also vulnerable to infection as the brain undergoes rapid postnatal development across the first years of life. Using a rhesus macaque (RMs) model we examined the long-term neurodevelopmental impact of postnatal ZIKV infection from infancy through the juvenile period. Thirty RMs were used in this study. At 1 month of age, 12 were infected with ZIKV (ZIKV-1), 6 received a single dose of poly-IC as an innate immune stimulated control (PIC), and 6 served as uninfected controls (UIC). At 7 months of age, 6 infants received ZIKV infection (ZIKV-7) to compare timing-specific effects of infection. Structural MRI scans were acquired at 3, 6, and 12 months of age to examine overall brain size (intracranial volume -ICV-), CSF, lateral ventricles (LV), amygdala (AMY) and hippocampal (HIPPO) volumes. All groups exhibit the expected increased brain growth across age, but significant groups differences emerged for the AMY and HIPPO. A Group x Age $F(6,51.935)=2.409$; $p=0.040$) interaction was driven by enlarged AMY volumes for ZIKV-1 compared to UIC at 3mo ($p=0.049$) and to PolyIC at 3 and 12mo ($p=0.009$, $p=0.006$, respectively). Interestingly, the Group x Age interaction for the HIPPO ($F(6,52)=2.562$; $p=0.030$) revealed that ZIKV-7 have smaller volumes than ZIKV-1 at 12mo ($p=0.005$). There were nonsignificant trends when Sex was added to the model, such that ZIKV-1 males, but not females, had larger AMY and HIPPO volumes than controls for ZIKV-7. When accounting for differences in brain size, most group effects were lost, suggesting regional effects might be partially driven by group differences in brain growth. These findings point to ZIKV neuroinvasion during infancy leading to altered development that resulted in increased amygdala growth in animals

infected at 1month after birth (equivalent to 4months in humans). We are currently testing the functional correlates of these neural changes. Future studies focused on interventions that mitigate negative consequences are critical to ensure treatment plans for at-risk communities.

Beyond Glasgow Coma Scale: Applying the Comprehensive Brain Injury Model to Pediatric Traumatic Brain Injury

Presenting Author: Jai Trivedi, Georgia Institute of Technology

Poster Number: 16

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Background: Traumatic brain injury (TBI) is a major cause of death and long-term disability worldwide, leading to profound personal, societal, and economic burdens, particularly in children and adolescents. Despite decades of investigation, clinical management and therapeutic trial design in TBI continue to be constrained by marked heterogeneity. Glasgow Coma Scale (GCS) alone is insufficient for long-term functional prognostication in pediatric TBI, as it characterizes the clinical manifestations of injury rather than the underlying structural or biological processes. In 2025, the NIH–NINDS TBI Classification and Nomenclature Initiative introduced the Comprehensive Brain Injury Model (CBI-M), a multidimensional framework encompassing four interrelated domains: clinical, biomarker, imaging, and modifier, providing a more precise classification method compared to GCS. To the best of our knowledge, this study is the first to investigate the applicability of the CBI-M framework to pediatric TBI. We examined whether operationalizing the CBI-M improves prediction of 6-month Pediatric Glasgow Outcome Scale–Extended (pGOSE) outcomes. Methods: In a prospective cohort enrolled at two emergency departments of a tertiary children's hospital (March 2017–June 2021; N = 592), prediction models were developed in a subset with 6-month pGOSE (n = 90). Unfavorable outcomes were defined as pGOSE 1–6. Twenty-eight predictors were screened with univariable logistic regression ($p < 0.20$), then pillar-specific multivariable models ($p < 0.10$), yielding a combined CBI-M model. Incremental discrimination was summarized with stepwise ROC. Discrimination is reported as AUC with 95% confidence intervals (CI). Results: The combined model retained GCS (adjusted odds ratio [aOR] 9.38; 95% CI 2.38–44.1), Ubiquitin C-terminal hydrolase-L1 (UCH-L1) ≥ 327 pg/mL (aOR 10.5; 95% CI 1.41–21.6), midline shift on CT (aOR 10.5; 95% CI 2.36–62.1), age ≤ 5 yr (aOR 1.27; 95% CI 0.312–4.95), and male sex (aOR 4.94; 95% CI 1.18–26.7). Versus GCS alone, CBI-M improved AUC (95% CI) for pGOSE 7–8: 0.909 (0.831–0.966) vs 0.811 (0.711–0.903); pGOSE 3–6: 0.746 (0.614–0.861) vs 0.579 (0.446–0.711); pGOSE 1–2: 0.980 (0.948–1.000) vs 0.957 (0.912–0.992). Conclusions: These findings suggest that integrating clinical, biomarker, imaging, and patient-modifier data provides superior prognostic discrimination compared with GCS alone. CBI-M–based approaches may ultimately support more precise risk stratification, prognostication, and personalized management strategies, representing an important step toward precision medicine in pediatric neurotrauma.

Poster Abstracts

CHD2-associated epilepsy: Expanding the Phenotypic Spectrum of CHD2-Associated Epilepsy: A Single-Center Experience with Six Patients

Presenting Author: Sonam Bhalla, Emory University, Children's Healthcare of Atlanta

Poster Number: 17

Co-Authors: Li, Mingyu; Bhalla, Sonam; Gujong Zhang

Background: CHD2 encodes an ATP-dependent chromatin remodeling protein that plays a critical role in chromatin organization and regulation of gene expression. Pathogenic variants in CHD2 have been associated with a broad spectrum of neurodevelopmental disorders, including epilepsy, developmental delay, autism spectrum disorder, and congenital anomalies. **Method** We retrospectively reviewed the clinical history, brain MRI findings, genetic testing results, and video-electroencephalographic (EEG) recordings of six patients with de novo CHD2 variants evaluated at Children's Healthcare of Atlanta. **Result** Age at seizure onset ranged from 18 months to 3 years, with a mean age of onset of 2.3 years. Generalized tonic-clonic seizures were the most common seizure type (4/5), followed by myoclonic seizures (2/5), eyelid myoclonia (2/5), and myoclonic-atonic seizures (1/5). EEG background activity was relatively normal or mildly slow in all patients. Generalized epileptiform discharges were present in all patients, with four patients also demonstrating focal or multifocal epileptiform abnormalities. Photosensitivity was identified in three patients, including one with photic-induced seizures during EEG recording. Three patients had a history of febrile seizures. All patients had drug-resistant epilepsy requiring multiple antiseizure medications; valproic acid was the most used medication. One patient underwent vagal nerve stimulation with uncertain benefit. Brain MRI findings were unremarkable in 4 cases and one case had mild cerebellar atrophy. Speech delay, including intellectual disability and autism was observed in all patients. **Conclusion:** Our findings are consistent with previous reports demonstrating that CHD2-related epilepsy is a developmental and epileptic encephalopathy characterized by early onset, developmental impairment, and refractory generalized epilepsy. Although no single clinical feature is pathognomonic, the combination of febrile seizures, photosensitivity, myoclonic jerks and eyelid myoclonia in younger children should raise suspicion for CHD2-related epilepsy and prompt genetic evaluation. Similar to prior cohorts, seizure control remained challenging, with all patients requiring multiple antiseizure medications and one patient undergoing vagal nerve stimulation without clear benefit. No treatment demonstrated superior efficacy within our cohort. Emerging evidence suggests that acetazolamide may provide seizure reduction in selected patients and warrants further investigation. Larger studies are needed to better define genotype-phenotype correlations and identify targeted therapeutic strategies for this rare epilepsy syndrome.

Predictors of vigabatrin-associated brain abnormalities on MRI in children: The Role of epilepsy etiology

Presenting Author: Hyoung Choi, Emory University

Poster Number: 18

Co-Authors: CHOI, HYOUNG; He, Zhulin; Prestel, Anna; Reddy, Kartik; Sankhla, Neal; Zhang, Guojun .

Background: Vigabatrin-associated brain abnormalities on MRI (VABAM) are characterized by reversible T2/FLAIR hyperintensity and diffusion restriction in deep gray and white matter structures in children treated with vigabatrin. Although VABAM is increasingly recognized, clinical factors associated with its development remain incompletely understood. We hypothesized that vigabatrin exposure characteristics and epilepsy etiology are associated with VABAM occurrence. **Methods:** We conducted a retrospective cohort study using an institutional medical record database to identify children treated with vigabatrin between August 29, 2019, and August 18, 2025. Inclusion required at least two brain MRI examinations obtained before and during vigabatrin treatment. VABAM was defined as new MRI abnormalities developing during vigabatrin therapy that met prespecified imaging criteria. Clinical variables, including demographics, treatment exposure, and epilepsy etiology, were compared between patients with and without VABAM. **Results:** Sixty-four patients met the inclusion criteria, of whom 18 (28.1%) developed VABAM. Higher peak vigabatrin dose (odds ratio [OR] 1.03, 95% confidence interval [CI] 1.01–1.06) and concomitant prednisolone therapy (OR 4.07, 95% CI 1.22–17.3) were independently associated with VABAM. Genetic epilepsy was more frequent in the VABAM-positive group (9/18, 50.0%), whereas structural epilepsy predominated in the VABAM-negative group (34/46, 73.9%). Although the specific monogenic disorders differed between groups, variants involving GABAA receptor subunit genes were identified in both. **Conclusions:** VABAM was independently associated with higher peak vigabatrin dose and concomitant prednisolone therapy. Distinct epilepsy etiologic profiles were observed between groups, with a higher proportion of genetic etiologies in the VABAM-positive group and distinct monogenic disorders represented in the VABAM-positive and VABAM-negative groups. These findings suggest that epilepsy etiology may contribute to susceptibility to VABAM and should be considered in future risk stratification studies.

Pediatric Brain Tumor Reporting and Data System (pBT-RADS), a Structured Reporting System for Improving Pediatric Brain Tumor Care

Presenting Author: Adam Goldman-Yassen, Emory University School of Medicine

Poster Number: 19

Co-Authors: GOLDMAN-YASSEN, ADAM; Reddy, Kartik; Martin, Joel; Fangusaro, Jason; and Weinberg, Brent

Background: There are currently no standards for clinical radiology reporting in pediatric neuro-oncology, and our institution's reporting methods do not include a specific structured template. The Brain Tumor Reporting and Data System (BT-RADS) was developed to maximize consistency between reading radiologists and clarity of reports, but its application in the pediatric population has not been explored and may be limited by the unique pathology and imaging features of pediatric brain tumors. We sought to assess stakeholder satisfaction with current reporting practices and to develop an adapted system for pediatric use. **Methods:** We conducted a survey of the current state of neuro-oncologic imaging reporting at our institution. The initial survey involved 18 clinicians—including pediatric neuro-oncologists, neurosurgeons, radiation oncologists, and neuroradiologists—using a 5-point Likert scale,

with 5 representing the most positive response and 1 the least positive. Responses were summarized using medians and interquartile ranges (IQR). Informed by these results, we developed a pediatric brain tumor reporting and data system (pBT-RADS) adapted from BT-RADS, accounting for factors specific to pediatric tumors and incorporating RAPNO criteria. Results: The median score for clear communication of results was 4 (IQR 3–4). The median score for maintaining consistency was 3 (IQR 2–4), and the median score for refraining from ambiguity was 3 (IQR 3–4). Respondents endorsed a desire for a structured format for both findings and impression, particularly one that would correlate with patient management. We identified specific pediatric tumors for which BT-RADS is limited and describe how the proposed pBT-RADS addresses these limitations. Conclusions: Current unstructured reporting in pediatric neuro-oncology leaves room for improved consistency and reduced ambiguity, and stakeholders support a structured template linked to patient management. We introduce pBT-RADS, adapted from BT-RADS with pediatric-specific factors and RAPNO criteria. Future evaluation and implementation of pBT-RADS in practice will further refine the template and allow assessment of its acceptance and utility in routine clinical use.

When the EEG Raises Concern: Early Recognition of DEND Syndrome Risk in an Infant with Neonatal Diabetes

Presenting Author: Vanessa Nguyen, Emory University

Poster Number: 20

Co-Authors: NGUYEN, VANESSA; Lowe, Kristina; and Ribeiro-Pinto, Anna

Background: Activating mutations within the KCNJ11 gene have been highly associated with endocrinologic conditions such as permanent neonatal diabetes mellitus but given that the specific potassium channel affected in these mutation (Kir6.2 subunit of KATP) is also expressed on other tissues, such as muscles and neuronal cells, certain mutations can present with neurological features. We present a case of a neonate admitted with profound hyperglycemia and respiratory failure. An EEG was done prior to the results of her genetic testing, and findings were concerning for DEND syndrome (Developmental delay and epilepsy accompanying neonatal diabetes) and ultimately her genetic testing confirmed a pathogenic variant in KCNJ11 (c.601C>T (p.Arg201Cys)). Methods: Single-patient case report. Results: Our patient was delivered at 37w2d with maternal pregnancy complications of fetal growth restriction. She was observed in the NICU for low birth weight and was discharged home on DOL 6. On DOL 16, following a well child visit for weight check, she was admitted to the pediatric intensive care unit due to apnea, lethargy, and hyperglycemia (>700 mg/dL). Our neurology team evaluated the patient to rule out central apnea given her prolonged intubation course, and as part of her work-up, an EEG was performed. Her EEG showed an excessively discontinuous background for gestational age and excessive multifocal sharp transients, suggesting underlying cortical irritability. In combination with her neonatal hyperglycemia requiring continuous insulin infusion, this was concerning for potential DEND syndrome related to KCNJ11 mutation. Her Invitae Monogenic Diabetes panel resulted with a pathogenic variant identified in KCNJ11 (c.601C>T (p.Arg201Cys)). Following these results, she was started on glyburide treatment for her hyperglycemia. About 6 days later after starting glyburide, she was extubated successfully. Repeat EEG about 1 month later had normalized. She had a prolonged hospital

course related to problematic glycemic control, but at the time of discharge, her neurological exam was normal. Conclusions: This case highlights the importance of early recognition of KCNJ11 mutation and consideration of neurological manifestations. With the initiation of appropriate treatment for glycemic control, typically with sulfonylureas, there can be considerable therapeutic benefit from diabetes management and neurological improvement.

Expanding the Clinical Spectrum of SETD1B-Related Neurodevelopmental Disorder: A Case Series of Three Children with Epilepsy and Developmental Impairment

Presenting Author: Anna Pinto, Emory University & Rafaela Dantas, Hospital Israelita Albert Einstein

Poster Number: 21

Co-Authors: Akialis, Kristen; Zhang, Guojun; DANTAS, RAFAELA; and PINTO, ANNA

Background: Pathogenic variants in SETD1B are an uncommon cause of neurodevelopmental disorder characterized by developmental delay, intellectual disability, epilepsy, autism spectrum disorder, and behavioral abnormalities. Although the phenotype is increasingly recognized, considerable variability exists in seizure presentation, neurodevelopmental outcomes, and treatment response. We describe three children with molecularly confirmed SETD1B-related disorder to further characterize the clinical spectrum and highlight diagnostic and therapeutic considerations. Methods: We performed a retrospective review of three pediatric patients evaluated at a tertiary pediatric epilepsy center with pathogenic or likely pathogenic SETD1B variants identified through clinical genetic testing. Clinical data including developmental history, seizure semiology, EEG findings, neuroimaging, genetic results, treatment response, and neurological outcomes were reviewed. Results: All three patients presented with early neurodevelopmental abnormalities preceding or accompanying epilepsy. Developmental delay was universal, with varying degrees of language impairment and cognitive dysfunction. Two patients exhibited autistic features and significant behavioral dysregulation. Epilepsy phenotypes were heterogeneous, including focal and generalized seizure types, with variable age at onset. EEG abnormalities ranged from multifocal epileptiform discharges to generalized spike-wave activity, while brain MRI findings were normal or demonstrated only nonspecific abnormalities. Genetic testing identified pathogenic or likely pathogenic variants in SETD1B, supporting the diagnosis in each patient. Antiseizure medication response varied, with one patient achieving seizure control while two experienced pharmacoresistant epilepsy requiring multiple therapeutic interventions. One patient achieved seizure freedom with VNS implantation. The phenotypic variability observed within this small cohort underscores the broad clinical expression of SETD1B-related disease. Conclusions: This case series expands the clinical characterization of SETD1B-associated neurodevelopmental disorder and reinforces the importance of considering SETD1B in children presenting with developmental delay, epilepsy, and behavioral abnormalities. Early genetic diagnosis facilitates accurate counseling, guides multidisciplinary management, and may improve access to emerging precision medicine approaches. Recognition of the variable epilepsy phenotype may also aid clinicians in earlier identification of affected patients.

Compound Muscle Action Potential Amplitudes in Newborn Screen Positive Spinal Muscular Atrophy (SMA)

Presenting Author: Sumit Verma, Emory University, Children's Healthcare of Atlanta

Poster Number: 22*Co-Authors: Verma, Sumit*

Background: To evaluate the utility of compound muscle action potential (CMAP) amplitudes as biomarkers of disease severity in newborn screening (NBS)-positive infants with spinal muscular atrophy (SMA). Methods: We conducted a retrospective review of 21 infants identified through SMA NBS (11 with 2 SMN2 copies and 10 with 3 SMN2 copies). Baseline and serial right median, ulnar, and fibular motor nerve CMAP amplitudes (millivolts, mV) were obtained during the study. Functional outcomes were assessed using the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND). Results: At baseline, infants with 2 SMN2 copies demonstrated significantly lower median, ulnar, and fibular CMAP amplitudes compared with infants with 3 SMN2 copies ($p < 0.05$). In contrast, baseline CHOP-INTEND scores did not differ significantly between the two groups. Prior to genetic confirmation, a right median CMAP amplitude ≥ 3.2 mV predicted ≥ 3 SMN2 copies. Following treatment, right median and fibular CMAP amplitudes demonstrated significant improvement over time, including in analyses accounting for SMN2 copies number. Conclusion: CMAP amplitudes obtained from multiple upper- and lower-extremity motor nerves provided objective electrophysiological measures that distinguished infants with two versus three SMN2 copies, despite similar baseline CHOP-INTEND scores. Furthermore, CMAP abnormalities were detectable in some cases before confirmatory genetic testing results became available. Serial CMAP measurements demonstrated significant longitudinal changes following treatment, whereas functional assessments approached ceiling values, supporting the potential value of electrophysiological monitoring in the era of disease-modifying therapies.

Neuromodulation with Rapid VNS Titration for Febrile Infection-Related Epilepsy or New Onset Refractory Status Epileptic: Single-Center OutcomesPresenting Author: Ahda Jbarah, Emory University, Children's Healthcare of AtlantaPoster Number: 23*Co-Authors: Jbarah, Ahda, MD; Shah, Ekta, MD; Vedala, Kishore, MD; Lin, Jenny, MD; Zhang, Goujon, MD; Chern, Joshua, MD; Oliver, Corinne, MSN; Aquino, Marleny, MD; Choi, Hyoung, MD; Sankhla, Neal, MD; Bhalla, Sonam, MD*

Rationale: Febrile Infection-Related Epilepsy Syndrome (FIRES) is a severe subtype of New-Onset Refractory Status Epilepticus (NORSE) presenting with medically refractory seizures following a febrile illness. These cases often require prolonged continuous anesthetic infusions and carry high morbidity and mortality. Vagus nerve stimulation (VNS) is an established therapy for drug-resistant epilepsy, and emerging reports suggest that early VNS implantation with rapid titration (daily increases in output current and duty cycle) may accelerate clinical response, reduce seizure burden, and facilitate weaning from anesthetics. However, data on safety and outcomes in pediatric FIRES remain limited. Methods: We conducted a retrospective chart review of four pediatric patients (aged 5–13 years) with FIRES or NORSE admitted to Children's Healthcare of Atlanta between 2023 and 2025. All patients received standard medical management and immunotherapy, followed by VNS implantation during the acute/subacute phase with rapid postoperative titration. Clinical demographics, neuroimaging, EEG findings, VNS

parameters, seizure burden, and outcomes were reviewed. Results: Median delay from status onset to VNS implantation was 43 days (range: 18–81). Daily rapid titration began on the day of surgery (n=1) or postoperative day 1 (n=3) until seizure burden significantly improved (Final settings: Patient 1: 2.25 mA, 51% duty cycle; Patient 2: 2.5 mA, 58%; Patient 3: 2.75 mA, 59%; Patient 4: 2.75 mA, 59%). Rapid titration facilitated weaning off continuous infusions in all patients. Three patients achieved marked clinical improvement and were discharged to rehabilitation; one died from multiorgan failure following prolonged hospitalization. Complications were minimal, with one patient developing mild obstructive sleep apnea. At latest follow-up, all surviving patients had significant seizure reduction without recurrence of status epilepticus (Patient 1: 1–3 brief seizures daily; Patient 2: 1–2 per week; Patient 4: 1–2 every 3–4 months). Conclusions: Early VNS implantation with rapid titration is a safe, feasible, and effective adjunctive treatment for pediatric FIRES and NORSE, aiding in status termination and anesthetic weaning. Further prospective studies are needed to define optimal timing and titration parameters.

A Multifactorial Framework of Developmental Psychopathology and Neuronal Maturation During Adolescence

Presenting Author: Dawn Jensen, Georgia State University

Poster Number: 24

Co-Authors: JENSEN, DAWN; Chen, Jiayu; Dai, Junqiang; Calhoun, Vince; Lui, Jingyu

Background: The development of psychopathology in adolescence is considered a multi-dimensional process comprising genetic vulnerability, adversity, and behavioral liability. The interplay of these combined factors with regard to the development psychopathology has been poorly understood. This study examines the contributions of genetic vulnerability, adverse childhood experiences (ACEs), and problematic behavior in a multifactorial framework, investigates its predictive power for psychopathology, and maps the associated neuronal maturation across adolescence. Methods: Summary variables for genetic vulnerability, ACEs, and problematic behavior were constructed using five waves of data from the Adolescent Brain Cognitive Development (ABCD) study, a population-based study of 11,878 children enrolled at age 10 years of age. These three factors were then used in a binomial logistic regression to assess their predictive ability for six psychopathology measures: depression, anxiety, adhd, somatization, conduct disorder, and oppositional disorder. Fractional anisotropy (FA) measures were calculated from subjects' diffusion images (dMRI). Latent growth curves for 69 regions were calculated, subject differences based on problematic behavior classifications were tested and significant regions had problematic behavior-specific growth trajectories plotted using multi-group mixture models. Results: The binomial regressions revealed the strong predictive power of the combined factors for diverse facets of psychopathology. When considered together in predictive modeling of the binomial regression, high genetic risk combined with high adversity and high problematic behavior levels performed well (>80%) at predicting psychopathology. Significant sex differences in problematic behavioral FA trajectories were found in the superior longitudinal fasciculus II. Conclusions: This application of a multifactorial framework to a population cohort of adolescents demonstrates the power multi-dimensional models have to predict psychopathology, supporting the gene x environment x behavior theories as the likely source of

both resilience as well as susceptibility. Adolescents experiencing increasing and high levels of problematic behavior had perturbed maturation within neuronal microstructures responsible for emotional processing.

FreeSurfer-Focal Observation & Control of Under/oversegmented Structures (FS-FOCUS): Quality Control Toward Trustworthy Volumetry in Clinical Neuroradiology

Presenting Author: Shayan Monabbati, Emory School of Medicine

Poster Number: 25

Co-Authors: Shayan Monabbati, Eswar Damaraju, Kaustav Bera, Prabhumallikarjun Patil, Kartik Reddy, Satish E. Viswanath

Purpose: Automated brain volumetry via FreeSurfer is entering clinical neurodevelopmental workflows; however segmentation outputs still require manual validation. For example, the corpus callosum in neurofibromatosis type 1 (NF1) is routinely under-segmented, biasing volumetry. We present FS-FOCUS, a standalone browser-based tool for region-level quality control (QC) of FreeSurfer segmentations. **Materials and Methods:** A retrospective single-center cohort of pediatric NF1 patients (Children's Hospital of Atlanta; T1w 3D MPRAGE/TFE; multiple Philips/Siemens scanners) was processed with FreeSurfer recon-all and reviewed in FS-FOCUS, which loads recon-all outputs in a browser with no FreeSurfer installation. A deterministic first pass flagged morphometric volume outliers and excessive Talairach rotation/head tilt for further neuroradiologist review via FS-FOCUS. FS-FOCUS was implemented as an interactive graphical user interface that overlays FreeSurfer segmentations on the source MRI, offering functionality including multi-planar visualization, automated segmentation-outlier flagging, and standardized per-subject quality grading. We compared within-NF1 cortical-thickness and regional-volume analyses before and after removing QC-flagged cases via FS-FOCUS. **Results:** 102 patients were initially included, from which 16 cases (post-contrast, duplicate, age ≥ 12 y) were excluded based on automatic demographic and image quality filtering. FS-FOCUS was used to flag 7/86 filtered cases as segmentation failures: 4 excessive Talairach rotation, 3 subcortical over/under-segmentations; originally considered acceptable via the standard pipeline. Prior to FS-FOCUS QC ($n=86$), patients with autism-spectrum comorbidity showed nominally smaller left caudal-middle-frontal cortical volume than those without neurocognitive comorbidity (6043 vs 7317 mm³; Cohen's $d=-0.60$; $p=0.009$). Removing the 7 flagged cases ($n=79$) lowered the comorbidity-free group's inflated mean volume (to 7033 mm³) and attenuated the effect ($d=-0.45$; $p=0.023$); cortical-thickness contrasts attenuated similarly. **Conclusion:** FS-FOCUS enables fast, region-level QC that catches segmentation failures which can be missed by automated pipelines to minimize impact on downstream volumetric group effects, supporting more reliable and objective volumetry in clinical neuroradiology.

Sex-based Disparities in Pediatric Traumatic Brain Injury Outcomes: A National Inpatient Sample (NIS)-based Analysis.

Presenting Author: Raisa Rani James, One Brooklyn Health- Brookdale University Medical Center

Poster Number: 26

Co-Authors: RANI JAMES, RAISA; Sunny, Angel; Daniel, Abhijith; Ann Thompson, Namitha and Tharakan, Binu

Background: Traumatic brain injury (TBI) is associated with significant morbidity and mortality, particularly morbidity in terms of cognitive and mental health outcomes. In addition, research suggests that there are significant sex disparities in terms of TBI outcomes in the pediatric age group, but it is a subject of controversy. The objective of this study was to assess the role of sex in in-hospital outcomes in Pediatric TBI patients to help better understand the disparities. **Methods:** We retrospectively analyzed data from the National Inpatient Sample (NIS) to identify pediatric patients (0-17 years) admitted with a primary diagnosis of TBI in 2016. We calculated demographic and clinical characteristics by sex using the Pearson χ^2 test. Multivariate logistic regression was performed to calculate the Odds ratio. Our primary outcome was inpatient mortality, and the secondary outcome was the length of stay. We used multivariate logistic regression to assess the effect of sex on TBI outcomes. **Results:** A total of 13,198 patients in the pediatric age group of 0-17 years was included in the study, out of which 8674 (65.7%) patients were males compared to 4524 (34.3%) females. When stratified by age group, there was no significant difference in mortality rates and length of stay among pediatric patients. In the pediatric age group (0-17 years), females stayed 0.2 days more compared to men; however, this data is not significant as $p\text{-value} > 0.05$. Women and men had a comparatively similar risk of mortality (odds ratio=0.95), but this result is not statistically significant as the $p\text{-value} > 0.05$ (0.822). **Conclusion:** Our study outcomes are similar to existing literature in terms of mortality following TBI however controversial in terms of length of hospital stay. To gain greater knowledge about these discrepancies, evidence-based guidelines need to be formulated from representative studies designed to understand what undeniably plays a role in this division. Forthcoming studies should focus on more measurable outcomes, such as hormone levels, differential expression of X-chromosome genes, mitochondrial pathophysiology, brain volume and swelling, cerebrovascular response, and excitotoxicity. In the meantime, providers of all specialties and training backgrounds should familiarize themselves with the challenges of caring for patients with TBI.

Electroencephalogram as a Tool to Improve Behavioral Intervention for Autistic Children: A Translational Clinical Case Study

Presenting Author: Alexandra Reilly, Emory School of Medicine Marcus Autism Center

Poster Number: 27

Co-Authors: Reilly, Alexandra; Argueta, Tracy; Key, Alexandra; and O'Guinn, K. Nicole

Background & Hypothesis: Individuals with profound autism have largely been excluded from research because current behavior-based assessments for autism are not designed for their skill levels. Thus, they often receive “floor” scores, making progress difficult to detect. Therefore, behavioral assessment alone cannot adequately characterize the skillsets or processes underlying learning barriers in children with profound autism. However, electroencephalogram (EEG) has been successfully used with other minimally verbal populations. Thus, we hypothesized that EEGs can successfully test auditory and language processing and inform behavioral intervention in a child with profound autism. **Methods:** The participant was an 8-year-old male who, over approximately 2.5 years of intervention, showed limited progress acquiring receptive identification skills, despite several intervention modifications and behavioral assessments. To better characterize his underlying receptive discrimination abilities, an EEG was completed using tasks assessing (a) speech sound discrimination, (b) known word recognition, and

(c) auditory memory for spoken language. Findings from the EEG were interpreted alongside behavioral observations to guide clinical decision-making and modifications to treatment programming. Results were used to switch from 2-dimensional to 3-dimensional stimuli (greater perceptual salience), reducing the duration of procedures for correcting errors (to maximize likelihood of attending to the correction). Results: The EEG demonstrated neural responses consistent with (a) intact discrimination of speech sounds; (b) limited differentiation between familiar words and nonwords suggesting limited receptive vocabulary; and (c) basic detection of repeated speech stimuli but limited spontaneous auditory memory and engagement with spoken language. Collectively, these findings suggest that the observed receptive language challenges were unlikely to reflect deficits in basic speech perception but instead may have been influenced by reduced attention to auditory stimuli. After EEG-based changes to his behavioral intervention, he learned 8 receptive identification targets in approximately 8 weeks, which led to meeting the discharge criteria from the intensive full-day program. Conclusions: This ongoing work demonstrates the potential utility of an EEG as a complementary tool for informing clinical decision-making within behavioral intervention practices. Integrating neural measures with behavioral assessment may improve clinical decision-making regarding learning barriers, individualized intervention planning, and provide an objective measure of treatment-related change alongside traditional behavioral data.

Kids Injury Detection Study (KIDSfast): Point-of-Care Biomarker Testing in Pediatric Traumatic Brain Injury

Presenting Author: Meena Verma, Children's Healthcare of Atlanta

Poster Number: 28

Co-Authors: VERMA, MEENA; Reisner, Andrew; Blackwell, Laura; Jaeger, Lindsay; Pierzchala, Amanda; Velasquez, Leslie; Muhammad, Maria; Khan, Myer; Trivedi, Jai; Frost, Kelsey

Background: Traumatic brain injury (TBI) remains a leading cause of morbidity and mortality in children. Rapid diagnostic information at the point of care (POC) may improve early risk stratification and management, yet data on POC blood-based biomarkers in pediatric TBI are limited. The i-STAT TBI system (Abbott) measuring glial fibrillary acidic protein (GFAP) and ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1) is currently approved for adults. This feasibility pilot study evaluates the use of a POC biomarker platform in children and its ability to predict CT-positive findings. **Design:** Prospective observational study. **Methods:** Children 0-21 years, presenting with TBI, within 72 hours post-injury were enrolled. Whole blood samples were obtained and analyzed using the i-STAT platform for GFAP and UCH-L1. Clinical data included Glasgow Coma Scale (GCS) score, head CT findings, need for neurosurgical intervention, intensive care unit admission, and length of stay. Biomarker levels were compared between patients with and without intracranial injury on CT. Receiver operating characteristic (ROC) curves were generated to assess diagnostic performance. **Results:** 29 patients were enrolled (mean age 9.6 ± 6.1 years). GFAP levels were significantly higher in patients with CT-positive (median 609 pg/mL, IQR 209–2571) compared with CT-negative patients (median 59 pg/mL, IQR 47–223). Similarly, UCH-L1 levels were elevated in CT-positive patients (median 486 pg/mL, IQR 209–2571) compared with CT-negative patients (median 87 pg/mL, IQR 87–164). The area under the curve (AUC) for prediction of intracranial injury was

0.805 for GFAP and 0.827 for UCH-L1. Conclusions: POC measurement of GFAP and UCH-L1 demonstrates promising ability to identify CT-positive findings in pediatric TBI. This may reduce reliance on CT imaging and limit exposure to ionizing radiation. These data suggest potential use in early triage, including pre-hospital and interfacility transport settings. This pilot study supports future prospective randomized trials to evaluate biomarker integration into pediatric TBI management.

Emerging Risk Factor in Pediatric Intracranial Gunshot Wounds: Age ≤ 5 Years

Presenting Author: Meena Verma, Children's Healthcare of Atlanta

Poster Number: 29

Co-Authors: VERMA, MEENA; Reisner, Andrew; Blackwell, Laura; Mulugeta, Makda; Javed, Mahwish

Background: Pediatric intracranial gunshot wounds (GSW) are a recognized cause of morbidity and mortality in the United States, with a marked rise in incidence and disproportionate increase among children ≤ 5 years. This reflects a broader increase in civilian firearm-related injury among children. The influence of social determinants of health (SDH) on these patients remains insufficiently characterized. Emerging evidence suggests a multifactorial etiology, including socioeconomic disruption during the COVID-19 pandemic and changes in firearm legislation. This study evaluates trends in incidence, severity, outcomes, and SDH in children ≤ 5 versus > 5 years, and how these evolved across key societal events. **Design:** Retrospective cohort study. **Methods:** Retrospective analysis was performed for 74 children aged 0–16 years (mean 8.6 ± 4.8) presenting to the emergency department with intracranial GSWs from January 2014 to December 2022. Pre-pandemic ($n=32$) and pandemic ($n=42$) cohorts were defined using 13 March 2020 (U.S. COVID-19 national emergency declaration). Clinical and social variables, including the Child Opportunity Index (COI), were analyzed. **Results:** Most patients were male (73%), Black (67.6%), and > 5 years of age (66.2%). During the pandemic, the proportion of patients ≤ 5 years increased by 62%, while those > 5 years decreased by 20.7%. Younger patients were more likely to undergo neurosurgical intervention (72% vs. 44.9%, $p=0.047$) and require inpatient rehabilitation (52% vs. 20.4%, $p=0.008$). Mortality among younger patients nearly doubled (12.5% to 23.5%), while remaining stable in older patients (41.7% vs. 40%). Children ≤ 5 years were more likely to reside in very low opportunity neighborhoods (68% vs. 30.6%, $p=0.006$), be publicly insured or uninsured (95.8% vs. 75.6%), and be Black (84% vs. 59.2%, $p=0.005$). **Conclusion:** Pediatric intracranial GSWs are increasing, particularly among children ≤ 5 years. Younger children demonstrated higher mortality during the pandemic and greater social vulnerability. Findings highlight the need for targeted prevention, firearm safety, responsible ownership, and caregiver education.

Early-Onset Duchenne Muscular Dystrophy in a 30-month-old Boy with Positive Family History: Clinicopathological Correlation and Early Diagnostic Challenges in a Resource-Limited Setting

Presenting Author: Iftekhhar Ahmed Sakib, Emory University School of Medicine

Poster Number: 30

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Background: Duchenne muscular dystrophy (DMD) is the most common inherited muscular dystrophy of childhood, yet diagnosis in low-resource settings is frequently delayed because molecular testing is often unavailable. We hypothesized that a confident diagnosis of DMD can be established using characteristic clinical features, markedly elevated serum creatine kinase (CK), and supportive muscle histopathology, and that failure to provide genetic counseling after diagnosis of an affected sibling represents a preventable missed opportunity for family-based care. **Methods:** We report the clinicopathological findings of a 30-month-old Bangladeshi boy presenting with progressive motor regression. Clinical history, neurological examination, laboratory investigations, cardiac assessment, muscle biopsy findings, family history, treatment, and follow-up were reviewed. Diagnostic assessment was based on phenotype, serum CK, conventional histopathology, and exclusion of alternative neuromuscular disorders because dystrophin immunohistochemistry and molecular genetic testing were unavailable. **Results:** The child developed progressive proximal muscle weakness from 18 months after normal early motor development. Examination demonstrated a positive Gowers' sign, waddling gait, lumbar lordosis, bilateral calf pseudohypertrophy, gluteal and thigh muscle wasting, hypotonia, and diminished deep tendon reflexes. Serum CK was markedly elevated at 9,013 U/L (approximately 53× the upper limit of normal). Muscle biopsy revealed marked myofiber size variation, hypertrophic and atrophic fibers, increased internal nuclei, endomysial fibrosis with fatty replacement, and focal inflammatory infiltrates, consistent with muscular dystrophy. Echocardiography showed preserved cardiac function (ejection fraction 60%). The patient's elder brother had died from DMD at 16 years of age, strongly supporting X-linked inheritance. Deflazacort, calcium, vitamin D supplementation, and physiotherapy were initiated, and the child remained clinically stable on follow-up. **Conclusion:** This case demonstrates that an accurate diagnosis of DMD remains achievable in resource-limited settings through careful clinicopathological correlation despite the absence of molecular confirmation. Equally important, it highlights that the greatest missed opportunity was not diagnostic but preventive: failure to provide genetic counseling and carrier assessment after the first affected child resulted in a second preventable case. Early recognition, timely corticosteroid therapy, multidisciplinary care, and family-centered genetic counseling remain essential for improving outcomes in low-resource settings.

Presurgical Hypothesis Accuracy and Surgical Outcomes in Pediatric Stereo-Electroencephalography: A Single-Center Study

Presenting Author: Joseph Abergel, Emory University School of Medicine

Poster Number: 31

Co-Authors: ABERGEL, JOSEPH N. ; Futch, Hunter S. ; Cosgrove, Megan ; Lin, Jenny; Laxpati, Nealen G.; Chern, Joshua J.

Background: Stereo-electroencephalography (SEEG) has become the predominant intracranial monitoring technique in pediatric epilepsy surgery programs. While the literature addresses safety and seizure outcomes, the accuracy of the presurgical hypothesis and its relationship to postoperative outcomes remain underexplored. This study analyzes concordance between the noninvasive presurgical seizure onset zone (SOZ) hypothesis and SEEG findings and examines whether hypothesis–SEEG concordance predicts postoperative seizure outcomes in a pediatric population. **Methods:** This

retrospective cohort study included 86 pediatric patients who underwent SEEG implantation at Children's Healthcare of Atlanta, between August 2019 and May 2025. All patients underwent comprehensive noninvasive presurgical evaluations to generate a ranked presurgical SOZ hypothesis. The SOZ hypothesis relation with SEEG was defined at the lobar or regional level within three cumulative definitions (H1 only, H1 or H2, and any hypothesis). Postoperative seizure outcomes were classified using the Engel Epilepsy Surgery Outcome Scale. Results: Mean age at implantation and seizure onset was 15.7 years and 5.7 years, respectively. 61.6% achieved Engel Class I seizure freedom and 77.9% achieved Engel Class I–II outcomes, comparable to the literature. Under the strictest H1-only definition, the presurgical hypothesis was concordant with SEEG-defined SOZ in 65.1% of patients (56/86), rising to 74.4% when secondary hypotheses were included and 93.0% under any-hypothesis concordance. H1-concordant patients had significantly greater odds of achieving seizure freedom than discordant patients (OR 2.55, 95% CI 1.03–6.32, $p = 0.042$). Although concordant patients also demonstrated higher odds of Engel Class I outcome under the H1-or-H2 (OR 1.56, 95% CI 0.59–4.14, $p = 0.370$) and Any-H (OR 3.00, 95% CI 0.52–17.36, $p = 0.202$) definitions, these associations weren't statistically significant. Conclusion: The directionality of the evidence indicates that presurgical hypothesis accuracy can be clinically meaningful. Concordance between the leading presurgical SOZ hypothesis and the SEEG-defined SOZ was associated with significantly greater odds of postoperative seizure freedom. The broader concordance definitions demonstrated similar trends, but insignificantly. These findings suggest that the accuracy of the primary presurgical hypothesis may have prognostic value and support further multicenter prospective studies to validate the role of hypothesis–SEEG concordance in surgical decision-making and long-term seizure outcomes.

Effects of Perinatal Opioid Exposure on Reward Related Behaviors

Presenting Author: Rachel Bond, Georgia State University

Poster Number: 32

Co-Authors: BOND, RACHEL; McWaters, Anna; Nyakoa, Judy; and Murphy, Anne

Opioid exposure during pregnancy, or perinatal opioid exposure (POE), oftentimes leads to diagnoses of Neonatal Abstinence Syndrome (NAS) in which infants exhibit symptoms of withdrawal at birth. Treatment and postnatal care for these infants has been well characterized and research following these infants into childhood has found that children diagnosed with NAS at birth display developmental delays physically, academically, and socially. Clinical research studying the long-term effects of POE throughout adolescence and into adulthood remains poorly understood. The Murphy lab has developed a clinically relevant, preclinical POE model that encompasses morphine use before, during, and after pregnancy using programmable infusion pumps implanted subcutaneously in young female rats. The lab explores a variety of effects POE might have on various biological systems and behaviors to encompass a holistic view of the long-term effects of POE. We have previously established that POE induces a moderate anhedonic state for both naturalistic and drug-related rewards. One leg of the project expands on this by exploring the effects of POE on prosocial behaviors, where we see deficits in social reward in morphine-exposed females and changes in the oxytocin system over adolescence and adulthood. Another leg of the project explores the propensity to use opioids following in utero exposure. Using a fentanyl self-

administration paradigm, we measure fentanyl intake. Our findings show that POE animals self-administer more fentanyl than controls and exhibit elevated orexin signaling in the lateral hypothalamus, suggesting that this system contributes to increased drug-seeking behavior. We aim to investigate whether FDA-approved orexin receptor inhibitors, which are currently prescribed to treat insomnia, can reduce fentanyl seeking and intake in these animals. We also aim to model the effect of POE and social isolation as children diagnosed with NAS frequently experience disrupted caregiving and social adversity during development. This project examines adolescent social isolation in a rat model of POE to determine its effects on reward-related behaviors and astrocyte-mediated glutamate homeostasis within the nucleus accumbens. By incorporating a clinically relevant postnatal stressor, this work aims to advance the translational relevance of POE models and identify potential neurobiological mechanisms underlying increased vulnerability to alcohol use disorder.

Neonatal Adversity on Brain Development and Behavior in a Preclinical Rodent NICU Model

Presenting Author: Liaa Ferede, Georgia State University

Poster Number: 33

Co-Authors: Nadja Brown, Liaa Ferede, Mirella Matos Ribeiro, Debbie Bangasser, Anne Z. Murphy

Roughly 1 in 10 infants is born preterm; those admitted to the NICU can undergo as many as 15 painful procedures per day - frequently without adequate analgesia and against a backdrop of incubator isolation and socioeconomic adversity. Existing preclinical models test these stressors in isolation, and thus fail to capture their cumulative impact. Clinical findings link NICU adversity to cortical thinning within the prefrontal cortex (PFC), a marker associated with depression and schizophrenia. The PFC regulates social behavior, decision-making, and reward processing. Because it is among the last brain regions to complete myelination, oligodendrocyte precursor cells (OPCs) are particularly vulnerable to early-life perturbation. Maternal separation and pain trigger premature OPC differentiation and arrest pre-oligodendrocyte maturation, depleting the pool required for proper myelination and white matter connectivity. Additionally, former NICU infants show impaired social bonding, a risk factor for later substance use. Early-life adversity disrupts corticolimbic endocannabinoid signaling and reduces forebrain CB1 receptor expression, a system crucial for mediating prosocial behavior and reward motivation via PFC-dopaminergic circuitry. We hypothesize that cumulative neonatal adversity (pain, maternal separation, and resource scarcity) drives grey matter loss via OPC dysfunction and hypomyelination, while simultaneously disrupting endocannabinoid signaling across developing PFC and reward circuits. This provides a novel mechanistic bridge connecting early NICU experiences to adolescent psychiatric disorders, maladaptive social behaviors, and substance use vulnerability. We test this hypothesis using a novel rodent model that integrates NICU stressors. Adolescent social behavior and motivation are evaluated using social assays, where we find that stressed rats exhibit delayed maturation of social circuitry (failing to show typical age-related play decline). Reward and substance vulnerability are assessed via operant sucrose and ethanol self-administration. Finally, structural outcomes are quantified using immunohistochemistry for CB1 receptor density alongside DTI and Luxol Fast Blue staining to evaluate white matter integrity and structural connectivity.

Electroclinical Characteristics of Epilepsy in Children With GLUT1 Deficiency Syndrome

Presenting Author: Isabel Paredes Cantos, Emory University School of Medicine

Poster Number: 34

Co-Authors: PAREDES, ISABEL; Choi, Hyoung Won; Furuta, Yutaka; Seim, Taylor; and Shah, Ekta

Hypothesis and Background: Glucose transporter type 1 deficiency syndrome (GLUT1DS) is a rare neurometabolic disorder caused by pathogenic variants in the SLC2A1, resulting in impaired glucose transport across the blood–brain barrier and chronic cerebral energy deficiency. Although epilepsy is a hallmark feature of GLUT1DS, the spectrum of seizure types, electroencephalographic findings, and predictors of seizure response to ketogenic diet therapy remain insufficiently characterized. We hypothesized that comprehensive characterization of electroclinical features in genetically confirmed GLUT1DS would provide insights into the clinical spectrum of epilepsy and describe potential relationships between baseline features and seizure outcomes following KDT. **Methods:** A retrospective chart review was conducted of children with GLUT1 deficiency syndrome who were followed in the Children's Healthcare of Atlanta ketogenic diet clinic between January 2014 and August 2026. Clinical data collected included age at seizure onset, seizure types, antiseizure medication history, cerebrospinal fluid-to-blood glucose ratios, developmental and neurological comorbidities, and serial electroencephalographic (EEG) findings. KDT-related variables included adherence, dietary modality, age at KDT initiation, feeding route, and blood β -hydroxybutyrate (BHB) concentrations. Given the small sample size, findings were summarized using descriptive statistics without formal statistical comparisons. **Results:** Nineteen patients had genetically confirmed GLUT1DS, whereas one patient had a variant of uncertain significance in SLC2A1 but was included based on a clinical phenotype consistent with GLUT1DS. Median age at diagnosis was 5 years (IQR, 2–11 years). Seventeen patients (85.0%) had seizures, with a median age at seizure onset of 8.5 months (IQR, 3–23 months). Among those with seizures, 13 (76.5%) had generalized seizures, 2 (11.8%) had focal seizures, and 2 (11.8%) had both. KDT was offered to 18 patients. Among 10 adherent patients, 6 (60.0%) achieved greater than 50% seizure frequency reduction following KDT initiation. **Conclusion:** In this single-center cohort of children with GLUT1DS followed at our ketogenic diet clinic, early-onset epilepsy was the predominant presenting feature, yet diagnosis remained delayed. These findings highlight the diverse electroclinical presentation of GLUT1DS and the importance of considering this treatable metabolic epilepsy in children with early-onset epilepsy and compatible seizure phenotypes, allowing timely evaluation for KDT.

Identification of Behaviors Relevant to Restricted Interests in Mice Lacking ASD Risk Gene Chd8

Presenting Author: Mya Peter, Emory University

Poster Number: 35

Co-Authors: PETER, MYA N.; Bhalerao, Janhavi; and Gourley, Shannon L.

Background. Chromodomain helicase DNA binding protein 8 (Chd8) is a high-risk gene for autism spectrum disorder (ASD). Loss of function is associated with varied symptoms, including restricted interests – referring clinically to intense interest in specific topics that is highly motivated and resistant to distraction. Despite the availability of model organisms bearing ASD-related mutations, including Chd8

mutant mice, existing assays overwhelmingly fail to measure behaviors relevant to restricted interests. The goal of the current investigation was to determine whether developmental Chd8 loss induces behaviors in mice that are reminiscent of restricted interests in humans. **Methods.** We genetically silenced Chd8 in the ventral hippocampus (vHC) because it has been implicated in such behaviors. Mice were evaluated for their ability to acquire and perform instrumental responses for a reward, to track reward contingencies, and to maintain motivation for reward and demonstrate behavioral persistence despite distracting conditions. **Results.** Developmental Chd8 loss improved contingency tracking, and Chd8-deficient mice demonstrated persistence in reward-related responding, despite distraction. Genetically silencing a transcriptional substrate of CHD8 produced similar behavioral effects. Given that difficulties in social communication are also a hallmark of ASD, we quantified social behaviors and found that mice were indifferent to social conspecifics. **Conclusions.** Thus, early-life Chd8 silencing induces features resembling restricted interests and social communication difficulties in ASD. Further investigation could aid in the development of more specialized support for individuals with ASD.

Exploring Novel Therapy in Pediatric Brain Tumor Using a High-Throughput Drug Screen

Presenting Author: Sunny Congrove, Emory University

Poster Number: 36

Co-Authors: CONGROVE, SUNNY; Lekha Koopari, Chandra; Mohanta, Sehasree, Kathuria, Annie; Joshi, Kaustubh; and DASGUPTA, BIPLAB

Diffuse Intrinsic Pontine Glioma (DIPG) is an aggressive pediatric brain tumor of the pons that is characterized by its diffuse infiltration, resistance to conventional chemotherapies, and median survival remains less than one year, which underscores the urgent need for new therapeutic strategies. However, the challenges of drug delivery across the blood-brain barrier and the rarity of the disease complicate the development of effective treatments. Therefore, this project focuses on repurposing existing central nervous system (CNS) penetrant drug compounds as potential therapeutic agents for DIPG. Using a high-throughput drug screening approach, a library of 788 clinically relevant compounds with known CNS bioavailability was evaluated for their ability to inhibit DIPG cell viability in vitro. An ex vivo organotypic brain slice model was optimized to evaluate drug responses in an environment that mimics in vivo tumor-brain interactions, thereby bridging the gap between traditional cell culture assays and in vivo models. In collaboration with the Kathuria Lab at Johns Hopkins, an additional ex vivo organoid model using brainstem organoids, tumor spheroids, and fusion assembloids was used to obtain functional readouts of electrical activity. From this study, we identified 5 drug compounds which will be used in in vivo mouse models of DIPG, and we highlight several potential target pathways for ongoing DIPG research.

Comparative Evaluation of Standard FreeSurfer and SynthSeg Brain Volumetrics in a Multi-Scanner Pediatric Cohort (Ages 1–20)

Presenting Author: Eswar Damaraju, Children's Healthcare of Atlanta

Poster Number: 37

Co-Authors: Damaraju, Eswar; Patil, Prabhumallikharjun; Reddy, Kartik; Palasis, Susan; and Goldmann-Yassen, Adam

Background: Automated brain volumetric segmentation in pediatric populations presents unique challenges due to rapid developmental changes, varying tissue contrast, and multi-scanner protocol variations. While traditional FreeSurfer pipelines are considered a gold standard, deep learning models such as SynthSeg offer rapid, contrast-agnostic segmentation. We aimed to evaluate and compare brain volumetric outputs between standard FreeSurfer and SynthSeg across a large, diverse pediatric dataset acquired across multiple MRI scanners at CHOA. Methods: We evaluated 3,500 pre-contrast T1-weighted MRI datasets from pediatric subjects aged 1 to 20 years, acquired across 7 different scanners. After image QC quality control, Standard FreeSurfer and SynthSeg pipelines were run on 2,700 datasets. Regional volumetrics were harmonized across acquisition sites using the NeuroCombat method. Multivariate volumetric outliers were identified as follows: Model Fitting: Age-associated developmental trajectories were modeled using Huber robust regression with flexible natural splines for age and sex as an additive covariate. Right-skewed volume distributions were $\log(1 + x)$ -transformed prior to modeling. Univariate QC: Model residual distributions for each structure were transformed into robust z-scores; regional outliers were identified using a threshold of $|z| > 3.5$. Multivariate QC: Principal component analysis was applied to the full residual z-score matrix. Robust Mahalanobis distances were computed using Minimum Covariance Determinant, and multivariate outliers were flagged using a chi2 critical value threshold. Subsequent comparisons were performed on shared cohort of N=1,955 subjects (923 Male, 1032 Female). Results: Across the shared N = 1,955 cohort, site harmonization effectively reduced scanner-dependent variance in both streams. The proposed outlier detection method to successfully identify multivariate outliers for standard FreeSurfer and SynthSeg pipelines. SynthSeg demonstrated high concordance with standard FreeSurfer across major subcortical and cortical structures, while significantly reducing compute wall-time. Robust regression growth models revealed comparable non-linear trajectory shapes across age, though baseline volumetric offsets were observed in specific regions sensitive to boundary contrast definitions. Conclusion: SynthSeg provides robust, scalable volumetric estimates in pediatric populations that closely align with standard FreeSurfer outcomes following site harmonization and rigorous outlier detection. Its resilience across multi-scanner data makes it a viable alternative for large-scale pediatric neuroimaging studies where computing efficiency and protocol variations are key constraints

mGlu1 Positive Allosteric Modulation Rescues Behavioral Deficits Following Developmental NMDAR Hypofunction

Presenting Author: Mac Jack Meadows, Emory University

Poster Number: 38

Co-Authors: Meadows, Mac; Gallinger, Isabel; Wolfe, Brenna; Heaton, Elizabeth; Pemu, Karena; and Luessen, Deborah

AIM: Adolescent exposure to phencyclidine (PCP) increases extracellular dopamine concentration in the dorsal striatum (DS), leading, in adulthood, to lasting alterations in striatal dopamine (DA) signaling and behavior deficits analogous to symptoms of adult schizophrenia. In preclinical models, we found that

metabotropic glutamate receptor subtype, mGlu1, negatively modulates DA release in the DS. Further, mGlu1-treated mice that completed amphetamine induced hyperlocomotion (AHL) showed the potential for mGlu1 positive allosteric modulators (PAMs) to become a drug candidate to recover behavioral deficits associated with the positive symptoms of schizophrenia. Given the potential for its striatal dopaminergic modulation and its decrease of sensorimotor impairment, we hypothesize that mGlu1 activation can recover sensorimotor impairments derived from chronic exposure to PCP during a critical point in development. **METHODS:** Male and female mice (Strains: C57/BL6 and GRM1-D1-KO - transgenic selective deletion of mGlu1 receptors in dopamine D1 receptor expressing cells) were injected with PCP (10mg/kg, s.c.) for 7 days (postnatal day 35-42). Saline- and PCP- treated mice were injected with AAV5-dLight1.1 into the DS. After 3 weeks of recovery, D'Light transients were recorded in response to a single injection of amphetamine (4 mg/kg, i.p.) in an open field. Pre-pulse inhibition (PPI) and AHL were also tested to determine sensorimotor performance in adult mice. VU6004909, a mGlu1 positive allosteric modulator (PAM), (30mg/kg, i.p.) was administered during photometry and behavioral studies. **RESULTS:** PPI is impaired and AHL is increased in PCP-treated mice compared to saline controls. However, when pre-treated with VU6004909, PCP-treated mice show recovery of PPI impairment and increased AHL response compared to saline controls. Further, in GRM1-D1-KO mice, AHL is increased compared to littermate controls, with VU6004909 partially blocking this phenotype. Ongoing photometry studies explore our overarching hypotheses that DS DA transmission will be increased in GRM1-D1-KO mice compared to littermate controls and VU6004909 will occlude dopamine inhibition. **CONCLUSIONS:** Overall, our study expands the current understanding of signaling mechanisms between mGlu1 and DA neuronal populations in the dorsal striatum. Given the promising recovery of sensorimotor impairment in preclinical models, our study also suggests that mGlu1 PAMs show therapeutic potential for the treatment of positive symptoms of schizophrenia.

Missed cases of Spinal Muscular Atrophy on Newborn Screening: increasing awareness and improving outcomes

Presenting Author: Gautham Sivakumar, University of Georgia

Poster Number: 39

Co-Authors: Verma, Sumit; and Sivakumar, Gautham

Spinal muscular atrophy (SMA) newborn screening (NBS) was put in place in Georgia in 2019 and uses an assay which detects the homozygous deletion of the SMN1 gene on exon 7. Approximately 5% of the SMA population are compound heterozygous for deletion including exon 7 and a non-functional frameshift mutation in the SMN1 gene and will be missed on NBS. This report contains two such patients born to non-consanguineous parents. **Methods:** Retrospective case studies of two full term healthy male births with normal SMA NBS results presented with severe weakness, respiratory and feeding difficulties at a median age of 3 months. **Results:** On neurological examination, infants had absent tendon jerks, tongue fasciculations, sea-saw breathing, lack of antigravity strength in bilateral legs and arms with early contractures. Creatine kinase and neurofilament light chain levels were elevated. Electrodiagnostic testing confirmed severe neurogenic changes affecting the motor neurons and or its axons. Rapid whole exome sequencing in both cases was unremarkable. However, due to the high index of clinical suspicion

for SMA, an SMN1 sequencing was performed and was positive, hence confirming the SMA diagnosis. Our patients had 2 SMN2 copies and were started on disease modifying treatment; however, had already suffered irreversible motor neuron loss. Discussion: SMA NBS is sensitive; however, there remains a small subset of SMA patients missed on NBS. High index of clinical suspicion, detailed neurological examination supported by electrodiagnostic and genetic SMN sequencing can help confirm the diagnosis, initiate disease modifying treatment and prevent further loss of motor neurons to improve outcomes.

Investigating Early-life Development and Progression of Motor Phenotypes in an Scn8a Mouse Model

Presenting Author: Grace Sohn, Department of Human Genetics, Emory University

Poster Number: 40

Co-Authors: SOHN, GRACE S.; James, Katie E.; and Wong, Jennifer C.

SCN8A encodes the voltage-gated sodium channel Nav1.6 and is highly expressed throughout the brain, including motor-relevant regions such as the cortex and cerebellum. Gain-of-function mutations in SCN8A increase Nav1.6 activity, resulting in neuronal hyperexcitability. Patients with SCN8A mutations exhibit a range of clinical phenotypes, including mild to severe seizures, developmental delay, intellectual disability and behavioral comorbidities. Despite presenting significant clinical burden, the onset and early progression of clinical phenotypes associated with SCN8A mutations in both patients and mouse models remain largely unknown. Since SCN8A is important for motor function, we hypothesize that harboring an SCN8A mutation will result in early-life impairments in gross motor behavior. Through this study, we aim to characterize the development of motor phenotypes in SCN8A-derived epilepsy and their underlying molecular contributions. To test our hypothesis, we used a mouse model expressing the human SCN8A R1620L (RL/+) mutation. RL/+ mutant mice recapitulate many phenotypes observed in human patients, including learning and memory deficits, hyperactivity, social behavior abnormalities, and spontaneous seizures. Early-life neurodevelopmental milestones were assessed in RL/+ and wild-type (WT) mice between postnatal days (P5-21). We also performed behavioral assays to measure gross motor function in 1, 2, and 4-month-old female and male mice. Motor coordination and learning were evaluated using an accelerating rotarod paradigm, while neuromuscular strength was assessed using a hanging grip assay. Our preliminary findings demonstrated that both RL/+ mutants and WT littermates exhibited comparable motor coordination and learning at 3-week and 2-month-old timepoints, with no significant differences between genotypes. Interestingly, we found that RL/+ mutants showed a reduced latency to fall during the hanging grip assay, suggesting reduced neuromuscular strength. Together, our findings suggest that the SCN8A R1620L mutation may affect distinct domains of behavior. For example, we found that early behavior in RL/+ mice appeared to have normal motor coordination, yet notable deficits in neuromuscular strength. Ongoing experiments will continue to investigate how these phenotypes evolve across additional timepoints. Ultimately, the findings from our study may shed light on the development and progression of motor behavior in patients with SCN8A mutations, potentially informing future studies investigating therapeutic strategies for SCN8A-associated behavioral comorbidities.

Influence of Genetic Mechanisms of Inheritance on Neuropsychological Outcomes of Duchenne Muscular Dystrophy

Presenting Author: Austin Wang, Georgia Institute of Technology

Poster Number: 41

Co-Authors: Wang, Austin; Kiefel, Jaqueline

Duchenne muscular dystrophy (DMD) is a progressive, X-linked recessive, neuromuscular disorder caused by mutations in the DMD gene, resulting in dysfunction of the dystrophin protein. Dystrophin protects the sarcolemma from contraction-induced damage, and its absence leads to progressive muscle degeneration and weakness. Affected children, often diagnosed within the first few years of life, experience rapid, progressive, generalized muscle weakness, leading to impaired ambulatory status and subsequent respiratory and cardiac insufficiencies that shorten overall lifespan. Significant knowledge gaps exist regarding the contribution of mutation origin to cognitive and neuropsychological phenotypes in DMD, as maternal carrier status may itself reflect genetic modifiers relevant to a child's outcomes. To address these gaps, we developed a combined neuropsychological and genetic surveillance protocol investigating DMD neuropsychological severity primarily in relation to mutation origin (de novo vs. maternally inherited), with exon locus and mutation type as secondary variables. We hypothesized that children with childhood-onset DMD demonstrate milder impairment than those with congenital DMD and that mutations downstream of the dystrophin gene will result in more severe impairments than mutations upstream of the gene. This longitudinal study uses a retrospective and prospective cohort design, combining existing clinical records with standardized testing of newly enrolled patients. Subjects are males aged 6–20 diagnosed with DMD without additional neurological dysfunction. Preliminary analysis of 19 participants (mean age = 12.49 years) revealed no significant difference in composite severity scores between de novo ($n = 9$) and maternally inherited ($n = 10$) mutations ($p = 0.43$). Exon locus showed a non-significant trend toward greater executive functioning and working memory deficits with downstream versus upstream mutations ($p = 0.19$); mutation type showed no significant association. These preliminary findings do not yet indicate a significant relationship between mutation origin and neuropsychological severity; however, difficulty distinguishing true de novo mutations from undetected maternal mosaicism may be underestimating a true effect. Continued enrollment alongside further analysis, will help determine whether mutation origin, independent of or interacting with locus and isoform involvement, can serve as an early biomarker for neuropsychological risk, informing earlier, targeted educational and therapeutic interventions for children with DMD.

Deciphering the Role of TCF20 in Human Cortical Development using iPSC-derived Brain Organoids

Presenting Author: Angelina Zhang, Emory University

Poster Number: 42

Co-Authors: Fuentes, Kevin; ZHANG, ANGELINA; Wen, Zhexing; and Zhou, Jian

Background: Transcription Factor-20 (TCF20) encodes a nuclear chromatin-binding protein and is haploinsufficient in TCF20 neurodevelopmental disorder (TAND), a condition marked by cognitive impairment and autistic features. Multiple independent genetic studies have established TCF20 as a

high-confidence neurodevelopmental disorder risk gene, underscoring its critical role in human brain development. Previous findings in primary rodent neurons have shown that Tcf20 coregulates Bdnf transcription, and knockdown of the gene reduces Bdnf expression, indicating that changes in Tcf20 expression can influence synapse density. Despite its strong genetic association, clinical significance, and rodent findings, the molecular and cellular mechanisms by which TCF20 regulates human neurodevelopment and its species-specific impact on the gene regulatory network remain largely unknown. Hypothesis: TCF20 deficiency alters the gene regulatory network, impacting neuronal differentiation, synaptic maturation, and neural network formation. Methods: To understand the role of TCF20 in human brain development, a human iPSC-derived model was used to generate isogenic heterozygous TCF20-deficient iPSCs. Cortical organoids were generated and collected at D56 to assess the impact of TCF20 haploinsufficiency on neurodevelopment at the cellular and molecular levels using immunostaining and single-cell RNA-seq (scRNA-seq). In parallel, neurons were generated from iPSCs and co-cultured with mouse astrocytes to investigate changes in neural network activity using microelectrode recordings. Results: Preliminary findings on changes in proliferation in D56 human iPSC-derived cortical organoids indicate that TCF20 deficiency reduces proliferation during early neurodevelopment, reflected in a lower ratio of Sox2+/Ki67+ cells. ScRNA-seq data show that TCF20-deficient organoids exhibit altered cell composition, with fewer glial cell types and more excitatory neurons, along with increased activity in differentiation and synaptic development pathways in radial glia and excitatory neurons. Additional microelectrode activity data in TCF20 haploinsufficient D14 hiPSC neurons cultured with mouse astrocytes show decreased mean firing rates and increased network burst frequency. Conclusion: The results indicate that TCF20 deficiency alters early human neurodevelopment and function, demonstrating its role in the pathogenesis of TAND.

QUASS-Enhanced AREX CEST MRI Reduces T1 Dependency in Pediatric Brain Tumors

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Poster Number: 43

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Background: Chemical exchange saturation transfer (CEST) MRI is sensitive to dilute metabolites and mobile proteins/peptides but remains sensitive to tissue T1 and the acquisition protocol in clinical settings. Pediatric brain tumors often exhibit substantial heterogeneity, which may limit the robustness of CEST MRI measurements. This study evaluated whether quasi-steady-state (QUASS) reconstruction of the apparent exchange-dependent relaxation (AREX) reduces T1-related variability in pediatric brain tumors. Methods and Materials: Fifteen pediatric brain tumor patients (11 low-grade and 4 high-grade) underwent multi-slice 3T CEST MRI using RF saturation at B1 = 0.7 μ T with a saturation time of 1.5 s. Lesion regions of interest were manually delineated on representative slices. Mean lesion values were calculated after excluding non-finite values and outlier voxels exceeding two standard deviations within each ROI. Conventional and QUASS-reconstructed amide (3.5 ppm) CEST metrics, including amide proton transfer-weighted (APT_w), chemical exchange saturation transfer ratio (CESTR), and AREX, were evaluated. APT_w was defined as conventional MTR asymmetry, whereas CESTR was calculated as the

difference between the fitted reference spectrum and the measured Z-spectrum ($CESTR = Z_{ref} - Z_{lab}$). Associations between lesion T1 and each metric were assessed using Pearson correlation and linear regression. Exploratory receiver operating characteristic (ROC) analysis was performed to evaluate discrimination between low- and high-grade tumors. Results: Conventional AREX showed a moderate correlation with lesion T1 ($r = -0.56$, $p = 0.030$), whereas QUASS-reconstructed AREX showed a weaker, non-significant correlation ($r = -0.29$, $p = 0.293$), indicating reduced T1 dependence. CESTR showed weak correlations with T1 before and after QUASS reconstruction (CESTRapp: $r = -0.23$, $p = 0.419$; CESTRQUASS: $r = -0.14$, $p = 0.607$). Across the cohort, QUASS reconstruction reduced apparent relaxation-related variability while preserving lesion contrast. Exploratory ROC analysis demonstrated modest discrimination between low- and high-grade tumors ($AUC = 0.545-0.705$), with conventional AREX achieving the highest performance ($AUC = 0.705$). Conclusions: QUASS-reconstructed AREX reduced T1 dependence in pediatric brain tumor CEST MRI while preserving lesion contrast. These findings support QUASS reconstruction as a more robust quantitative CEST approach for clinical evaluation of pediatric brain tumors.

Developmental Prefrontal Interneuron Dysfunction Underlies Persistent Cognitive Deficits Following Adolescent Cocaine Exposure

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Poster Number: 44

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Aim: Exposure to psychostimulants, such as cocaine, during adolescence produces persistent changes in the prefrontal cortex (PFC) which parallel cognitive deficits seen in adulthood. Further, adolescent exposure to psychostimulants impairs inhibitory transmission in the PFC in adulthood, suggesting that enhancing PFC inhibitory transmission may be a promising strategy to reverse drug-induced cognitive deficits. Activation of the mGlu1 subtype of metabotropic glutamate receptor increases inhibitory transmission in the PFC and working memory by selective excitation of somatostatin-expressing GABA interneurons (SST-INs). Therefore, we hypothesize that repeated exposure to cocaine during a critical developmental period in adolescence disrupts PFC inhibition via SST-INs and drives working memory impairments in adulthood which can be mitigated by activation of mGlu1. **Methods:** Male and female mice were injected once daily with cocaine (20 mg/kg, i.p.) for 7 days (PND 35-42). Behavioral and electrophysiological testing was conducted between 10-12 weeks of age. mGlu1 positive allosteric modulators (PAMs), SST- and PV-Ai9 tdTomato mice, whole-cell patch-clamp electrophysiology, maze- and touchscreen-based automated cognition testing. **Results:** We found that repeated administration of cocaine during a critical adolescent period impaired PFC SST-IN, but not parvalbumin-expressing interneuron (PV-IN), firing compared to saline-treated mice. Adolescent cocaine exposure significantly decreased the frequency of spontaneous excitatory postsynaptic currents onto SST-INs but not PV-INs. These findings were paralleled by adolescent cocaine-induced impairments in spatial working memory in adulthood. Importantly, these physiological and behavioral effects of adolescent cocaine exposure were reversed by selective mGlu1 activation. Lastly, repeated amphetamine administration during the same adolescent critical period did not result in impaired SST-IN function or spatial working memory in

adulthood. Conclusions: These studies show that: 1) cocaine, but not amphetamine, exposure during an adolescent critical period induces persistent and selective deficits in PFC SST-IN function and cognition in adulthood and 2) selective activation of mGlu1 with PAMs represents a novel strategy for reversing cocaine-induced cognitive impairment

CHOA Neurosciences: Uncovering How to Empower Patients on their Journey

Presenting Author: Nadja Kadom, Emory University

Poster Number: 45

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Background: Patient empowerment refers to patient's and families' ability to navigate healthcare with confidence, self-efficacy, and sustained agency. Empowerment contributes to higher healthcare quality, safety, patient experience, and value. It is currently unknown which distinct skills and strategies patients could employ to succeed in their healthcare journey. We hypothesized that a study using patient interviews could help elucidate such skills and strategies. Methods: We conducted a prospective, exploratory qualitative study at a pediatric healthcare system, IRB-approved and HIPAA-compliant. The team developed an interview guide iteratively supported by targeted literature review. Recruited patient families completed voluntary, one-hour virtual interviews that were recorded, transcribed, and uploaded to the coding platform (Dedoose® v10, Manhattan Beach, California, USA). Two team members coded the interviews and developed parent and child codes independently, then convened to combine codes and themes. Results: A total of 5 participants, all mothers, females, with a mean age of 51.4 years (range 41- 68 years), completed interviews. Three hold bachelor's degrees, one master's degree, and one completed some college. All participants had a chronic care journey. The qualitative analysis revealed the following three domains and themes (in parentheses): 1- Advocacy (Apprising, Championing social justice in the provision of healthcare, Committing, Connecting, Mediating, Safeguarding, Valuing), 2- Gaining access (Goals and habits, Being eligible to access, Finding out about a resources, Having the means to access), 3- Positive Functioning (Attention and awareness, Comprehension and coping, Emotions, Goals and habits, Virtues and relationships, Building trust, Having a sense of control, Finance, Beliefs). Conclusion: Patients and families employ a wide range of skills and strategies during their healthcare journey in CHOA neurosciences. Our study identifies new opportunities for interventions across the pediatric care journey that could be implemented at CHOA towards patient empowerment. Examples include planning inpatient days with family quiet time included and coaching families in self-care. Future work will translate these findings into practical tools and evaluate their implementation and impact.

Repeated sevoflurane exposure leads to persistent plasma biomarkers of inflammation and neurobehavioral changes in infant rhesus macaques

Presenting Author: Jessica Raper, Department of Pediatrics, Emory University School of Medicine

Poster Number: 46

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Background: Clinical studies and animal models suggest that general anesthesia exposure during infancy can result in long-lasting neurobehavioral impairments. Considering that millions of children each year undergo procedures that require anesthesia, it is important to investigate the mechanism of anesthesia-induced neurotoxicity to ultimately develop ways to protect the vulnerable developing brain. We have previously reported that repeated sevoflurane exposure in rhesus macaques during the first month of life alters emotional responses to an acute stressor and impairs visual recognition memory. We have also shown alterations in peripheral cytokines within 24 hours after anesthesia exposure, as well as altered synaptic ultrastructure in the hippocampus and dorsolateral prefrontal cortex at 4 years of age. We hypothesize that general anesthesia exposure induces inflammation leading to lasting alterations in the brain that result in neurobehavioral impairments. **Methods:** The present study sought to examine whether neurobehavioral changes after repeated sevoflurane exposure were linked to persistent alterations in peripheral cytokine biomarkers. Sixteen infant rhesus macaques were randomly assigned to either receive repeated sevoflurane exposure (three 4-h exposures) or serve as unexposed controls. At 6 months of age, all animals underwent blood sample collection and an acute stress test. **Results:** Sevoflurane exposure in infancy increased granulocyte macrophage colony-stimulating factor (GM-CSF: $t[14]=1.97$, $p=0.035$) but decreased monocyte chemoattractant protein-4 (MCP-4: $t[14]=3.14$, $p=0.004$) plasma levels at 6 months of age. During the acute stressor, sevoflurane-exposed macaques emitted fewer vocalizations during the most salient threat condition (Group X Condition: $F(2,28) = 4.76$, $p=0.017$), which negatively correlated with GM-CSF levels ($r=-0.43$, $p=0.035$). **Conclusions:** Clinical studies have reported social communication deficits in children with repeated anesthesia exposure, which may be similar to the decreased vocalizations observed in sevoflurane exposed macaques. Additionally, the correlation between altered cytokines and vocalizations suggest a potential link between anesthesia-induced inflammation and long-term behavioral changes. Taken together these data suggest that plasma cytokine levels may be useful biomarkers for detecting anesthesia induced neurocognitive changes in clinical studies. Future directions include clinical studies to examine these biomarkers in children after repeated anesthesia exposure and preclinical studies that test perioperative treatments to mitigate anesthesia-induced inflammation and neurobehavioral alterations.

A Gamified Framework for Multimodal Memory Assessment in Adults and Children with Epilepsy

Presenting Author: Taylor Shade, Emory University

Poster Number: 47

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Rationale: Disagreement between functional outcomes and neuropsychological performance among epilepsy patients suggests that traditional cognitive assessments cannot fully evaluate function. Recent technological advancements enable the creation of sophisticated cognitive assessments that simulate real-world scenarios to better evaluate human memory. We developed a gamified assessment to study critical aspects of memory that are at risk in adults with epilepsy, and present preliminary data on a pediatric version of this task. **Methodology:** We used Unity Game Engine to develop a stand-alone

measure of multimodal memory, the Emory Pediatric Multimodal Learning Test (EPMLT). This task consists of learning and delayed recall blocks, where subjects view professionally developed videos of individuals engaged in everyday activities each in a unique setting. Subjects must recall traditional verbal material, but also multifaceted visual scenes depicting complex stories that unfold over time (visual narrative). We used a virtual delivery platform, allowing for any recall delay, and machine learning for automated transcription, scoring, and interpretation. We collected data at the immediate, 30-min and 1-week intervals for 10 pediatric epilepsy patients, 40 adult epilepsy patients, and 15 healthy controls. Performance between subgroups was assessed with a mixed design ANOVA, and within group differences with paired t-tests. Results: Healthy controls perform better than children and adults with epilepsy across all facets of the EPMLT ($p < .001$). Children performed significantly better remembering visual content compared to verbal content ($p < .01$), in contrast to adults who performed better on verbal memory tasks ($p < .001$). We found relatively stable memory across sessions in presurgical children. Performance declined for most tasks after one week in the child sample, with decline tending to be greater for patients than controls. Conclusions: The EPMLT appears to be internally reliable and we observed many similarities between pediatric and adult performance. Children with epilepsy were better at the visual narrative aspect of the task than adults, which may relate to greater familiarity with gamified tasks. Overall, we believe these novel tasks hold the potential to identify and address cognitive overlooked vulnerabilities in epilepsy patients (e.g., rapid long-term forgetting), ultimately contributing to the development of tailored interventions and improved patient outcomes.

Comparative Analysis of Glymphatic System Function and White Matter Microstructural Integrity in Pediatric MOG-Associated Disorder and Multiple Sclerosis

Presenting Author: Leonardo Tang, Emory University

Poster Number: 48

Co-Authors: TANG, LEONARDO; Goldman-Yassen, Adam; Damaraju, Eswar; Wheeler, Austin; Gombolay, Grace; Palasis, Susan; Shishido, Yuri; and Mao, Hui

Background: Pediatric myelin oligodendrocyte glycoprotein-associated disorder (MOGAD) and multiple sclerosis (MS) are distinct demyelinating diseases with overlapping clinical presentations that result in long-term disability. To identify quantitative mechanism-specific neuroimaging biomarkers to differentiate these disorders, this study evaluated glymphatic system function using the DTI-ALPS index and assessed regional white matter microstructural damage using multi-metric tract-based spatial statistics (TBSS). Methods: This cross-sectional study included pediatric patients MOGAD, MS, and healthy controls. Glymphatic clearance was estimated with bilateral DTI-ALPS indices at the lateral ventricular projection and association fibers. ANCOVA analysis adjusted for age, sex, and scanner strength. Voxel-wise TBSS analysis of diffusion metrics, including fractional anisotropy (FA), geodesic anisotropy (GA), and radial diffusivity (RD), was performed. Significant voxels were registered to the JHU atlas, yielding tract-specific volumetric involvement ratios that were mapped to functional pathways. Results: The cohort comprised 28 MOGAD (M/F=6/22, median age 10.5), 26 MS (M/F=3/23, median age 17), and 24 controls (M/F=10/14, median age 13). After covariate adjustment, MOGAD patients demonstrated significantly reduced DTI-ALPS indices in both the left ($p=0.0386$) and right ($p=0.0173$)

hemispheres compared to healthy controls, indicating impaired glymphatic clearance, while the MS cohort showed no significant differences compared to controls. While TBSS revealed widespread demyelination (decreased FA, increased RD) in both cohorts, topographic signatures differed. MOGAD displayed maximal decreased FA in the forceps major (0.746), correlating with visuomotor pathway disruption. MS exhibited maximal FA reductions in the left inferior longitudinal fasciculus (0.919) and bilateral parahippocampal cingulum (left: 0.965, right: 0.930), predominantly impacting emotional and memory pathways. MOGAD patients also exhibited significantly decreased GA. Conclusion: DTI-ALPS reveals glymphatic dysfunction in pediatric MOGAD patients, while multi-metric TBSS demonstrates distinct, disease-specific topographic signatures of white matter microstructural damage between MOGAD and MS, providing a neuroanatomical basis for their differing clinical phenotypes. Future work is needed correlating these findings with neuropsychological disability and how differences can impact patient treatment.

Divergent Effects of Antiviral and Anti-Inflammatory Immunomodulators in a Mouse Model of West Nile Neuroinvasive Disease

Presenting Author: Kathleen Weimer, Emory University

Poster Number: 49

Co-Authors: WEIMER, KATHLEEN; McSwain, Leon; Falko, Karyna; Sokolsky, Marina; Gershon, Timothy; and Murray, Kristy

Background: West Nile virus (WNV) is the most prevalent mosquito-borne illness in the United States. Of those infected, ~1 in 150 develop West Nile neuroinvasive disease, a severe manifestation characterized by meningitis, encephalitis, and/or acute flaccid paralysis often resulting in long-term neurological sequelae or, in ~10% of cases, death. Currently, there are no approved therapeutics for WNV infection, and the mechanisms driving disease severity remain incompletely understood. We hypothesize that severe WNV disease is driven, in part, by dysregulated host inflammatory responses and that therapeutic modulation of these pathways can improve clinical outcomes. Here, we evaluated two host-directed therapeutic strategies in murine models of WNV infection: Resi-POx, a nanoparticulate TLR7/8 agonist that stimulates innate antiviral immunity, and the neurokinin-1 receptor (NK1R) antagonist CH123001, which suppresses substance P-mediated neuroinflammation. Methods: C57BL/6 mice were infected with WNV strain 385-99 and treated with Resi-POx [5 mg/kg, intraperitoneally (IP), every other day] beginning on either day 0 or day 2 post-infection. Brain tissues were evaluated with immunohistochemistry for viral antigen (4G2), microglial/macrophage activation (IBA1), T-cell infiltration (CD3e), and apoptosis (cC3). In a separate study, infected mice received CH123001 [10 mg/kg, IP] on days 4 – 6 post-infection as either a single-dose or daily regimen. Substance P expression in the brain was assessed throughout infection and treatment. In all studies animals were monitored for clinical signs and survival and viral burden was quantified by qPCR. Results: WNV infection resulted in widespread CNS viral antigen, microglial activation, T-cell infiltration, and neuronal apoptosis. Resi-POx treatment reduced viral burden in peripheral tissues and the brain but did not improve survival. In contrast, NK1R antagonism improved survival despite minimal effects on CNS viral load. Lower brain Substance P RNA levels were associated with prolonged survival (Spearman's $\rho = -0.7463$), with expression significantly

lower in survivors than non-survivors ($p = 0.0026$). Despite conferring survival benefit, WNV RNA levels did not differ significantly among treated and untreated groups at 7 days post-infection ($p = 0.0644$). Conclusions: These findings support a pathogenic role for neuroinflammation in WNV neuroinvasive disease and suggest that effective therapies may need to target both viral replication and inflammatory injury.