# POSTER LIST

1 **Neuronal polarity and structure are not disrupted by binucleation**

**Presenter(s):** Selena Akay **Role(s):** Undergraduate student 11am–noon

**Author(s):** Selena Akay

When cortical pyramidal neurons differentiate, they polarize so that they form only one axon but multiple dendrites. The mechanisms of how this occurs are still not fully understood. We previously investigated how loss of scaffolding protein Cep55 affects brain development since mutations to this protein have been linked to brain malformations in humans. Cep55 knockout (KO) mice exhibited small brain phenotype and increased binucleated cells. This led us to question whether polarization and structure of cells are disrupted by binucleation. We hypothesized that neurons with two nuclei would make two axons instead of one. To first ensure that loss of Cep55 did not affect neuronal polarity, we used dissociated neuron cultures derived from Cep55 control and KO mouse embryos and found no significant difference in neuronal polarity between the two by analyzing the number of axons and stage counts. As expected, we found increased binucleated neurons in our Cep55 KO cultures compared to control cultures using immunocytochemistry. Finally, we investigated if binucleated neurons produce two axons instead of one by pooling the data from the Cep55 control and KO cultures. We found that the polarization of the binucleated neurons was not significantly different compared to mononucleated neurons by analyzing the number of axons and stage counts. None of the binucleated neurons had two axons and axon lengths were not significantly different between mononucleated and binucleated neurons. Surprisingly, our results suggest that binucleation does not have a significant effect on neuron polarization, and that neuronal binucleation does not produce two axons.

2 **2D CAIPI accelerated 3D multi-slab diffusion-weighted EPI combined with qModeL reconstruction for fast high-resolution microstructure imaging**

**Presenter(s):** Reza Ghorbani Alikelayeh **Role(s):** Graduate student 11am–noon

**Author(s):** Chu-Yu Lee, Reza Ghorbani, Merry Mani

In this work, an accelerated 3D multi-slab diffusion-weighted EPI (3D ms-DWI) method that facilitates high spatial and angular resolutions without long scan times is proposed. It targets the principal bottleneck of standard 3D ms-DWI, which is the prolonged multi-shot kz encoding, by introducing two key innovations in both acquisition and reconstruction.

First, we employ a shot-selective 2D CAIPI sampling design for the ky-kz phase-encoding axes, enabling aggressive under-sampling in both the in-plane (ky) and through-plane (kz) directions. A dedicated 2D navigator echo is acquired for each shot to capture per-shot phase information. Incorporating these navigator measurements into a unified forward model compensates for shot-to-shot diffusion-induced phase variations and maintains image fidelity. Second, the proposed method leverages the substantial redundancy inherent in diffusion MRI, where multiple b-values and directions span a 6D k-q space. By randomizing the sampled kz lines across various diffusion directions, we ensure complementary kz coverage. We show that k-q accelerations close to a factor of 12 can be achieved with a reconstruction error < 3% for both single and multi-shell data. All these under-sampled data are then combined in a single reconstruction that applies both spatial Total Variation and a learned q-space manifold constraint through a denoising autoencoder. The proposed joint 6D reconstruction method, qModeL, integrates every diffusion-weighted volume simultaneously, distributing the under-sampling burden across directions and bolstering overall SNR. Extensive validation on healthy volunteers, including single-shell and multi-shell acquisitions at 1 mm isotropic resolution, demonstrates the viability of 3D ms-DWI for advanced neuroimaging studies.

3 **Behavioral Outcomes in a Mouse Model of Febrile Status Epilepticus**

**Presenter(s):** Everett Altherr **Role(s):** Postdoctoral Scholar noon–1pm

**Author(s):** Everett Altherr, PhD; Howard Goodkin MD-PhD

Febrile status epilepticus (FSE) is a prolonged seizure in the setting of a febrile illness without evidence of direct central nervous system infection. Children with a history of FSE are more susceptible to future temporal lobe epilepsy, motor and verbal developmental delays, cognitive deficits, and psychiatric illness such as depression. The aim of the present study was to determine if FSE leads to motor dysfunction and a depressive phenotype in mice. We also tested the efficacy of antidepressant drugs in treating the depressive phenotype. Using the tail suspension and forced swim behavioral assays, we discovered that an early life episode of FSE spared motor function but lead to a depressive phenotype in adolescent mice. This depressive phenotype persisted in adulthood. We found that compared to vehicle, both the selective serotonin reuptake inhibitor fluoxetine and the norepinephrine reuptake inhibitor desipramine ameliorated the depressive phenotype in adolescent mice. Desipramine recapitulated this finding in adult mice as well. In contrast, the GABAA positive allosteric modulator allopregnanolone failed to treat depressive symptomology in both adolescent and adult mice. Taken together, our findings indicate that experimental FSE leads to a depressive phenotype in mice, and that phenotype is reversible with systemic treatment of antidepressant drugs fluoxetine and desipramine. Future studies will focus on assessing neurological changes following FSE and determining if those are mediating factors in conferring a depressive phenotype.

4 **The Effect of Sibling Relationships on Entropy in Infants' Brains**

**Presenter(s):** Samantha Barnett **Role(s):** Undergraduate student 12pm - 1pm

**Author(s):** Samantha Barnett

Sibling relationships play a large part in socialization throughout infancy, a time when a child's interactions are often limited mostly to family members. However, the neural effects of sibling relationships in infancy are not well understood. This study aims to investigate how sibling relationships affect brain signal entropy, a measure of neural complexity that can be used as an index of neurodevelopment. As part of a larger ongoing study, 12 month old infants with and without an older sibling undergo EEG while watching videos of siblings engaging in joint and parallel play. EEG data will be subjected to multiscale entropy analysis, and a two-sample-t-test will be used to compare entropy values between groups of infants with and without siblings. I hypothesize that infants with siblings will display an increase in neural entropy compared to only children due to the increased socialization throughout their early life. This study will provide insight into the neurological effect of sibling relationships and the part siblings play in social development

5 **Investigating the Association Between Sibling Composition and ADOS Risk Levels**

**Presenter(s):** Charly Beasley **Role(s):** Undergraduate student 11am–noon

**Author(s):** Charly Beasley

This study explores the correlation between the number and type of siblings and autism risk levels in early childhood. Prior research has examined autism risk factors such as heritability, sibling recurrence, and birth order, but little is known about sibling composition in relation to autism risk. In the current study (n=16), autism risk was measured in participants with at least one full or maternal half-sibling using the Autism Diagnostic Observation Schedule (ADOS), the gold-standard diagnostic tool which classifies toddlers into three categories: Little-to-No Risk, Mild-to-Moderate Risk, and Moderate-to-Severe Risk. Maternal siblings were chosen due to their shared gestational environment with the participant. Siblings were quantified via total sibling count, total full sibling count, and total maternal half-sibling count, stratified by sibling sex for the comparison of risk scores across children with different sibling types and totals. Preliminary analysis used ordinal logistic regression models in Jamovi to test three models, each including a single predictor: total siblings, total full siblings, and total maternal half-siblings. None of the models yielded statistically significant results (p-values: 0.118, 0.169, 0.556 respectively), though total and full sibling counts were weakly associated with higher risk, while half-sibling count showed a non-significant negative trend. These results suggest no strong relationship between sibling composition and ADOS classification, though patterns may inform future research with larger samples. Future research should consider additional variables in a larger sample to better assess how sibling composition may impact an infant's development.

6 **Man vs. Machine: Can AI Rival Neurosurgeons in Targeting the VIM for Focused Ultrasound Thalamotomy?**

**Presenter(s):** Daniel Beck **Role(s):** Staff noon–1pm

**Author(s):** Daniel Beck; Emmanuel Cuny, MD; Shayan Moosa, MD

Transcranial MRI-guided focused ultrasound (MRgFUS) enables noninvasive lesioning of the ventral intermediate nucleus (VIM) of the thalamus to treat essential tremor (ET). Since the VIM is not directly visible on MRI, its location is estimated using indirect targeting based on nearby anatomical landmarks. Variability in brain anatomy and human error can make precise targeting difficult, potentially increasing treatment time, number of sonications, and risk of side effects. A novel machine learning algorithm, OptimMRI (RebrAIn Corp.), performs automated VIM targeting using 18 anatomical landmarks per hemisphere. Trained on a large dataset of successful MRgFUS cases, it offers a level of precision and consistency that would be impractical for a human to replicate. However, it remains unknown whether this algorithm can outperform expert neurosurgeons in clinical targeting accuracy. We identified 15 challenging cases from a cohort of 120 ET patients treated with MRgFUS by a single neurosurgeon. In these cases, the original target was adjusted by more than 1 mm due to suboptimal clinical response or side effects. We will compare the final lesion location with both the neurosurgeon's initial plan and the target predicted by OptimMRI. We hypothesize that the OptimMRI-predicted target will more closely match the final therapeutic lesion than the neurosurgeon's original target, as measured by mean Euclidean distance. Analysis is ongoing and expected to be completed within the next month.

7 **Exploring the Role of Microglia in Engram Representations of Social Memories**

**Presenter(s):** Eva Campbell **Role(s):** Undergraduate student 11am–noon

**Author(s):** Eva A. Campbell, Walter Tatera, Sabrina Lee, Brenda Sanchez, Piotr Kraszewski, Elise C. Cope

Social memory deficits are characterized by the inability to recognize familiar individuals. The neural mechanisms underlying these devastating impairments are poorly understood. The hippocampal CA2 subregion and its excitatory projection to ventral CA1 (vCA1) are essential for processing, storage, and retrieval of social memories. Memories are encoded in neuronal ensembles termed “engrams,” which are activated during learning and reactivated upon recall. Microglia, the brain’s immunocompetent cells, are known to modulate neuronal activity, indicating a mechanism by which microglia-neuron interactions may shape engram representations of social memories. We observed marked social memory deficits in mice depleted of microglia via colony-stimulating factor 1 receptor inhibitor, PLX-3397. When allowed to repopulate, microglia exhibited morphological changes, including increased soma volume and reduced process complexity. Current work utilizes the Targeted Recombination in Active Populations (TRAP2) tamoxifen-inducible genetic system to investigate how microglia regulate neuronal activity. We crossed TRAP2+/+ with ZsGreen+/+ reporter mice to permanently “tag” neurons activated during social memory encoding; combined with immunolabeling of reactivated neurons expressing Fos (activation marker) during memory retrieval, putative “engram” neurons can be identified. TRAP2+/-;ZsGreen+/- mice were depleted of microglia with PLX-3397, subjected to novel and familiar social interactions, and perfused to examine Fos with immunolabeling. ZsGreen+ and Fos+ cell counts in CA2 and vCA1 will reveal whether microglia depletion alters neuronal activity in response to a novel or familiar conspecific, respectively. ZsGreen+/Fos+ co-labeled cell counts will elucidate whether microglia modulate social memory engrams. Future work will explore how changes in CA2 neuronal activity influence microglia-neuron interactions.

8 **Simultaneous Skull and Brain Monitoring in Transcranial MRgFUS Surgeries Using a 3D Stack-of-Spirals Sequence**

**Presenter(s):** Sheng Chen **Role(s):** Graduate student 11am–noon

**Author(s):** Sheng Chen, Steven P. Allen, John P. Mugler III, G. Wilson Miller, Craig H. Meyer

Purpose: To develop an MRI approach for simultaneous skull and brain monitoring in clinical transcranial MR-guided focused ultrasound (MRgFUS) surgeries.

Methods: A 3D stack-of-spirals dual-echo sequence was implemented, incorporating spiral-out ultrashort-TE (UTE) acquisition, spiral-retraced-in-out normal-TE (NTE) acquisitions, and fat suppression pulses. The variable TE technique enabled achieving a UTE as short as 0.05ms, allowing T1 mapping of the skull using the variable flip angle (VFA) method. A fixed NTE was selected based on Bloch simulation to enhance phase measurement accuracy using the proton resonance frequency (PRF) shift method in the brain. This method integrates spiral deblurring methods, in-plane trajectory measurement, and B1-mapping-based correction of T1 mapping, and was evaluated in both laboratory and clinical setups.

Results: During laboratory cooling, estimated temperatures closely matched with the ground truth, with standard deviations of 0.60 °C and 0.57 °C per gel ROI, and demonstrated a linear relationship with cortical bone T1 (2.51ms/ °C). A similar trend was observed during laboratory heating (3.86 ms/ °C). In phantom heating in a clinical environment, a concurrent increase in gel temperature and bone T1 was observed at the boundaries, peaking at 12 °C and 7.5ms, respectively. In patient scan results, B1 correction reduced variability in the T1 map of the skull’s top region, while the estimated brain temperature remained stable with a standard deviation of 0.95 °C.

Conclusions: The proposed method, integrating the 3D stack-of-spirals dual-echo sequence and corrections for both blurring artifacts and the B1 field, enabled simultaneous skull-temperature-change detection and brain thermometry with high accuracy and precision under transcranial MRgFUS conditions.

9 **Accessing genetically defined cell types in the Superior Colliculus with transgenic mouse lines**

**Presenter(s):** Chen Chen **Role(s):** Graduate student noon–1pm

**Author(s):** Chen Chen, Yuanming Liu, Jianhua Cang

Recent studies have revealed diverse neuron types in the superior colliculus (SC), a midbrain structure critical for sensorimotor transformation. Here, as an important step towards studying the function of these subtypes, we characterize ten transgenic mouse lines based on a recently published molecular atlas of the superficial SC. We show that Cre or fluorescence expression in some lines corresponds specifically to certain transcriptomic neuron types. These include two GENSAT lines that have been used to target morphological cell types in the SC and three knock-in lines. In contrast, such a correspondence is not seen in other tested mice. Importantly, the expression pattern of marker genes in all these lines is highly consistent with the molecular atlas. Together, our studies support a correlation between morphological and transcriptomic neuron types, identify useful lines for targeting SC neuron types genetically, and demonstrate the validity of the single-cell transcriptomics data.

10 **Regulation of Microglial Immune Functions by SHP-1 in Multiple Sclerosis**

**Presenter(s):** Nicholas Cormas **Role(s):** Undergraduate student noon–1pm

**Author(s):** Nicholas Cormas; Joshua Samuels; John Lukens, PhD

Relapsing-Remitting Multiple Sclerosis (RRMS) is a debilitating autoimmune disease affecting nearly three million people worldwide with no cure. RRMS is characterized by cycles of demyelination and remyelination of neuronal axons. Microglia, the brain's sole resident immune cells, clear degraded myelin and cellular debris, release pro-inflammatory cytokines that recruit peripheral immune cells, and provide supportive factors for remyelination. The phosphatase SHP-1 negatively regulates the TREM2-SYK immune signaling axis, which is essential for protective microglial phagocytosis. However, reduced SHP-1 expression in peripheral macrophages is clinically linked to an enhanced inflammatory profile in RRMS patients, suggesting that impaired SHP-1 signaling may worsen myelin pathology in RRMS. To elucidate the specific role of microglial SHP-1 in RRMS pathology, we generated SHP-1fl/fl Cx3cr1Ert2Cre mice harboring conditional deletion of microglial SHP-1 and Cre-negative littermate controls. Mice underwent Cuprizone-mediated demyelination, and brain sections were harvested during demyelination or remyelination post-Cuprizone withdrawal. Immunohistochemistry of the Corpus Callosum revealed that SHP-1 deficient microglia exhibited an increase in phagolysosomal engulfment of degraded myelin basic protein (dMBP) despite no change in the overall dMBP volume in the demyelination phase. In the remyelination phase, SHP-1-deficient microglia exhibited significant increases in microglial coverage and phagolysosomal engulfment of dMBP despite an exacerbation of overall dMBP accumulation. Notably, follow-up staining revealed that mice lacking microglial SHP-1 exhibited a higher coverage of CD169+ macrophages in the Corpus Callosum, indicating increased recruitment of inflammatory peripheral immune cells. These findings suggest that microglial SHP-1 may play a neuroprotective role against deleterious inflammatory cascades that worsen RRMS progression.

11 **Investigating the role of Cd59 in oligodendrocyte development**

**Presenter(s):** Veronica Coyle **Role(s):** Graduate student 11am–noon

**Author(s):** Veronica Coyle, Kenneth Do, Sarah Kucenas

Myelination is an essential process in vertebrates where select axons are encased in a myelin sheath which accelerates action potential conduction and metabolically supports the axon. Myelin is an extension of the membrane of myelinating glia; oligodendrocytes in the central nervous system (CNS) and Schwann cells in the peripheral nervous system (PNS). Developmental myelination is a complex process involving cell proliferation, target selection, myelin wrapping and compaction. Various disorders, including leukodystrophies and demyelinating diseases, lead to abnormal myelination, resulting in cognitive defects, motor problems and more. Treatments are limited, and efforts are underway to illuminate the mechanisms driving myelin development in order to develop therapeutics.

Recently, the Kucenas lab identified cd59 as highly expressed during myelinating glial cell development. cd59 encodes a small GPI-anchored glycoprotein called Cd59, best known for inhibiting complement-induced lysis of self-cells. Cd59 also participates in immune signaling, apoptosis, and vesicular secretion. To investigate the role of Cd59 in developmental myelination, our lab used CRISPR-Cas9 genome editing to create zebrafish cd59 mutants. The lab showed mutant Schwann cells over-proliferate but display peripheral hypomyelination and perturbed nodes of Ranvier. My project aims to decipher the role of Cd59 in oligodendrocyte development. My preliminary studies show disrupted node of Ranvier development and increased instances of “paranodal bridging” between internodes. I hypothesize that Cd59 regulates node of Ranvier formation by facilitating exocytosis of axon-myelin adhesion proteins necessary for node of Ranvier development, as Cd59 has previously been described to play an essential role in exocytosis in other biological contexts.

12 **Genetic mosaic analysis of abscission genes Cep55 and Kif20b in the developing cortex**

**Presenter(s):** Hayley Dingsdale **Role(s):** Postdoctoral Scholar 11am–noon

**Author(s):** Hayley Dingsdale, Elizabeth Ross, Jackson Byars, Savera Shetty, Erik Miao, Klaudia Filipek, Noelle Dwyer

Tight regulation of neural stem cell (NSC) division in the developing cortex is crucial for generating the correct number and placement of neurons and glia. Our previous data show that disrupting the last stage of cell division – in which daughter cells undergo the final separation – via functional knockout of abscission proteins Cep55 and Kif20b, drastically affects cortical development. Knockout cortices show altered cell fates, cell death and microcephaly. In germline mutant brains however, abnormal brain structure and abundant apoptosis make it difficult to isolate autonomous from non-autonomous effects. To overcome this, here we use Mosaic Analysis of Double Markers (MADM) to generate cortex-specific, fluorescently-labelled sparse knockout cells within an otherwise normal size brain. With knockout cells expressing EGFP and wildtype cells expressing tdTomato, we have been able to show that cells lacking Cep55 or Kif20b have altered survival compared to their wildtype counterparts; cells in upper layers of the cortex appear more vulnerable to these effects. In addition, preliminary data suggests that knockout cells in the MADM brain may be less vulnerable to remaining stuck in cell division, as the percentage of knockout cells that are binucleate appears lower than in the germline mutant. Further analyses will improve our understanding of the complex cell interactions occurring during cortical development, and the short- and long-term consequences of disrupted cell division.

13 **The Influence of Feeding Type on Language Development in Premature Infants**

**Presenter(s):** Emily Douglas **Role(s):** Undergraduate student 11am–noon

**Author(s):** Emily Douglas

Prematurity is strongly associated with an increased risk in cognitive, motor, and language development in infants/toddlers. Preterm children, even moderate-late preterm, are at risk for poorer language performance than term-born children. The well-understood importance of breastfeeding for infants has caused increased initiatives for promoting breastfeeding practices in the neonatal intensive care unit (NICU) due to premature babies' known susceptbility towards delayed development. This study aims to investigate the relationship between feeding method (breastfed from breast, breastfed from bottle, formula-fed) received specifically by preterm infants and their language development.

Parents reported the proportion of weekly feedings their child received from each of the three offered feedings types – namely breastfed from breast, breastfed from bottle, and formula-fed – by way of a NICU Behavioral Questionnaire. This data was compared to the corresponding Language Standard Scoring from the Bayley Scales of Infant and Toddler Development Test received by each participant at around 24 months of age. We hypothesize that the NICU babies who received a higher proportion of weekly breastfeedings will receive higher Language Standard Scores than their bottle-fed or formula-fed counterparts. This research will provide valuable information regarding the relationship between feeding type and language development in a uniquely vulnerable population, premature infants.

14 **Activation of Periaqueductal Gray Neurons Proximal to Kindled Seizures that Present with Apnea**

**Presenter(s):** Selena Garcia DuBar **Role(s):** Postdoctoral Scholar 11am–noon

**Author(s):** Selena Garcia DuBar, Sebastian Moeller Rivera, Ian Wenker

Sudden Unexpected Death in Epilepsy (SUDEP) is defined as the sudden, unexpected, and unexplained death of a person with epilepsy and accounts for up to 17% of all epilepsy-related deaths. There is increasing evidence that seizure-induced apnea (SIA) is the primary cause of SUDEP. Our work using preclinical models of epilepsy shows that SIA occurs during the tonic phase, minutes before terminal asystole. We have also previously observed that SIA is not impacted by forebrain inhibition; thus, we hypothesize that overactive brainstem neural circuitry is what produces SIA.

A rapid kindling model in mice was used, which produces seizures on a modified Raine scale that include wild running/jumping (stage 6), tonic extension and SIA (stage 7), and death from SIA (stage 8). Breathing rate, EEG power, and heart rate were assessed for each condition. TRAP2 mice were kindled until reaching their first behavior stage 6 or 7 to observe activated neuronal populations in mice experiencing seizures. In a subset of these experiments, we performed in situ hybridization to assess the subtypes of activated neurons.

Most notably, we found more activated neurons in the periaqueductal gray (PAG) of mice that had seizures with apnea versus mice with seizures without SIA. The activated neurons were mostly glutamatergic. These results suggest that excitatory neurons in the PAG are activated during seizures to produce apnea and SUDEP. The PAG represents a potential target for intervention to prevent apnea and SUDEP that can be examined in future studies.

15 **Investigating the genetic basis of variation in neural stem cell reactivation in Drosophila melanogaster.**

**Presenter(s):** Tai Ferree **Role(s):** Undergraduate student noon–1pm

**Author(s):** Tai Ferree, Taylor Nystrom, Sarah Siegrist, PhD

Neurogenesis is the process by which neural stem cells (NSCs) divide and differentiate to produce the neurons and glia that compose the nervous system. During neurogenesis, NSCs go through periods of proliferation and quiescence, a dormant yet actively regulated state in which cells exit the cell cycle but maintain the ability to re-enter and resume activity. NSCs leave quiescence and resume division in a process called “reactivation,” which is cued by cell intrinsic and extrinsic factors. Since various pathways influence reactivation, we asked about the impact of genetic variation. In Drosophila melanogaster, most work investigating neurogenesis has been performed in a limited number of genetic backgrounds. As such, the impact of genetic variation on reactivation remains unknown. In this project, we conducted a genome-wide association study to investigate how genetic variation affects reactivation. We analyzed NSC reactivation in genetically distinct lines of Drosophila and confirmed that genetic variation affects the timing of reactivation. We then identified rugose, CG4267, oseg2, and bicra as genes significantly associated with variation in reactivation. Our results from in vivo genetic knockdowns indicate that rugose and CG4267 do not have a role in regulating reactivation. Genetic knockdowns of oseg2 and bicra to validate their potential involvement are currently ongoing. This work yields insight into Drosophila neurogenesis and provides the opportunity for further exploration into the identified genes. Understanding the genetic basis of reactivation will contribute to a more detailed understanding of NSC development and may provide a framework for research into neurodevelopmental disorders.

16 **ApoE2 Protects Against Neurodegeneration by Alleviating Translational Stress Induced by Tau Pathology**

**Presenter(s):** Weronika Gniadzik **Role(s):** Graduate student noon–1pm

**Author(s):** Weronika Gniadzik, Maja Wierzbińska, Eliana Sherman, Tian Zhang, Lulu Jiang

Objectives: Apolipoprotein E (APOE) is a key genetic factor in Alzheimer's disease (AD), with the APOE2 variant linked to reduced risk. However, how different APOE genotypes affect AD pathology remains unclear. Studies suggest that APOE influences lipid metabolism, amyloid-beta deposition, and tau pathology in neurons and glial cells. This study aims to elucidate the role of APOE2 in splicing and translation driving tau pathology.

Methods: We hypothesize that ApoE-mediated translational and spliceosomal regulation influence tau aggregation in neurons and glial cells in AD. To test this, we use 3D neuron-glial brain assembloid models (Masteroids) derived from human iPSCs representing ApoE2 and isogenic ApoE3 genotypes. ApoE2 and ApoE3 iPSCs were differentiated into neuronal, astrocytic, and microglial-like cells in 2D cultures. Neuronal cells were seeded with tau oligomers to simulate pathology. Masteroids, formed by combining these cell types, were analyzed for tau aggregation, with underlying pathways investigated using mass spectrometry.

Results: The advanced Masteroid model of AD replicates the complex cellular interactions of the human brain and reveals isoform-specific differences in protein translation and splicing between ApoE variants. Proteomic analysis indicates that ApoE2 Masteroids exhibit reduced translational stress in response to tau pathology compared to ApoE3. This suggests that ApoE2 maintains translational homeostasis and may mitigate aberrant RNA processing associated with tau pathology.

Conclusions: Our findings suggest that ApoE isoforms differentially regulate protein translation and splicing, influencing tau pathology in AD. In this disease, translation and spliceosomal activity are compromised, whereas ApoE2 appears to exert a protective effect by reducing translational stress.

17 **A Comprehensive LC-MS Metabolomics Approach Reveals a Novel Panel of Markers in an APOE4 Mouse Model of Alzheimer's Disease**

**Presenter(s):** Reyhan Haider **Role(s):** Undergraduate student noon–1pm

**Author(s):** Reyhan Haider, Meth Jayatilake, Shivani Bansal, Amrita Cheema, Bill Rebeck

Alzheimer's disease is a neurodegenerative disease affecting millions of individuals around the world. However, all FDA-approved drugs for Alzheimer's disease offer only symptomatic treatment, with limited effect on slowing disease progression. APOE is a major genetic risk factor for the disease. Individuals with one copy of the APOE (E4) allele have a 3-fold likelihood of developing the disease, while individuals with two copies are 15 times more likely to have the disease. But, the mechanisms for how E4 increases the likelihood of developing Alzheimer's Disease is largely unknown. This study utilized liquid chromatography-mass spectrometry (LC-MS) to gain insight into the molecular impact of differential E4 expression on metabolic predictors of Alzheimer's Disease development cerebellum tissue samples from wild-type and E4-expressing mice at ages 6, 12, 18, and 21 months. Our results identified 64 metabolites demonstrating increases or decreases at 6 months. Tracing these markers throughout the mouse lifespan revealed these markers are also changed in a similar manner at 18 months, indicating that molecular dysregulations are stable across time. Comparing metabolic profiles between sexes reveals that APOE4 has a more drastic effect in females at 12 months, showing how APOE4 can adversely affect populations susceptible to Alzheimer's disease. This study sheds light on the potential metabolite candidates and the overall molecular impact of E4 to improve early diagnosis and preventive measures in regard to Alzheimer's disease.

18 **Profiling cerebrospinal fluid metabolites in traumatic brain injury and stroke**

**Presenter(s):** Chaitali Harge **Role(s):** Staff 11am–noon

**Author(s):** Chaitali Harge, Andrew P Carlson

Neurological disorders like traumatic brain injury (TBI) and stroke are the leading causes of deaths worldwide. They can affect patient's cognitive function, motor skills and sensory perception. At a clinical level, TBI and stroke can be managed by maintaining adequate oxygenation, cerebral perfusion pressure, cerebrovascular pressure as well as analysis of cerebrospinal fluid (CSF). TBI and stroke can disrupt the blood-brain barrier, causing leakage of substances from blood into CSF, altering its composition. Injured brain tissue can also release specific molecules into the CSF. Analysis of such molecules in TBI and stroke patients can help determine CSF signatures in patient recovery. Recent data science advances provide tools to analyze complex data from CSF samples to identify potential biomarkers. We analyzed metabolite profiles present in CSF after TBI and Subarachnoid Hemorrhage (SAH) stroke. We characterized patterns in CSF metabolites and physiological indicators in TBI and SAH patients with poor and good recovery outcomes. We are further utilizing detailed data obtained through CSF mass spectrometry to identify specific molecules that are significantly altered following TBI/SAH. Combining CSF data with other neuromonitoring assessments may be used to build robust predictive models for TBI/SAH prognosis.

19 **Prefrontal-Alpha Asymmetry as a Moderator Between Infant Temperament and Toddler Development**

**Presenter(s):** Elise Harris **Role(s):** Undergraduate student 11am–noon

**Author(s):** Elise Harris, Winnie Chang, Que Nguyen, Meghan Puglia

Identification of developmental delays in early childhood is crucial for timely intervention, and understanding underlying neurological and behavioral mechanisms can improve predictive development models. Prior research demonstrates individual relationships between infant temperament, frontal alpha asymmetry (FAA) measured via electroencephalography (EEG), and domains of toddler development. However, little is known about how all three variables interact and how FAA might moderate these interactions. This study examines early indicators of developmental differences by integrating temperament, neurological, and developmental variables to deepen our understanding of early indicators of developmental differences. At 12 months, participants (n=35) underwent an EEG paradigm to assess FAA and completed the IBQ-R temperament questionnaire. At 24 months, participants returned to the lab to complete the Bayley-4 developmental assessment. Statistical analyses explore the relationships between EEG, IBQ-R, and Bayley-4 data to evaluate their multivariate interaction. Contrary to the hypothesis, we found significant relationships between positive temperament and right-frontal activation ($\beta$ = -1.20, p = .03), as well as between high adaptive-behavior developmental functioning and right-frontal activation ($\beta$ = -21.03, p = .05). Additionally, no moderation effects were observed among the three variables, also contradicting the hypothesis. These results highlight the need for further exploration of other factors that may contribute to the neurological and behavioral mechanisms underlying developmental differences.

20 **Co-Morbid Seizures in Frontotemporal Dementia: What Do They Tell Us?**

**Presenter(s):** Syeda Amrah Hashmi **Role(s):** Research Fellow noon–1pm

**Author(s):** Syeda Amrah Hashmi, Jaideep Kapur, Mark Quigg, Anelyssa D'Abreu, Carol Manning, Ifrah Zawar

Rationale: Seizures are associated with accelerated cognitive decline in dementia. Comorbid seizures are common in Frontotemporal dementia(FTD) yet remain understudied. This retrospective, single-center study investigated the risk factors, characteristics, and outcomes of FTD patients with(FTD+SZ) and without seizures(FTD-SZ).

Methods: All patients coming to our hospital with clinically-diagnosed FTD from 2011-2024 were classified into 1)FTD+SZ) and2)FTD-SZ. FTD+SZ was defined as having any seizure observed. FTD was classified into behavioral-variant FTD(bvFTD),sematic-variant-primary-progressive aphasia(svPPA) or non-fluent-primary-progressive-aphasia(nfPPA). Data on baseline demographics, seizure characteristics, and outcomes were obtained from EMR. Data were analyzed using Pearson's Chi-squared test, fisher exact test, or t-tests.

Results: Of 326 FTD patients(average age of dementia onset=64+9years, 46% female) who met the inclusion criteria, 10%(N=33) had seizures. The average age of seizure-onset was 63+13years in FTD+SZ. Traumatic brain injury(TBI) was the only significant risk factor for seizures in FTD(FTD+SZ=8 (24%) vs FTD-SZ=18(6%), p<0.001). All other characteristics were comparable among the groups. bvFTD was more prevalent in FTD+SZ compared to FTD-SZ(58% vs 50%). Of these, 16(48%) had epilepsy, seven (21%) had one-time unprovoked seizures, and seven(21%) had provoked seizures due to secondary causes. Fourteen(42%) patients had focal-epilepsy, 11(33%) had generalized-epilepsy, and epilepsy type was unknown for the remaining 8(24%) patients. Five(36 %) patients with focal epilepsy were diagnosed with temporal-lobe-epilepsy. For patients with focal epilepsy, 12(86%) patients had focal seizures with impaired awareness, 3(21%) of whom experienced secondary generalization. Twenty-five(76%) achieved control on ASMs and seizures self-resolved in the remaining 8(24%)FTD+SZ.

Conclusions: Around 10% of FTD patients experience seizures. TBI was the most frequent risk factor associated with seizures in FTD. Seizures are more commonly associated with the behavioral variant of FTD. In FTD, focal epilepsy is most common, with temporal lobe epilepsy being the most prevalent subtype. The majority achieved seizure control. While not uncommon, seizures in FTD have a favorable outcome.

21 **TEST-RETEST RELIABILITY: PH-BASED STRUCTURAL CONNECTIVITY**

**Presenter(s):** Xin He **Role(s):** Undergraduate student noon–1pm

**Author(s):** Xin He

Reliable brain connectivity features are essential for reproducible neuroscience research. This study applies Persistent Homology (PH), a topological data analysis method, to evaluate the test–retest reliability of structural brain network features. Using data from the HCP-Development dataset, we analyzed structural connectivity matrices from 636 participants, including 635 with retest scans.

For each subject, we computed three PH-based metrics: Backbone Strength (BS), Backbone Dispersion (BD), and Cycle Strength (CS). These features describe the strength, dispersion, and cyclicity of connectivity patterns. We then assessed test–retest reliability using Intraclass Correlation Coefficient (ICC) analysis with a two-way random-effects model.

Our results show that Backbone Dispersion (BD) exhibited excellent reliability (ICC = 0.924), followed by BS (0.770) and CS (0.708). These findings suggest that PH-derived features, particularly BD, provide stable representations of structural brain organization, while CS may reflect more variable, state-dependent properties.

22 **Susceptibility Source Separation MRI Development for Mouse Brain Applications**

**Presenter(s):** Timothy Ho **Role(s):** Graduate student 11am–noon

**Author(s):** Timothy Ho

Recent advances in Susceptibility Source Separation (SSS) Magnetic Resonance Imaging (MRI) algorithms have improved the ability to analyze diamagnetic calcium and paramagnetic iron susceptibility sources, offering new opportunities to study disease progression for neurological disorders. Histologically, calcium and iron not only serve as key biological markers but also as major contributors to MRI contrast. The objective of this study is to develop MRI methods to investigate the progression of neurodegenerative disease in the murine brain. We propose a series of advancements in MRI techniques, spanning hardware improvements, pulse sequence development, and post-processing data analysis. Current methodologies suffer from low spatial resolution, long acquisition times, and inaccurate separation of paramagnetic and diamagnetic sources. Specifically, the overarching goal is to address three challenges in current preclinical imaging protocols: first, the development of custom MRI coils to improve sample signal coverage; second, the implementation of accelerated data acquisition protocols to produce more accurate results while facilitating clinical translation; and third, the validation of algorithms evaluating the paramagnetic and diamagnetic properties of different regions of the murine brain. This proposed work is significant for advancing our understanding of the underlying mechanisms of neurodegenerative disorders. Beyond its immediate application to neurodegenerative disease models, the methodologies could be adapted to study a wide range of neurological conditions, such as Alzheimer's disease, Parkinson's disease, and traumatic brain injury. Ultimately, our research strives to bridge the gap between the histological properties of the brain and the mechanisms of neurodegenerative diseases in a preclinical setting.

23 **Impact of Gestational Age at Birth on Functional Connectivity of Memory and Inhibitory Control Systems in Preterm Neonates: Whole-Network Analysis**

**Presenter(s):** Ava Hogan **Role(s):** Research Assistant noon–1pm

**Author(s):** Ava Hogan*, Gabby Snetkov*, Mia Tan*, Grace Flynn*, Analia Marzoratti, Anna Youngkin, Tanya Evans PhD

*equal contributions

This study investigates the impact of gestational age (GA) at birth on the functional connectivity (FC) of brain regions related to declarative memory and inhibitory control in preterm (PT) neonates. Using resting-state functional MRI (rsfMRI) in a multiple linear regression model, FC was examined between the hippocampus and somatomotor network, associated with declarative memory, and the anterior cingulate cortex (ACC) and default mode network, related to inhibitory control. Results suggest that FC between these regions varies with GA at birth, potentially contributing to cognitive and behavioral outcomes later in life, such as difficulties in attention and emotional regulation. Further, these results highlight the heterogeneity of the PT population and suggest that early alterations in brain connectivity may serve as biomarkers for neurodevelopmental challenges. This study underscores the need for early interventions targeting memory and cognitive control systems to support developmental outcomes of PT infants.

24 **Assessment of extracellular matrix and perineuronal nets in epilepsy**

**Presenter(s):** Silky Hou **Role(s):** Staff 11am–noon

**Author(s):** Silky Hou, Bhanu P. Tewari, Harald Sontheimer

Perineuronal nets (PNNs) are highly organized extracellular matrix (ECM) condensations that normally envelop inhibitory neurons and regulate synaptic plasticity. Previously we have reported profound disruption of PNN in mice cerebral cortex and hippocampus in glioma-associated and brain infection-induced models of epilepsy. In the present study, we sought to systematically analyze the changes in ECM and PNNs after acute status epilepticus and chronic epilepsy to understand the role of ECM and PNN in epileptogenesis. We induced acute seizures in C57BL/6 mice by injecting either pilocarpine or Theiler's murine encephalomyelitis virus and dissected mice brains after 7 days and 45 days of acute seizure induction. Using a combination of markers including NeuN and PV for neurons, and WFA and Aggrecan for PNNs, we performed immunohistochemistry and confocal imaging on PFA fixed brain sections obtained from acute and chronic seizure groups. We observed a continuum of changes in the PNNs ranging from subtle structural defects to pronounced loss of PNNs in the cerebral cortex and hippocampus. We also observed an upregulation of PNNs and interstitial ECM in several brain regions after the acute phase. Subsequently, in the chronic phase, some of these changes persisted while others reverted in different brain regions. These observations suggest an involvement of ECM and PNN in epileptogenesis. However, further studies are needed to understand whether and how these changes impact the process of epileptogenesis.

25 **Axonal spheroid engulfment by phagocytic glia regulates axon degeneration**

**Presenter(s):** Sarah Hunter-Chang **Role(s):** Graduate student noon–1pm

**Author(s):** Sarah Hunter-Chang, Tanvika Vegiraju, Charlene Kim-Aun, Brynn Manke, Christopher Deppmann*, Sarah Kucenas* *Co-corresponding authors

Neurodegeneration and axonopathies are driven by axon degeneration, which in turn can be influenced by glial responses. Phagocytic glia contribute to breakdown by engulfing axonal material exposing a phosphatidylserine (PS) “eat me” signal. Seemingly in contrast, recent studies found that professional phagocytes, macrophages, can slow axon degeneration. Here, we seek to elucidate an axon-protective phagocytic pathway targeting axonal spheroids, bubble-like swellings ubiquitous on degenerating axons, using a zebrafish peripheral nerve injury model and complementary in vitro neuron-macrophage co-cultures. We first confirmed the protective effects of macrophages in both models. We then tested whether engulfment is required for protection, with ongoing studies using PS receptor-deficient macrophages in vitro and PS binding inhibitors in vivo supporting this requirement. We next identified spheroids as targets for selective macrophage engulfment, and our preliminary studies indicated that spheroid engulfment inhibits pro-degenerative factor release. Collectively, these studies demonstrate that macrophages slow axon degeneration by engulfing spheroids. However, because only a subpopulation of macrophages were seen contacting spheroids in vivo and because we previously found that SCs can also eliminate spheroids, we hypothesized that SC ablation in vivo would also hasten axon degeneration. Surprisingly, there were no differences in axon degeneration rates between SC conditions, but macrophages were increasingly phagocytic in the absence of SCs, indicating possible compensation. Therefore, spheroid engulfment by a range of professional and unprofessional phagocytes may represent a novel regulatory mechanism in axon degeneration.

26 **Mechanisms of Sudden Death in a Mouse Model of Tuberous Sclerosis Complex**

**Presenter(s):** Marissa Incer **Role(s):** Staff noon–1pm

**Author(s):** Marissa C. Incer, BS; Ian C. Wenker, PhD

Seizures are a key feature of Tuberous Sclerosis Complex (TSC), and sudden unexpected death in epilepsy (SUDEP) is the most common cause of death. However, little is known about the underlying mechanisms of SUDEP in this population. We have previously shown early fatality in a Scn8a mouse model of epilepsy is due to seizure-induced apnea (SIA). Therefore, we hypothesize that SIA is the cause of SUDEP in two commonly used mouse models of TSC: fl-Tsc1; Syn1-Cre and fl-Tsc1; GFAP-Cre . Mice underwent surgery to implant headsets that chronically record electroencephalogram (EEG) and electrocardiogram (ECG). After recovery, the mice were placed in whole-body plethysmography chambers to record breathing. All biosignals and footage were analyzed in LabChart 7 and Spike2. Both mouse strains routinely displayed seizures that included spike wave discharges (SWD), convulsions, and altered breathing and cardiac function. Not all seizures were presented with SWD despite convulsions and rearing still occurring. Eventually, the mice experienced a fatal seizure. We detected an SIA during the tonic phase of fatal seizure in a fl-Tsc1; GFAP-Cre mouse but were unable to in the fl-Tsc1; Syn1-Cre mice. The mechanism of death in fl-Tsc1; GFAP-Cre mice appears similar to that of previous mouse models where SIA is initiated during the tonic phase and breathing does not recover, leading to death. Additionally, some fl-Tsc1; Syn1-Cre mice displayed a trend where heart rate decreases before dramatically increasing before death. Once the mechanism of SIA is better understood, more targeted treatments can be developed to help TSC patients.

27 **Hummingbird-HOPE Pilot Study: Measuring Hope in the Context of Progressive Illness**

**Presenter(s):** Anna Jesus **Role(s):** Faculty 11am–noon

**Author(s):** Areesheh Khan; Anna Jesus MD, MBE; Sarah Jones, MD; Erin Plews-Ogan, MD, MPH; Margaret Plews-Ogan, MD, MS; Rebecca J. Scharf, MD, MPH

Background: Living with a progressive neuromuscular disease comes with significant medical burden, but may also present an opportunity for learning and adaptability that may be under-recognized. This pilot study aims to recognize the positive attributes patients gain while navigating medical complexity.

Study Participants & Setting: The survey was distributed in neuromuscular clinics at a university hospital. Results were analyzed for 44 respondents between June and October 2024. The ages of the participants ranged from 5 – 72 years old.

Materials / Methods: The Turbocharged Living Scale was created by Drs. Jim and Peggy Plews-Ogan with the aim of recognizing new skills such as hope, adaptability, and resilience gained with neuromuscular disease. This pilot study adapted this survey into three versions: 1) Adults/ Adolescents; 2) Youth/ Children; and 3) Caregivers. Four post-survey questions using a 5-point Likert scale (strongly disagree to strongly agree) were implemented to quantify patient perceptions. Data from each question were combined into three nominal categories of Agree, Neutral, and Disagree.

Results: The most common response from patients was “Agree” for all post-survey questions. 36% of participants reported they were never asked about their personal strengths prior to this survey and 58% wished there was a way to document the skills they have gained. We recorded a variety of responses that included concepts of resiliency, hope, and adaptive skills.

Conclusion: Turbocharged Living Scale may help foster conversation between patients, caregivers, and healthcare providers around these skills and the perspective that comes with living with a progressive neurological condition.

28 **Role of hippocampal perineuronal nets in social memory in mice.**

**Presenter(s):** Bhadra Kadangal & Evelyn Gouldin **Role(s):** Undergraduate students noon–1pm

**Author(s):** Bhadra Kadangal*, Evelyn Gouldin*, Lata Chaunsali, Bhanu P. Tewari, and Harald Sontheimer

* These authors contributed equally.

Perineuronal nets (PNNs) are highly organized condensations of the extracellular matrix (ECM). PNNs restrict synaptic plasticity by stabilizing neuronal connections. Consequently, PNNs contribute to memory regulation. While PNNs primarily encase GABAergic interneurons, in the CA2 area of the hippocampus, PNNs also surround excitatory pyramidal neurons. The CA2 area regulates social memory, an important form of memory necessary for engaging in social interactions and maintaining relationships. Due to the implication of PNNs in synaptic plasticity and the role of the CA2 region in social memory, we hypothesized that CA2 PNNs influence social memory processes. The baseline social memory of adult C57BL/6 mice was assessed using a direct interaction behavior task. CA2 PNNs were then disrupted by injecting the bacterial-derived enzyme chondroitinase ABC, and subsequent social memory was assessed using the same behavior task. We confirmed CA2 PNN digestion using immunohistochemistry and confocal imaging techniques. Compared to penicillinase-injected control mice, we observed disrupted social interaction behavior of mice upon PNN digestion. Enzymatic digestion of PNNs is temporary and PNNs reform within days. Given this, we assessed whether social interaction behavior returns to baseline 14 days post-injection with regrowth of PNNs. Indeed, our data indicates that PNN regrowth reinstates normal social interaction behavior. Our results suggest that CA2 PNNs are a critical component of social memory functions. These findings are pertinent to Alzheimer's disease and other neurodegenerative diseases in which PNN loss may cause social memory deficits.

29 **Predicting Neurodevelopmental Outcomes in Preterm Infants Using Maternal-Neonatal Determinants and Perinatal Interventions During Neonatal ICU Admission**

**Presenter(s):** Zoë Kitchings **Role(s):** Undergraduate student noon–1pm

**Author(s):** Zoë G. Kitchings, Madelyn G. Nance, Winnie Chang, Meghan H. Puglia

The critical care that infants and their birth parents receive during gestation and parturition shape life-long developmental mechanisms and moderate the impact of pre-existing medical conditions within the mother-infant dyad. The complex processes by which delivery method, modifiable perinatal interventions, and inherent medical determinants influence social-emotional maturation are not fully understood. This study aims to identify clinical factors associated with an increased risk of developmental delay to optimize neonatal care and direct future research. We extracted data from 63 preterm infants' electronic health records, including maternal obstetric history, perinatal data, and relevant diagnoses during an initial admission in UVA's Neonatal Intensive Care Unit (NICU). At 22-26 months corrected age, participants completed the Bayley Scales of Infant Development (BSID) and Autism Diagnostic Observation Schedule (ADOS). Extracted infant health metrics were utilized in iterative regression modeling to predict BSID and ADOS scores. To evaluate the predictive accuracy of optimized models, we utilized confusion matrices. 44 infants (70%) were born via cesarean section and 22 (35%) had behavioral ratings indicating risk of developmental delay. The optimized model predicted BSID behavioral rating with 81% accuracy and ADOS score severity with 57% accuracy. Significant interactions were observed with delivery methods such that cesarean sections were associated with lower performance on neurodevelopmental assessments. These results suggest a potential influence of delivery method on long-term cognitive development in premature infants. Further study is needed to elucidate underlying mechanisms and ensure the current understanding of cesarean safety, which primarily emphasizes respiratory outcomes, also considers potential long-term neurodevelopmental effects.

30 **Self-Reported Valence and Arousal Responses to Neutral Visual Stimuli are not Influenced by Preceding Exposure to Positive or Negative Tactile Stimuli**

**Presenter(s):** Lauryn Kumpe **Role(s):** Undergraduate student noon–1pm

**Author(s):** Lauryn G. Kumpe, Meghan H. Puglia, Madelyn G. Nance

People's arousal and valence states can fluctuate in reaction to external experiences. The Open Affective Standardized Image Set (OASIS) offers a database of images that previous research has shown are reliable in eliciting a consistent, specific emotional response in viewers while the International Affective Digitized Sounds (IADS) provides an auditory database of sounds that similarly provokes consistent emotional responses. Using a selection of stimuli from each database with positive, neutral, or negative valences, we compared participants' behavioral and physiological responses to our own collection of tactile stimuli in order to begin to establish a standardized tactile database. Focusing on the self-reported behavioral responses to neutral visual stimuli that directly followed a tactile stimulus, the reports show that participants' visual self-reports are not statistically significantly influenced by a preceding positive, neutral, or negative tactile experience. These findings may indicate that the self-reported behavioral reactions to varying stimuli are not at risk of being skewed by the valence or arousal factor of previous stimuli.

31 **MEK signaling as a therapeutic vulnerability of KRAS-driven somatic brain arteriovenous malformations**

**Presenter(s):** Gabrielle Largoza **Role(s):** Graduate student 11am–noon

**Author(s):** Gabrielle E. Largoza, Matthew R. Hoch, Richard J. Price, Joshua D. Wythe

Brain arteriovenous malformations (bAVMs) are abnormal, direct connections between arteries and veins that bypass normal intervening capillary vasculature, resulting in tissue hypoxia and cell death. Furthermore, these fragile, dilated, and tortuous vascular anomalies form pathologic shunts between high-pressure arteries and low-resistance veins, making bAVMs a major cause of hemorrhagic stroke in young adults and children. While open surgical resection remains the standard treatment, approximately 20% of patients are ineligible due to excessive risk, underscoring the need for alternative therapeutic strategies .

Our sequencing of bAVM patient samples identified somatic KRAS gain-of-function mutations. Further in vitro studies demonstrated that mutant KRAS preferentially signals through the MAPK/ERK cascade, establishing it as a promising therapeutic target. While previous work has demonstrated that MEK inhibition can prevent bAVM formation, the more translationally relevant question of whether MEK inhibition can stabilize or regress pre-existing bAVMs remains unknown.

To investigate this, we developed a postnatal mouse model whereby endothelial-specific expression of mutant KRASG12D is induced via focal 4-OHT injection while bAVM formation and progression is monitored longitudinally via time-of-flight MRI-assisted angiogram. AI-guided analysis of 3D imaging suggest that the FDA-approved MEK inhibitor, trametinib, may stabilize and regress bAVMs in mice, with findings further supported by off-label compassionate use in a small pediatric cohort. Moreover, higher resolution tissue clearing and 3D imaging of these vascular malformations in our preclinical murine model has revealed key alterations in cellular dynamics, including defects in cell polarization and junctional stability, which may drive the extensive pathologic vessel remodeling observed in bAVM patients.

32 **Oligodendrocyte tmem125b Regulates CNS Myelin Targeting and Growth**

**Presenter(s):** Andrew Latimer **Role(s):** Staff noon–1pm

**Author(s):** Andrew J. Latimer, Rebecca Wu, Sarah Kucenas

Efficient nervous system function in vertebrates is achieved by ensheathment of axons by myelin. Not every axon is myelinated, however, and cell structures such as dendrites and soma remain unmyelinated. How appropriate axon targets are selected, myelin sheaths become stabilized and grow and excess and ectopic myelination is corrected is incompletely known, but recent studies have begun to identify molecules that regulate these stages of myelin sheath formation. The myelin proteome consists of more than 1,000 proteins, most of which remain unstudied. We performed RNA-sequencing to identify new genes that regulate developmental myelination in zebrafish and found that tmem125b is highly enriched specifically in myelinating oligodendrocytes (mOLs). Tmem125 is also expressed in mouse mOLs, suggesting a conserved function during vertebrate CNS myelin development. We used CRISPR/Cas9 to generate tmem125b mutant alleles and found that in tmem125b mutant embryos myelin sheaths are shorter and myelin inappropriately wraps neuronal cell bodies. Cell body wrapping increases through larval stages, but surprisingly it decreases as juvenile development progresses. We are currently focused on determining how tmem125b regulates proper myelin targeting and growth, but are further interested in learning the mechanisms that correct myelin mistargeting in mutant embryos.

33 **Art of Brain Data: Neurodiversity Through Aesthetic Data Visualization**

**Presenter(s):** Siwen Liao **Role(s):** Undergraduate student 11am–noon

**Author(s):** Siwen Liao

Data is not merely a collection of numbers — it is a dynamic medium which, when transformed into art, can reveal the profound beauty and complexity concerning the human brain. Historically, research has highlighted a notable disparity in ASD diagnoses, with males being diagnosed significantly more frequently than females. By re-envisioning data as art, the gap between rigorous scientific inquiry and creative expression is bridged, offering a fresh perspective on gender differences among individuals with and without Autism Spectrum Disorders (ASD) where data becomes a bridge that inviting viewers to engage with and reflect on the intricacies of brain structure. Drawing on over 300 3D brain surface models from the Autism Centers of Excellence (ACE) study, our approach blends advanced MRI neuroimaging, multivariate statistical analysis, and cutting-edge 3D printing technology. MRI-derived brain data was taken and used with Linear Discriminant Analysis (LDA) to reduce dimensionality, classify the data into groups, and transform these insights into physical 3D-printed brain models. Our result is a physical visualization of the brain data where each sculpture serves as a tangible narrative, celebrating both the subtle and striking differences between male and female brains, whether neurotypical or affected by ASD. By embracing "data as art," we encourage a more holistic understanding of neurodiversity; an understanding that not only informs but also resonates on an emotional and aesthetic level.

34 **Maternal Bonds: Could Postpartum Depression Affect Infant Development?**

**Presenter(s):** Katherine Littlejohn **Role(s):** Undergraduate student 11am–noon

**Author(s):** Katherine Littlejohn

Postpartum depression is when a mother faces long-term depression symptoms following the birth of their infant that may last up to a year. Wanting to study the emotional connection between a mother and child, my goal was to use the Bayley language assessment scores of the infant with the caregiver's Edinburgh Postnatal Depression Scale to determine if there was a correlation between the two variables. I hypothesized that the variables have a negative correlation, as one of the depression symptoms is emotional distance, and I wanted to see if that had any effect on development. The Edinburgh Postnatal Depression Scale consists of a series of experience-based questions that the caregiver completes at their first visit (6-8 weeks after a baby is born). The Bayley assessment is completed by the infant at around two years of age at the family's second visit. As a result, the study uses longitudinal data. I ran a correlation test using Excel and discovered that there was no correlation between the variables: r- squared = 0.003. This was the desired outcome, as it provides evidence that the variables are independent of one another. For future studies, I would like to compare the results of direct interaction between the mother and child with the Bayley scores, as I believe this would provide clearer results of their connective development. For example, a mother's tone or word choice with their child could affect their developing language skills.

35 **P2RY12 REGULATES MICROGLIAL IMMUNO-METABOLIC STATES**

**Presenter(s):** Aida Lopez **Role(s):** Graduate student noon–1pm

**Author(s):** Aida Lopez

Microglia are the resident immune cells of the CNS and are integral to maintaining homeostasis. In disease, microglia are powerful mediators of neuroinflammation. Understanding the molecular pathways involved in microglial function is pivotal for advancing neurobiological research and developing effective strategies for CNS disorders. In this context, P2RY12 is a G protein-coupled receptor (GPCR) that is enriched in microglia in the brain parenchyma and is part of the transcriptional signature of homeostatic microglia. Conversely, P2RY12 is downregulated in many neurological conditions.

In our study, we compared the transcriptional profiles of P2RY12 knockout (KO) microglia to wild-type (WT) microglia. Our results revealed significant upregulation of genes involved in immune signaling and metabolic regulation in P2RY12-deficient microglia, including the key metabolic regulator PGK1, which plays a role in glycolysis and energy production.

We also examined the response of P2RY12-deficient microglia to LPS-induced inflammation. In WT microglia, LPS treatment upregulated key genes involved in the oxidative stress response. However, in P2RY12KO microglia, these genes showed minimal induction, indicating a dysfunctional antioxidant response. This suggests that P2RY12 is required for mounting a robust antioxidant response and for the proper management of oxidative stress during microglial immune activation.

These results highlight the critical role of P2RY12 in regulating microglial immune and metabolic responses under both homeostatic and inflammatory conditions, providing insights into its involvement in CNS pathophysiology.

36 **Neural correlates of language acquisition in infancy**

**Presenter(s):** Beverly Lundeen **Role(s):** Undergraduate student 11am–noon

**Author(s):** Beverly Lundeen, Cabell Williams, Allison Baines, Winnie Chang, Que Nguyen, Meghan H. Puglia

Delays or difficulties in language ability are associated with a range of disorders in children and adults; thus, it is crucial to investigate the neurological basis of language acquisition in infancy to understand cognitive outcomes. Power spectral density (PSD) is used to analyze the frequency of neural activity recorded by electroencephalography (EEG). Higher frequencies such as the beta and gamma waves are associated with active cognitive processing. This study aims to analyze whether PSD in beta and gamma bands in brain areas responsible for language processing during infant engagement in an auditory listening task would positively predict language ability in toddlerhood. At eight months of age, two independent samples of infants underwent EEG recordings while listening to speech and nonsocial auditory stimuli. At 16 months of age for one sample (N=32), parents completed the Infant Behavioral Questionnaire and the Infant Developmental Checklist to assess language ability. At 24 months of age for the second sample (N=28), infants completed a language assessment via the Bayley-4 Scales for Infant and Toddler Development and parents completed a Bayley-4 questionnaire. A linear regression analysis revealed a significant positive association between beta power at eight months in language regions and Bayley-4 language scores at 24 months in sample two ($\beta$=15.70, p=.027, adjusted $R^2$=0.14). No significant relationships were found in the gamma band or in either wave band for sample one. These results provide insight into the neurological underpinnings of early language acquisition which may inform predictive developmental models.

37 **Effect of Endothelial Cells on Oligodendrocyte Progenitor Cell Morphology**

**Presenter(s):** Joseph Maliakkal **Role(s):** Graduate student 11am–noon

**Author(s):** Joseph Maliakkal, Samuel Agro, Kyle J. Lampe, Lakeshia J. Taite

Remyelination requires oligodendrocyte progenitor cells (OPCs) to migrate to the site of demyelination, differentiate into oligodendrocytes, and deposit myelin. This process, however, is often ineffective. Endothelial cells (ECs) have been shown to influence OPC proliferation and migration. Further understanding the interactions between these two cell types could lead to therapeutic remyelination strategies by regulating OPC behavior. As OPC differentiation is presaged by changes in morphology, in this study, we investigated the effect of ECs on OPC morphology.

OPCs were cultured in four different conditions: OPC media, Endothelial Growth Medium-2 (EGM), conditioned EGM (collected after culturing ECs in EGM for a day), and co-culture with ECs in EGM. Morphological features (area and form factor ((4*pi*area)/perimeter^2 )) of OPCs in the different conditions were significantly different. The difference between OPC cultures in OPC media and EGM is likely to be due to serum present in EGM. The differences between the cultures in EGM and conditioned EGM indicate that signaling molecules secreted by ECs and present in the conditioned media cause a change in OPC morphology. For the OPCs co-cultured with ECs, the morphology was different. However, this condition had a much larger number of cells and contact inhibition of the cells could have affected OPC morphology. The results indicate that soluble signals secreted by ECs influence OPC morphology, potentially affecting their behaviour, especially differentiation. Further studies will examine specific differentiation markers.

38 **Deciphering the role of tenascin-n in peripheral spinal motor nerve development**

**Presenter(s):** Charles Marcucci **Role(s):** Graduate student 11am–noon

**Author(s):** Charles G. Marcucci, Coleman Blanton, Andrew J. Latimer, Sarah C. Kucenas

Peripheral motor nerves are an integral component of the nervous system comprised of many diverse cell types. Congenital disorders, degeneration, and injuries that lead to peripheral neuropathies can severely affect quality of life. Current, treatment strategies for these conditions primarily focus on pain management and physical therapy. With a more complete understanding of how peripheral motor nerves are assembled during development, we could design more effective treatment strategies that would facilitate regeneration of damaged nerves. An understudied component of peripheral motor nerves are perineurial glia (PG), a central nervous system (CNS)-derived cell that forms the perineurium of peripheral motor nerves, a layer critical for blood-nerve-barrier function. PG are integral to ventral motor nerve assembly as disruption of PG specification results in aberrant motor nerve formation. To begin to uncover the molecular mechanisms that drive these processes, I mined transcriptomic data generated by our lab and found that tenascin-n (tnn) is one of the highest differentially expressed genes in PG. Tenascins, a family of extracellular matrix glycoproteins, are crucial during neurodevelopmental; more specifically a tnn family member, tnc, is involved in motor axon outgrowth in zebrafish. Therefore, I hypothesized that tnn is vital for peripheral spinal motor nerve assembly. I have defined the expression dynamics and continue to investigate the functional role of tnn in zebrafish ventral motor nerve assembly. These experiments will shed light on a novel, fundamental role for tnn in neurodevelopment and have the potential to inform the design of future therapeutic strategies to repair peripheral motor nerves.

39 **The Influence of Feeding Type on Infant Sootheability: Investigating Physical, Auditory, and Visual Soothing Methods**

**Presenter(s):** Jessica Medlin **Role(s):** Undergraduate student noon–1pm

**Author(s):** Jessica Medlin; Meghan H. Puglia, PhD

The role of infant feeding methods—such as breastfeeding and formula feeding—have been a focal point in developmental psychology and neurology, with numerous studies examining how different feeding practices might influence various aspects of early development, including soothing behaviors. Soothability, or the ability to calm in response to discomfort or stress, is an essential aspect of infant well-being, particularly in the first six months when infants are highly dependent on caregivers for emotional regulation. This study aims to determine whether breastfeeding corresponds to sootheability in a sample of 89 four-month-old infants. Further, we investigate any possible differences in soothability based on physical, auditory, and visual modes of soothing. Parents reported the proportion of weekly meals an infant was fed via breastfeeding, expressed breast milk, and formula, and completed the Infant Behavioral Questionnaire, a measure which includes infant and delayed infant sootheability. We hypothesize that breastfed infants will exhibit higher immediate soothing scores and lower delayed soothing scores compared to the formula-fed infants. Further, we hypothesize that physical touch will have the greatest impact on soothing, especially for breastfed infants. This research will provide valuable insights into early caregiving strategies and the role of different soothing modalities.

40 **Electrochemical detection of serotonin in sert mutant Drosophila larvae**

**Presenter(s):** Emily Miller **Role(s):** Graduate student 11am–noon

**Author(s):** Emily Miller, B. Jill Venton

Drosophila melanogaster is an excellent model to study the effect of diseases such as depression and Parkinson's on the dynamics of neurotransmitters. 5-Hydroxytryptamine (5-HT), or serotonin, is a neurotransmitter associated with neurological diseases such as depression. These diseases can occur from dysregulation of serotonin transporters (SERT) not allowing for the reuptake of serotonin to occur efficiently. Selective serotonin reuptake inhibitors (SSRIs) are the most prescribed antidepressants, blocking SERT to increase the amount of circulating serotonin. The goal of this study is to understand the effect of sert on the dynamics of serotonin release. Two mutant fruit fly lines, dSERT16 and dSERTΔ3.9 are electrochemically tested to determine the affect these genetic mutations have on the real-time reuptake of serotonin. dSERT16 is a partial loss of function mutant with the promotor region of the DNA removed that codes for dSERT. dSERTΔ3.9 is a complete loss of function mutant, with removal of the dSERT coding sequence. dSERTΔ3.9 slows reuptake of serotonin significantly, and the serotonin does not go back to baseline with t50 unable to be calculated after 30s. It is expected that dSERT16 will also slow reuptake but not as substantially as there is still possibility of SERT being present. Future directions of this project include the testing of these mutations and wild type fly on SSRIs like escitalopram to determine the effect when sert is mutated. Other smaller mutations in the sert gene could also be tested to detect how that influences SSRI efficacy.

41 **Alterations in Perineuronal Nets within the Hippocampal CA2 Region are Associated with Age-Related Social Memory Dysfunction**

**Presenter(s):** Jacqueline Moats **Role(s):** Graduate student noon–1pm

**Author(s):** Jacqueline M. Moats, Katherine Sponaugle, Jessica M. Kilmer, Elise C. Cope

Aging is accompanied by several non-pathological brain changes that, even in the absence of disease, deleteriously influence cognitive capacities. One of the lesser-known cognitive deficits associated with aging is impairments in social memory, or the inability to recognize and remember previously encountered individuals. To investigate this, we compared social memory in young (3-month-old) and aged (18-month-old) mice. Aged mice failed to recognize recently encountered conspecifics but retained intact long-term memories of their cagemates, suggesting that aging selectively impairs recent, but not remote, social memory. The CA2 region of the hippocampus, an area critical for social memory processing, contains a high abundance of perineuronal nets (PNNs)—condensed forms of extracellular matrix that surround certain neurons, limiting their plasticity. In the CA2, PNNs are found surrounding both excitatory and inhibitory cells, and disrupting CA2 PNNs impairs social memory. Here, we used the plant-based lectin Wisteria floribunda agglutinin (WFA) to examine PNNs and observed a robust age-related reduction in WFA+ PNNs within the CA2, with a decrease within the CA2 covered in WFA+ PNNs. Since CA2 PNNs surround PCP4-labeled excitatory pyramidal cells and PV+ inhibitory interneurons, we next analyzed these populations separately. We found a decrease in WFA+ PNN intensity in both populations, with a more pronounced decrease in PCP4+ cells. These findings demonstrate that CA2 PNNs are diminished with advanced age and suggest their disruption may contribute to age-related impairments in recent social memory. Ongoing work is examining additional hippocampal CA2 PNN components to further clarify their role in social memory decline.

42 **Characteristics of Subclinical Rhythmic Electrographic Discharges Of Adults (SREDA)**

**Presenter(s):** Sebastian Moeller Rivera **Role(s):** Undergraduate student noon–1pm

**Author(s):** Sebastian Moeller Rivera; Clara Dowadu, MD; Brianna Bagalkotkar, MD; Nathan B. Fountain, MD

Subclinical rhythmic electrographic discharges of adults (SREDA) is a benign EEG variant that mimics seizure activity but is not associated with seizures or any underlying pathology. Although important to recognize, it is rarely reported in the literature. This study aims to determine the incidence of SREDA in a retrospective electroencephalogram (EEG) analysis. We searched EEG reports and electronic medical records of 152,314 EEGs and found 11 patients with EEG reports mentioning SREDA. We reviewed EEGs and reports to confirm the presence of SREDA, determine its characteristics, and identify any additional EEG abnormalities. We also examined the patients' medical comorbidities, the reasons their referring physicians requested EEGs, and whether the patients were later diagnosed with epilepsy. We conclude that SREDA is a rare EEG pattern (0.00009% prevalence rate) and that is important to recognize as distinct from seizure activity to avoid unnecessary treatment.

43 **Role of IL12Rβ2 signaling on OPC differentiation and remyelination**

**Presenter(s):** Stephanie Moy **Role(s):** Graduate student 11am–noon

**Author(s):** Stephanie Moy, Andrea Merchak, Alison Curtis, Jakenzie Fletcher-Thrower, Farooq Khan, Alban Gaultier

Multiple sclerosis (MS) is a multifaceted, chronic disorder of the central nervous system in which the myelin sheath is destroyed due to an immune-mediated response. Despite decades of work, MS has no cure and remains a debilitating disease. Oligodendrocyte precursor cells (OPCs) are a glial subtype with the ability to differentiate into myelinating oligodendrocytes and replace the loss of myelin. The pathways that stimulate OPC differentiation toward remyelination are an emerging area of research in the development of therapeutics to combat MS and other demyelinating disorders. Mice deficient in IL-12 receptor beta 2, Il12rb2-/-, are highly susceptible to experimental autoimmune encephalomyelitis (EAE), an animal model of MS, suggesting a protective role of IL12Rβ2 signaling. IL-12 receptor mRNA transcripts have been shown to be expressed by Sox10+ cells which including the oligolineage, but the role of IL12Rβ2 signaling during remyelination has not been established. To test the effect of IL-12 signaling on OPC differentiation, we incubated primary OPCs from wildtype or Il12rb2-/- mice and found that Il12rb2-/- cultures do not differentiate compared to cultures from C57Bl/6J mice. Brains from 2-, 10-, and 24-week C57Bl/6J and Il12rb2-/- mice showed similar numbers of OPCs and oligodendrocytes, but Il12rb2-/- mice displayed greater demyelination 10 days-post-lysolecithin-mediated demyelination. Taken together, these results suggest that the absence of IL12Rβ2 signaling inhibits differentiation of OPCs into myelinating oligodendrocytes in vitro and may delay remyelination in vivo. Investigating IL12Rβ2 signaling on oligolineage cells may elucidate new pathways to promote OPC differentiation during demyelination.

44 **Targeted neuroprotection via lactate receptor, HCAR1, in neonatal hypoxic ischemic encephalopathy**

**Presenter(s):** Hannah Mulhern **Role(s):** Staff 11am–noon

**Author(s):** Hannah Mulhern, Maria Marlicz, Ellie Kain-Kuzniewski, Jaideep Kapur, Jennifer Burnsed

Background: Hypoxic ischemic encephalopathy (HIE) is a leading cause of neonatal death and neurodevelopmental deficits. There is a critical need for novel and adjuvant therapies, as the only available neuroprotective treatment for HIE is therapeutic hypothermia (TH). Recently, lactate, which is increased in the serum and brain after neonatal HI, was found to have a G protein-coupled receptor, hydroxycarboxylic acid receptor 1 (HCAR1) and direct signaling effects in the brain, including on neuronal excitability. A few studies have found that supraphysiologic doses of exogenous lactate may be neuroprotective in neonatal HI rodent models but the mechanism remains unknown. A direct agonist of HCAR1, dihydroxybenzoic acid (DHBA), would avoid off target effects possible with lactate.

Objective: To compare seizure burden in a neonatal HI mouse model after administration of DHBA vs. vehicle.

Methods: Postnatal day (p)9 C57Bl/6 mice underwent stereotactic cranial electrode implantation, then HI on p10 (unilateral carotid ligation+8%FiO2x60min). Mice were randomized to a single dose of DHBA (3g/kg, SQ) or vehicle solution (saline). Continuous video electroencephalography (EEG) was recorded for 30 minutes before, during, and 30 minutes after hypoxia and analyzed for seizures using LabChart Pro software. GraphPad Prism was used to analyze data using a 2-sided t-test.

Results: 16 mice were used, 4 died during hypoxia (3 DHBA group, 1 vehicle) and were excluded from analysis. Mean total seizure time in the DHBA group was significantly less than that in the vehicle group (DHBA 238.3±151.3 sec vs vehicle 1032±366.2; p=0.007; n=5 DHBA, 2 vehicle). Time to first seizure during hypoxia was not significantly different between the groups (DHBA 33.9±21.1sec vs vehicle 12.88±12.61sec; p=0.26).

Conclusions: Mice given a single dose of direct HCAR1 agonist, DHBA, experienced shorter total seizure time during neonatal hypoxia-ischemia. Ongoing work will further examine the potential neuroprotective effect of HCAR1 neuroprotection in neonatal HIE.

45 **Causal Analysis of Graph Signals for Brain Effectome Inference**

**Presenter(s):** Srikar Mutnuri **Role(s):** Graduate student noon–1pm

**Author(s):** Srikar Mutnuri, Aniruddha Adiga, Srinivasan Venkatramanan, Madhav V. Marathe

Understanding the directed interactions between brain regions is critical for analyzing neuro-degenerative diseases like Alzheimer's (AD). Traditional functional connectivity (FC) methods capture statistical associations but fail to infer causal relationships, limiting their ability to reveal structural disruptions in disease progression. In this exploratory work, we propose a causal graph inference and spectral analysis framework for EEG signals. Specifically, we leverage Granger causality and spectral graph methods to construct and analyze the effective connectome (effectome) of the brain. Our work reveals that AD networks exhibit lower algebraic connectivity ($\lambda 2$), reduced modularity (eigenvalue gaps), and increased structural sensitivity to perturbations, compared to healthy individuals. Additionally, we simulate diffusion processes on the inferred graph topology to model signal propagation, demonstrating disrupted information flow in AD-affected networks.

46 **Ciliary Gene Togaram1 Influences Brain Development**

**Presenter(s):** Clarissa Nassar **Role(s):** Graduate student 11am–noon

**Author(s):** Clarissa Nassar, Savera Shetty, Selena Akay, Sarah Khan, Noelle Dwyer

Joubert Syndrome (JS) is an autosomal recessive disorder characterized by a midbrain and hindbrain malformation, and it is part of a class of disorders known as ciliopathies. Ciliopathies are caused by mutations in genes that encode proteins related to the primary cilium, a microtubule-based sensory organelle that acts as a cellular antenna. Multiple single gene causative mutations have been found to cause JS, but the cause of this disorder remains unknown in many individuals. Homozygous TOGARAM1 mutations have been found in patients with JS and studies in model organisms have found structural and functional abnormalities when this gene was mutated. These data suggest that Togaram1 plays an important role in cilia formation, thus impacting brain development by hindering important developmental signaling pathways. To explore the role of Togaram1 in the developing mammalian brain, we are characterizing the gross morphology and cellular changes in a Togaram1 knockout mouse model. Our preliminary results indicate that Togaram1 KO animals have altered neural stem cell proliferation and abnormal localization and generation of neurons. These findings shed light on the function of Togaram1 within primary cilia and in neural stem cells. Ultimately, this research will improve the field’s understanding of different factors that influence mammalian brain development.

47 **Effects of early-life infection and immune signaling on neuroblast reactivation in Drosophila larvae**

**Presenter(s):** Omina Nazarzoda **Role(s):** Graduate student 11am–noon

**Author(s):** Omina Nazarzoda, Michelle L. Bland, Sarah E. Siegrist

Building a healthy adult brain is a complex process. Neural stem cell proliferation and differentiation to make neurons and glia, neuropil extension, and synaptogenesis followed by pruning depend on optimal nutrient, resource, environmental and genetic conditions. These processes are tightly regulated because errors can have severe impacts on the developing brain and consequent adult behavior. For example, infection and aberrant immune activation, especially early in development, is associated with disrupted growth and cognitive development in children. The fruit fly Drosophila melanogaster has been used extensively to study both neural development and immune signaling. From these studies we know that Drosophila neural stem cells, or neuroblasts, grow and proliferate in a nutrient-dependent manner through growth signaling pathways and give rise to the neurons and glia of the brain. Drosophila has two humoral immune pathways, Toll and Imd, and data from our labs show that chronic Toll signaling results in reduced larval growth and small adults. We hypothesized that an early-life infection would activate immune signaling in larvae and lead to disruptions to brain development. Indeed, infecting freshly-hatched larvae with Erwinia carotovora carotovora 15 (Ecc15) induces the antimicrobial peptide Drosomycin, a Toll pathway target. Feeding Ecc15 to freshly-hatched larvae delays neuroblast reactivation from quiescence by 24h compared to uninfected controls. Likely as a consequence of this delay, the infected

larvae have smaller brains than controls. Activating Toll signaling in the absence of infection also results in lower neuroblast proliferation rate. These results so far suggest that infection perturbs neural development, and the effects might be mediated by the immune system. Future work will be conducting RNAi experiments to silence components of immune pathways and assess the effects of infection on brain development. Our established larval infection model together with the expansive Drosophila genetic toolkit will enable us to unravel the biology of brain development and plasticity in response to early-life infection and immune signaling challenges.

48 **Digital Organoid: A Biologically Inspired Neural Network for Image Classification**

**Presenter(s):** Ethan Nelson **Role(s):** Graduate student noon–1pm

**Author(s):** Ethan Nelson, John Darrell Van Horn

Artificial Neural Networks (ANNs) and Spiking Neural Networks (SNNs) imitate the nervous system’s design of neurons (nodes) communicating through axons (edges). While SNNs improve upon ANNs by incorporating time dynamics in the model’s inputs, both methods do not capture the time dynamics of signals between neurons in the network. These dynamics have been shown to encode information in the brain, such as in audio processing. To capture these dynamics, we introduce the Digital Organoid, a spherical graph network that models the signals between neurons as traveling waves. The name and shape of the system take inspiration from brain organoids: neural cell cultures used to study neural development. Each axon in the network has electrophysiological properties determined by the physical dimensions of the system that govern the signal wave behavior. The network takes input stimuli using UV Mapping to project images onto the surface of the sphere. The Digital Organoid extends SNNs to capture the dynamics of signals between neurons over time and distance because of their physiological characteristics. A future extension of this work will include modifying node positions to manipulate signal speeds via a reinforcement learning agent. The agent’s behavior will be guided by the difference between the output node firing results and a pre-determined output node firing configuration for image classification. Digital Organoids will be deployed in parallel using UVA’s GPU Neo Cluster to emulate an evolutionary process. This extension will result in a system whose learning process is governed by conformational changes in the Digital Organoid's shape.

49 **The 5XFAD mouse model of Alzheimer's disease displays a delayed recovery from Clostridioides difficile infection clinical symptoms**

**Presenter(s):** Ashley Nguyen **Role(s):** Undergraduate student 11am–noon

**Author(s):** Ashley Nguyen, Suemin E. Yang, Deiziane V. S. Costa, Maria L. G. Morais, Cirle A. Warren

Introduction: Clostridioides difficile (C. difficile), an obligate anaerobic, spore-forming gram-positive bacillus, is the primary cause of hospital- and community-acquired diarrhea associated with antibiotic use worldwide. C. difficile infection (CDI) affects nearly half a million patients in the US annually, particularly the elderly. Previous studies have suggested that delirium and dementia may be associated with CDI and influence outcomes in humans. The mechanism of how dementia contributes to disease severity remains unknown. Here, we investigated whether Alzheimer's disease-associated amyloid pathology (5xFAD mouse model) influences the clinical outcome of CDI. Methodology: Wild-type (WT) and 5xFAD mice (5 months old) were infected with C. difficile (VPI 10463, oral gavage), monitored daily for weight loss, clinical symptoms, and C. difficile shedding for 7 days post-infection. C. difficile shedding was determined by PCR for TcdB gene. Results: 5xFAD infected mice had significantly worse diarrhea and higher total clinical score compared to WT infected mice on day 4 post-infection. Additionally, the 5xFAD infected mice also appeared to recover slower from the body weight loss. No significant differences in C. difficile shedding in stools was detected between WT and 5xFAD infected mice, suggesting that the host response, and not pathogen burden, may contribute to these differences in clinical outcomes. Conclusion: Our preliminary data shows that amyloid pathology—a defining characteristic of Alzheimer's disease—appears to aggravate CDI. Further investigations will be needed to better understand how the amyloid pathology impairs CDI and whether CDI contribute to worse neuroinflammation and cognitive outcome in host with amyloid neuropathology.

50 **Microglial Absence Exacerbates Kainic Acid-Induced Seizures in FIRE Mice**

**Presenter(s):** Audrey Nguyen **Role(s):** Undergraduate student noon–1pm

**Author(s):** Audrey Nguyen, Synphane Gibbs-Shelton, Ukpong Eyo

Seizure disorders involve sudden, uncontrolled electrical disturbances in the brain that affect individuals of all ages. While various antiseizure drugs exist, many remain ineffective for a large portion of patients, highlighting the need for alternative treatment strategies. The activation of immune cells in the central nervous system, specifically microglia, is essential in maintaining neural homeostasis. As primary contributors to neuroinflammation, microglia play a role in seizure development and severity, but their exact role remains poorly understood. This study aims to determine the role of microglia in chemoconvulsive and hyperthermic seizures by using FIRE mice, which exhibit a nearly complete absence of brain microglia while leaving other macrophage populations unaffected.

Through genetic deletion of the fms-intronic regulatory element (FIRE) in the Csf1r gene, we generated FIRE mice to investigate the involvement of microglia in chemoconvulsive and hyperthermic seizure models. Our results showed that FIRE knockout mice exhibited exacerbated Kainic acid (KA)-induced seizures compared to FIRE heterozygous and wild-type littermates. However, no differences in seizure susceptibility were observed between FIRE knockout, heterozygous, and wild-type groups. Additionally, we evaluated the contribution of macrophages to seizure susceptibility during chemoconvulsive seizures by comparing FIRE knockout mice with FIRE knockouts treated with PLX3397, a macrophage-depleting drug. No significant differences were observed, supporting the idea that microglia, rather than other macrophages, primarily regulate seizure severity in chemoconvulsive seizures. Overall, our results demonstrate that microglia play a protective role in chemoconvulsive seizures, but not in hyperthermic seizures, suggesting that their involvement may be model-specific.

51 **Oscillation frequency-dependent modulation of the prefrontal cortex using low-Intensity Focused Ultrasound: impact on downstream mesolimbic dopamine**

**Presenter(s):** Greatness Olaitan **Role(s):** Graduate student 11am–noon

**Author(s):** Greatness O. Olaitan, Kenneth Okojie, Wendy Lynch, B. Jill Venton

Synchronized neural oscillations are fundamental to cognitive function, orchestrating inhibitory and excitatory neurotransmission and downstream signaling. Disruption of these temporal couplings leads to neural isolation, diminished signal propagation, and cognitive deficits. We hypothesized that applying Low-Intensity Focused Ultrasound (LIFU) parameters to mimic specific oscillatory patterns would modulate dopamine neurotransmission. Building upon prior findings demonstrating LIFU's impact on dopamine release, we investigated the effects of frequency-modulated LIFU of the prelimbic cortex (PLC) on dopamine release in the nucleus accumbens core (NAcc). After three consecutive 80-seconds long LIFU stimulations with a 30 minutes stimulation interval, we found that LIFU can both excite and inhibit dopamine release in an oscillation-frequency dependent manner. Employing a theta (8 Hz)-coupled beta (16 Hz) oscillations led to a 58% reduction in dopamine release and decreased astrocytic activation. Conversely, theta (5 Hz)-coupled gamma (50 Hz) frequency LIFU resulted in a 28% increase in NAcc dopamine levels for 90 minutes post-stimulation, paralleling the enhanced neuronal and astrocytic activation observed via immunohistochemistry. Theta-coupled beta oscillations led to a 58% reduction in dopamine release and decreased astrocytic activation. Beta-delta (16:2 Hz) coupling produced milder inhibitory effects, while beta-theta (28:7 Hz) coupling showed no significant impact, similar to anatomical and sham controls. While a similar level of inhibition was observed in females, non of the tested parameters significantly excited dopamine. Thus, these results indicate that LIFU can selectively modulate dopamine release by mimicking specific oscillatory patterns, offering potential therapeutic applications for disorders involving dopamine dysregulation.

52 **Sex Differences in Fentanyl's Impact on Mesolimbic Dopamine Activity**

**Presenter(s):** Greatness Olaitan **Role(s):** Graduate student noon–1pm

**Author(s):** Greatness Olaitan, Jill Venton, Wendy Lynch

Opioid use disorder (OUD) has reached epidemic proportions in the United States, with synthetic opioids like fentanyl driving a dramatic increase in overdose deaths. In 2021 alone, approximately 107,891 drug overdose fatalities were recorded, with opioids responsible for nearly 75% of these deaths. Understanding the neurobiological mechanisms underlying opioid addiction is crucial for developing effective interventions, particularly regarding potential sex differences in response to these substances.

Fentanyl, a potent synthetic opioid, significantly modulates mesolimbic dopamine (DA) neurotransmission through μ-opioid receptor activation. This study investigates sex-specific alterations in DA signaling within the nucleus accumbens (NAc) of male and female rodents following fentanyl exposure. Using in vivo fast-scan cyclic voltammetry, we measured fentanyl-induced changes in electrically stimulated DA release within the NAc. Male and female rats underwent intermittent intravenous fentanyl self-administration for 10 days, and DA dynamics were assessed on Day 10 under varying stimulation parameters. Western blot analysis of phosphorylated ERK (pERK) was also conducted to evaluate neuronal activity.

Preliminary results indicate significant sex differences in fentanyl-induced DA release. Males exhibited sharper increases in DA levels with stimulation, while females showed a more gradual response. Interestingly, drug-naïve females had higher DA release than males, but this trend reversed after fentanyl exposure. Additionally, females demonstrated greater fentanyl-induced neuronal activity.

These findings highlight critical sex-dependent differences in opioid-induced neuroadaptations within the mesolimbic circuit, emphasizing the need for tailored interventions to address sex-specific vulnerabilities to OUD. Future research should explore the effects of fentanyl withdrawal on mesolimbic function to inform targeted addiction treatment strategies.

53 **Jam proteins mediate oligodendrocyte myelin targeting during zebrafish neurodevelopment**

**Presenter(s):** Andrew Perl **Role(s):** Graduate student noon–1pm

**Author(s):** Andrew Perl, Drew Latimer, Sarah Kucenas

In vertebrates, nerve impulse transmission often depends on the myelination of axons by specialized glial cells. Glial ensheathment by myelin simultaneously insulates and nourishes the axon, and can increase the speed of neurotransmission by orders of magnitude. In the central nervous system (CNS), oligodendrocytes (OLs) myelinate only select axons in the brain and spinal cord under physiological conditions. Why they don't myelinate other structures, including neuronal cell bodies, is not fully understood. To probe the cellular and molecular mechanisms underlying this myelin targeting specificity during development, we explored our own and publicly available single-cell RNA sequencing datasets. Among the candidate genes which met our search criteria were junctional adhesion molecules (Jams) 2 & 3 and their zebrafish orthologs (jams 2a, 2b, 3a and 3b). JAMs are transmembrane proteins involved in tight junction formation and other diverse functions, but the role they play in the CNS is largely unexplored. Using CRISPR/Cas9 genome modification, our group produced zebrafish larvae harboring mutations in each of these four jam genes that have myelin targeted inappropriately to neuronal cell bodies. Using these mutant lines, we are investigating the role of Jam proteins in myelin targeting during CNS development using in vivo time-lapse imaging, RNAscope, and electron microscopy. When complete, our studies will provide a fuller understanding of the mechanisms that drive developmental myelin targeting in the CNS, which is a prerequisite for devising effective remyelination therapies for demyelinating and dysmyelinating diseases like multiple sclerosis and leukodystrophies.

54 **The Gut-Brain Connection: Frontal Alpha Asymmetry in Relation to the Montreal Feeding Scale**

**Presenter(s):** Gray Powell **Role(s):** Undergraduate student noon–1pm

**Author(s):** Gray Powell, Meghan H. Puglia

A healthy and diverse diet contributes to a healthy gut-brain axis through the gut microbiome, which has been shown to contribute to feelings of happiness. Frontal alpha asymmetry is a measurement of the disparity in electroencephalography (EEG) alpha signals between the left and right frontal lobe. Increased frontal alpha asymmetry at rest correlates to greater feelings of depression, anxiety, and stress. As children begin to eat solid foods and expand their diet, it is essential that their gut microbiome is healthy and diverse. There has been little research conducted on how diet can contribute to a developing brain and how it can serve as an indicator of healthy brain development. My study examines how healthy feeding habits (determined by the Montreal Feeding Scale) relate to resting frontal alpha asymmetry EEG data in children at age two years old. Understanding feeding habits and food intake will allow parents to make informed decisions about their child's feeding habits and how they can promote healthier brain development. This research will also allow the scientific community to better understand the influence of diet on the health and happiness of the brain, specifically young children's brains, allowing us to take preventative measures and make informed decisions regarding early childcare. I anticipate that my research will show a positive correlation between frontal alpha asymmetry at rest and Montreal Feeding Scale scores, where decreased frontal alpha asymmetry relates to healthier feeding habits.

55 **Association of MoCA Scores with Advanced Diffusion MRI Metrics**

**Presenter(s):** Mahsa Rajabi **Role(s):** Graduate student 11am–noon

**Author(s):** Mahsa Rajabi, Merry Mani

The Montreal Cognitive Assessment (MoCA) is a widely used screening tool for detecting mild cognitive impairment by measuring multiple cognitive domains, including visuospatial ability, naming, attention, language, abstraction, memory recall, and orientation. Meanwhile, diffusion magnetic resonance imaging (dMRI) offers quantitative biomarkers that can detect subtle microstructural alterations in brain tissue, potentially reflecting cognitive changes associated with aging or neurodegenerative processes. In this study, we investigated the relationship between MoCA performance and advanced dMRI parameters in fifteen adult participants ranging in age from 30 to 79 years.

Each subject underwent a standard MoCA test, yielding both total scores and domain-specific sub-scores, as well as a high-resolution diffusion scan. The dMRI data were processed to extract metrics sensitive to intraneuronal, extracellular, and free-water compartments. These measures capture different aspects of brain tissue complexity, including neuronal density, myelin integrity, and extracellular water diffusion. Correlation analyses were conducted to examine the association of diffusion metrics with MoCA performance across the various domains while accounting for demographic factors such as age, sex, and education.

Preliminary findings suggest that certain diffusion metrics, particularly those reflecting microstructural integrity (Da and De), demonstrate reasonable associations with MoCA total scores and selected cognitive subdomains. These results underscore the potential utility of advanced diffusion imaging as a noninvasive biomarker of cognitive function. Larger-scale studies are warranted to validate these findings and to elucidate the precise biological underpinnings linking dMRI metrics and cognitive performance.

56 **Base Editing Rescue of Seizures and SUDEP in SCN8A Developmental Epileptic Encephalopathy**

**Presenter(s):** Caeley Reever **Role(s):** Graduate student 11am–noon

**Author(s):** Caeley M. Reever, Alexis R. Boscia, Tyler C.J. Deutsch, Mansi P. Patel, Shrinidhi Kittur, Raquel M. Miralles, Erik J. Fleischel, Atum M. L. Buo, Matthew S. Yorek, Charles R. Farber, Manoj K. Patel

SCN8A, encoding the voltage-gated sodium channel Nav1.6, plays a key role in facilitating neuronal excitability. Mutations in SCN8A, particularly gain-of-function missense variants, are associated with SCN8A developmental and epileptic encephalopathy (DEE), a severe epilepsy syndrome characterized by spontaneous seizures and sudden unexpected death in epilepsy (SUDEP). The recurrent SCN8A variant R1872W destabilizes inactivation of the sodium channel, resulting in neuronal hyperexcitability and seizure onset. Current treatments, anti-seizure medications (ASMs), broadly target sodium channels, are ineffective in SCN8A DEE patients and are associated with significant side effects, highlighting the need for targeted therapies. In this study, we utilized base editing as a therapeutic strategy to correct the R1872W SCN8A variant. Using engineered cell lines, we identified targeting constructs that successfully reverted the R1872W variant to the reference allele. The most effective construct, along with a paired successful guide RNA, was packaged within a dual PhP.eB-AAV delivery system. This dual AAV therapy (SCN8A-ABE) was administered to mice expressing the R1872W variant at P2. Treatment with SCN8A-ABE significantly increased survival of mice expressing R1872W, and either significantly reduced or completely inhibited seizure occurrence. Assessment of editing efficiencies revealed approximately 30% conversion of the mutant allele in hippocampal/cortex RNA of mice. Electrophysiological recordings revealed attenuation of seizure-associated neuronal hyperexcitability and pathogenic sodium channel behavior in treated mice. Comorbid movement disorders and anxiety-like behaviors were also improved in treated mice. These findings demonstrate the potential of base editing as a novel effective therapeutic approach for SCN8A DEE, addressing the underlying driver for the disease.

57 **The Effects of Abscission Protein Cep55 on Cortical Cell Fate**

**Presenter(s):** Elizabeth Ross **Role(s):** Undergraduate student 11am–noon

**Author(s):** Elizabeth Ross

Precise control of neural cell division is integral to the function and development of the cortex of the brain. Cep55 is a protein that aids this division by signaling the recruitment of proteins that sever dividing daughter cells during abscission. Cep55 knockouts particularly affect the brain, exhibiting cortexes with increased apoptosis and a decline in cortical thickness. With the use of a mosaic analysis with genetic markers technique (MADM), MADM mice, while having knockout cells, will continue to survive and can be analyzed throughout development. MADM relies on the recombination of chromosomes to generate a fluorescently labelled genetic mosaic. This process generates Cep55 knockout cells within the cortices of mice, along with Cep55 wild-type and heterozygous cells. After MADM sections are collected, they undergo Cleaved Caspase 3 and Phosphohistone H3 antibody staining to identify cells undergoing apoptosis and mitosis, respectively. Across prenatal development, results showed an increase of apoptosis from embryonic day 12 to 16 that declined by postnatal day 0. Less apoptosis in MADM Cep55 heterogenous mice was seen across this developmental period compared to the Cep55 wild-type mice cortexes. Within neural cell mitosis, there was an increased rate of division among MADM Cep55 heterogenous mice than the wild types. Compared to full Cep55 knockout mice, the MADM Cep55 heterogenous mice similarly demonstrate altered cell death, this could suggest that it is altered by cell-autonomous forces of the knockout. The rate of division could also suggest that the cortical organization is being altered.

58 **Morphological network alterations in Autism Spectrum Disorder and sex-related differences.**

**Presenter(s):** Nooshin Safari **Role(s):** Postdoctoral Scholar noon–1pm

**Author(s):** Nooshin Safari, Javier Rasero

Autism spectrum disorder (ASD) is marked by heterogeneous neurodevelopmental alterations, complicating the identification of reliable neural biomarkers. We apply the Morphometric INverse Divergence (MIND) network approach to assess morphology-based connectivity in ASD using data from 317 individuals aged 8–18 years, including 166 with ASD. T1-weighted MRI data were processed with FreeSurfer to extract cortical thickness, volume, surface area, mean curvature, and sulcal depth. Morphometric similarity was estimated via symmetric Kullback–Leibler divergence. Network-based statistics were used to identify significant connectivity differences ($p_{fwe} < 0.05$) in cohort (ASD vs Control) and gender-by-cohort interaction while controlling for age, intracranial volume, and site. We identified significant morphology-based connectivity alterations between individuals with ASD and the control population across multiple brain regions. The most affected connections involved the entorhinal cortex, precuneus, lateral occipital cortex, and pars opercularis—regions linked to memory, self-referential processing, visual integration, and motor coordination. These regions are embedded in the default mode network (DMN), salience network (SN), and central executive network (CEN), indicating disrupted integration across systems involved in social cognition and sensory processing. Significant morphology-based connectivity alterations correlated with scores for restricted and repetitive behaviors, self-injurious behaviors, stereotyped behaviors, and adaptive functioning in ASD.

Although the gender-by-cohort interaction wasn't significant, separate analyses within the ASD group revealed distinct gender profiles. Males with ASD showed greater connectivity involving the parahippocampal and fusiform regions; females showed stronger connectivity between the precuneus and entorhinal cortex. These findings highlight the potential of morphology-based connectivity as a biomarker for ASD and sex-related differences.

59 **Two-photon FLIM and PLIM Imaging to Investigate Metabolism and Oxygen Tension in Live Animals.**

**Presenter(s):** Vijay Kumar Sagar **Role(s):** Postdoctoral Scholar 11am–noon

**Author(s):** Vijay Kumar Sagar, Andrés Norambuena, Evelyn Pardo, Horst Wallrabe, Shagufta R Alam, Ammasi Periasamy

The state-of-the-art fluorescence lifetime imaging (FLIM) is a non-invasive and quantitative optical imaging technique to track metabolism at the molecular level in a biological system; FLIM can also be applied to labeled moieties. Unlike conventional single photon excitation, two-photon illumination improves the penetration depth in tissues due to less light scattering and reduced phototoxicity of infrared (IR) wavelengths to examine thick biological samples. Two-photon FLIM is an ideal technique for tracking metabolic changes in live cells and animals based on the bound and free coenzyme NAD(P)H lifetime parameters. We apply this FLIM technique to quantify changes in the bound coenzyme NAD(P)H in both wild type (WT) and Alzheimer disease (AD) animal models before and after stimulation with nutrients (amino acid). Another application of this technique is Phosphorescence Lifetime Microscopy (PLIM) to sense oxygen tension levels in live cells, tissue and animal model specimens. The PLIM fluorophore “Ruthenium” is often used as an oxygen sensor based on its fluorescence lifetime. As a proof of principle, the results of this PLIM technique applied to WT mouse brain will be presented. This allows simultaneous acquisition of both measurement of NAD(P)H and oxygen tension using FLIM (nanoseconds) and PLIM (microseconds).

60 **Social memory dysfunction coincides with microglia-dependent remodeling of hippocampal CA2 perineuronal nets**

**Presenter(s):** Brenda Sanchez **Role(s):** Graduate student noon–1pm

**Author(s):** Brenda Sanchez*, Sabrina Lee*, Colin M. Remy, Eva A. Campbell, Elise C. Cope

*Authors contributed equally

Social memory dysfunction is a feature of different neuropsychiatric and neurodegenerative disorders. The hippocampal CA2 region and its connections form a circuit critical for social memory. The CA2 has a high abundance of perineuronal nets (PNNs), condensed extracellular matrix structures that ensheath particular neurons and regulate their plasticity. While previous work suggests PNNs may serve as a potential therapeutic target for social memory, the specific cellular and molecular processes regulating CA2 PNNs remain unexplored. Microglia, the brain’s resident macrophages, participate in the homeostatic remodeling of PNNs and contribute to their loss in disease. Here, we explored the role of microglia in remodeling CA2 PNNs under homeostatic conditions. We fed mice pexidartinib (PLX3397) to deplete microglia and observed social memory impairments. Although we did not find differences across all structural components of CA2 PNNs, we observed increased intensity of Wisteria floribunda agglutinin (WFA), which labels glycosaminoglycan chains attached to chondroitin sulfate proteoglycans (CSPGs), and increased intensity of the CSPG aggrecan. This indicates that microglial elimination causes an accumulation of some, but not all, PNN components. We examined PNNs in other hippocampal regions and found little to no change in mice lacking microglia, suggesting the CA2 may be more vulnerable to microglial-mediated PNN remodeling. Next, we investigated whether microglial repopulation reverses CA2 PNN accumulation. We found that restoration of microglial numbers coincided with a reduction of WFA+ PNN intensity in the CA2 back to control levels. Ongoing studies are exploring PNN turnover rates induced by microglial depletion and repopulation in the CA2.

61 **Astrocyte activation by 7-ketocholesterol is mediated by microglia**

**Presenter(s):** Kayal Sankar **Role(s):** Staff 11am–noon

**Author(s):** Kayalvizhi Radhakrishnan, Yiyu Zhang, Oluwaseun Mustapha, Thaddeus K Weigel, Clint M Upchurch, Xiaodong Tian, Franklin Herbert, Wenyuan Huang, Norbert Leitinger, Ukpong B Eyo, Huiwang Ai, Heather A Ferris

Oxidative stress plays a significant role in the pathophysiology of Alzheimer's disease. 7-ketocholesterol (7-KC) is a potent pro-inflammatory molecule produced as a result of cholesterol oxidation contributing to the disease pathology. In the current study we see increase of 7-KC levels in 3xTg mice as assessed by mass spectrometry. To further investigate the process of oxidative stress in pathological conditions, we developed an astrocyte specific genetically encoded fluorescent indicator. We used this sensor to show that 7-KC increased oxidative stress in astrocytes both in vivo and in vitro. Intriguingly, this activation of astrocytes by 7-KC was only in presence of microglia. When the microglia were depleted the astrocyte activation by 7-KC disappeared. 7-KC was shown to activate microglia alone, in a microglial cell line or in a mixed glial culture in vitro. Subsequently, the activated microglia increased oxidative stress in astrocytes. These findings indicate that 7-KC contributes to increased oxidative stress in astrocytes and microglia play a crucial role in mediating this increase in astrocytic ROS.

62 **Assessing Mother-Child Interaction and Early Childhood Development in Rural Tanzania**

**Presenter(s):** Rebecca J Scharf **Role(s):** Faculty noon–1pm

**Author(s):** Daniel Nguyen, Amber Young, Erling Svensen, Sarah Elwood, Elizabeth Rogawski McQuade, Eliwaza Bayo, Ladislaus Blacy, Estomih Mduma, Mark DeBoer, Rebecca J Scharf

Parent-child interactions are critical for early childhood development, particularly in low-resource settings, where risks like malnutrition and enteric diseases are common. The Observation of Maternal-Child Interaction (OMCI) tool evaluates these interactions, and the Malawi Developmental Assessment Tool (MDAT) assesses childhood cognitive, motor, language, and social development. This study focuses on the rural region of Haydom, Tanzania, where new insights into early caregiving practices are needed.

This study of 246 children aimed to evaluate the OMCI as a culturally-relevant, and to explore how mother-child interactions influence development. OMCI assessments were conducted at 12 months, with mothers engaging with their children using picture board books. Scores were based on behaviors like pointing, naming objects, praising the child, and mutual enjoyment. MDAT assessments were conducted at both 18 and 24 months.

OMCI scores found variability in mother/child interactions. The mean child score was 10.39 (SD 2.75) out of 21, while the mean maternal score was 21.26 (SD 3.99) out of 36. Higher child OMCI scores at 12 months were associated with better MDAT scores at 18 and 24 months, suggesting that more engaged interactions predict better developmental outcomes. These findings held even after adjusting for gender, income, maternal education, and assets.

The OMCI tool was successfully implemented in rural Tanzania, revealing wide variability in mother-child interactions. This study demonstrates the predictive value of early mother-child interactions for later developmental outcomes in a low-resource rural setting. Future research should examine the long-term effects of these interactions on language, cognitive, and social-emotional development.

63 **NGF-regulated extracellular vesicles: A novel mechanism for target-dependent circuit development?**

**Presenter(s):** Jonathon Sewell **Role(s):** Graduate student 11am–noon

**Author(s):** Jonathon Sewell, Eli Zunder, Chris Deppmann, Bettina Winckler

During early development, integration of neurons into functional circuits relies on developmental cues that often communicated over long distances. In the sympathetic circuit of the autonomic nervous system, sympathetic postganglionic neurons that receive sufficient Nerve Growth Factor (NGF) survive, while insufficient NGF induces apoptosis. Upstream, sympathetic preganglionic neurons also depend on NGF for survival and development. However, these neurons do not express the NGF receptor, TrkA, nor have access to soluble NGF, which raises the question: how is this process NGF-dependent when NGF is not directly involved?

Our group has shown that TrkA can be retrogradely trafficked from the distal axon of cultured sympathetic postganglionic neurons and secreted at the cell body on extracellular vesicles (sympathetic EVs). Additionally, sympathetic EV secretion is regulated by NGF-TrkA signaling cascades. Thus, we hypothesize that NGF-induced EVs induce progressive signaling responses in recipient preganglionic neurons that support development.

Using suspension mass cytometry, we assayed sympathetic EV-dependent signaling changes in spinal cord cultures with single-cell resolution. In neuronal cell populations, we observe changes in cell signaling pathways related to increased survival and DNA damage response, which is not observed with HEK293-derived EV treatment. Additionally, we observe distinct responses from neuronal to non-neuronal cells, suggesting cell type specificity.

In summary, we show with our high-throughput assay that sympathetic EVs induce signaling changes in a cell type- and EV source-dependent manner. Thus, we have documented the existence of TrkA-positive sympathetic EVs regulated by NGF signaling that are signaling-competent, pointing to a novel mechanism for target-dependent circuit development.

64 **Strategies for Addressing Eligibility Verification and Participant Fraud in Digital Research**

**Presenter(s):** Chris Sheehan **Role(s):** Staff noon–1pm

**Author(s):** Christina Sheehan, Anna Arp, Shannon Reilly, Ishan Williams, Carol Manning, Virginia Gallagher

Background: Although digital recruitment provides researchers with the opportunity to recruit large and varied samples, it frequently exposes research studies to individuals who misrepresent their identity and study eligibility to access research-related incentives. Fraudulent participation compromises the integrity of research and places a significant strain on study resources. We discuss lessons learned and strategies for contending with fraudulent participants in a remote, online survey study employing digital recruitment.

Results and Discussion: The study recruited through disease-related research registries and e-distributions, social media platforms, and local news email blasts. Shortly after study initiation, staff noticed suspicious patterns in participant-provided information and eligibility. Trends included discrepant contact information, multiple survey submissions sharing identical contact information with different responses, and nonsensical personal information. Over six months, the study received 255 prescreening eligibility survey submissions. Of these submissions, study staff identified 142 (55.69%) as concerning for fraud.

The research team developed rigorous protocols to address fraudulent participation. The primary mitigation strategy involved a multi-step authentication process. Participants were asked to answer a series of questions about their personal information and study eligibility before speaking with a member of the study team to confirm their responses. The research team also employed reverse-foil questions and open-ended responses throughout surveys to assess participant authenticity.

Conclusion: The prospect of leveraging online platforms and social media to reach an expanded pool of participants is exciting to many researchers. However, digital recruitment poses considerations and risks that differ significantly from clinic and in-person recruitment. Researchers should carefully consider the implementation of proactive strategies against participant fraud to preserve study resources and validity.

65 **Exploring the Role of ApoE4 in Alzheimer's Disease Using an Innovative Neuron-Glial Assembloid Model**

**Presenter(s):** Eliana Sherman **Role(s):** Staff 11am–noon

**Author(s):** Eliana Sherman, Kevin Qui, Rebecca Roberts, Sihan Li, Lucille Shichman, Lucie Ide, Weronika Gniadzik, Aiying Zhang, Alev Erisir, Lulu Jiang

Objectives: Exploration of the pathophysiology of Alzheimer's disease (AD) has been hampered by the lack of systems that accurately recapitulate the full profile of disease progression. We developed a three-dimensional (3D) assembloid model with iPSC-induced neurons, astrocytes, and microglia to investigate the pathophysiology, protein-protein interactions, cellular mechanisms, and interventional strategies for AD. In the current study, we aim to elucidate the mechanism of the risk isoform ApoE4 in regulating the pathogenesis of AD.

Methods: ApoE4 and its isogenic control ApoE3 iPSC lines were differentiated into neuronal, astrocytic, and microglial cells in 2D culture. The neuronal cells were seeded with tau oligomers. Subsequently, the three cell types were mixed together to generate 3D Microglia-Astrocyte-Neuronal spheroids (Masteroids). These Masteroids were challenged with Aβ oligomers on day seven of the 3D culture. Pathological accumulation of tau and Aβ was examined at four weeks after treatment. Underlying molecular pathways were deciphered using single cell RNA sequencing analysis.

Results: Analysis of the Masteroid cultures after four weeks revealed accumulated β-amyloid deposition, tau pathology, neurodegeneration, astrogliosis, and microglial activation in the conditions challenged with oligomeric tau propagation and/or Aβ oligomers stress. Single cell transcriptomic analysis revealed novel impacts of ApoE4 and its synergistic exacerbation of AD pathology with oligomeric tau.

Conclusions: We generated a 3D brain assembloid model that effectively recapitulates key features of AD pathology. This model offers an advanced platform to study cellular and molecular mechanisms of disease progression and reveal distinct pathways in which the ApoE4 isoform regulates the pathogenesis of AD.

66 **Prematurity, the theta/beta ratio, and ADHD detection: a longitudinal EEG study**

**Presenter(s):** Sophia Stewart **Role(s):** Undergraduate student noon–1pm

**Author(s):** Sophia Stewart; Meghan Puglia, PhD

Attention-deficit/hyperactivity disorder (ADHD) is one of the most prevalent neurological disabilities. It is frequently diagnosed during childhood and characterized by decreased ability to focus, impulsivity, and hyperactivity, all of which can impact scholastic achievement, sociability, and overall higher-level functioning. Studies show biomarkers exist to predict a possible ADHD diagnosis later in life. For example, an infant's theta/beta ratio (TBR) measured through electroencephalography (EEG) can act as a biomarker to predict the chance of a future ADHD diagnosis. Studies have shown a decrease in the theta/beta ratio of infants can be associated with development of ADHD-relevant temperamental traits as the child progresses to their toddler years. While this correlation has been identified, little research exists surrounding whether gestational age has an impact on the TBR. Finding an association between the two proves relevant, as premature babies are more likely to be diagnosed with ADHD during childhood than full term babies. My study examines potential differences between the TBRs of full term and preterm infants at 0-4 months, and then at around 24 months. It also measures the progression of the average TBR values in each group from 0-4 months to 2 years. Gaining insight about this possible correlation would potentially allow for earlier intervention for ADHD and give parents the opportunity to watch their children for symptoms throughout their development. I anticipate my research will show a positive correlation between gestational age and TBR ratio, as I predict the premature infants will have decreased TBRs.

67 **Q-Space Trajectory Imaging: Expanding Microstructural Insights via Efficient Model Fitting**

**Presenter(s):** Wenwen Sun **Role(s):** Graduate student 11am–noon

**Author(s):** Wenwen Sun

Q-space trajectory imaging (QTI) extends conventional diffusion approaches by integrating linear, planar, and spherical b-tensors to capture richer isotropic and anisotropic information. This multi-track sampling enables more accurate characterization of crossing fibers, partial volume effects, and orientation dispersion. Critically, QTI's linearized framework simultaneously estimates the mean diffusion tensor and a full 6×6 covariance tensor, facilitating derivation of a broader set of microstructural parameters—such as microscopic fractional anisotropy (μFA) and isotropic/anisotropic kurtosis measures. These parameters distinguish intrinsic micro-level anisotropy from macroscopic orientation complexity, thus providing a clearer view of tissue organization than standard tensor models.

The dataset used in our work is openly available from the Hormone Health Study (HHS), comprising 22 young female participants who completed three MRI sessions on a Siemens 3T Prisma scanner. Each participant underwent QTI sequences involving multiple b-values (0–2000 s/mm$^2$) and diverse tensor shapes (four spherical, four linear; total 107 directions). This design ensures sensitivity to restricted diffusion components while preserving robust signal-to-noise.

In terms of diffusion model fitting, even though QTI estimates more parameters than DKI, its direct, linear approach requires minimal computation: for a single subject with 107 directions, the complete QTI model can be fit in about two minutes, whereas iterative DKI fitting (60 directions) took approximately 17 minutes. Thus, QTI emerges as a rapid yet comprehensive diffusion framework, offering an expanded array of biologically meaningful parameters alongside notably faster computation—an advantageous profile for broad application.

68 **Quantifying the contributions of intermediate filaments to sensory neuron development**

**Presenter(s):** Isaiah Swann **Role(s):** Graduate student noon–1pm

**Author(s):** Isaiah Swann, Jonathon Sewell, Laura Digilio, Chan Choo Yap, Max Lu, Chris Deppmann, Eli Zunder, Bettina Winckler

Intermediate filaments (IFs) constitute a highly conserved superfamily of ubiquitous, cell-specific cytoskeletal proteins with nearly 70 genes encoded in mammals. In neurons, IFs are involved in developmental axon outgrowth, axon caliber/integrity, injury signaling, and regeneration. While all neurons express IFs, not every neuron expresses the same subtype(s), suggesting a specific functional role for each IF. One subtype, peripherin, is expressed primarily in the peripheral nervous system and upregulated coincidently with developmental axon outgrowth and during axon regeneration after injury. Mutations in peripherin are linked to several degenerative nerve diseases, such as peripheral neuropathies and amyotrophic lateral sclerosis (ALS). Still, how peripherin contributes to normal neuronal physiology and pathophysiology is unknown. I hypothesize that peripherin is required for the proper abundances of neuron subtypes of the dorsal root ganglion (DRG) and is a necessary component of IF networks of developing and regenerating DRG neurons. Here, I leverage imaging mass cytometry, a multiplexed spatial proteomics technique, to define "IF codes", cell type-specific IF protein expression patterns, across development and within neuronal subtypes of the murine DRG. Additionally, I address the consequences of peripherin knockout for the abundances and IF networks of specific DRG neuron subpopulations. Current efforts will improve our understanding of fundamental IF, especially PRPH, neurobiology and set the stage for future studies focused on defining "IF codes" in the injured DRG and elucidating the mechanistic underpinnings of PRPH activity in developing and injured axons.

69 **Harnessing spatial imaging mass cytometry to explore Lacritin's potential in restoring Alzheimer's disease homeostasis**

**Presenter(s):** Swaroop Thonda **Role(s):** Postdoctoral Scholar 11am–noon

**Author(s):** Swaroop Thonda, Gordon W Laurie

Treatment options for Alzheimer's disease (AD) are limited despite recent advances. The ocular surface tear protein 'lacritin', recently discovered to be distributed in the cerebral spinal fluid (CSF) and plasma, may be beneficial. Under the conditions of immune or protein aggregate stress, lacritin transiently accelerates autophagy to restore oxidative phosphorylation through mitochondrial fusion. Via a largely different signalling pathway, it regenerates neurons. In preliminary studies, we have identified the presence of lacritin monomer and the transglutaminase 2 inactivated dimer form of lacritin within human CSF samples. Intracerebroventricular administration of the C-terminal lacritin synthetic peptide ('N-104') resulted in the stimulation of autophagic flux and a reduction in imaging mass cytometry (IMC)-detectable Aβ levels in mRFP-eGFP-LC3B/5xFAD mice. Our working hypothesis is that lacritin is an unappreciated dual homeostasis and restorative activity in the CNS. The presence of bioactive monomeric lacritin may be selectively deficient in the cerebrospinal fluid of individuals with AD. In these instances, the use of replacement therapy is potentially transformative. Our immediate goal is to utilize the IMC antibody panel to decipher single-cell and spatial proteomic profiles with ‘N-104’ peptide treatment in different-aged mRFP-eGFP-LC3B/5xFAD mice and then seek to validate its therapeutic benefit in AD human brain slice cultures. Our long-term goal is to harness this information towards the development of an early-onset AD therapeutic.

70 **Patterns of Cortico-Tectal Input Across Species: An Evolutionary Comparative Analysis**

**Presenter(s):** Christopher Turner **Role(s):** Undergraduate student noon–1pm

**Author(s):** Christopher Turner; Arda Kipcak; Alev Erisir, MD, PhD

The superior colliculus (SC) is a highly conserved midbrain structure within the tectum that integrates multisensory information to generate spatial maps of salient stimuli, facilitating orienting behaviors critical for survival. While the SC exhibits distinct morphology, connectivity, and function across species, the circuit and cell-type specific mechanisms that underlie the differential visuospatial reflexive behavior remain incompletely understood. In this study, I catalogue the corticotectal projections across the mouse, cat, tree shrew, and monkey. These species were selected based on their evolutionary divergence from primates (mouse), complex cortical integration and phylogenetic proximity to primates (tree shrew), and highly developed sensorimotor and visuospatial reflexive systems (cat and monkey). To investigate projection intensity from discrete cortical regions to SC, I performed a data-mine and analysis of the Allen Mouse Brain Connectivity Atlas anterograde tracer experiments. This analysis revealed 20 unique cortical regions projecting to the SC in functionally organized, yet distinct patterns across the anterior-posterior, medial-lateral, and superficial-deep gradients. In the tree shrew, I conducted an rgAAVtdtomato tracer injection into the SC of one animal, identifying 27 unique cortical regions expressing fluorescent signal in cell bodies. Cat and monkey input patterns were obtained through a literature review. These findings reveal species-specific differences in corticotectal circuits that may underlie variations in visuospatial processing and sensorimotor adaptations. By comparing these connectivity patterns, this study provides insight into the evolutionary divergence of SC circuitry and its implications for reflexive behavior across mammals.

71 **Using Atypical Functional Connectivity in Autism Spectrum Disorder Risk Prediction with Multivariate Machine Learning Methods**

**Presenter(s):** Shriya Varada **Role(s):** Undergraduate student 11am–noon

**Author(s):** Shriya Varada

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social behavior and cognitive processing. Diagnosis cannot be made until age 2 and depends on behavioral assessment. This study aims to use measures of functional connectivity, or intrinsic temporal correlations between brain regions, at 0-2 months of age to predict ASD risk in preterm infants via multivariate analysis. Spontaneous electroencephalography data was collected during rest at 0-2 months in preterm infants (n=40), and the Autism Diagnosis Observation Schedule was used to assess ASD symptoms in the same infants around two years of corrected age. We demonstrated that magnitude-squared coherence, the similarity of frequency between two signals, in the alpha band was significantly greater in preterm infants with low concern for ASD (n=7) than those with high concern (n=10), thus establishing a detectable difference in brain activity between risk groups early in life. We also calculated phase coherence, the similarity in oscillations of different brain waves, and multiscale entropy, a measure of neural variability and complexity, to better capture the nonlinear dynamics of brain function. We intend to build and test a support vector regression machine learning model to predict ASD symptom scores, as this type of model is particularly well suited for high dimensional data. Successful predictive modeling based on EEG data from such young infants will show promise for the discovery and definition of biomarkers to facilitate earlier diagnosis, which would encourage optimal outcomes for long-term social development in children with ASD.

72 **The Role of MMP-9 in Central Nervous System Pericyte-Endothelial Cell Uncoupling and Subsequent Vessel Leakage in Hyperglycemia**

**Presenter(s):** Yashasvisai Veeramasu & Corrina Peachey **Role(s):** Undergraduate students noon–1pm

**Author(s):** Corrina Peachey, Yashasvisai Veeramasu, Kareem El-Ghazawi, Shayn M. Peirce

Diabetic retinopathy is a common microvascular complication of Type 2 Diabetes (T2D) characterized by capillary leakage and degeneration. Capillaries are essential for nutrient, oxygen, and waste exchange between blood and tissues. Pericytes are specialized cells that wrap around the abluminal surface of capillary endothelial cells to regulate blood flow and provide structural stability. In hyperglycemia, retinal pericyte cell bodies have been shown to uncouple from their associated vessels and extend their processes to other capillaries, a potential contributor to vessel leakage. Matrix metalloproteinase-9 (MMP-9) degrades the basement membrane and is elevated in T2D. This study aims to investigate the relationship between MMP-9, pericyte-endothelial cell uncoupling, and blood vessel leakage in the retinas of hyperglycemic mice. Pericyte lineage-traced hyperglycemic and normoglycemic mouse retinas were whole-mounted and immunostained for MMP-9 or fibrinogen to evaluate MMP-9 activity and vessel leakage within proximity to pericyte uncoupling. The immunostained retinas were imaged using confocal microscopy. Total pericyte count, pericyte uncoupling, and fluorescence per area of MMP-9 and fibrinogen were quantified. These findings will aid in determining underlying mechanisms of microvascular dysfunction of the central nervous system in T2D with potential to inform therapeutic strategies and targets.

73 **Unraveling the Neural Circuitry of Energy Balance with Molecular Connectomics**

**Presenter(s):** Addison Webster **Role(s):** Postdoctoral Scholar noon–1pm

**Author(s):** Addison N. Webster*, Jordan J. Becker*, Chia Li, Dana C. Schwalbe, Damien Kerspern, Eva O. Karolczak, Catherine B. Bundon, Roberta A. Onoharigho, Maisie Crook, Maira Jalil, Elizabeth N. Godschall, Emily G. Dame, Adam Dawer, Dylan Matthew Belmont-Rausch, Tune H. Pers, Andrew Lutas, Naomi Habib, Ali D. Güler, Michael J. Krashes, John N. Campbell

Identifying neurons which are synaptically connected is a fundamental challenge in neuroscience, especially in the hypothalamus. Here we develop a new method combining monosynaptic rabies with single-cell transcriptomics to identify connected neurons in a genetically tractable manner: “RAMPANT” (Rabies Afferent Mapping by Poly-A Nuclear Transcriptomics). We applied RAMPANT to two populations of arcuate hypothalamus (ARC) cells: Agouti-related peptide (AgRP) neurons and POMC neurons. After infecting these neurons and their primary afferents with rabies-H2b-mCherry, we isolated mCherry+ cell nuclei for droplet-based single-nuclei RNA-sequencing, profiling the transcriptomes of 13,748 cells in total. We identified 34 molecularly distinct inputs to AgRP neurons from the mediobasal and paraventricular hypothalamus, several of which we validated by RNA FISH, and 47 inputs to POMC neurons from across the hypothalamus. Among the AgRP afferents were a feeding-activated, GLP1-sensing, inhibitory neuron population which suppresses appetite and body weight and mediates the effects of the GLP1 analogue liraglutide on energy balance. Comparing ARC afferents to POMC and AgRP neurons revealed an unexpected degree of overlap, raising the possibility that the activity of these populations is coordinated by common inputs. Our results shed light on the circuits and signaling pathways which shape AgRP and POMC neurons’ role in energy balance.

74 **Possible regulation of neuronal excitability in Temporal Lobe Epilepsy (TLE) by Perineuronal Nets (PNNs) acting as Ca2+ buffers**

**Presenter(s):** Reuben Weitzman **Role(s):** Undergraduate student 11am–noon

**Author(s):** Patrycja Oleniacz, Reuben Weitzman, Himesh Chandel, Harald Sontheimer

Temporal Lobe Epilepsy (TLE) is the most common form of localized epilepsy characterized by occurrences of unprovoked, repetitive seizures originating from the medial or lateral temporal lobe. Brain extracellular matrix (ECM) disruption has been implicated in multiple epilepsies, but the ECM-epilepsy link is not fully understood. The brain ECM accounts for ~15% of whole brain volume and consists of neuronal interstitial matrix (NIM), filling most of the extracellular space, perineuronal nets (PNNs), tightly surrounding the soma of some neurons in specific regions of the brain, and basal membrane (BM), part of the blood-brain-barrier (BBB). PNNs are particularly dense, mesh-like ECM structures of high tortuosity and highly negative charge that surround the soma of mostly inhibitory interneurons. They have been suggested to function as selective ion diffusion barriers and may potentially influence neuronal excitability.

Previous research in our lab suggests that, in mice models of TLE, PNNs undergo remodeling. One of the striking features of PNN remodeling in TLE was the production of PNNs around the excitatory granule cells in the dentate gyrus, where PNNs usually do not appear. The dentate gyrus was indicated to be hyper-excitable in TLE and proposed to act as a gate for spreading seizures. De novo-formed PNNs in the dentate gyrus were proposed to contribute to increasing granule cell excitability, however the mechanism is unknown.

PNNs consist of abundant chondroitin sulfate polymers attached to chondroitin sulfate proteoglycans anchored on the hyaluronan backbone, and crosslinked with tenascin C, with other proteins. We confirmed that chondroitin sulfate binds K+, Ca2+, Mg2+, and Fe3+, with a higher degree of binding of Ca2+ and Mg2+. Our data suggests that chondroitin sulfate has a high buffering capacity towards Ca2+ and releases Ca2+ after enzymatic degradation. Ca2+ is one of the main signaling ions in the brain. Extracellular Ca2+ levels were indicated to modulate neurotransmitter release and short synaptic plasticity in terms of paired-pulse facilitation effect. Our data indicated that in epileptic mice, in granule cells that had abnormal PNNs around, paired-pulse facilitation effect changed from

paired pulse depression towards facilitation. This supports the theory that abnormal PNNs around granule cells in epilepsy may contribute to increasing synaptic excitability of granule cells via buffering of extracellular Ca2+. Further studies are needed to confirm that the measured effect was dependent on PNNs.

75 **Clinical Phenotypes of Epigenetic Biomarker Positive versus Biomarker Negative PPD**

**Presenter(s):** Elizabeth Wenzel **Role(s):** Postdoctoral Scholar noon–1pm

**Author(s):** Elizabeth S. Wenzel, Zachary Kaminsky, Kayla Pennycuff, Meeta Pangtey, Jennifer L. Payne

Objective: Postpartum depression (PPD) can be predicted by 3rd trimester methylation at two estrogen-responsive genes (TTC9B, HP1BP3), but the mechanism(s) by which these epigenetic changes lead to PPD are unknown. We investigated whether clinical characteristics (psychiatric histories, depression onset, stress/anxiety/trauma) differ between those with (Bio+) and without (Bio-) these biomarkers of PPD risk.

Methods: Participants (N=210) completed clinical diagnostic interviews and stress/anxiety/trauma questionnaires at up to 7 study visits during pregnancy and postpartum. Biomarker status was determined using 3rd trimester blood samples. Linear mixed effects models compared outcomes between groups. Mediation models assessed the average causal mediation effect of anxiety on the relationship between biomarker status and PPD.

Results: Bio+ individuals had a greater history of generalized anxiety (X2=8.3, p=.005) and bipolar II disorders (X2=8.3, p=.003) and more often had antenatal-onset of depression (X2=8.03, p=.009). Bio- individuals more often became depressed between 3-6 months postpartum. Bio+ individuals scored higher on the perinatal anxiety screening scale (PASS, p=.02), perceived stress scale (PSS,p<.001), and state-trait anxiety index (STAI)-trait subscale (p=.04). There was a stronger positive association between Recent Life Changes (RLCQ, p=.006) and Childhood Traumatic Events (CTES, p=.04) and Edinburgh Postnatal Depression Scale (EPDS) scores in Bio+ individuals. Anxiety outcomes on the PASS (95%CI:0.02-0.12), PSS (95%CI:0.03-0.14), and STAI-Trait (95%CI:0.01-0.09) mediated the relationship between biomarker status and PPD development.

Conclusions: Findings suggest distinct clinical phenotypes between Bio+ and Bio- PPD, and a role of anxiety/stress in Bio+ PPD. This presents an opportunity to investigate mechanisms in more homogenous groups based on biomarker status.

76 **The Impact of Preterm Birth on Early Vocalizations and Motor Reflex Development in Mice**

**Presenter(s):** Rachel Woods **Role(s):** Undergraduate student noon–1pm

**Author(s):** Rachel Woods, Mya Marquez, Emily McCoy, Adema Ribic

Premature birth is associated with deficits in motor function (Gemperli et al., 2024), cognitive performance (McCoy et al., 2024), and visual processing (Witteveen et al., 2023) in adulthood. However, the early developmental mechanisms underlying these impairments remain unclear. Understanding how prematurity influences early neurodevelopment can provide insight into its long-term effects. Using a previously established mouse model of preterm birth (Witteveen et al., 2023), in which pregnant mice received mifepristone injections two days before delivery, we investigated milestone achievement in preterm and term-born mouse pups. Mice underwent ultrasonic vocalization (USV) and motor reflex testing during the first two weeks of life, as these measures predict overall developmental outcomes.

Mother isolation-induced USVs were recorded from postnatal days (PND) 0 to 14 using a specialized microphone and analyzed with DeepSqueak software. Preliminary findings suggest no significant differences in vocalization output at PND0; however, preterm mice exhibited altered USV patterns and reduced output at PND3 and PND8. Motor development was assessed using the righting reflex task, measuring a pup's ability to reorient after being placed on its back. Preliminary data from term mice indicate decreasing righting time with age, with a significant drop between PND6 and PND7.

Further testing will include expanded USV and motor reflex analyses to assess developmental trajectories in preterm mice. By focusing on vocalization patterns and motor function over time, we aim to identify specific early neurodevelopmental alterations associated with prematurity, providing a foundation for future research on the precise neural mechanisms underlying preterm-related developmental disorders.

77 **Hippocampal PNN loss is associated with delirium-like cognitive impairment in old mice after anesthesia, surgery, and a simulated ICU environment (ASI)**

**Presenter(s):** Jeffrey Wooters **Role(s):** Undergraduate student 11am–noon

**Author(s):** Jeffrey Wooters*; Navya Atluri*, PhD; Jinny Park, BA; Michal Jedrusiak, MD; Hari Prasad Osuru, PhD; Nadia Lunardi, MD, PhD

Postoperative delirium (POD) is a type of acute cerebral dysfunction that manifests with dementia-like symptoms; however, there remains no actionable pharmacological target for delirium. One emerging area of research is the perineuronal net (PNN), an extracellular structure surrounding inhibitory parvalbumin-expressing (PV+) interneurons in the hippocampus. Our findings may reveal that delirium is not simply a result of neuronal impacts but that PNNs are the missing piece of the puzzle.

18–20-month-old and 3–4-month-old C57BL/6J mice were randomly allocated to ASI or control groups. ASI mice underwent anesthesia, sedation and simulated ICU conditions, while control mice received no treatment. Cognition was assessed using Y-maze and open-field behavioral tests. Brain tissue was collected to quantify PNN-surrounded PV+ neurons. We examined PNN sulfation patterns by staining with chondroitin sulfate (CS) isomers and LC-MS. GraphPad Prism 9 was used for analysis.

Old ASI mice had fewer entries to the Y-maze novel arm ($p=0.0138$) and exhibited abnormalities in spatial memory in the AST test compared to controls ($p=0.036$). PNN density was significantly lower in the hippocampus of delirious old mice relative to controls ($p=0.0010$). An increased molar % of C4S6S/E ($p=0.0443$) and increased representation of C4S/A and C6S/C ($p<0.0001$) isomers in CA2 was shown in old mice. Young mice subjected to the same conditions did not show a significant change of PNNs nor behaviors relative to controls. Our findings show that a decrease in PNN density in old mice is associated with delirium-like symptoms, while PNNs of young mice are more resilient against ASI.

78 **Low-Rank Tensor Dictionary Learning for Denoising High b-Value Diffusion MRI**

**Presenter(s):** Kang Yan **Role(s):** Graduate student noon–1pm

**Author(s):** Kang Yan, Craig H. Meyer

Diffusion MRI is a powerful tool for investigating micro-structural tissue properties, especially at high b-values. However, the inherently low signal-to-noise ratio (SNR) at high b-values poses challenges in accurately characterizing these properties. Conventional SNR enhancement methods, such as MR signal averaging, offer only a $\sqrt{N}$ improvement with an N-fold increase in acquisition time, while higher magnetic field strengths, though beneficial, introduce artifacts and require costly hardware.

Denoising algorithms provide a promising alternative by enhancing SNR post-acquisition. While state-of-the-art methods exploit image redundancy, they often either sacrifice spatial resolution or degrade in performance under high noise levels, limiting their clinical utility. To address these challenges, we propose a novel low-rank tensor dictionary learning (LTDL) algorithm that preserves spatial resolution while significantly improving performance in high-noise conditions, thereby maintaining diagnostic accuracy.

We validated LTDL using numerical simulations, publicly available datasets, and healthy volunteer scans at b-values of 1000 and 2000 s/mm$^2$. Comparisons with state-of-the-art methods—MPPCA and gl-HOSVD—demonstrated LTDL's superior performance. At a b-value of 1000 s/mm$^2$, LTDL achieved the highest peak SNR (PSNR) (44.125 for diffusion-weighted images), outperforming MPPCA (39.670) and gl-HOSVD (41.972). This trend remained consistent at 2000 s/mm$^2$, with similar improvements observed in in vivo data.

Our results highlight LTDL as a robust denoising method for high b-value diffusion MRI, offering enhanced SNR without compromising spatial resolution, making it a valuable tool for clinical and research applications.

79 **Heart Rate Modulation by the Insular Cortex: Evidence from Direct Cortical Stimulation**

**Presenter(s):** Shuqi Ye **Role(s):** Staff 11am–noon

**Author(s):** Shuqi Ye, BS; Mark Quigg, MD; Dan Wang, PhD; Xiaohan Zhang, BA; Sihe Wang; Angela Han; Aryan Mhaskar; Alex Lin; Averie Jacobson; Jared Chung; Shayan Moosa, MD; W. Jeffrey Elias, MD; Chang-Chia Liu, PhD

The location and function of cortico-cardiac regulation by the insular cortex remain unclear. We used direct electrical stimulation of the insular cortex in non-epileptic patients to delineate how insular sub-regions influence cardiac rhythm.

ECGs were obtained from 6 subjects (4 females, 65.64 ± 11.51 years) enrolled in a chronic pain DBS trial. Longitudinal insular depth electrodes (10 contacts, 5mm spacing) were implanted bilaterally. Bi-polar stimulations (50Hz, bi-phasic, 250μs PD, 2-8mA) were delivered in 10-30s trains. Insular sub regions were defined by side (Left/Right), and by the central sulcus (Anterior/Posterior). The mean ± one standard deviation of immediate pre-stimulation (~30s) R-R intervals (RRI) was used to identify cardiac responses. Two-proportion Z test was performed to test for significance, $\alpha = 0.05$.

One hundred and 96 stimulations were delivered to the LA (81), RA (60), LP (23), and RP (32) insular subregions. Ninety-three of these stimulations evoked RRI responses. Greater proportion of RRI decrease vs. increase were found following either left or right insular stimulation ($p < 0.05$). Greater proportion of RRI decrease vs. increase were found following posterior insular stimulation ($p < 0.01$). Higher stimulation current is more likely to trigger a cardiac response, especially RRI decrease ($p < 0.05$).

Preliminary results suggest a role for the insular cortex in cardiac rhythm. Greater proportion of heart rate increase following direct insula stimulation. Heart rate respond differently along antero-posterior axis, but there was no obvious left/right side difference. Higher stimulation current is more likely to increase heart rate.

80 **BEG-GAE: A Novel GNN Framework Integrating Neuroimaging and Behavioral Information to Understand Adolescent Psychiatric Disorders**

**Presenter(s):** Ellery Yu **Role(s):** Staff noon–1pm

**Author(s):** Ellery Yu; Aiying Zhang, PhD

Functional connectivity (FC) is widely used to study various psychiatric disorders, but its consistency is often undermined by significant inter-subject variability. While these differences can be reflected in behavioral characteristics, few studies have combined them with FC. To this end, we propose a novel graph learning framework that enhances the differentiation of psychiatric disorders by integrating FC and behavioral characteristics. Additionally, we apply Grad-CAM to enhance model interpretability by identifying key regions of interest involved in distinguishing individuals with psychiatric disorders from healthy controls. Experiments with the Adolescent Brain Cognitive Development dataset highlighted two critical insights: the thalamus and specific ROIs within the somatomotor and cingulo-opercular networks play a critical role for identifying psychiatric disorders. Additionally, visualization of latent representations demonstrated that individuals with externalizing disorders, specifically Oppositional Defiant Disorder, can be distinguished from healthy controls. These findings underscore the utility of our graph learning framework for identifying psychiatric disorders and suggest its promise for improving diagnostic accuracy.

81 **Tau Oligomerization-Driven Nuclear Membrane Disruption Pathology in Alzheimer's Disease: Rupture, Invagination, and Lamina Damage**

**Presenter(s):** Shuo Yuan **Role(s):** Postdoctoral Scholar noon–1pm

**Author(s):** Shuo Yuan, Nicholas Essepian, Eliana Sherman, Weronika Gniadzik, Lulu Jiang

Physiologically, the microtubule-associated protein tau stabilizes microtubules, but under stress it undergoes oligomerization, phosphorylation, and somatodendritic accumulation. Tau misfolding and aggregation are hallmarks of tauopathies including Alzheimer's disease (AD), which correlates with cognitive decline. Previous research including ours has identified oligomeric tau (oTau) as the most toxic species, potentially through its role in nuclear membrane disruption. This study explores the dynamic interaction between oTau and nuclear envelop, as well as the mechanisms mediating this interaction. We apply the light-inducible optoTau system (4R1N Tau::mCherry::Cry2Olig) to monitor the spatiotemporal recruitment of oTau to nuclear envelop in human iPSC-derived neurons. Through live-cell imaging, immunocytochemistry, and Western Blot analysis, we found that tau oligomerization initiates nuclear membrane invagination, nuclear deformation and hyperphosphorylated tau accumulation at sites of nuclear disruption. Moreover, tau oligomers target the nuclear lamina by binding nuclear lamins, leading to nuclear rupture. The direct binding of oTau with lamin B receptor and nuclear lamina disruption were further confirmed in the humanized P301S tau (PS19) transgenic mouse. Ultrastructural analysis by electron microscopy revealed that tau-induced nuclear invaginations elicit chromatin remodeling, which may underlie gene expression dysregulations in AD pathogenesis. Notably, the correlation between nuclear lamina disruption and pathological tau deposition was also validated in AD postmortem brain tissues. In summary, tau oligomer-mediated nuclear damage may be a key driver of neurodegeneration. Therapeutic strategies targeting tau oligomerization and its interactions with nuclear membrane could represent a novel approach to mitigating disease progression in tauopathies including AD.

82 **Predictors of Late-Onset Epilepsy in Persons with Dementia**

**Presenter(s):** Ifrah Zawar **Role(s):** Faculty noon–1pm

**Author(s):** Ifrah Zawar, Mark Quigg, Emily Johnson, Soutik Ghosal, Carol Manning, Jaideep Kapur

IMPORTANCE: The risk of developing epilepsy substantially increases after the age of 60(late-onset epilepsy[LOE]), particularly in people with cognitive decline(PWCD, i.e., dementia and/or mild cognitive impairment). Epilepsy is associated with worse cognitive and mortality outcomes in PWCD. Identifying PWCD at risk for developing LOE can facilitate early screening and treatment of epilepsy. Our study investigated factors associated with LOE in PWCD. METHOD: This longitudinal, multicenter study is based on participants from 39 US Alzheimer's Disease Research Centers from 9/2005–12/2021. Of 44,713 participants, 25119 PWCD were identified. Of these,14,685 were included who did not have epilepsy at enrollment, had >2 visits, and were >60 at the most recent follow-up. We investigated the association between various factors and LOE development in PWCD. The primary outcome was LOE, defined as seizures starting at or after 60. Those who did not develop LOE but were >60 at follow-up served as controls. A multivariable Cox regression analysis assessed the association between various factors and LOE. Independent variables included age, sex, and socio-economic factors (education, race, ethnicity), cardiovascular risks (hypertension, diabetes, hyperlipidemia), cerebrovascular disease (stroke or history of transient ischemic attack[TIA]), other neurologic comorbidities (Parkinson's disease[PD], traumatic brain injury), cognition (age of dementia-onset, dementia severity, type of dementia: Alzheimer's disease [AD] vs. non-AD), genetics (APOE4 status), lifestyle (alcohol abuse, smoking), and depression. RESULTS: Of the 14,685 participants (7,355(50%) female; mean age: 73.82+8.5 years) who met the inclusion criteria, 221 (1.5%) developed LOE during follow-up. After adjusting for demographics, cardiovascular risks, neurologic comorbidities, genetics, cognitive factors, and depression, the following were associated with a higher risk of developing LOE: APOE4 allele (aHR:1.39, 95%CI:[1.04,1.86],p=0.03), dementia-onset before 60 (adjusted hazard ratio(aHR):2.46, 95% confidence interval[CI]:[1.53,3.95],p<0.001), worse cognition (aHR:2.35, 95%CI:[1.97,2.79],p<0.001), AD dementia subtype (aHR:1.68, 95%CI:[1.13,2.49], p=0.01), stroke/TIA [aHR:2.03, 95%CI:[1.37,3.01],p<0.001]), and PD (aHR:2.53, 95%CI:[1.08,5.95],p=0.03). In sensitivity analysis, using an alternative LOE definition of epilepsy-onset after 65 revealed the same factors associated with LOE. CONCLUSION AND RELEVANCE: Our study showed that the APOE4 allele, dementia-onset before 60, AD dementia subtype, worse cognition, stroke/TIA, and PD are associated with LOE development in PWCD. PWCD with these risk factors may be considered for routine screening with an EEG for early identification of LOE.

83 **Neurodevelopmental Biomarkers and Lived Experiences: Understanding Late Autism Diagnosis Across Gender and Sex**

**Presenter(s):** Sarah Zeffouni **Role(s):** Undergraduate student noon–1pm

**Author(s):** Sarah Zeffouni

Autism Spectrum Disorder (ASD) has long been studied through a predominantly male-centered lens, leading to significant diagnostic disparities for females, gender-diverse individuals, and racially/ethnically diverse populations. Late autism diagnosis (LDx), often occurring after age 12, is linked to poorer quality of life, including heightened rates of anxiety, depression, and limited access to support. This study, part of the Autism Centers for Excellence (ACE) Network, seeks to identify biobehavioral predictors of late diagnosis and address barriers to early identification.

Using a multimodal approach, this research integrates behavioral assessments, neuroimaging (MRI), and qualitative interviews to examine sex-, gender-, and race/ethnicity-based differences in cognitive and neural profiles associated with diagnostic timing. Machine learning models analyze neuroimaging data alongside phenotypic measures to develop personalized biomarkers distinguishing LDx from early-diagnosed (TDx) individuals. Preliminary findings suggest that camouflaging behaviors, clinical biases, and sociocultural barriers contribute to diagnostic delays, particularly for females and gender-diverse individuals. AI-driven methods further reveal unique neurodevelopmental patterns that differentiate LDx from TDx groups.

This research advances understandings of autism beyond the traditional male-centric framework, informing the development of gender- and culturally sensitive diagnostic criteria. By integrating diverse perspectives and leveraging AI for precision diagnostics, these findings hold the potential to transform clinical practice, ensuring earlier recognition and support for historically underdiagnosed populations. This work contributes to a more inclusive and equitable approach to autism diagnosis and care.

84 **EEG Alpha Oscillatory Dynamics Reflect Affective Modulation of Pain by Personally Meaningful Music**

**Presenter(s):** Xiaohan Zhang **Role(s):** Staff 11am–noon

**Author(s):** Patrick Realyvasquez, Nicholas P. Cherup, Xiaohan Zhang, Siny Tsang, Ayshah Asmat, Jahred Rosa-Sullivan, Pati Castro Martinez, Mathieu Roy, Shuqi Ye, Dan Wang, Jeff Liu, Patrick H. Finan

Music is a promising non-pharmacological approach to pain modulation, yet the underlying neural mechanisms remain incompletely understood. This study examined how different types of music modulate EEG responses to long-lasting heat pain stimulation, with a focus on alpha oscillatory activity.

Forty-four healthy participants underwent EEG recording while exposed to painful heat stimuli (Pain 50/100) applied to the ventral forearm. Each stimulus was delivered at the midpoint of a 60-second music clip. Participants listened to personally meaningful positive music, research-assigned negative music, and neutral instrumental music in an order-randomized block design. EEG alpha power and peak alpha frequency were analyzed time-locked to the pain stimulus, and pain intensity and unpleasantness ratings were collected before and after each condition.

Our results showed that positive music significantly reduced both pain intensity and unpleasantness, while negative music significantly increased pain unpleasantness. EEG analysis revealed a significant increase in heat pain-related alpha power during positive music ($p = 4.62e\text{-}60$) and a significant decrease in peak alpha frequency during negative music ($p = 3.61e\text{-}6$). No significant modulation of alpha activity was observed during negative or neutral music.

Personally meaningful positive music was associated with increased alpha oscillatory responses to painful stimulation and lower subjective pain ratings. These results suggest that music may influence both neural and perceptual aspects of pain and that alpha power could serve as a potential marker for affective modulation in pain-related EEG research.

85 **Neurophysiological Markers of Pain Relief After Focused Ultrasound Mesencephalotomy for Head and Neck Cancer**

**Presenter(s):** Xiaohan Zhang **Role(s):** Staff noon–1pm

**Author(s):** Xiaohan Zhang, Shuqi Ye, Dan Wang, Charlotte Ream, Alex Lin, Aryan Mhaskar, Averie Jacobson, Jared Chung, Shayan Moosa, W. Jeff Elias, Jeff C. Liu

Mesencephalotomy has been used to relieve head and neck cancer pain but is limited by invasiveness and risk of stereotactic inaccuracy. Focused ultrasound (FUS) offers a noninvasive and precise alternate. This clinical trial evaluates the safety and feasibility of FUS mesencephalotomy for cancer-related pain. Here, we report findings from a sub-study investigating resting-state EEG changes as potential neurophysiological correlates of pain relief.

Four male subjects with intractable cancer-related pain underwent FUS mesencephalotomy. Resting-state EEG was recorded before and one week after treatment. Data were filtered, artifact-cleaned, and z-score normalized. EEG signals were segmented into 5-second epochs, and power spectral density (PSD) was estimated using the MATLAB pwelch function with a 50% overlapping Hamming window to minimize spectral leakage. Dominant band power was calculated as the band power integral over sum power integral for delta, theta, alpha, beta, and gamma bands. The dominant frequency peak (6–14.5 Hz) was identified, and its power was expressed as a fraction of total power (0–55 Hz). Differences were assessed using Wilcoxon rank-sum tests ($p < 0.05$).

No consistent changes were observed in delta, theta, alpha, or beta band power following treatment. However, gamma band power increased in responders and decreased in non-responders ($p < 0.001$). Dominant frequency significantly decreased in responders but not in non-responders ($p < 0.05$).

Preliminary findings suggest that resting-state EEG—particularly gamma band power and dominant frequency—may reflect early neurophysiological changes associated with response to FUS mesencephalotomy. Larger studies are needed to validate these results.