



# **Annual Neuroscience Symposium & Poster Session**

**STAR Campus  
Newark, DE**

**Friday, October 28, 2022**

***The Delaware Center for Neuroscience  
Research  
and  
The Delaware Chapter of the Society for  
Neuroscience***



# Annual Delaware Neuroscience Research Symposium

STAR Tower, Newark, DE 19702

Friday, October 28, 2022



8:30 – 9:00 am		Registration and coffee/bagels
9:00 – 9:15 am	<b>Welcome and Overview</b>	<b>Melissa Harrington, Assoc. VP for Research, Delaware State Univ.</b> <b>Anna Klintsova, Professor of Psychological &amp; Brain Sciences, Univ. Delaware</b>
9:15 – 10:15 am	<b>Session I: Short Talks</b> <b>Moderator: Anna Klintsova</b>	<p><b>9:15 – 9:30 am Rachel Clein, University of Delaware</b> <i>Novel computational approach reveals altered group dynamics in Shank3b mutant mice</i></p> <p><b>9:35 – 9:50 am Katrina Milbocker, University of Delaware</b> <i>Disentangling Abnormalities in Myelin Ensheathment Across Adolescence and Adulthood in a Rodent Model of Fetal Alcohol Spectrum Disorders</i></p> <p><b>9:55 – 10:10 am Mohamed Khalife, University of Delaware</b> <i>MC4Rs facilitate fear extinction learning and ACTH-driven neuroprotection after early life seizures</i></p>
10:15 – 10:25 am		<b>BREAK</b>
10:25 – 11:20 am	<b>Session II Short Talks (cont'd)</b> <b>Moderator: Anna Klintsova</b>	<p><b>10:25 – 10:40 am Nicholas Cottam, Delaware State University</b> <i>Cerebellar structural, glial, and neuronal defects in a mouse model of spinal muscular atrophy</i></p> <p><b>10:45 – 11:00 am Dinesh Kumar Verma, PhD Delaware State University</b> <i>SEN-1 inhibition reduces damages from preformed fibrils of alpha-synuclein and alleviates Parkinson's disease-related signs in mice</i></p> <p><b>11:05 am – 11:20 am Malek Elsayyid</b> <i>Neuronal extracellular vesicle biogenesis and glial uptake</i></p>
11:25 – 12:25 pm	<b>Session II Lightning Talks</b> <b>Moderator: Anna Klintsova</b>	<p><b>11:25 am – 11:30 am Jerome Roehm, University of Delaware</b> <i>Topological Data Analysis and Stimulus Space Classification</i></p> <p><b>11:30 am – 11:35 am Maelyn Arcodia, University of Delaware</b> <i>Control of Balance During Walking in Individuals with Parkinson's Disease</i></p> <p><b>11:35 am – 11:40 am Zachary Gemzik, University of Delaware</b> <i>Optogenetic Theta Stimulation of the Medial Septum Facilitates Spatial Working Memory</i></p> <p><b>11:40 am – 11:45 am Janace Gifford, University of Delaware</b> <i>Vulnerability to postpartum anhedonia and underlying neuroimmune and resting state function in Sprague Dawley rats</i></p> <p><b>11:45 am – 11:50 am Dionne Williams, Delaware State University</b> <i>Ameliorating the effects of an environmental toxin in a Drosophila model of Parkinson's Disease</i></p> <p><b>11:50 am – 11:55 am Taylor Campbell, University of Delaware</b> <i>Stress &amp; the Epigenome: A Role for Behavioral Interventions</i></p> <p><b>11:55 am – 12:00 pm Tobenna Amanfo, Delaware State University</b> <i>Synaptobrevin (Vamp2) dominant negative prevents glutamate exocytosis by astrocytes</i></p> <p><b>12:00 pm – 12:05 pm Andy Lam, PhD, University of Delaware</b> <i>Protective Impact of Vitamin B12 in an Alzheimer's Disease Model</i></p> <p><b>12:05 pm – 12:10 pm Emylee Kerslake, University of Delaware</b> <i>Impact of High Dietary Glucose on A<math>\beta</math>-induced Proteotoxicity in C. elegans</i></p> <p><b>12:10 pm – 12:15 pm V. A. N. Talabattula, PhD, Delaware State University</b> <i>Role of the Astrocytic mGluR Pathway in the development of Neuronal Synchrony</i></p>



## Annual Delaware Neuroscience Research Symposium



12:30 – 1:30 pm	<b>Networking Lunch and Posters Set Up</b>	
1:30 pm	<b>Introduction of speaker</b>	Soonmoon Yoo, PhD, Sr. Research Scientist Nemours Children's Health
1:35 – 2:30 pm	<b>Keynote speaker</b>	Dr. Jeff Twiss Professor, SmartState Chair in Childhood Neurotherapeutics, Associate Dean for Research and Graduate Studies, Univ. of South Carolina <b>Venturing into axons, from heretical ideas to growth acceleration</b>
2:30 – 4:30 pm	<b>Poster session and judging of student posters</b> 2:30 – 3:30 pm presenters stand by odd numbered posters 3:30 – 4:30 pm presenters stand by even numbered posters Refreshments @3:30pm	
5:00 pm	<b>Announcement of poster award winners</b>	



## Annual Delaware Neuroscience Research Symposium



### Keynote talk

## Venturing into axons, from heretical ideas to growth acceleration



*Jeffery L. Twiss, M.D., Ph.D.  
Associate Dean for Research & Graduate Studies,  
College of Arts & Sciences  
SmartState Chair in Childhood  
Neurotherapeutics  
University of South Carolina, Columbia, SC*

Jeff Twiss completed the MD, PhD program at Medical University of South Carolina. He did a clinical residency and fellowship in anatomic pathology and neuropathology at Stanford Medical Center, followed by post-doctoral training in neurobiology at Stanford University. He started his independent research career in 1996 focusing on molecular neurobiology and continued with clinical work in neuropathology. His group has made seminal contributions to the field of neural repair and how post-transcriptional mechanisms contribute to neural connectivity. They discovered that intra-axonal protein synthesis is needed for regeneration of peripheral nerves and are now leveraging that and other discoveries to develop new therapeutic strategies for neural repair. His research program has been continually funded by NIH since 1994 and has garnered support from numerous other federal as well as private agencies. He was appointed as SmartState Endowed Chair in Childhood Neurotherapeutics at the University of South Carolina in 2013 and currently serves as Associate Dean for Research and Graduate Studies in the College of Arts and Sciences.



## Annual Delaware Neuroscience Research Symposium



# Abstracts of Oral Presentations



**Tobenna Amanfo, Murali K. Temburni, V.A.N. Talabattula**

Delaware State University

### **“Synaptobrevin (Vamp2) dominant negative prevents glutamate exocytosis by astrocytes”**

We established pure neuron only and mixed (astrocyte and neuron) cultures on multi-electrode arrays (MEAs) from the embryonic chick optic tectum with the goal of testing the role of astrocytes in the development of neuronal network activity. Our preliminary results indicate that astrocytes are necessary for neuronal cultures' synchronous activity of neurons. Mixed neuron and astrocyte cultures show random spiking activity without synchronization. Astrocytes have been shown to modulate network activity by releasing gliotransmitters like glutamate, D-serine, and ATP. We hypothesize that glutamate sensing at tripartite synapses via mGluRs elevates local calcium within astrocyte processes. With sufficient activation, the localized calcium elevation crosses a threshold causing a calcium-induced calcium release (CICR) within the astrocyte leading to glutamate exocytosis. We targeted the SNARE protein Synaptobrevin (Vamp2) within astrocytes as crucial for communication with neurons via its molecular induction of vesicle docking. We proposed to test this model by expressing a truncated Vamp2 subunit (Vamp2 DN) which acts as a dominant-negative to block exocytotic release. Astrocytes expressing the Vamp2DN are expected to release significantly less glutamate upon calcium elevation, thereby reducing synchrony of neuronal activity. We have generated primary astrocyte lines expressing the synaptobrevin dominant-negative (Vamp2DN) along with the glutamate sensor iGluSnFR. We demonstrate that Vamp2DN expressing astrocytes have significantly reduced glutamate exocytosis when CICR is induced with Ionomycin. We will co-culture the Vamp2DN astrocytes with neurons and record network activity on MEAs (Multi-Channel Systems). With these tools, a more comprehensive molecular model for astrocyte involvement in generating neuronal synchrony can be developed.



**Maelyn Arcodia, Ashwini Sansare, Elizabeth Thompson,  
Hendrik Reimann, John J. Jeka,**  
University of Delaware

### **“Control of Balance During Walking in Individuals with Parkinson’s Disease”**

Majority of falls occur during walking and are the leading cause of injury for older adults (OH) and high fall-risk populations such individuals with Parkinson’s disease (PD). Humans use three sensory systems to maintain their balance: visual, vestibular, and proprioception. It is known that OH rely on vision while PD have proprioceptive deficits. These sensory deficits may contribute to fall-risk. Previously, we showed how young healthy (YH) individuals regain upright stability when walking in a visually challenging environment. YH use multiple balance mechanisms; *lateral ankle roll, step placement, and push off*, to control their center of mass (CoM) to regain upright stability. However, it is unknown how OH or PD respond under the same condition. This study aims to understand how OH and PD use the balance mechanisms to regain stability during a visually perceived fall. Eleven individuals with PD and four age matched OH walked on an instrumented treadmill for 10 two-minute trials in a virtual reality environment. At randomized heel strikes, the visual field was briefly rotated, resulting in a perceived fall to the side. Kinematic responses were measured using motion capture data. Following a visual perturbation, both groups shifted their CoM in the opposite direction of the perceived fall. The PD group had a larger CoM displacement post-perturbation than the OH group. PD group also prioritized different balance mechanisms than the HO group following a visually perceived fall suggesting that the pathology of Parkinson’s disease may play a role in upright stability during walking.



**Taylor Campbell, Tania Roth**

University of Delaware

### **“Stress & the Epigenome: A Role for Behavioral Interventions”**

Aversive caregiving in early life is a risk factor for aberrant brain and behavioral development. This outcome is related to epigenetic dysregulation of the *Bdnf* gene. The *Bdnf* gene encodes for brain-derived neurotrophic factor (BDNF), a neurotrophin involved in early brain development, neural plasticity, learning, and memory. Disruptions in caregiver-infant interactions lead to increased methylation and decreased expression of the *Bdnf* gene. One way to mitigate this effect is hypothesized to be through aerobic exercise. Exercise increases BDNF at the protein and gene expression levels, making it an exciting target for therapeutic interventions. To our knowledge, exercise has never been studied as a therapeutic intervention in preclinical rodent models of caregiver maltreatment. To that end, the current study investigated the effect of an adult voluntary wheel running intervention on *Bdnf* aberrant methylation and expression in the prefrontal cortex and hippocampus of rats who experienced aversive caregiving in infancy. We employed a rodent model (Long Evans rats) wherein rat pups experienced intermittent caregiver-induced stress from postnatal days 1-7 and were given voluntary access to a running wheel (except in the control condition) from postnatal days 70-90 as a young adulthood treatment intervention. Current results indicate that maltreatment and exercise affect *Bdnf* gene methylation in an exon, CG site (loci where methyl groups attach), and sex specific manner. Data collection is ongoing, further demonstrating the dynamic nature of DNA methylation. This work is funded by the National Institutes of Health: Eunice Kennedy Shriver National Institute of Child Health & Human Development (1R01HD087509).



**Rachel Clein, Megan Warren, Josh Neunuebel**

University of Delaware

### **“Novel computational approach reveals altered group dynamics in Shank3b mutant mice”**

Autism spectrum disorders (ASDs) are highly heritable neurodevelopmental conditions characterized by deficits in social behavior and communication. While the influence of genetic modifications on ASD-like phenotypes in individuals is well-studied, the impact of ASD symptoms on group dynamics is less clear. Here, we used a preclinical mouse model of Phelan-McDermid syndrome, a monogenic form of ASD resulting from mutations of the SHANK3 gene (Peca et al., 2011), to investigate group social dynamics. We continuously recorded audio and video data using a sound source localization system (Warren et al., 2018) while mixed-sex groups (2 males and 2 females per group) of either Shank3b knockout mice (KO;  $n = 6$  groups) or wild-type controls (WT;  $n = 7$  groups) freely behaved for five hours. To quantify collective behavior, we developed a computational approach that assessed social cohesion over time based on the spatial location of each mouse relative to the other mice.

When assessing how individual members regulated the social cohesion of their group, we found that KO females contributed significantly more to group cohesion than KO males, but there were no differences between WT males and females (Kruskal-Wallis with Dunn-Sidak post hoc correction;  $H(3) = 14.77$ ,  $p < 0.05$ ). We next applied a progressive k-means clustering algorithm to the cohesion values and identified eight categories of group behavioral events. The eight types of group behavioral events, on average, lasted from 0.6 to 1.7 seconds, occurred 928 to 15,899 times, and had cohesion values ranging from 5.09 (more cohesion) to 36.14 (less cohesion). A stochastic first order Markov chain model demonstrated that the temporal patterning of behavioral events was altered in KO groups relative to WT (Chi Square Goodness of Fit Test,  $X^2(63) = 1391.8$ ,  $p < 0.001$ ). The vocal rate was also significantly higher in WT groups, but only during behavioral events defined by small inter-individual distances (Wilcoxon rank sum tests, all significant U values  $> 60$ , all significant p values  $< 0.05$ ). During these behavioral events, the vocal activity could accurately predict the genotype of the group. Our results suggest that genetic modifications to the SHANK3 gene lead to group-level alterations in social dynamics, thus providing further insight into how social deficits in individual animals may impact collective behavior.



**Nicholas C. Cottam, Tiffany Bamfo, Melissa Harrington,  
Christine Charvet, Khan Hekmatyar, Jianli Sun**

Delaware State University

### **“Cerebellar structural, glial, and neuronal defects in a mouse model of spinal muscular atrophy”**

Spinal Muscular Atrophy (SMA) is a neuromuscular disease that affects as many as 1 in 6,000 individuals at birth, making it the leading genetic cause of infant mortality. SMA is best defined by motor neuron dysfunction due to a deletion or mutation in transcripts of survival motor neuron protein (SMN), which leads to degeneration and dysfunction in the anterior horn of the spinal cord. A growing number of studies indicate that SMA is a multi-system disease, but the cerebellum has received little attention even though it plays an important role in motor function with widespread pathology reported in the cerebella of SMA patients. In this study, we use the SMN $\Delta$ 7 mouse model to assess SMA pathology in the cerebellum using structural and diffusion magnetic resonance imaging, immunohistochemistry, and electrophysiology. Magnetic resonance imaging revealed a significant disproportionate loss in cerebellar volume, decrease in afferent cerebellar tract formation, and abnormal microstructure. Histology staining revealed a selective lobule-specific degeneration of Purkinje cells and abnormal structural foliation and glial cell arrangements. Lastly, patch-clamp electrophysiological recordings revealed a decrease in spontaneous firing of cerebellar output neurons in the SMN $\Delta$ 7 mice relative to controls. Our findings reiterate the necessity to expand the characterization of SMA pathology beyond the spinal cord. We suggest that cerebellar defects due to decreased SMN levels impairs the functional cerebellar output in motor control, and that cerebellar pathology may be necessary to address in order to achieve comprehensive treatment and therapy for SMA patients.

**Malek Elsayyid, Jessica Tanis**

University of Delaware

## **“Neuronal extracellular vesicle biogenesis and glial uptake”**

Extracellular vesicles (EVs) are membrane-enclosed bioactive molecules released by nearly all cells. The role of EVs in the progression of neurodegenerative diseases such as Alzheimer’s Disease (AD) has only recently been appreciated, with evidence of pathological EV cargo contributing to the spread of the disease. Understanding how EVs are biosynthesized, package biomolecular cargo, and affect change in target cells is imperative to understanding intercellular signaling and pathogenesis. EVs can be released from cilia, microtubule-based specialized organelles that protrude from the neuron surface similar to antennae sending and receiving signals. In *Caenorhabditis elegans*, EVs bud from the cilia of sensory neurons and can be uptaken by surrounding glia or released into the external environment through pores in the animal’s exoskeleton.

We have identified the ion channel, CHLM-1, as a novel EV cargo. Loss of the GTPase RAB-28 results in a buildup of ectopic EVs in the extracellular space between the neuronal cilium and glia, suggesting its role as a negative EV release regulator. I have found that the number of EVs containing the ion channel CLHM-1 increases in *rab-28* mutants whereas other EV subpopulations are unaffected. CLHM-1 may be among the proteins packaged into the excess EVs shed in the lumen of *rab-28* mutants and could therefore be taken up by the glia. Using super-resolution microscopy, I have shown neuronal-derived tdTomato-tagged CLHM-1 colocalizing with GFP labeled glial cells in the male tail sensory neurons *in vivo*. This data suggests that G-protein activity may differentially regulate EV subpopulation biogenesis, while neuron-glia crosstalk affects EV release into the surrounding environment.



**Zachary Gemzik, Amy L. Griffin**

University of Delaware

### **“Optogenetic Theta Stimulation of the Medial Septum Facilitates Spatial Working Memory”**

Spatial working memory (SWM) is the ability to process and maintain spatially-relevant, goal-directed information over a temporal gap, and relies on an intact hippocampus (HPC). The medial septum (MS) is necessary for the generation of theta, (4-12 Hz) oscillations in the HPC and SWM (Mizumori et al., 1990). A recent study from our lab showed that optogenetic suppression of MS delivered during the delay period of a delayed non-matched to position task disrupted choice accuracy, suggesting that MS activity is necessary for the maintenance of spatial information during SWM tasks (Gemzik et al., 2020). Based on these previous findings, we hypothesized that MS-generated theta facilitates the maintenance of spatial information to enable optimal SWM task performance.

To test this hypothesis, we examined the effects of optogenetic MS theta stimulation delivered during the delay period of a SWM-dependent task. We first trained rats (N=10) to perform a delayed alternation task with a 10s delay. After rats reached asymptotic performance, we injected an excitatory optogenetic viral vector encoding a blue light-activated cation channel, channelrhopsin-2 (AAV5-hSyn-hChR2-EYFP) into the MS and implanted an optogenetic fiber above the injection site. We also implanted two of these rats with LFP electrodes aimed at the MS and HPC to verify the effectiveness of our stimulation procedures in inducing theta oscillations. We challenged SWM demand by adding a long (30s) delay period in addition to the short (10s) delay. We predicted that MS theta stimulation would facilitate choice accuracy especially for the longer delay. Each testing session consisted of 10 trials each of 4 different conditions that were pseudo-randomly interleaved within the session: red (638nm/control) or blue (470nm/excitatory) laser stimulation at theta frequency (6Hz) delivered during a short (10s) or long (30s) delay period.

As predicted, for the control stimulation, choice accuracy was significantly lower on the 30s delay trials vs. the 10s delay trials, verifying that longer delay periods pose a significant challenge to SWM. This delay-dependent decrease in choice accuracy was eliminated by delivering MS theta stimulation during the delay period (rmANOVA: laser color x delay length,  $F(1,9) = 11.48$ ,  $p = 0.008$ ; post-hoc Holm test, red/control 10 vs. 30s,  $p = 0.004$ ; 10s red/control vs. blue/excitatory,  $p = 0.921$ ; 30s red/control vs. blue/excitatory,  $p = 0.01$ ). These findings support the hypothesis that MS theta stimulation facilitates SWM and suggest that MS may equip HPC neurons with a temporal framework upon which to process and organize task-relevant information on a theta frequency timescale.



**Janace Gifford, Jaclyn Schwarz**

University of Delaware

### **“Vulnerability to postpartum anhedonia and underlying neuroimmune and resting state function in Sprague Dawley rats”**

Approximately 60% of new mothers experience postpartum mood disturbances known as the “baby blues.” Fortunately, most new mothers recover within a few weeks but a significant subset (10-15%) go on to develop postpartum depression (PPD). The present study aimed to examine the onset of anhedonia and associated changes in neuroimmune and endocrine function as well as altered resting state brain function postpartum. First time dams underwent a series of sucrose preference tests (prior to breeding and postpartum) to examine depressive-like behavior. Previous data revealed pre-pregnancy, most rats exhibit a strong sucrose preference (>80%) but immediately postpartum approximately 40% of new mothers display anhedonia suggesting some mothers are susceptible and others resilient to this onset of postpartum anhedonia. To better understand these individual differences, brain tissue was collected from animals at either postnatal day 2 or 9 and assessed for neuroimmune function. Fecal samples were also collected and assayed for estradiol and corticosterone levels. Results indicated an increase in IL-6 in susceptible animals in the dorsal hippocampus and medial prefrontal cortex (mPFC) at P2 and P9 time points as well as decreased BDNF in the mPFC at P2 and P9. Increased corticosterone postpartum was observed in resilient animals while no differences were observed in estradiol. Further, results suggest susceptible animals have altered default mode network integration between P3 and P10. Overall, this work aims to better understand and predict susceptibility or resiliency to postpartum anhedonia with hopes to proactively identify risk factors associated with PPD to aid in the development of future targeted therapeutics.

Funded by R21MH122862 to JMS



**Emylee Kerslake, Andy Lam, Jessica Tanis**

University of Delaware

### **“Impact of High Dietary Glucose on A $\beta$ -induced Proteotoxicity in *C. Elegans*”**

Alzheimer’s disease (AD) is the leading neurodegenerative disorder worldwide, with an estimated 50 million individuals currently afflicted. Pathological features of this debilitating condition include amyloid-beta (A $\beta$ ) accumulation, bioenergetic defects, increased oxidative stress, and impaired glucose metabolism. Since there is currently no disease-modifying treatment for AD, it is essential to understand how modifiable risk factors such as diet impact disease onset and progression. It is difficult to determine the impact of specific nutrients in humans due to complex diet, organismal complexity, genetic diversity, and indirect effects of the gut microbiome. Individuals with abnormal blood sugar levels and glucose utilization are at greater risk for AD, likely because glucose is required to fuel neuronal function. Yet we lack an understanding of how the interplay between glucose and other macro/micronutrient availability impacts brain health. To define how diet impacts A $\beta$  proteotoxicity we use *C. elegans* that express toxic human A $\beta$ 1-42 in the body wall muscles, which induces robust time-dependent paralysis, reduced ATP levels, and increased reactive oxygen species (ROS). We discovered that glucose supplementation accelerated paralysis in A $\beta$  animals that consumed OP50 *E. coli* yet had no effect on worms fed HB101 *E. coli*. While vitamin B12 can protect against A $\beta$ -induced proteotoxicity, B12 is not the factor in the HB101 diet that nullifies the toxic effects of excess glucose levels. To determine how this diet was protective we performed RNA-Seq and observed downregulation of the predicted facilitated glucose transporter F14E5.1 in animals fed HB101. Loss of F14E5.1 slowed A $\beta$ -induced paralysis, bioenergetic defects, and ROS accumulation in A $\beta$  animals fed OP50. In the presence of excess glucose, the F14E5.1(tm3206) mutation abrogated accelerated A $\beta$ -induced paralysis, resulting in a similar time to paralysis regardless of the diet consumed. These findings suggest that F14E5.1 impacts A $\beta$ -induced proteotoxicity, potentially by modulating glucose metabolism.



**Mohamed Rabieh Khalife, Patrick Jasinski, Khalil Abed Rabbo, Mohamed Ouardouz, Rod C. Scott, Matthew Mahoney, Amanda Hernan**

University of Delaware and Nemours Children's Health

### **“MC4Rs facilitate fear extinction learning and ACTH-driven neuroprotection after early life seizures”**

Pediatric epilepsy is a common neurological disorder characterized by recurrent unprovoked seizures, but often associated with severe cognitive impairments and psychiatric comorbidities that are detrimental to the patient's quality of life and not improved with current treatment approaches (Sherman et al., 2007; Reilly et al., 2014). Rodents with a history of early life seizures (ELS) have significant deficits in spatial learning and memory, sociability, attention, and fear extinction learning. We have previously shown that exogenously administered ACTH, a hormone in the HPA-axis, is effective at preventing learning impairments after ELS. Here we show that this prevention is dependent on melanocortin 4 receptors, neuropeptide receptors agonized by ACTH that are expressed on neurons and glia in the brain. ELS and ACTH treatment are associated with long-term alterations in PFC neuronal firing modulation at baseline during an open field task, as well as during learning in a fear extinction task. These results suggest that ACTH treatment improves cognitive outcome after ELS through a mechanism that bypasses the systemic effects of cortisol release and potentially normalizes local PFC networks independently from altering seizure parameters. Taken together, these data elucidate the mechanism behind the improvement in ELS outcome with ACTH treatment and suggest that MC4R agonists may be a novel therapeutic strategy for improving outcome in pediatric epilepsy.



**Andy Lam, Jessica Tanis**

University of Delaware

### **“Protective Impact of Vitamin B12 in an Alzheimer’s Disease Model”**

Alzheimer’s disease (AD) is a devastating neurodegenerative disorder with no effective treatment that currently afflicts ~50 million individuals worldwide. Some AD risk factors including genetic predisposition and aging are non-modifiable while other risk factors such as diet can be altered to slow disease onset and progression. However, the complexity of the human diet and the indirect effects of the microbiome make it challenging to identify protective nutrients. Multiple factors contribute to AD pathogenesis including amyloid-beta ( $A\beta$ ) deposition, energy crisis, and oxidative stress. Transgenic expression of toxic human  $A\beta$  peptides in *C. elegans* body wall muscles generate robust time-dependent paralysis as well as AD-like pathological features. We discovered that  $A\beta$ -expressing *C. elegans* fed HB101 *E. coli* exhibited delayed paralysis, higher ATP levels, decreased mitochondrial fragmentation, and reduced reactive oxygen species (ROS) compared to those raised on OP50 *E. coli*. Mild vitamin B<sub>12</sub> deficiency was observed in animals grown on OP50, but not HB101. B<sub>12</sub> supplementation delayed  $A\beta$ -induced paralysis and protected against the increase in ROS and energy crisis observed in animals fed OP50, but did not have an additive beneficial effect on those that consumed HB101. Providing dietary B<sub>12</sub> to deficient adult  $A\beta$  animals delayed paralysis, suggesting potential for vitamin B<sub>12</sub> as a therapy to target proteotoxic stress later in life. Vitamin B<sub>12</sub> had this protective effect by acting as a cofactor for methionine synthase (METR-1), impacting the methionine/S-adenosylmethionine (SAME) cycle. Phosphatidylcholine (PtdCho), a major component of membranes, can be synthesized by SAME-dependent methylation of phosphoethanolamine. Choline supplementation delayed  $A\beta$ -induced paralysis of animals that consumed OP50 but offered no additional protection for those fed HB101. These data are consistent with a model in which vitamin B<sub>12</sub> dependent methionine/SAME cycle activity increases PtdCho production to reduce  $A\beta$  proteotoxic effects.



**Katrina A. Milbocker, Anna Klintsova**

University of Delaware

### **“Disentangling Abnormalities in Myelin Ensheathment Across Adolescence and Adulthood in a Rodent Model of Fetal Alcohol Spectrum Disorders”**

Fetal Alcohol Spectrum Disorders (FASD), a class of developmental disorders that may result from prenatal alcohol exposure, affects 1 in 20 infants in the U.S. annually (May, 2018). FASD-affected individuals have poor executive function, increasing their risk for educational, employment, and legal issues (McLachlan et al., 2020).

Diminished executive function capacity is linked to disrupted corpus callosum myelination during adolescence (Jacobson et al., 2017; Kar et al., 2021). However, targeted interventions that support neurodevelopment in FASD-affected youth are limited. This multimodal study investigates the potential for a myelin-stimulating adolescent intervention to restore corpus callosum myelination using a rodent model of FASD. Female Long-Evans rat pups underwent either intragastric intubation of alcohol in milk substitute (5.25 g/kg/day) or intubation without alcohol exposure (sham-controls) from postnatal days (PD) 4 through 9 targeting the rodent brain growth spurt at the onset of corpus callosum myelination (Milbocker & Klintsova, 2020; Dobbing & Sands, 1979).

Adolescent rats from both groups were randomly selected to receive a voluntary exercise intervention or remain sedentary from PD 30-42. Previous work from our lab has shown that this intervention mitigates neuroanatomical impairments to gray matter regions in the FASD-affected brain (Klintsova et al., 2013). Using in vivo neuroimaging, we confirmed that corpus callosum maturation is delayed across adolescence in our model ( $p < .05$ ). However, we did not detect any main or interactive effects of adolescent exercise intervention on myelination. To validate this finding, we perfused a cohort of rats from each time point and collected fixed brain tissue to quantify changes to myelin basic protein density in corpus callosum pre- and post-intervention. Preliminary results show that the density of myelin basic protein is increased in the FASD-affected brain across adolescence, and a significant interaction confirms that exercise intervention reduces myelin density to control levels in the FASD-affected brain ( $F_{1,30} = 9.2$ ,  $p = .005$ ). Unexpectedly, preliminary ultrastructural analysis of myelin ensheathment in corpus callosum suggests that the percent of axons with abnormal ensheathment is highest in adult rats with previous alcohol exposures that underwent the intervention ( $F_{1,24} = 6.8$ ,  $p = .02$ ), potentially resulting from upregulated myelin sheath production following intervention exposure. Together, these data demonstrate that adolescent exercise intervention stimulates white matter development, and that ongoing research is needed to detect nuanced changes in vivo using neuroimaging. These experiments showcase the capacity for Delaware researchers to answer complex questions concerning prevalent neurodevelopmental disorders using available cutting-edge resources.



**Jerome Roehm, Chad Giusti**

University of Delaware

### **“Topological Data Analysis and Stimulus Space Classification”**

Neurons in the mammalian hippocampus called place cells encode known environments. As an animal navigates a physical space, specific place cells will fire at increased rates when the animal is in the corresponding locations. Amongst an enormous amount of noise, neural firing patterns that mimic those seen when the animal is moving can be found when the animal is at rest. These firing sequences are known as sharp wave ripples. My research uses topological and other data analysis techniques to “read the mind” of the animal when it is at rest but is thinking about navigation. In this presentation, I will give a brief overview of topological data analysis and its application to navigation in neuroscience. More specifically, given a sequence of neural firings from place cells, I determine if the firings can represent the animal thinking about navigating an environment or if it is more likely to be noise or non-motor signal. If the sequences can be interpreted as encoding an environment, my results allow me to reconstruct the environment (linear track, square area, circular track, etc.) from the neural firing patterns alone, not using any behavioral data. This research into sharp wave ripples could impact the way that we understand memory.



**V.A.N. Talabattula, Michael Moore, Rhonda Dzakpasu, Murali K. Temburni**

Delaware State University

### **“Role of the Astrocytic mGluR Pathway in the development of Neuronal Synchrony”**

Synchronous oscillations are necessary for establishing functional neuronal networks in normal vertebrate brain development – however, the mechanisms of neuronal synchronization are not fully understood. Existing models of synchronous activity assume that it is intrinsic to neurons. Astrocytes have been shown to modulate oscillatory activity in networks of neurons possibly by releasing gliotransmitters like glutamate and ATP. We have established pure and mixed (astrocyte and neuronal) cultures from the developing chicken brain (optic tectum) and recorded neuronal network activity using three different the multi-electrode array systems, MED64, Axion and Multichannel Systems. Our preliminary results indicate that astrocytes are necessary for synchronous activity of neurons in culture. To further dissect the molecular pathways involved, we targeted the metabotropic glutamate receptor (mGluR) pathway within astrocytes as a mechanism by which astrocytes influence synchronous firing. Astrocytes express mGluRs that consist of the same subunits and stoichiometry as those expressed in neurons.

To test this model, we expressed the calcium sensor GCaMP6F to assay  $\text{Ca}^{++}$  activity and a truncated mGluR subunit (mGluR DN) which acts as a dominant negative by blocking downstream signaling of the mGluR1 pathway using the lentiviral vector pUltrahot in primary chick astrocytes. Preliminary results show that astrocytes expressing the mGluR DN have reduced calcium elevation upon mGluR stimulation.

Lastly, we will take a pharmacological approach and add the mGluR1 antagonist, A841720, to neuron-astrocyte co-cultures and pure neuronal cultures. Synchronous activity will be recorded using the MCS MEA system and network activity parameters such as synchrony index (SI), spike amplitude and spike rates will be determined. We expect that the mGluR1 antagonist treated cultures will have a reduced Synchrony Index.



**Dinesh Kumar Verma, Anurupa Ghosh, Kwadwo Ofori, Darice Wheeler, Gabriela Cabrera, Y. Hwan Kim**

Delaware State University

### **“SEN-1 inhibition reduces damages from preformed fibrils of alpha-synuclein and alleviates Parkinson’s disease-related signs in mice”**

Small Ubiquitin-like modifier (SUMO) conjugation is a dynamic post-translational modification on lysine residues, catalyzed by SUMO-specific ligases and removed by SUMO-specific proteases (SENPs). The physiological consequences of (de)SUMOylation in Parkinson’s disease (PD) pathology are not well understood. In this study, we characterized which isoform of SENPs is involved in detaching SUMOs from  $\alpha$ -synuclein when 1-methyl-4-phenylpyridinium (MPP<sup>+</sup>) or pre-formed fibrils (PFF) of  $\alpha$ -synuclein induces toxicity, in the scope of understanding the idiopathic mechanisms of PD pathology.

After PFF or MPP<sup>+</sup> exposure to N27 rat dopaminergic cells, we found that SENP-1 expression was particularly elevated among other SENP family proteins, such as SENP-1, 3, 5, 6, 7 and 8. An increase in SENP-1 expression and a decline in SUMO-1 level were detected in PFF-treated primary cortical neuron culture, midbrain and striatum of PFF injected C57Bl/6 mice and the SNpc of human PD patient brains. The knock-down of SENP-1 by siRNA resulted in an increase of SUMO-1 level in PFF-treated N27 cells. Next, we assessed various commercially available SENP-1 inhibitors targeting SENP-1 suppression and found significant decreases in the levels of ROS and protein aggregates, derived from PFF toxicity.

Since a SENP-1 inhibitor, Momordin lc was more efficacious than others based on our *in vitro* assays, we have orally treated Momordin to PFF-injected >12-month-old mice at two doses (10 or 50 mg/kg) for 6-7 weeks. The oral SENP-1 inhibition alleviated motor deficits induced by PFF injection in behavioral tests, such as rotarod, nesting, grooming, hindlimb clasping and pole test. In the striatum and midbrain region of PFF injected mice, immunohistochemical analyses revealed the increased levels of protein aggregates in Thioflavin-T staining and phosphorylated alpha-synuclein, a pathological marker, were significantly reduced by Momordin treatment. These results were further verified by an increase in the number of TH<sup>+</sup> neurons in the SNc and enhanced TH intensity in the striatum in a blinded analysis. Taken together, our results strongly suggest that SENP-1 inhibition can be applied to halt and further reverse the pathology of PD, due to the reduction of protein aggregation and oxidative stress.



**Dionne Williams, Hakeem Lawal**

Delaware State University

### **“Ameliorating the effects of an environmental toxin in a *Drosophila* model of Parkinson’s Disease”**

Parkinson’s Disease (PD) is a neurodegenerative disorder characterized in part by the selective loss of dopaminergic neurons in the substantia nigra pars compacta. Although the precise cause of PD is not yet fully understood, environmental factors are known to contribute to the etiology of a vast number of cases. Rotenone, a pesticide that inhibits Complex 1 of the mitochondrial Electron Transport Chain, is one such toxin. Importantly, there is no known cure for PD and effective treatment options are severely limited both in number and efficacy. We are interested in developing neuroprotective strategies that may lead to more effective treatments for the disease. This project studies the effects of rotenone-induced toxicity in adult *Drosophila melanogaster* and the neuroprotective capacity of dacarbazine, a possible anti-PD drug that was identified in a previous pharmacological screen. We hypothesized that dacarbazine will confer protection against rotenone-induced toxicity and mitochondrial dysfunction. Further, we measured the effect of rotenone on mitochondrial oxygen consumption rate (OCR) using the Seahorse Analyzer and tested whether treatment with dacarbazine can ameliorate the effects of the rotenone inhibition of the mitochondria and we present preliminary data on the effect of dacarbazine on OCR in adult *Drosophila melanogaster* brains and in Schneider (S2) cells.



## Annual Delaware Neuroscience Research Symposium



# Abstracts of Poster Presentations



### Poster #17

Muhammad Abeer , Michael Gitcho

Delaware State University

#### **“Increased expression of the small heat shock protein 27 may reduce aggregation of transactive response DNA binding protein 43”**

A major pathological protein in both amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) is Transactive response DNA binding protein 43 (TDP-43). Recently, pathological TDP-43 was discovered as a secondary pathology in up to 50% of Alzheimer's disease (AD) cases. Several studies reported that TDP-43 binds to heat shock protein family B (small) member 1 (HSPB1 or HSP27) but no functional evaluation of this interaction has been explored. In response to stress, heat shock proteins work to help fold native proteins in order to reduce aggregation. Inducing expression of HSP27 has been shown to be protective of many other disease conditions and has been shown to reduce aggregation of amyloid in AD. The overall goal of the current project is to utilize both primary neuronal cultures and mice that are selectively expressing pathogenic TDP-43, HSP27, and apolipoprotein E (apoE) in the brain and spinal cord in order to characterize the effect of HSP27 overexpression on TDP-43 and apoE. This will give us a better model to understand TDP-43 proteinopathies.

In the present study, we hypothesize that increased expression of HSP27 may reduce TDP-43 aggregation and alter mitochondrial morphology. A new transgenic mouse model was developed to selectively drive human HSP27 and pathological TDP-43 with a defective nuclear localization signal (DNLS) in the hippocampus and neocortex using the  $Ca^{2+}$ /calmodulin protein kinase (Camk2a) tetracycline inducible system. We evaluated the following genotypes: wild-type, Camk2a/NLS, Camk2a/HSP27 and Camk2a/HSP27/TDP43DNLS at 4 months of age for immunohistochemistry, biochemistry (solubility fractionation), and Western blot. Preliminary *in vitro* results show that cells overexpressing HSP27 reduce aggregation and protein levels of TDP43. Mice overexpressing HSP27 in a TDP43DNLS background in the hippocampus show a reduction of aggregated TDP43. We also examined protein changes altering processing of full length TDP-43 into N- and C-terminal fragments. Besides, samples were treated against human specific TDP; no differences were observed between CK2/NLS and CK2/HSP/NLS mice. Interestingly, HSP27 overexpression modulated endogenous apoE expression. We will also explore interactions between HSP27 and apoE. To identify HSP27-apoE interactions, we will induce HSP27 and apoE isoforms in cellular and mice models. Immunohistochemical and bioenergetic experiments will be carried out to evaluate the overall brain and mitochondrial morphology upon HSP27 overexpression. Overall, our initial data suggests that modifying HSP27 expression may provide a point of therapeutic intervention for TDP-43 proteinopathies.



### Poster #36

Eman Alsaqabi, Stephen J. DiBianca, Ashwini Sansare,  
Khushboo Verma, John J. Jeka, Hendrik Reimann

University of Delaware

### **“The Role of Sensory Deficits in Neural Control of Balance During Walking in Parkinson’s Disease”**

Loss of balance is a major problem in people with Parkinson’s disease (PwPD). Although Parkinson’s disease is mostly characterized by motor impairments, its stability issues might be due to sensory deficits, especially in proprioception. Various balance mechanisms were identified in literature for keeping stability in response to sensory fall stimuli. These mechanisms use either lower extremities’ (LE) proximal or distal joints. When responding to postural perturbations, PwPD favor the use of their proximal joints. A technique called stochastic resonance stimulation (SR) has shown promising results in overcoming sensory deficits and enhancing sensory processing. SR is sub-sensory noise that improves the sensitivity of a sensory system to detect signals, allowing smaller stimuli to reach sensory detection threshold. However, it is not known whether SR can improve balance in PwPD during walking. **Purpose/Hypothesis:** The aim of this study was to: 1) investigate the effects of SR on balance control during visually perturbed walking. We hypothesized that electrical SR stimulation reduces the variability in the gait parameters including Center of Mass (CoM) excursion in PwPD. **Subjects:** Ten subjects with clinical diagnosis of Parkinson’s disease, stages I – III, were recruited. **Methods:** In the first experimental session, participants underwent several clinical tests to assess balance control. In the second session, we determined the sensory thresholds to noisy electric stimulation for each subject at six stimuli sites in the LE and determined the optimal SR intensity. The optimal intensity was identified by calculating margin of stability (MOS) at different intensities and the one resulting in higher absolute value indicates better stability, thus, considered the optimal. Then, subjects walked on a self-paced treadmill in a virtual environment with and without visual perturbations. SR was administered in half of these trials, in randomized order. From these trials, Area Under the Curve (AUC), which is derived from the CoM excursion was obtained. AUC indicates an overall response to visual falls. This outcome variable was assessed using repeated-measures ANOVA, considering differences between the two sides in PwPD. **Results:** No significant differences were found in the AUC between the trials with SR stimulation and those without stimulation ( $P = .286$ ). Similarly, no significant differences were found when comparing the affected sides to the less-affected sides among the PD participants ( $P = .241$ ). **Conclusion:** Using SR stimulation to enhance balance control in PwPD showed insignificant effect in terms of reducing medio-lateral sway (CoM excursion) in response to visual perturbation while walking.



### Poster #1

**Mitra Assadi, Richard Fischer, Terry PhD**

Christiana Care

### **“Enhancing the behavioral and linguistic outcomes in autism spectrum disorder using transcranial magnetic stimulation”**

#### **Aims:**

To determine the effects of unilateral repetitive Transcranial Magnetic Stimulation (rTMS) of the inferior parietal lobule (IPL) on social/behavioral deficits in children and young adults with ASD. To assess the differential effects of rTMS of the left versus right IPL on linguistic abilities and executive function in ASD.

#### **Rational:**

Autism spectrum disorder (ASD) encompasses a range of limitations in reciprocal social and communicative milestones, as well as restrictive and/or repetitive patterns of behavior which lead to significant functional challenges impacting individuals throughout their lifespan. There are major shortcomings in the existing pharmacological interventions; they are of limited efficacy, target a subset of problematic behaviors, and fail to improve social cognition. To overcome these limitations, our group studies the use of neurostimulation to mitigate the social and cognitive manifestations of ASD. Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive neurostimulation technique that alters cortical excitability by repeated induction of electromagnetic activity. A prevailing hypothesis in ASD proposes that mirror neuron dysfunction in the IPL contributes to the core deficits.

#### **Methods:**

We are recruiting patients 5-25 years of age with confirmed ASD and offer 10 sessions of TMS, delivering 2000 stimulations per session, according to our IRB approved protocol. Participants are randomized to receive active stimulation to either the left or right IPL (with sham stimulation to the contralateral side) in a prospective, double-blind fashion. Outcome measures include neuropsychological testing administered at baseline, after completion of TMS, and 3 months later.

The neuropsychological test battery consists of:

D-KEFS: Verbal Fluency task

Flanker: attention/executive functioning

DCCS: cognitive flexibility

SRS-2: Social Responsiveness Scale

RRBs: Repetitive Behavior Scale



### Poster #13

**Angeline-Claudia Atheby, Lindsey M. Ruggiero, Hakeem Lawal**

Delaware State University

### **“Pesticide Interactions in *Drosophila* Model of Environmental Toxicity”**

Parkinson’s Disease (PD) is a progressive neurodegenerative disorder characterized in part by the loss of dopaminergic neurons in the substantia nigra pars compacta. Epidemiological studies indicate that exposure to certain pesticides and herbicides increase an individual’s likelihood of developing PD. While the full catalog of pesticides that may pose risks for PD is not currently known, some potentially toxic compounds are commonly used for agricultural or gardening purposes and may be purchased at local stores. The objective of this study, therefore, was to determine whether different combinations of these pesticides and herbicides have either a synergistic or additive effect on toxicity in *Drosophila*. We first established a dose response curve in the following pesticides: acephate, atrazine, and diuron. We then exposed *Drosophila* to different combinations of the compounds at a concentration at which each alone was minimally toxic. We performed survival and locomotion ability analyses on each experimental group. Here, we report that combinations involving atrazine and diuron show strong decreases in survival that were greater than each single pesticide alone. We also present data on our analysis of the synergistic effect in the locomotion assay. Together, our data suggest that exposure to some combinations of commonly used pesticides may render increased susceptibility to environment toxins and their deleterious effects.



### Poster #2

**Mona Batish, Robert E. Akins**

Nemours Children's Health

### **“Epigenetic Changes Associated with Perinatal Encephalopathy and Neuromotor Dysfunction”**

Cerebral palsy is a set of common, severe, motor disabilities categorized by a static, nondegenerative encephalopathy arising in the developing brain and associated with deficits in movement, posture, and activity. Spastic CP, which is the most common type, involves high muscle tone and is associated with altered muscle function including poor muscle growth, contracture, increased extracellular matrix deposition, microanatomic disruptions, musculoskeletal deformities, weakness, and difficult movement control. These muscle-related manifestations of CP are major causes of progressive debilitation and frequently require intensive surgical and therapeutic intervention to control. Current clinical approaches involve sophisticated consideration of biomechanics, radiologic assessments, and movement analyses, but outcomes remain difficult to predict. There is a need for more precise and personalized approaches involving omics technologies, data science, and advanced analytics. In particular, an improved understanding of muscle involvement in spastic CP is needed. Unfortunately, the fundamental mechanisms and molecular pathways contributing to altered muscle function in spastic CP are only partially understood. In this presentation, we discuss recent studies supporting the emerging hypothesis that epigenetic phenomena, especially differential DNA methylation and altered regulatory RNA, play significant roles in musculoskeletal manifestations of CP.

**Funding:** This study was funded by a P20 GM103446 grant to APC.



### Poster #5

**Megan Bone**, Katarzyna D. Rosikon, Tempalyn Wiggins, Mahlet Mersha, Harbinder S. Dhillon\*, Hakeem Lawal

Delaware State University

### **“Embryonic asymmetry and Development of Function Neuronal Connectivity”**

The relationship between laterality and functional asymmetry has particular relevance for the development of an organism. Most animals, including humans, appear symmetrical externally but display visceral lateral asymmetry with a bias for one enantiomeric body plan over the other. The nematode lab model *Caenorhabditis elegans* also shows predominantly bilaterally symmetric external anatomy, but with clear internal L/R asymmetry that is established during early embryogenesis. The point at which the sperm enters the embryo during fertilization becomes the posterior end of the embryo. Dorso-ventral polarity is established during the second cleavage of the anterior cell, AB, into the anterior blastomere posterior and anterior blastomere anterior cells (ABp and ABa) defining the dorsal-ventral axis of the animal. This division yields two spindles which are initially parallel to the L/R axis and shift at an angle of 20° in an anti-clockwise manner. It has been proposed that the foundations of neuronal LR asymmetry in adult worms are laid in early embryonic decisions.

Our working hypothesis is that a mutation in *gpa-16* in which mutant animals demonstrate embryonic spindle and visceral organ reversal will also result in anatomical and functional reversal of asymmetric chemosensory ASE neuron pairs. To test this idea, we have examined mutants in the *C. elegans gpa-16* which is likely to be involved in the determination of handedness. And we report that a temperature-sensitive *gpa-16* mutant (*it143*), when reared at non-permissive temperature of 25° C, yields close to 70% unviable embryos, but of the survivors 40% are sinistral. Previous studies have clearly shown the reversed spindle orientation of sinistral animals during their 4-6 cell developmental stage. The 70% embryonic lethality observed at non-permissive temperature has not been examined, though it may hold a clue to genetic mechanisms governing L/R establishment. In order to unravel the fate of these embryos at the critical stage for L/R axis establishment we have examined the *gpa-16 t.s (it143)* and the *gpa-16 deletion (ok2349)* mutant embryos at their 4-6 cell stages. Additionally, we are working towards maintaining these embryos through adulthood in efforts to observe whether there is a relationship between embryonic laterality and adult neuronal laterality. This contributes to our understanding of the embryonic mechanisms responsible for establishing laterality in adult organisms.

\* This author is deceased



### Poster #27

Giovanna Arantes de Oliveira Campos, Kim V. Nguyen,  
Linda J. Hoffman, Katie R. Jobson, Nora S. Newcombe, Ingrid R. Olson

Temple University

### **“Relating the fornix to episodic memory and spatial navigation in development”**

The cognitive abilities of remembering past experiences and of knowing how to navigate an environment are both essential throughout one's life. Neutrally, episodic memory and spatial navigation depend on medial temporal lobe structures (e.g. hippocampus) and the white matter tracts that connect them (e.g. fornix). While the non-human animal literature provides rich evidence that severing the fornix leads to multiple memory impairments, observing similar relationships in humans has been a challenge. Diffusion magnetic resonance imaging (dMRI) offers us a unique opportunity to investigate the correlates of fornix structure measures and episodic memory as well as spatial navigation non-invasively. Several studies have found correlations between fornix microstructure and autobiographical memory in adults, but fewer have investigated this relationship in children. Additionally, the literature on human navigation and the fornix is virtually non-existent. Additionally, the literature on human navigation and the fornix across all ages is virtually non-existent. **With participants undergoing a real-world encoding experience, we will directly relate spatial and episodic memory with fornix microstructure from late childhood to adulthood.** In our study, children (8-13YOs) and young adults are taken on a tour that combines a real-world spatial experience with sixteen episodic events. On the second day of testing, participants undergo a diffusion-weighted imaging (DWI) scan. Linear modeling revealed that spatial navigation significantly predicted better episodic recall and recognition, with adults (N = 41) recalling more events than children (N = 23, currently). DTI analyses are ongoing with plans to extract fornix and arcuate fasciculus (control tract) microstructure using probabilistic tractography and to perform free water correction. We will run multilevel linear models with microstructure metrics interacting with age and predicting spatial composite score and episodic memory variables, individually. We hope to further tease apart the nuances of this interconnected network and track its developmental trajectory.



### Poster #20

Sophia Crisomia, Roxana G. Burciu, Jae Woo Chung

University of Delaware

### “Free Water as a Biomarker for Parkinson’s Disease Subtypes”

#### Objective:

To evaluate progression-related changes in the brain structure of individuals with Parkinson’s disease (PD) who have a tremor dominant (TD) motor phenotype versus a Postural Instability and Gait Difficulty (PIGD) motor phenotype. Brain changes were assessed over a period of two years using 1) free water (FW), a previously validated progression marker in the posterior substantia nigra (pSN) in PD, and 2) voxel-based morphometry (VBM), a technique used to assess changes in gray matter volume.

#### Background:

Motor symptoms in PD vary among individuals, which prompted clinicians to subtype PD based on clinical features into TD and PIGD. Evaluating the impact of subtype on disease progression in the brain may inform the development of subtype-specific treatments.

#### Methods:

Diffusion MRI and T1-weighted imaging were downloaded from the Parkinson’s Progression Marker Initiative (PPMI). Study cohorts included 20 TD and 7 PIGD. FW values for multiple bilateral regions in the basal ganglia, cerebellum, thalamus and brainstem were calculated at three time points: baseline, year 1, and year 2, and VBM for gray matter structures as baseline and year 2. Groups were matched on sex, age, cognitive status using the Montreal Cognitive Assessment Test, and severity of symptoms off medication using the motor section of the MDS - Unified Parkinson’s Disease Rating Scale (MDS-UPDRS-III) at baseline. Baseline clinical and imaging measures were analyzed with independent samples t-test and longitudinal changes with repeated measures ANOVA.

#### Results:

We found no group differences at baseline in total MDS-UPDRS-III, rigidity, and posture and gait subscores from the MDS-UPDRS-III, or FW in any regions. Bradykinesia and rest tremor subscores differed between groups, with PIGD being slower and TD exhibiting more rest tremor. Importantly, results revealed increases in FW over time in PIGD but not TD in the thalamus, middle cerebellar peduncle, red nucleus, and cerebellar lobule V. Both groups experienced an increase in FW in the pSN, caudate, and globus pallidus. None of the groups exhibited progression-related changes in the gray matter volume based on the VBM analysis.

#### Conclusions:

The FW analysis demonstrated different patterns of progression of brain changes, with TD-related changes limited to the basal ganglia circuit versus additional and more extensive changes spanning the cerebello-thalamo and brainstem networks in PIGD. Results also suggest that FW imaging is more sensitive than conventional MRI at depicting subtype-related brain changes over a short period of time and could serve and may serve as a biomarker for PD subtypes.



### Poster #15

**Esther Daniel**, Esther Abiona, Dionne Williams, Hakeem Lawal

Delaware State University

### **“Testing the Effect of a Putative Neuroprotective Agent in a *Drosophila* Model of Parkinson’s Disease”**

Parkinson’s disease (PD) is the second most common neurodegenerative disease whose pathological hallmarks include the progressive loss of specific neuron populations within the basal ganglia. Features of PD include the display of resting tremors, speech difficulties, stiffness, and lack of coordination. Currently, there is no known cure for PD, and there are limited treatment options available. However, we seek to contribute a pharmacological intervention against the disease by analyzing the effects of a potentially therapeutic compound, dacarbazine. Currently, dacarbazine is used for cancer treatment; however, we hypothesize that it can serve as a treatment for PD as well. We are testing the efficacy of this compound in *Drosophila* using rotenone, a commonly used pesticide that we and others have previously deployed to model sporadic PD. In this study, we tested the ability of dacarbazine to ameliorate the neurotoxic effects of rotenone upon exposure to *Drosophila*. We utilized a prior regimen of rotenone and combined it with dacarbazine. We then measured the effect of that combination (as compared to controls) on survivorship and locomotion, two common experimental read-outs for neurotoxicity. Our findings unveiled promising results similar to the ones we hypothesized. We theorize that further research, experimentation, and analysis would help clarify the precise effect that dacarbazine has on PD models, and ultimately it may uncover a useful therapeutic intervention against PD.

This research was supported by funding from the Delaware INBRE program, by an NIH/K01 Career Development Award to HL, as well as by an NIH/INBRE Research Independence Award to HL.



### Poster #39

Abigail Diaz, Kathleen Brewer-Smyth

University of Delaware

### **“Neurological and Childhood Abuse Histories of Women Who Commit Violence against Themselves and Others”**

#### **Background/Purpose**

It is critical to identify risk factors for violence against self and others in order to develop evidence-based prevention strategies.

#### **Theoretical Framework**

Due to growing threats of suicidal females committing homicide and other violence, this study identifies risk factors for these behaviors.

#### **Methods (Design, Sample, Setting, Measures, Analysis)**

Further analyses were conducted of data from private interviews and examinations of female prison inmates. Analyses compared females who have ( $n = 41$ ) and have not ( $n = 92$ ) attempted suicide; and those who committed a violent crime and/ or attempted suicide ( $n = 84$ ) to those who did not attempt suicide or commit a violent crime ( $n = 71$ ).

#### **Results**

Bivariate logistic regressions revealed that females who committed a violent crime and/ or attempted suicide experienced greater childhood physical abuse (CPA) ( $OR=1.088$ ;  $95\%CI=1.015-1.166$ ), childhood sexual abuse (CSA) ( $OR=1.128$ ;  $95\%CI=1.020-1.247$ ), total childhood abuse ( $OR=1.075$ ;  $95\%CI=1.022-1.130$ ), and abuse resulting in healthcare access ( $OR=1.316$ ;  $95\%CI=1.035-1.672$ ) compared to those who did not attempt suicide or commit violent crimes. Abuse resulting in healthcare access was the only significant variable adjusting for associated variables. Abuse-related healthcare access was often due to traumatic brain injuries (TBI). Though females who attempted suicide and/ or committed a violent crime had more neurological histories, especially TBIs, more incarcerated adult family members during childhood, and were more likely under the influence of alcohol at the time of their crime, these were not significant in bivariate or multivariate logistic regressions. Those who were under the influence of alcohol at the time of committing a violent crime had more suicide attempts than others. The mean number of suicide attempts of those convicted of homicide and other violent crimes was almost 3 times greater than others. CSA predicted more suicide attempts per person.

#### **Conclusions & Implications**

Both childhood physical and sexual abuse are risk factors for attempting suicide and/ or committing violent crimes. This is especially true for those with abuse-related injuries resulting in healthcare access that often occurred due to TBI. Health care providers released women because their injuries were not life threatening; yet they were life threatening for themselves and victims of their subsequent violent crimes including homicide. Females accessing health care for abuse-related injuries present a critical opportunity to prevent suicide, homicide, and other violent crimes by victims.



### Poster #35

Stephen J. DiBianca, Hendrik Reimann

University of Delaware

### “Visual Motion Detection during Walking and Standing”

**Background and Aims:** A visual motion detection threshold is an estimate of the smallest movement of the visual field detectable by a participant. These threshold values are typically obtained while sitting. In this study we aim to: 1) test whether a visual motion detection threshold can be reliably measured during standing and walking; and 2) investigate whether visual motion detection thresholds differ during standing and walking.

**Methods:** Twenty-nine subjects stood on and walked along a self-paced, instrumented treadmill inside a virtual environment displayed on a large dome. Participants performed a 2-alternative forced choice experiment in which they discriminated between a counterclockwise (“left”) and clockwise (“right”) rotation of a visual scene projected on a large dome. A 6 down 1 up adaptive staircase algorithm was used to change the amplitude of the rotation. A psychometric fit to the participants’ binary responses provided an estimate for the detection threshold at a target value of 89%.

**Results:** A strong correlation exists between thresholds obtained from walking trials one and two ( $R = .84$ ) and standing trials one and two ( $R = .73$ ). Average thresholds obtained during walking (1.03 degrees) are higher than average thresholds obtained during standing (.73 degrees).

**Conclusion:** Visual motion detection thresholds can be obtained during both walking and standing in which the balance system is challenged. These results indicate that the reliability of visual information for balance control may be different between standing and walking. An individual’s threshold of motion detection may be an indicator of how much their balance control system is influenced by visual perturbations and could be of use as a clinical assessment tool.



### Poster #18

**Matthew Dopler**, Keyshawn Cox, Charmise Preddie, Tyler Petersen, Miranda Kotey, Whitney Smith, Sharee McGriff, Sanaz Arezoumandan, Michael Gitcho

Delaware State University

### **“Rapid progression, pathology, and reduced lifespan in a triple mutant TDP-43 mouse model”**

**Background and Aims:** A visual motion detection threshold is an estimate of the smallest movement of the visual field detectable by a participant. These threshold values are typically obtained while sitting. In this study we aim to: 1) test whether a visual motion detection threshold can be reliably measured during standing and walking; and 2) investigate whether visual motion detection thresholds differ during standing and walking.

**Methods:** Twenty-nine subjects stood on and walked along a self-paced, instrumented treadmill inside a virtual environment displayed on a large dome. Participants performed a 2-alternative forced choice experiment in which they discriminated between a counterclockwise (“left”) and clockwise (“right”) rotation of a visual scene projected on a large dome. A 6 down 1 up adaptive staircase algorithm was used to change the amplitude of the rotation. A psychometric fit to the participants’ binary responses provided an estimate for the detection threshold at a target value of 89%.

**Results:** A strong correlation exists between thresholds obtained from walking trials one and two ( $R = .84$ ) and standing trials one and two ( $R = .73$ ). Average thresholds obtained during walking (1.03 degrees) are higher than average thresholds obtained during standing (.73 degrees).

**Conclusion:** Visual motion detection thresholds can be obtained during both walking and standing in which the balance system is challenged. These results indicate that the reliability of visual information for balance control may be different between standing and walking. An individual’s threshold of motion detection may be an indicator of how much their balance control system is influenced by visual perturbations and could be of use as a clinical assessment tool.



### Poster #36

**Carmen Dressler, Mariyah Jiwanji, William Foster, Benjamin Dunham, Ishmail Abdus-Sabor, Nathan Fried, Mathieu Wimmer**

**Temple University**

### **“Measuring pain in a chronic inflammatory rat model using a novel high speed videography-based pain scale”**

Chronic pain is a socio-economic burden affecting more than 30% of people worldwide. This multi-dimensional condition has a significantly negative impact on the quality of life, increasing with the duration of pain. The transition from acute to chronic pain and its etiology and risk factors are poorly understood, despite the efforts that have been made to better understand the neurobiology of pain. We recently established a novel pain scale using high-speed video imaging, and by combining face grimace with paw kinematics into a single reliable pain score in rats. By mapping sub-second mechanically evoked behaviors to eight stimuli in both males and females, we transformed the data into a single dimension using statistical and machine learning approaches to generate an easily interpretable pain score. Previous research has relied on reflexive paw withdrawal assays that result in binary responses in rats, limiting the range of pain scores and hindering the data interpretation. In a recent publication, we demonstrated that our novel pain scale generated pain scores that distinguished and accurately predicted innocuous stimuli from painful pinpricks in males and females.

To study chronic pain, we combined the use of the rat pain scale and the Complete Freund's Adjuvant (CFA)-induced chronic pain rat model. The hind paw was injected with CFA (100 ul) to induce inflammatory pain; controls received saline. Pain scores were generated using the novel pain scale at regular intervals for 5 weeks in order to delineate changes in pain sensitivity caused by CFA and the associated recovery. One advantage of this approach is that both nonpainful and painful stimuli can be used to assess pain, allowing the assessment of allodynia or hyperalgesia. In males, light pin pricks, which register in the pain domain prior to CFA treatment, caused a higher pain score following CFA treatment. This increase lasted until day 21 post CFA treatment. Surprisingly, this effect was not present in females. Our results highlight the fact that validating protocols in females is necessary, considering that CFA-based assays historically include mostly males. These studies lay the foundation to better understand the mechanisms underlying inflammatory pain as well as those promoting its chronicity. These kinds of approaches could facilitate both drug discovery efforts to improve pain therapeutics and be deployed to test existing pain-relieving compounds in a more rigorous and systematic way in male and female rats.



### Poster #37

**Julia Gray, Ashwini Sansare, Moira van Leeuwen, Sjoerd Bruijn, Hendrik Reimann**

University of Delaware

### **“Step time modulation is used as a balance mechanism in slow walking”**

Controlling balance while walking requires regulation of each step based on the body's Center of Mass (CoM). Our study explored how the neural control processes of walking change with steady state walking at varying cadences. Specifically, we ask whether step time is actively modulated with the goal of maintaining balance, and how the relationship between step time modulation and CoM changes with cadence. Prior work in robotics has shown that it is possible to maintain balance by only regulating step timing in a quadruped walker. Here we are applying this concept to human locomotion and ask whether humans use this mechanism in normal walking. For example, when a body leans to one side while walking, the stance time on that leg increases. If humans also use this step timing mechanism to regulate balance, then CoM displacement should predict step time. In our study, we measured this relationship by fitting walking data in a linear regression model. We measured the slope and explanatory power of this linear relationship between CoM and step time and analyzed changes with walking cadence. 24 young healthy participants walked at one of five designated metronome paces (50, 75, 100, 120, and 140 bpm) on a self-paced treadmill in trials of 100 strides. They completed three trials at each cadence, with order of metronome pace randomized within blocks of five trials. We measured kinematic data from 44 markers in Qualisys Motion Capture, kinematic data from force plates captured kinetic data. Left footstep time was calculated as the time between a left heel strike and the following right heel strike, and the whole-body CoM position was calculated relative to stance foot ankle position and velocity. The slopes of our linear models significantly decrease in magnitude as the cadence increases, eventually trending towards zero. This showed that the step time mechanism was impacted by CoM more intensely at 50 and 75 bpm. We found low  $R^2$  values throughout our dataset that trended downward as the cadence increased. Additionally, the variability of the outcomes decreases as walking cadence increases. Our results suggest that step timing may be a mechanism of balance regulation for people walking at slower cadences. Because clinical populations walk at slower cadences, this mechanism may be a form of compensation for step placement and ankle torque methods of balance regulation.



### Poster #29

Sarah Gustafson, Ian Smith, Anna Klintsova

University of Delaware

### **“Dose-dependent increase in levels of apoptosis observed in the nucleus reuniens after single-day alcohol exposure during third trimester development”**

Fetal Alcohol Spectrum Disorders (FASD) affect as many as 2-5% of live births in the US and result in an array of symptoms including lower brain volume, brain abnormalities, and behavioral deficits, including impaired executive functioning and spatial working memory (May et al., 2018; Vorgias, 2021). The nucleus reuniens of the midline thalamus (Re) is crucial for proper executive functioning and spatial working memory in rodents, making it a region of interest in FASD research (Dollerman-Van der Weel et al., 2019). To understand how Re is damaged in an animal model of FASD we examined levels of apoptosis, programmed cell death that manifests as cytomorphological changes (chromatin condensation and nuclear fragmentation) in Re after neonatal alcohol exposure in a dose- and time-dependent manner. Two different time points during the rodent brain growth spurt (corresponding to the third trimester of human pregnancy) were studied; Long Evans rat pups received either moderate (3g/kg) or high (5.25g/kg) doses of alcohol in a milk substitute via intragastric intubation on postnatal day (PD) 7 or 9. Control sham intubated (SI) pups were intubated but received no liquid. Pups were anesthetized and perfused intracardially twelve hours after the first dose and brain tissue was collected; tissue was then sectioned coronally and stained with cresyl violet to identify apoptotic cells based on cytomorphological characteristics. Using an unbiased stereological approach, apoptotic body counts in Re were obtained. Preliminary analyses revealed a significant main effect of postnatal treatment on apoptotic cell number in Re [ $F(2, 19) = 5.245, p = 0.028$ ]. Tukey-corrected *post hoc* analyses revealed that animals in the high alcohol group, regardless of time point, exhibited significantly higher levels of apoptosis than both the sham intubated group ( $p = 0.0072$ ) and moderate alcohol group ( $p = 0.0152$ ). Moderate groups did not significantly differ from the control groups in terms of apoptotic cell number. These results provide supporting evidence that alcohol exposure causes significant apoptosis within the Re in a dose-dependent manner regardless of timing of exposure. Adding to prior studies, these results further our understanding about the impact of AE during the third trimester.



### Poster 31

Mary Beth Hall, Elina Rodriguez, Nikhila Indukuri, Jaclyn Schwarz

University of Delaware

#### **“Effects of maternal immune activation with lipopolysaccharide on auditory fear conditioning and a second-hit immune response in adult offspring”**

Epidemiological evidence suggests that maternal immune activation during gestation increases the risk for offspring to experience symptoms of developmental disorders later in life, of which males are more likely to be diagnosed than females. The goal of this project is to elucidate how maternal immune activation (MIA) with lipopolysaccharide (LPS) may lead to changes in brain and behavioral processes in adult offspring. Sprague-Dawley dams were injected with LPS (50ug/ml/kg, i.p.) or saline on embryonic day (E)15. After birth, offspring were weaned and then left undisturbed until adulthood. On P90, offspring were tested in a Latent Inhibition of auditory fear conditioning task. Latent inhibition is when animals show lower levels of a learned behavior (freezing) if the rat is pre-exposed to an innocuous stimulus (tone) before it is paired with an aversive unconditioned stimulus (footshock). *Deficits* in latent inhibition are when the animal still shows high levels of freezing to the conditioned stimulus (tone), even with pre-exposure to that stimulus. After behavioral testing, the rats were given a second immune challenge (50ug/ml/kg LPS or saline) and euthanized 4 hours later to examine whether MIA influences the immune response in adult offspring. Half brains were dissected to collect brain regions of interest, including dorsal hippocampus (dHP). Preliminary data suggest that during the training phase of the Latent Inhibition task, E15 saline offspring pre-exposed to the tone (Pre-CS group) froze less than those *not* pre-exposed to the tone (Pre-Cnxt group), suggesting that latent inhibition was achieved. However, in Pre-Cnxt rats, E15 LPS rats froze less than E15 saline offspring, suggesting that MIA may interrupt normal acquisition of auditory fear conditioning. Further, in Pre-CS rats, both E15 LPS and saline offspring froze at comparable levels, suggesting that tone pre-exposure may support auditory fear learning, rather than a latent inhibition response, in E15 LPS rats. Additionally, preliminary dHP tissue analyses show that, regardless of E15 treatment, adult LPS increases IL-6, but not IL-1 $\beta$ , expression compared to adult saline treatment. This suggests that MIA does not affect the immune response within dHP of adult offspring. Future studies will examine the effects of MIA on cytokine expression in other tissues and on other learning and anxiety behaviors. These findings will provide us with a better understanding of how early-life environmental factors affect later-life brain and behavioral processes, and how they may be differently dysregulated in males and females.



### Poster #38

**Patrick Jasinski**, Mohamed Rabieh Khalife, Mohamed Ouardouz, Matthew Mahoney, Rod C. Scott, Amanda Hernan

Nemours Children's Hospital

### **“Neural Activity Patterns on Different Timescales”**

How do neurons encode information about stimuli and behavior? One way that this can be done is by simply changing their rate of firing. Another way involves changing the pattern of firing. This includes changes in the distribution of interspike intervals, the auto correlogram, and changes on a longer timescale such as those involving bursting. The focus of this research is on quantifying and understanding these changes in the pattern of firing. Patterns of neuronal firing underlie cognition, and can become disorganized under neurological diseases, particularly epilepsy. Understanding how normal patterns subserve healthy cognition and how these diseases alter them requires robust, unbiased quantification.

We have used generalized linear models and custom-built bursting and firing pattern recognition software to find neurons recorded in our lab that change their average firing rate, but not their pattern of firing exhibited by the auto correlogram and distribution of interspike intervals, neurons that change both their firing rate and pattern, and neurons that show otherwise interesting modifications of their behavior on longer timescales. These findings may have implications for how neurons encode information in a healthy state and how this facility may be affected under various diseases.



### Poster #21

Sydney Ku, Amelia Cuarenta, Molly Dupuis, James Flowers II, Reza Karbalaei, Cori Ardekani, Mathieu Wimmer, Debra Bangasser

Temple University

### **“Postpartum resource scarcity alters the nature of maternal defensive behavior in rats”**

Postpartum affective disorders, such as postpartum depression and anxiety disorders, are debilitating diseases with limited treatments. Two extremely high-risk factors for postpartum affective disorders are postnatal stress and low socioeconomic status (SES). A low SES environment can be mimicked using a limited bedding and nesting (LBN) manipulation, in which the dam's access to nesting materials is restricted during the beginning of the postpartum period. Furthermore, the dam and pups reside on a customized metal grate, which induces additional postnatal environmental stress. Previously, we found that the LBN manipulation alters dams' behavior, increasing pup-directed behavior (passive nursing, blanket nursing, arched back nursing, licking, and grooming of pups) and decreasing self-care (self-grooming, eating, and drinking): a phenotype which likely reflects hyperarousal. Conversely, dams exposed to extremely enriched postnatal environments display very little time on the nest and overall decreased frequency of nursing.

Given this clear, demonstrable effect of resource availability on maternal care and postpartum affective behavior, we sought to leverage our LBN model to expand current knowledge and understand how both postnatal chronic stress and resource scarcity affect postpartum affective behavior. On postnatal day (PND) 2, Long Evans dams (60-100 days old) were placed in either standard housing (ample bedding, cotton nestlets, and enrichment,  $n = 11$ ) or LBN ( $n = 9$ ) housing conditions. On PND10, we ran dams through a resident/intruder task to elicit aggression, where a late adolescent (50-75 days old) male intruder rat was placed in the dams' home cage for 15 minutes. Each resident/intruder interaction was recorded with a GoPro, then hand scored using SolomanCoder for various forms of aggression. Though data analysis is still ongoing, our preliminary findings indicate that LBN does not alter the frequency or likelihood of aggressing. Rather, LBN appears to affect the nature of aggression: LBN dams pin the intruder significantly less than control dams and, if at all, for significantly shorter durations. This pattern of aggression in LBN dams is consistent with a more defensive type of aggression versus a more offensive type displayed by control dams. We are currently conducting RNA sequencing on the medial amygdala (MeA) in control and LBN dams to ascertain how resource scarcity alters transcription in this key region for aggression. Together, these studies will reveal mechanisms by which resource scarcity alters maternal defensive behavior. Clinically, this work may reveal novel targets for treating postpartum anxiety disorders, particularly symptoms regarding overprotective or anxious parenting.



### Poster #21

**Elise Lemanski, Bailey Collins, Jordan Case, Elizabeth Wright-Jin**

University of Delaware

#### **“Establishing a Novel Model of Neonatal Hypoxic Ischemic Encephalopathy”**

Neonatal Hypoxic Ischemic Encephalopathy (HIE) causes neural injury through impaired circulation of blood and oxygen to the brain in the perinatal period and is the leading cause of cerebral palsy in children born at term, with worse deficits seen in affected boys. The treatments for HIE are limited to therapeutic hypothermia which has limited success and is restricted to a short window of effectiveness. The current established animal model for HIE is the Rice-Vannucci model which involves a unilateral carotid artery ligation followed by prolonged moderate hypoxia. While this model has been well established, it produces a hemispheric stroke-like injury that is not typical of human pathology. Additionally, surgery is necessary for carotid artery ligation which may require recovery time as well as induce additional stress and trauma on the animals. For this reason, we have adopted an altered model of HIE which utilizes maternal immune activation via LPS in addition to a shorter, but more severe hypoxia. To establish this model, hypoxia was performed at different timepoints, either on P2, P4, or P7. Measurements included cortical thickness, as well as microglial density in the hippocampus, pons, and corpus callosum. Surprisingly, LPS exposure had no effect on cortical thickness but led to a decrease in microglial density in both the hippocampus and pons. While hypoxia did not have much effect alone, when paired with LPS the microglial density was raised to control levels. This model did not lead to clear motor changes and so was adjusted to hypoxia with 37°C at P6, which preliminarily appears to induce a motor deficit. Current and future directions include determining the location and extent of neural injury, fully characterizing the motor profile of affected animals, and quantifying any microglial changes in number, morphology, or transcript as a marker of neuroinflammation.



### Poster #10

Vasilios Lomis, Malek Elsayyid, Jessica Tanis

University of Delaware

#### **“Exploring the effects of the CIL-1 Phosphatidylinositol 4,5-bisphosphate 5-phosphatase on extracellular vesicle biogenesis”**

Small, bioactive vesicles which get secreted into extracellular space are known as extracellular vesicles (EVs). These EVs can transport various protein, RNA, and metabolite cargoes, enabling communication between cells. A single cell can release multiple distinct EV subpopulations, each with different cargo enrichment, which can result in different functionalities. In *C. elegans*, EVs bud from sensory neuron cilia and then are either up-taken by surrounding glia or discharged into the environment where they play a role in animal-to-animal communication. Two significant cargoes include the polycystin-2 channel PKD-2 and the voltage-gated calcium channel CLHM-1, both of which are released in EVs from *C. elegans* neuronal cilia. These EVs are visualized by tagging CLHM-1 with tdTomato (tdT) and PKD-2 with green fluorescent protein (GFP). EVs with PKD-2 appear to be released at the ciliary distal tip, while CLHM-1 is released in EVs from the ciliary base. Prior research shows the ciliary transition zone restricts certain proteins and lipids to different ciliary compartments, which may impact EV cargo sorting and biogenesis. I am investigating the impact of the phosphatidylinositol 4,5-bisphosphate 5-phosphatase CIL-1, which is known to cause defects in ciliary localization of PKD-2 on EV shedding. It remains unclear whether *cil-1* mutants have altered phosphoinositide levels, lipids that regulate both trafficking and TRPP protein channel activity. Further, it is unknown if the localization of other ciliary proteins such as CLHM-1 is impacted by the loss of *cil-1*. Finally, we do not know if EV shedding or cargo sorting is impacted by the loss of this phosphatase. I am currently imaging animals containing the *cil-1* mutation with various fluorescently labeled proteins to better understand the role of CIL-1 on protein trafficking within the cilia and in EV biogenesis.



### Poster #3

**Michael Moore**

Delaware State University

### **“Imaging Facility at Delaware State University”**

The Imaging Facility at Delaware State University is a multi- user core facility that offers advanced imaging and spectroscopy instruments with scientific and technical expertise in optical microscopy, spectroscopy and computation image analysis. The mission is to advance transformative excellence in research, innovation and education and to provide a vital support structure to the faculty and students in specialized facilities.

The core facility houses state of the art optical and electron imaging instruments. Currently the facility has three confocal microscopes, a Zeiss LSM 780 and a Zeiss LSM 510 both on loan through a partner Bioimaging core at the University of Delaware, and a Crest Optics xLight V3 Spinning disk confocal. The facility has a Wide-Field inverted Fluorescence DIC microscope and several advanced bright field microscopes with extended contrast techniques (e.g. Polarized light, Dark-Field, Phase Contrast, DIC). In addition, we have a Bruker Innova AFM a Bruker Anasys nanoIR2-s AFM system, and a FEI Quanta FEG 250 scanning electron microscope with EDS, EBSD, and ESEM. The imaging facility also hosts a uv-vis spectrophotometer, FTIR, and an ISS-K2 spectro-fluorimeter. Furthermore, the data collected is archived on a server housed with-in the facility and the data is analyzed on our power workstations in our Image Analysis room. We have several commercial software packages, Huygens Deconvolution, Topo Maps 3D, Imaris, Avizo, Metamorph, MATLAB and more.

In addition to providing services to the research community and industry users the OSCAR imaging facility hosts several middle school and high school workshops throughout the year. The facility has hosted several of these workshops for INBRE summer internship students. We coordinate with the multitude of summer science-based programs on campus providing tours and workshops. These workshops are part of our mission to educate the next generation of scientist.



### Poster #23

**Teneisha Myers**, Elizabeth A. Birmingham, Brigham T. Rhoads, Lisa A. Briand

Temple University

### **“The Influence of the Estrus Cycle on Sociability Following Adolescent Social Isolation”**

Adolescence is a critical period of development for establishing social relationships. It is also characterized by high levels of reward seeking. During adolescence, brain circuits are plastic and can be greatly influenced by the environment and individual's experiences. Exposure to chronic stress during this time leads to alterations of brain structure and function and can have a negative impact on social behavior. Our lab has examined the influence of adolescent social isolation on social interaction both during adolescence and in adulthood. Results showed that adolescent social isolation leads to decreased sociability in female mice and increased sociability in male mice in adulthood while not affecting social interaction during adolescence in either sex. To determine if gonadal hormones may play a role in the sex differences seen in social behavior, the present study examined whether the effect on sociability seen in isolated females is mediated by the estrus cycle. We did not detect a significant effect of estrus cycle on sociability in either group housed or socially isolated females. However, we did find that following lavage stress, the socially isolated females exhibited increases in sociability compared to group housed controls. This was in direct contrast to our initial finding that social isolation stress decreased sociability in females. We are currently examining whether this difference is due to stress induced by the lavage procedure. We hypothesize that social isolation may prime females to be more sensitive to the effects of stress and further work is underway to examine the effects of other stressors on sociability in group housed and isolated mice.



### Poster #19

**Kwadwo Ofori, Anurupa Ghosh, Dinesh Kumar Verma, Gabriela Cabrera, Darice Wheeler, Sung Hwan Moon, Soo Jin Lee, Y. Hwan Kim**

Delaware State University

### **“A novel NOX inhibitor alleviates Parkinson’s disease pathology in PFF-injected mice”**

Parkinson’s disease (PD) is the most prevalent motor neurodegenerative disorder, resulting from the decline of dopaminergic neurons in the midbrain. Although numerous genetic mutations have been identified in PD pathology, a key pathological hallmark is misfolded protein aggregation called Lewy body formation. Thus, it has been emphasized to develop therapeutics to halt the Lewy body formation to prevent dopaminergic neuronal loss in the nigrostriatal pathway. Despite the causes upstream, oxidative stress-mediated damage in downstream often underlines PD pathology. Therefore, ultimately regulating oxidative stress can be an effective approach to preventing PD pathological progress. Here we assessed the efficacy of an exogenous reactive oxygen species (ROS) regulator, nicotinamide adenine phosphate (NADPH) oxidase (NOX) inhibitor, compound-11 which was synthesized by Aptabio Therapeutics. The compound is a safe and specific inhibitor for NOX-1, 2, and 4, based on our preliminary assessments. Using rat dopaminergic cells and alpha-synuclein preformed fibrils (PFF)-injected mouse model, we tested the novel NOX inhibitor as a potential therapeutic for PD. PFF is known to be a pathogenic form of alpha-synuclein leading to rapid protein aggregation for recapitulating PD pathology. In our *in vitro* assays, the novel compound enhanced cell viability and reduced cytotoxicity against PFF exposure at a wide range of concentrations (1 nM-10  $\mu$ M), but we confirmed that 1  $\mu$ M was an optimal concentration *in vitro*. We also found a significant reduction in ROS and protein aggregation in Thioflavin-T stain with the compound treatment in N27 cells. After 7-8 weeks of oral treatment (5 or 25 mg/kg), starting 3 months post-PFF injection using 12-month-old mice, we found that both doses of the compound treated mice (n=6-7/group) showed a significant reduction in motor deficits assessed by behavioral assays, such as grooming, nesting, rotarod, hindlimb clasping, and pole test, in a blinded assessment. Further, in immunohistochemistry, the treatment reduced the level of protein aggregation and prevented or reversed the dopaminergic neuronal loss in the striatum and Substantia Nigra, suggesting that the inhibition of NOX can be a viable option for developing potential therapeutics for PD.



### Poster #28

Natalie Onesi, Ian Smith, Anna Klintsova

University of Delaware

### **“Response of Critical Executive Function Circuit to Developmental Alcohol Exposure in a Rodent Model of Fetal Alcohol Spectrum Disorders”**

Fetal Alcohol Spectrum Disorders (FASD) is a range of developmental disorders defined by deficits in physical, behavioral, and cognitive functioning from prenatal exposure to alcohol. As many as 1 in 20 live births in the United States have been exposed to sufficient alcohol exposure (AE) to produce lasting, significant impairments in these areas. A notable effect of AE is damage seen to executive function (EF), a set of cognitive processes involved in goal-directed behaviors. EF regulation has been associated with coordinated activity of the hippocampus (HPC) and medial prefrontal cortex (mPFC). However, the nucleus reuniens of the thalamus (Re) has been identified as a facilitator for reciprocal communication between the HPC and mPFC. Previous research has demonstrated that developmental AE can specifically damage the Re, compromising communication between structures. It is therefore hypothesized that damage to the structural integrity of the mPFC-Re-HPC circuit is linked to EF deficits associated with FASD by compromising the synchrony between the mPFC and HPC.

This study used a rodent model of third trimester binge alcohol exposure to examine the behavioral and neuroanatomical alterations to the Re resulting from neonatal AE. In the present study an Object-in-Place (OIP) associative memory task was used as a behavioral measure of mPFC-Re-HPC functionality. In addition to behavioral data, cells expressing the immediate early gene cFos, a marker of neuronal activation, were quantified in the Re. An impairment of associative memory formation accompanied by a decrease in the number of cFos-expressing neurons in the Re were expected as a result of exposure to alcohol.

No significant effect of postnatal treatment was found on memory formation between sample and test phases. However, a significant improvement in female performance between sample and test phases was found regardless of postnatal treatment. Additionally, no significant effect was found on the number of cFos-positive cells within the Re, indicating that the activation of the Re neurons was not compromised during this task. Lastly, an Open-Field test was implemented to test for anxiety-like behaviors during testing. It was found that there was an intubation effect on rearing, especially present in males. It was also found that there were sex differences in locomotion, with females moving more in general. This study is important in examining what mechanistic alterations are related to AE and how they are involved in deficits associated with FASD.



### Poster #12

**DaShan Osborne, Hakeem Lawal**

Delaware State University

#### **Effects of aging on cholinergic synaptic release in the central nervous system**

Acetylcholine (ACh) is a ubiquitous chemical found in both the central nervous system (CNS) and peripheral nervous system (PNS). In the CNS, ACh is synthesized in the cytoplasm of cholinergic neurons and stored in synaptic vesicles. Vesicular Acetylcholine Transporter (VACHT) is a protein that transports ACh from the cytoplasm to the synaptic vesicles. Despite the wealth of knowledge regarding the regulation of ACh synaptic transmission, including the fact that cholinergic decline is an important feature of aging, not much is understood about how cholinergic release is mediated late in the lifespan or the role of VACHT in that process. We are interested in systematically determining how ACh synapses are altered during aging, and what role changes in expression or function of VACHT may play in that process.

Here we use *Drosophila melanogaster* as a model, and immunohistochemistry to visualize age related changes in the expression of VACHT, as well as changes in its localization to synaptic vesicles relative to the plasma membrane. For this study, *Drosophila* were separated into 3 age groups (0-7 days old; 28 days old; 56 days old), as well as male and female, per age group. The brains were dissected and visualized under a fluorescent microscope. Data from this study are still in the gathering stages. We hypothesize that there will be a change in the expression and localization of VACHT as the neurons age. Future studies will focus on synaptic physiology, and how age-related changes and the overexpression of VACHT, effect synaptic vesicle localization and synaptic transmission.

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K01 Career Development Grant to H.O. Lawal



### Poster #16

**Yoonwoo Park**, Madison Endres, Lisha Shao, Daniel Bushey, Masayoshi Ito, Ulrike Heberlein

University of Delaware

### **“Investigating the role of a cluster of dopaminergic neurons in the regulation of motivational state in *Drosophila*”**

Reward processing is a fundamental function of the brain which shapes the appetitive and consummatory behavior of animals. Subsequently, the consumption and motivation to consume rewards, including food and sex, depend on the internal state as well as the value of the rewarding stimuli. Accordingly, understanding how motivation is represented and regulated in the nervous system is essential not only for understanding reward-driven behaviors but also pathophysiology of disorders, such as depression and addiction, as well. Dopaminergic neurons (DANs) have been shown to signal for reward value and risks in various species. Yet the effects of DANs vary due to the heterogeneity in their location, projection, and transcriptional profiles and the role of DANs in reward evaluation remains to be fully explored. Many clusters of DANs have been identified throughout the *Drosophila* brain that mediate distinctive aspects of reward processing. Recently, our lab identified a previously uncharacterized cluster of DANs that may mediate the animal's motivation to engage in reward-driven behaviors. Specifically, we identified two cell types in the paired posterior medial 3 (PPM3) cluster of DANs that projects to the fan-shaped body. We show that optogenetic activation of these PPM3 neuron is rewarding to the flies, manifested as showing positional preference for and forming appetitive memories with the neuronal activation. Interestingly, the activation of PPM3 elicit a synchronized proboscis extension response, which is known to be an indicator of food preference. Subsequently, we explored the role of these neurons in the regulation of feeding and mating behaviors. While there is much to be explored, the combined results appear to allude to a role of regulation of motivation in PPM3 that may shed light on the mechanisms of homeostatic and hedonic regulation of rewarding stimuli.



### Poster #4

**Rabiul Rafi**

University of Delaware

### **“CD24 Is Essential for Maintaining Proper Lens Stiffness and Lens Volume”**

The lens of the eye is a specialized structure that is integral for vision. Aberrations of the lens can cause many visual impairments, including cataracts. Although there are modern surgical procedures that can reverse cataracts, cataractous lenses can present specific biomechanical problems (e.g. increased stiffness) that make them more difficult to operate on. For this reason, we analyzed the biomechanical properties of cataractous lenses, specifically formed by the absence of the CD24 protein. The CD24 protein is a heavily glycosylated cell adhesion molecule that contributes to the development of a healthy lens. In its absence, the lens structure becomes compromised which leads to the development of a sclerotic ring (a concentric deformity in the lens), refractive discontinuity, and cataract formation. Age is a factor that mediates these changes and as such, we investigated the biomechanical properties of CD24 knockout lenses in mice for multiple age groups. At 20 weeks old, the knockout lenses are visually similar to the wild-type lenses. Around 39 weeks old however knockout lenses display a sclerotic ring within the lens. Finally, at 50+ weeks old these lenses also develop nuclear cataracts. As such, these age groups were selected to understand the lens biomechanics of CD24.

To quantify the biomechanical properties of these lenses, we utilized the coverslip technique proposed by Cheng et al. on mice lenses. Using this technique, we captured images of the lenses as incremental weight (per coverslip) was applied. Analysis of these images on FIJI ImageJ allowed us to calculate many types of biomechanical properties such as equatorial and axial strain (how the dimensions of the lens shape change), volume, and resiliency (to what extent the lens reverted to its original shape after the load was removed). Our findings generally suggest that the differences caused by an absence of CD24 are more pronounced in older age groups. Interestingly, at 50+ weeks knockout lenses are less stiff at lower pressure compared to wildtype but show increased stiffness at higher pressure (more coverslips placed on the lens) which is not the case for the other two age groups. Our findings also have allowed us to characterize other biomechanical properties such as lens volume, which we found to be smaller in the knockout lenses across all age groups. Although these findings help shed light on the nature of CD24 protein within the lens, future research could be conducted.



### Poster #33

**Elina Rodriguez, Mary Beth Hall, Daria Willis, Jaclyn M. Schwarz**

University of Delaware

#### **“Effects of maternal immune activation on maternal care behavior and neonatal reflex development in male and female offspring”**

Developmental disorders, such as autism spectrum disorder and learning disabilities, in offspring are associated with immune activation that occurs during pregnancy. Notably, males are more likely than females to experience symptoms of developmental disorders. The inflammatory response within pregnant mothers is thought to introduce toxins or proteins to amniotic fluid and impact early offspring development. Prenatal maternal inflammation has also been shown to result in fewer nurturing behaviors toward pups, which may influence pups' socialization and learning. The goal of this project is to determine the effects of maternal immune activation (MIA) on neonatal reflex development in offspring and pup-directed maternal care behaviors. On embryonic day 15 (E15) in Sprague-Dawley rats, dams were injected with lipopolysaccharide (LPS; 50ug/ml/kg, i.p.) or saline. To examine maternal care, two 30-min recordings were collected throughout pup development on postnatal days (P)1-P5, P10, P15, and P20. Recordings were coded for frequency of various nursing styles (arch, low-arch, blanket, passive) as well as pup-directed behaviors (licking, stepping, proximity to nest during resting). Furthermore, two male and two female offspring per litter (scores combined for N=1/sex) were assessed for acquisition of neonatal development reflex behaviors from P3-P21, including posture, righting, cliff avoidance, and grasping. We found that offspring that experienced E15 LPS acquired forelimb grasping, hindlimb grasping, and cliff avoidance behaviors significantly earlier in development compared to pups that received E15 saline. LPS-treated dams displayed greater frequencies of passive nursing (P3, P5), and low-arch nursing (P4) relative to saline-treated dams. LPS-treated dams also displayed fewer frequencies of sleeping near pups (P2, P3) and sleeping away from pups (P5) relative to saline-treated dams. These findings provide insight into the impact of MIA on postnatal development and how differences in maternal care may be involved. Further studies will explore the potential neural correlates of these behavioral disparities between LPS- and saline-treated dams and offspring.



### Poster #22

**Paris Junior Roserie,** Elizabeth B. Smedley, Charlotte C. Bavley,  
Camryn Krumbhaar, Maddie Funk, Carmen Dressler, Lisa Briand, Deepu Murty,  
Mathieu Wimmer

Temple University

### **“The hippocampus plays a role in the incubation of craving for sucrose”**

Incubation of craving refers to the intensification of cue-induced reward-seeking behaviours over a period of abstinence from natural rewards or drugs of abuse. There is extensive data on the neural circuits that are critical to reward-seeking behaviour, namely, the nucleus accumbens (NAc) and Pre-Frontal Cortex (PFC). The hippocampus has not been considered as much, although there is evidence that it is important for consolidating rewarding memories. Recent studies have discovered that certain subregions in the hippocampus encode different features of memory; more specifically, the dorsal hippocampus supports the consolidation of neutral spatiotemporal details, while the ventral hippocampus supports the consolidation of rewarding features of the memory. The ability to create strong associations between drug use and contextual stimuli may play a role in addiction and relapse by triggering cue-induced reward-seeking behaviours. Here, we posit that the ventral hippocampus (vHPC) and dorsal hippocampus (dHPC) play different causal roles in the incubation of craving and relapse behaviour. In this study, we sought to delineate the dorsal and ventral hippocampus functionality associated with reward-seeking behaviours. Male rats self-administered sucrose for 10 days. A subgroup of animals was tested for cue-induced sucrose seeking on day 1, while the remaining rats were split into sham, vHPC or dHPC lesion groups. Surgerized animals endured 30 days of forced abstinence and were then tested for cue-induced sucrose seeking. Lesions to the dorsal hippocampus significantly intensified the incubation of craving compared to a sham group. Conversely, lesions to the ventral hippocampus slightly dampened reward seeking following 30 days of abstinence. Overall, these findings suggest that the dorsal hippocampus plays a vital role in relapse behaviour and future directions should explore the molecular modifications that are developing in the hippocampus during abstinence.



### Poster #11

**Katarzyna Rosikon, Hakeem Lawal, Rosaria Formisano,  
Harbinder S. Dhillon\***

University State University

### **“Excitatory synaptic release mechanisms in *Drosophila* and *Caenorhabditis elegans*”**

Excitatory neurotransmitter release and clearance are highly controlled processes, whose modulation is precisely controlled through different sets of modulators. Dopamine and acetylcholine are the key neurotransmitters involved in executive function, motor control, cognition, reinforcement and reward, and their homeostatic dysfunction is implicated in Parkinson’s disease, dementia, and addiction amongst other neuro-pathologies. However, despite the wealth of knowledge in how these molecules are regulated *in vivo*, an integrated picture for their homeostasis remains unclear. By using organism model systems, we are able to investigate in depth the mechanisms of excitatory synaptic release. We utilize *Caenorhabditis elegans* model to test the hypothesis that functional interactions between individual feedback components from the DOP-2 auto-receptor and the DAT-1 membrane transporter merge to form a complex central hub responsible for modulating synaptic vesicle levels. We used an *in vivo* functional imaging approach involving the use of a switchable optical sensor (SEpHluorin) in Fluorescent Recovery After Photobleaching (FRAP)-based assays. Our FRAP recovery data from individual synaptic puncta show that both DOP-2 auto-receptor and DAT-1 transporter provide inhibitory elements in modulating synaptic vesicle fusion. Our current focus is on measuring synaptic fusion rates of *dop-2;dat-1* double-deletion mutants in FRAP experiments. In addition, we are investigating their genetic interaction through behavioral assays, namely, SWIP and mechano-sensory habituation. We are also using synaptopHluorins to identify for the first time, the trafficking domain in the *Drosophila* vesicular acetylcholine transporter, which is responsible for the packaging of acetylcholine into synaptic vesicles for subsequent exocytotic release. Specifically, by utilizing CRISPR-generated endogenously tagged (using pHluorins) putative *Vacht* C-terminal mutants, we are testing the hypothesis that two amino acid residues at the C terminus control the localization of VACHT to synaptic vesicles. Taken together, this work would significantly advance our understanding of the mechanisms that control the synaptic release of essential neurotransmitters dopamine and acetylcholine and could help identify potential therapeutic strategies against disorders related to the aberrant function of those systems.

\* This author is deceased.



### Poster #14

**Yolanda Rush, Jeff Donlea, Hakeem Lawal**

Delaware State University

### **“Analyzing Sleep Deprivation using Chronic and Acute Toxin Exposure to Wild-type *Drosophila* Models”**

Paraquat is an herbicide commonly used for grass and weed control. Exposure to paraquat increases oxidative stress, leading to cell damage and death. Persistent paraquat exposure may increase the risk for Parkinson's disease (PD), resulting in loss of function in the dopamine neuron cells. Because sleep disruption can be an early symptom of neurodegenerative diseases, including PD, we tested whether sleep is altered in fruit flies treated with paraquat. Two lines of wild-type *Drosophila melanogaster* (Canton-S, Cs, or wild-caught population cage flies, PCF) flies fed paraquat or vehicle control of different concentrations. 2mM of paraquat is considered our chronic pesticide exposure, while 10mM of paraquat is our acute exposure. After three trials, we report that chronically exposed CS flies developed less sleep over time. The acute exposure to CS flies decreased their amount of sleep, but they did not survive past the first day. PCF flies could survive much longer with both chronic and acute levels of pesticides but still showed similar trends of decreased sleep.



### Poster #9

John Salsini-Tobias, Dr. Andy Lam, Rachel Wang, Dr. Jessica Tanis

University of Delaware

### **“Effects of vitamin B12 supplementation on chemotaxis in *C. elegans* with neuronal amyloid- $\beta$ ”**

Alzheimer’s disease (AD) is a neurodegenerative disorder characterized by atrophy of neurons in the brain and has an estimated 5.8 million cases in the United States. Notably, evidence suggests that build-up of toxic amyloid-beta ( $A\beta$ ) in the brain is a pathogenic feature of AD. Due to limitations with complexity of mammalian systems, *C. elegans* provide a useful model to examine how the modifiable risk factor diet affects  $A\beta$ -induced proteotoxicity. Expression of toxic  $A\beta$  in *C. elegans* body-wall muscles causes time-dependent paralysis, allowing for easy determination of factors that impact proteotoxicity. Previously the Tanis lab showed that supplementing with vitamin B12 protected against  $A\beta$  induced paralysis and bioenergetic defects by impacting the methionine/SAMe cycle. Phosphatidylcholine (PtdCho) has been observed at reduced levels in individuals with AD and can be synthesized by SAMe-dependent methylation of phosphoethanolamine. Supplementation with PtdCho also protects against  $A\beta$ -induced proteotoxicity. To further explore the protective potential of vitamin B12 and PtdCho, we are using a *C. elegans* strain that expresses  $A\beta$  pan-neuronally, which exhibits chemotaxis defects in response to the attractant isoamyl alcohol (IA). Attraction to IA was quantified with a chemotaxis index (CI). Our results showed all groups were attracted to the IA treatment, with a lesser attraction observed for  $A\beta$ -expressing animals without supplementation. This suggests that  $A\beta$  was detrimental to chemotaxis ability and that vitamin B12 and choline supplementation is protective against  $A\beta$ -induced proteotoxicity in this neuronal model. Conditioning the animals to IA in the absence of food before performing the assay results in a negative CI as the animals learn that IA is associated with starvation. We are currently performing conditioning trials to investigate how  $A\beta$  expression and dietary supplementation of these animal’s impact learning.



### Poster #6

Diana Sanchez, Miki Ii

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#### **“The distinct genetic interactions between *endu-2* and the apoptotic pathway genes in motor neuron development and degeneration in *Caenorhabditis elegans*”**

ENDU-2 is an endoribonuclease that regulates gene expression. It is known that this endoribonuclease plays an important role in the regulation of the neurons in *C. elegans*. Its human counterpart ENDOU has been used as a biomarker in certain cancers whereas, in other model organisms, such as *Drosophila*, a loss of function mutation of *endu-2* ortholog can cause neurodegeneration. This implies that ENDU-2 is involved in the prevention of neurodegeneration.

Motor neuron degeneration is the major cause of neuromuscular disorders. Some diseases, like ALS, can decrease the life expectancy of individuals and for others, it causes strain on daily life. While there are possible treatments for MNDs there is no cure as little is known about the mechanism that motor neurons play.

Dr. Ii's research group found that *endu-2* mutants display a drastic decrease in locomotion for the forward movement that begins in early adulthood. This trait mimics the symptoms of ALS. Because *endu-2* and apoptotic pathway genes work together to regulate neurons such as ADL chemosensory neurons and oxygen-sensing neurons, we hypothesize that ENDU-2 and apoptotic pathway genes play a role in the prevention of motor neuron degeneration.

In Aim 1, I examined how *endu-2* and apoptotic mutants affected locomotion and pharyngeal pumping in young adult worms in developing motor neurons. We found that the development of motor neurons is regulated by genetic interactions between *endu-2* and the two apoptotic pathway genes: *egl-1* and *ced-3*. Surprisingly, the relationships between *endu-2* and the two apoptotic pathway genes in the regulation of the motor neurons were different from the ones we observed in the ADL neurons and oxygen-sensing neurons that regulate cold tolerance and low-oxygen tolerance, respectively.

In Aim 2, I examined the reduction of locomotion in aging worms and life span in *endu-2*, the apoptotic pathway genes' single mutants, and the double mutants. As we expected, we observed the same relationship between *endu-2* and the two apoptotic pathway genes as the ones we observed in the ADL neurons and oxygen-sensing neurons.

Taken together, these results suggest that ENDU-2 acts on different target proteins' mRNAs depending on the stages of motor neurons, such as during the course of development and maintenance of the neurons in adulthood. We propose a novel role of ENDU-2 in the regulation of the development and maintenance of neurons via changes in the target mRNAs.



### Poster #30

Ian Smith, Katrina Milbocker, Tania Roth, Anna Klintsova

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### **“Exploring the effects of alcohol exposure on myelin-related gene expression and potential epigenetic markers in a rodent model of fetal alcohol spectrum disorders”**

Fetal Alcohol Spectrum Disorders (FASDs) are a group of prevalent but preventable developmental disorders that result from alcohol exposure (AE) *in utero*. FASDs are a major concern for public health with 1.1 – 5% of children born in the United States affected (May et al., 2018). Some morphological changes in the brain brought on by AE are improper myelination and growth of white matter commissural and projection tracts (Wilhelm and Guizzetti, 2016; Mathews et al., 2021). Indeed, myelination of white matter is disrupted in children and adolescents with AE (Jacobson et al., 2017; Kar et al., 2021; Treit et al., 2013). Deficits in the proliferation and differentiation of oligodendrocyte precursor cells (OPCs) have been linked to many neurological disorders, including developmental disorders (Berry & Lu, 2020). Patterns of epigenetic modifications have been closely associated with cell fate specification and differentiation, suggesting a crucial role for epigenetic mechanisms in the regulation of these functions. Notably, class I histone deacetylases (HDACs) such as HDAC1 and HDAC3 are highly involved in regulating OPC development (Berry and Lu, 2020). This study investigated the effect of binge AE (5.25 g/kg/day, two doses 2 hours apart) during postnatal days (PD) 4-9 on *Hdac1* and *Hdac3* expression, as well as gene expression of the OPC marker platelet-derived growth factor receptor A (*Pdgfra*) and mature oligodendrocyte marker myelin basic protein (*Mbp*) in male and female Long Evans rat pups at two postnatal timepoints. On PD10 or PD15, brains were extracted and flash frozen; RNA was isolated from medial prefrontal cortex (mPFC) and corpus callosum (CC); RT-PCR was used to assess quantitative expression of gene targets. Preliminary analyses revealed a significant main effect of postnatal treatment on *Mbp* expression in CC at PD10 [ $F(2, 45) = 3.428, p = 0.0411$ ]. *Post hoc* analyses revealed significantly lower gene expression in AE males compared to suckle control males, suggesting an effect of the combined intubation procedure and AE in males at PD10. Additionally, there was a significant main effect of postnatal treatment on *Hdac3* expression in mPFC at PD10 [ $F(2, 46) = 7.093, p = 0.0021$ ] with suckle control animals exhibiting significantly higher gene expression compared to either AE or sham intubated animals, suggesting an effect of intubation stress on *Hdac3*. This ongoing study will help us understand the early onset mechanisms by which AE affects OPC development and subsequent gray and white matter myelination.



### Poster #24

John Stout, Allison George, Henry Hallock, Amy L. Griffin

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### **“Harnessing prefrontal-hippocampal theta synchrony through brain machine interfacing”**

Distant brain regions are thought to communicate when their neural activities become synchronized, an idea known as communication through coherence. In rats, the theta oscillation (4-12Hz) is a prominent brain rhythm that coordinates neural activity. For decades, it has been demonstrated that prefrontal-hippocampal theta coherence is strongly correlated with successful decision making on spatial working memory tasks. But whether prefrontal-hippocampal theta interactions can be harnessed to improve memory guided decision making is unknown. Moreover, the neurobiological mechanisms supporting high theta synchrony states remain poorly understood. To address these problems, we developed software that supports brain machine interfacing. Namely, we created automated analytical procedures to detect states of high and low magnitude prefrontal-hippocampal theta synchrony and employed these procedures to test various questions. First, we implemented these techniques to detect states of high and low magnitude theta coherence as rats performed a spatial working memory task. Trials presented during high prefrontal-hippocampal theta coherence led to improved choice outcomes, indicating that endogenous brain rhythms can be harnessed to improve memory-guided decision making. When prefrontal-hippocampal theta coherence was high, prefrontal theta oscillations emerged and were led by the hippocampus. Implementation of our newly developed algorithms to a previously collected dataset revealed that prefrontal action potential discharging synchronized to local theta rhythms during high prefrontal-hippocampal theta coherence states. However, we found no evidence of enhanced prefrontal neuronal representation, indicating that heightened states of theta coherence led to improved choice outcomes through rhythmic coordination of neuronal activity patterns within the prefrontal cortex. Current research is focused on combining our brain machine interfacing techniques with optogenetic perturbations to understand how prefrontal oscillations emerge to support synchrony. Our findings represent the development and implementation of brain machine interfacing procedures to understand the contributions of neural synchrony on behavior.



### Poster #8

Karli Sunnergren, Jessica Tanis, Andy Lam

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### **“Exploring the Role of Altered Homocysteine Metabolism in an Alzheimer’s Disease Model”**

Elevated levels of homocysteine result in oxidative stress, and hyperhomocysteinemia is a modifiable risk factor for Alzheimer’s Disease (AD). Homocysteine is converted to methionine-by-methionine synthase (METR-1), which requires vitamin B12 as an essential cofactor, but can also be broken down into cystathionine by the enzyme cystathionine beta synthase (CBS-1). We recently discovered that dietary vitamin B12 was protective in a *C. elegans* AD model (GMC101) that expresses the toxic A $\beta$ 1-42 peptide, delaying A $\beta$ -induced paralysis, increasing ATPs levels, reducing mitochondrial fragmentation, and decreasing reactive oxygen species, all without impacting A $\beta$  levels. The protective effect of vitamin B12 required METR-1, indicating that B12 functions as an enzyme cofactor to increase methionine levels. However, we also found that too much methionine had a detrimental effect on A $\beta$ -expressing animals. Through RNA-Seq of wild type and A $\beta$  animals that were fed OP50 *E. coli*, which induces mild B12 deficiency, and HB101, which provides adequate B12, we discovered that the HB101 diet caused an increase in *cbs-1* expression. qRT-PCR shows that vitamin B12 supplementation of the OP50 diet is sufficient to increase *cbs-1* transcript levels in A $\beta$  *C. elegans*, although this does not extend to wild type animals. This raises the possibility that altering *cbs-1* transcription may serve as a mechanism to regulate methionine levels. CBS-1 function in *C. elegans* has not been thoroughly described, so we used CRISPR to create a *cbs-1* knockout. We found that loss of *cbs-1* resulted in severely delayed developmental timing, a significant increase in lifespan, and reduced brood size compared to control animals. Additionally, loss of *cbs-1* in A $\beta$  animals eliminated the protective effect of the B12 rich HB101 diet on A $\beta$  paralysis, suggesting that a B12-induced increase in homocysteine metabolism through the transsulfuration pathway may contribute to the reduced A $\beta$  proteotoxicity observed in animals fed a B12 rich diet.



### Poster #32

Brooke Van Weele, Janace Gifford, Jaclyn Schwarz

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#### **“The effects of limited bedding and nesting on anxiety and maternal behavior in postpartum rats”**

Postpartum depression is a common and serious mental illness that many mothers struggle with. Similarly, to humans, female rats have also demonstrated symptoms of postpartum depression (PPD) their first two days after giving birth. The purpose of this research project is to examine postpartum female rats after being placed in stressful living conditions and how it may alter their overall stress and anxiety. The rats used for this study were separated into two groups who received differing bedding conditions, LBN or control. LBN consists of much less bedding than usual (250mL), whereas control consists of more than usual bedding volume (4000mL). Our hypothesis was that rats under LBN conditions would demonstrate more stress and anxiety compared to rats under control conditions. In order to measure their anxiety levels, animals underwent several behavior tests to show the impact postpartum anhedonia has on their maternal behavior. These tests include, sucrose preference, marble burying, elevated plus maze (EPM), hoarding behavior, and pup retrieval tests. Average pup weight was observed in each bedding condition group to see if their living conditions altered weight and general growth of their pups, an indication of maternal behavior. Our hypothesis was supported by a few of the tests we conducted. For instance, the results for the elevated plus maze, marble burying, and the pup weight all show that rats under LBN conditions demonstrate higher levels of stress and anxiety. However, there were no correlations between living condition and their general maternal behavior in the other behavioral tasks observed. There is research continuing to be conducted in the Schwarz Lab on postpartum depression in rats, in which maternal behavior will be analyzed more heavily.



### Poster #7

Tempalyn Wiggins, Harbinder S. Dhillon\*

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### “Centrioles at the Center of Asymmetric Left/Right Axis Development”

Multicellular eukaryotes display an anatomical and functional asymmetry in all three spatial dimensions. Extensive scientific studies of the developmental mechanisms involved in embryogenesis have provided significant progress in elucidating the processes of dorsal/ventral and anterior/posterior axes development, also described as organismal x- and y- axes. Recent research focusing on the left/right or z-axis has provided insights into the mechanisms involved in its development including the roles of microtubules and ciliary movement.<sup>1</sup> However, the asymmetric gene expression required to form the z-axis with asymmetric left/right laterality remains unexplained. Uncovering the role of centriole-chromatid recognition which results in specific cell destinations during asymmetric cell divisions of embryogenesis would uncover a novel mechanism of transcriptional regulation of ensemble-like gene sets in embryo development.

My objective is to test the HYPOTHESIS that long-lived paternal centrioles have a preordained cell destination which can be mapped through cell lineages in embryonic development and the aberration of which leads to reversed/atypical asymmetrical embryo laterality. I am testing whether the centrioles can bind specifically to the initial paternal chromosomes to provide a mechanism whereby particular chromatids of particular paternal origin are located to specific cells during embryogenesis with resultant organismal laterality. Using the *C. elegans* invertebrate model with its small number of chromosomes, its completely defined cell divisions from the initial P/AB division of the zygote through the 959 cells of the fully differentiated organism, and its thoroughly mapped cell lineages provides an excellent model to conduct this investigation.<sup>4</sup> Additionally, the highly conserved nature of centriole structure and genetics across eukaryotes makes *C. elegans* a broadly applicable model for this study. To determine the pattern of paternal centriole distribution until the establishment of the z-axis, I have imaged the movement of paternal centrioles during embryonic cell cycles on Zeiss-510 confocal microscope. Preliminary results suggest that a specific cellular trajectory does not exist; however, a sex specific difference needs to be further elucidated.

\*This author is deceased.



### Poster #34

Daria Willis, Mary Beth Hall, Jaclyn Schwarz

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#### **“The effects of maternal immune activation on cytokine expression in fetal brain and maternal spleen”**

Maternal immune activation (MIA) in rodents has been shown to produce offspring with altered behavior and expression of neural and glial factors, similar to symptoms seen in disorders such as autism spectrum disorder, schizophrenia, and general learning disabilities. Thus, rodent models of MIA are useful in studying changes that may underlie these neurodevelopmental disorders. In this project, MIA is produced with lipopolysaccharide (LPS), a gram-negative component of bacterial cell walls that is used to mimic an innate immune response by triggering the production and expression of immune-associated genes, cytokines, and proteins. On embryonic day (E)15, pregnant Sprague-Dawley rats were injected with LPS (i.p., 50ug/ml/kg) or sterile saline; non-pregnant rats also received LPS or saline. At either 2-, 4-, or 24-hours post-injection, brain and peripheral tissue were collected from adult females and fetuses. Quantitative, real-time polymerase chain reaction (qRT-PCR) was used to examine differences in cytokine expression between LPS and saline groups in pregnant and non-pregnant females. We also examined the immune response of male vs. female fetuses following MIA. Preliminary analysis of maternal spleen tissue shows that LPS administration elevated IL-6 expression relative to the 18S housekeeping gene after 2, 4, and 24 hours. Furthermore, expression of the male specific Sry gene in fetal tail samples was used to determine sex and one male and one female fetus were selected from each litter for further tissue analysis. Preliminary analysis of whole fetal brains shows an interaction between time point and treatment group, with IL-6 elevated at 2 and 4, but not 24 hours post-injection. Further studies will elucidate the expression of other cytokines in additional maternal brain and peripheral tissues following immune activation.