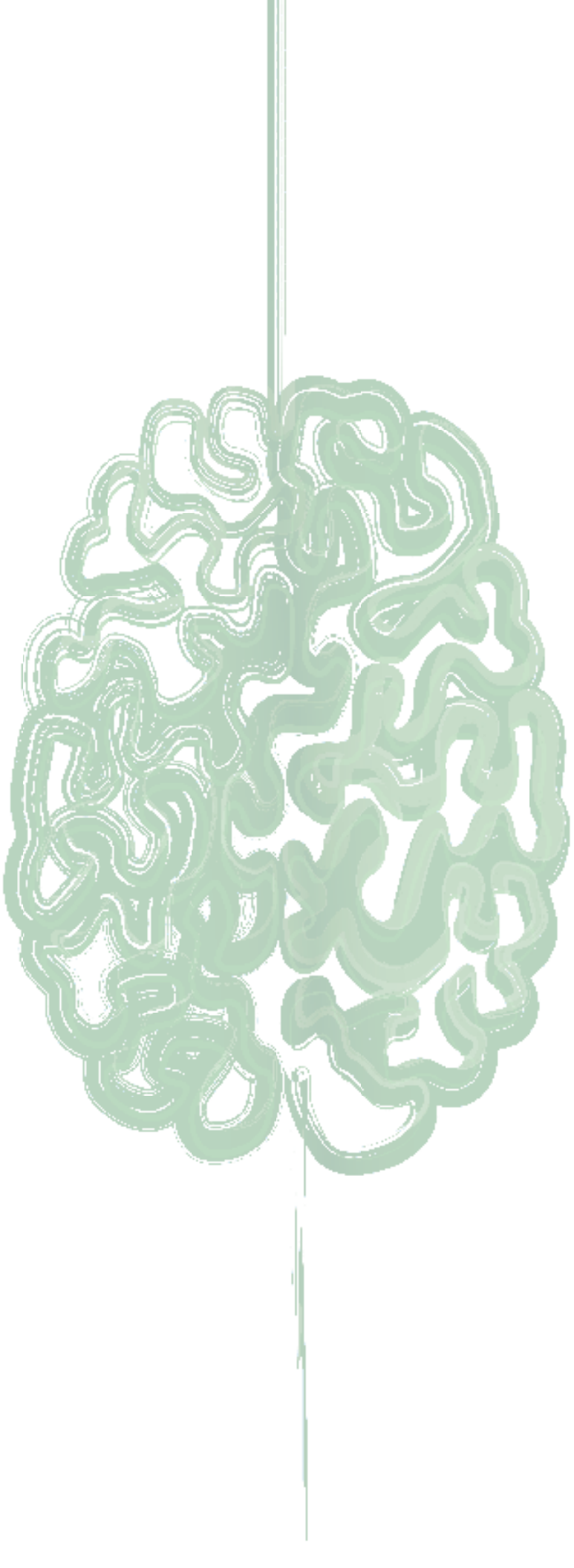

2023 FUN Undergraduate Poster Session

Abstracts

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Poster #1 **Poster Board: XX94**

HIPPOCAMPAL NEURAL STEM CELL PROXIMITY TO VASCULATURE EMERGES DURING POSTNATAL DEVELOPMENT IN MICE

India S. Carter, Nidhi Devasthali, Angela L. Saulsbery, Elizabeth D. Kirby

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Adult neurogenesis, the process of creating new neurons throughout life, occurs in two main areas of the mammalian brain; the subventricular zone and the dentate gyrus (DG) of the hippocampus. The surrounding vasculature within each of these niches is an important source of support for adult neurogenic processes. Within the DG, the vasculature is especially dense and neural stem cells (NSCs) and their immediate progeny exist in especially close proximity to local blood vessels in adulthood. This unique arrangement is hypothesized to support adult neurogenesis in several ways, such as by providing scaffolding for progenitors and neuroblasts to migrate tangentially through the DG, as well as by providing NSCs access to circulating support molecules such as growth factors. Though the proximity of the adult NSCs to vessels is well established, little is known about how it develops. To characterize the development of NSC proximity to blood vessels, we quantified the distance from radial glia-like NSC bodies to the nearest blood vessel in mice between 2 and 9 weeks of age, a time period covering from early formation of the major DG cell layers to adulthood. We identified NSCs and endothelial cells in wildtype mice perfused at 2, 3, 5 and 9 weeks of age using immunofluorescent phenotypic markers in fixed tissue slices. We found that from 2 weeks to 9 weeks of age, there was a progressive reduction in the distance between NSC bodies and the nearest blood vessel. These findings suggest that the association of RGL NSCs with vasculature is not a preserved feature from early development, but rather one that arises de novo during postnatal maturation. They further imply that the development of the RGL NSC neurogenic vascular niche is not complete until adulthood. Further characterization of the development of the neural stem cell niche and surrounding vasculature will provide insight into the unique mechanisms that ensure preservation of neurogenesis in the adult DG.

FUN Member Sponsor: Elizabeth Kirby

Theme A: Development

Poster #2 **Poster Board: XX93**

EXPRESSION OF AUTISM-RELATED INTEGRIN β3 IN MOUSE CEREBRAL CORTEX AND HIPPOCAMPUS

Hollyn N. Cook, Ellie C. Vinson, Anna R.Kalinowski, Hilda V.Rodriguez, Collin J. Denzler, George S. Vidal

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A strong association exists between mutations in integrin β3 (Itgb3) and autism spectrum disorder. Integrins (a class of heterodimeric cell adhesion molecules) are required for normal structural development of dendrites and synapses. The function of integrin β3 in cerebral cortical and hippocampal neurons and glia in vivo was unknown until recent studies from our lab showing that Itgb3 is required for normal dendritic arborization of layer II/III pyramidal neurons in vivo in a cell-specific manner (https://doi.org/10.1186/s13041-020-00707-0), and that it is required in forebrain excitatory neurons and astrocytes for normal social and grooming behaviors in mice (https://doi.org/10.1186/s12868-022-00691-2). These and other prior studies suggest that integrin β3 is required in neurons of the cortex and hippocampus for normal brain function, and that its postnatal expression could be developmentally regulated. However, Itgb3 expression in cerebral cortex and hippocampus is not well understood. We set out to characterize Itgb3 expression utilizing fluorescent in situ hybridization (RNAscope), which localized Itgb3 transcripts throughout the cortex and hippocampus of early postnatal and juvenile mice. Results suggest a strong laminar pattern of Itgb3 expression in layer V of the cortex, and a pattern of expression strongly restricted to stratum pyramidale of hippocampal region CA3. These patterns appear to peak during the early postnatal period and persist into early adulthood. Taken together, our results suggest that Itgb3 is expressed in cortex and hippocampus during the time when dendrites of excitatory pyramidal neurons develop en masse.

Funding Support: NINDS K01 NS107723

FUN Member Sponsor: George Vidal

Theme A: Development

Poster #3 **Poster Board: XX92**

EFFECT OF EMBRYONIC CORTISOL EXPOSURE ON NEURONAL MARKER GENE EXPRESSION IN ZEBRAFISH LARVAE

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Exposure to prenatal stress is known to correlate with neurodevelopmental disorders and negative health outcomes later in life. Cortisol is the primary hormone mediating the impacts of prenatal stress. Cortisol has been reported to regulate gene expression of specific neuronal marker genes in adult tissues. We tested how early prenatal cortisol exposure affects mRNA gene expression of different neuronal marker genes in zebrafish using reverse transcription quantitative polymerase chain reaction (RT-qPCR). At 3 hours post fertilization (hpf), zebrafish embryos were treated with 5 uM cortisol solution or vehicle solution. Treatment solutions were fully refreshed daily until 5 days post fertilization (dpf). RNA was then extracted from pooled samples of larvae and converted to cDNA. Gene expression was measured using gene-specific primers with RT-qPCR. Tested genes included markers for different types of neurons (e.g. glutamatergic, GABAergic, glycinergic) and glia. Differential gene expression analysis was conducted by comparing cortisol-treated samples with vehicle-treated samples using standard methods incorporating primer amplification efficiency values. No significant differences in neuronal marker gene expression based on cortisol treatment were found. These data indicate that this level of embryonic cortisol exposure does not regulate these specific genes in 5dpf zebrafish, suggesting cortisol may not directly affect early development of these types of neurons and glia.

FUN Member Sponsor: Cora Dunnum

Theme A: Development

Poster #4 **Poster Board: XX91**

SOCIAL EYE-GAZE DEFINES DISCOURSE BOUNDARIES IN NATURAL PLAY INTERACTIONS

Imuetiyan E. Eweka, Crystal Lee, Casey .Lew-Williams .

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Children are often exposed to different social environments that bolster language learning. In these environments, caregivers help children develop their language skills by providing social cues that encourage word learning. These cues include social eye-gaze and gestures, and research demonstrates that these cues enhance joint-attention to objects of play, and facilitate learning of those labels (Baldwin, 1993). The complexity of language acquisition from social cues in a naturalistic, dynamic setting is not taken into account by these experimental approaches, even though in-the-moment connections are a crucial part of word learning (Lee & Lew-Williams, 2022). We hypothesize that the benefits of in-the-moment social cues are present within natural discourse. Caregivers can produce social cues to define discourse boundaries. We predict this will facilitate children to discover topics of discourse, identify referents of discussion, and capitalize on linguistic input. We attempt to address the first of these predictions: the relationship between caregiver social cues and discourse structure. We test this question by analyzing natural caregiver-child interactions (N = 44). We code each video of unstructured play for moments of joint attention, eye-gaze, and discourse topics. We predict that caregivers will produce social cues more frequently at the beginning of discourse topics, suggesting they are using such cues to indicate shifts in discourse structure. Our findings will broaden the lens through which social cues occur and their effects on word learning. Caregiver social cues may be presented in systematic ways to provide structure and scaffold the continuous input children receive, bolstering their vocabulary acquisition.

FUN Member Sponsor: Princeton Neuroscience Institute Summer Internship Program

Theme A: Development

Poster #5 **Poster Board: XX90**

MALE MICE ARE MORE SUSCEPTIBLE TO DEVELOPMENTAL STRESS IN A TWO-HIT PARADIGM: EFFECTS ON ADULT MOOD-RELATED BEHAVIOR, SOCIAL BEHAVIOR, AND GLUCOCORTICOID RECEPTOR EXPRESSION

Anya P. Gemos, Colleen E. Donahoe, Surya G.Daniel, Isabella .Craus, Zachary M. Palermo, Nikol Lupu

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Early adversity is known to increase the likelihood of developing mental illness later in life, but there is less research examining the possible cumulative impact of multiple early adverse events. This study focused on the long-term effects of a two-hit model composed of stressors during childhood and adolescent development and evaluated behaviors related to mood and sociability in adulthood in both males and females. Maternal separation was used to model early adversity and stressful events in childhood, while social isolation was used as a stressor in adolescence. Male and female CD-1 mice were exposed to either maternal separation (MS; PND 2-12), adolescent social isolation (ASI; PND 35-56), a combination of both (MS-ASI), while controls experienced no stress CON. Overall, results suggest males are more susceptible to developmental stress exposure than females across multiple behavioral tests. For example, we found higher anxiety in all three developmentally stressed male groups compared to controls in the elevated plus maze (EPM total time in open arms, $p=0.003$) with a similar but not significant pattern exhibited in the novelty suppressed feeding paradigm for latency to eat. In the social preference test, once again males were more affected, as developmentally stressed male groups showed higher preference for social contact in a three-chamber test compared to controls, while in the females there was no effect of treatment condition (treatment effect on time near social cup, $p=0.037$; sex effect for time near social cup, $p<0.001$). Treatments did not appear to impact measures of depression in either the forced swim test or sucrose preference test. Further, there was no overall impact of treatment on locomotor behavior in an open field. Ongoing analyses seek to assess potential changes in glucocorticoid receptor protein levels in the hippocampus following the developmental stress treatments to assess whether similar sex differences can be detected in the brain.

Funding Support: Emmanuel College

FUN Member Sponsor: Melanie Leussis

Theme A: Development

Poster #6 **Poster Board: XX89**

EXAMINING FINE MOTOR FUNCTION AND POTENTIAL EFFECTS OF AN NMDA RECEPTOR PARTIAL AGONIST IN 22Q11.2 DELETION SYNDROME MICE USING A STRING-PULLING BEHAVIORAL TASK

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Alterations of genes within the 22 chromosome, specifically the 22q11.2 region, contribute to neuropsychiatric and neurodevelopmental disorders, including autism spectrum disorder and schizophrenia. Several neurodevelopmental disorders, including the 22q11.2 microdeletion (22q11.2DS) have been associated with abnormalities in cerebellar function that may result in deficits in gross and/or fine motor skills. The current study sought to examine motor function in the 22q11.2DS mouse model and determine the effects of an NMDA receptor (NMDAR) agonist intervention on this behavior. Female C57BL/6-Del(16Dgcr2-Hira)1Tac mice (n=9) and their age- and sex-matched wild-type controls (n=7) were subjected to a subchronic, 1-week dosing of an NMDAR partial agonist (D-cycloserine; 30mg/kg, i.p.) or saline, starting at 4-6 week old. Five days following injections, mice were assessed for fine motor skills using a rodent string-pulling task. On day 1, mice were habituated to 20 strings (100% cotton) of which half were baited to contain ½ a piece of a cheerio and dipped in sweetened condensed milk. All mice pulled at least 18 of the 20 strings and moved to day two of the test trial in a clear Plexiglas rectangular string-pulling apparatus (13.3 cm × 7.5 cm × 26 cm). String-pulling behavior was captured using a Sony Handycam camcorder, positioned at a perpendicular angle to the apparatus, with settings at 60 frames/second and a shutter speed of 1/1000. Initial measures collected from the string-pulling task included amount of time to approach string and duration of time spent engaged in string-pulling behavior. To determine if there were any differences in these measures based on differences in the scent of strings (e.g., unscented versus scented), mice were provided a series of strings to pull which are baited (with cheerios) or scented (one string with the scent of the mouse's bedding from their home cage and two strings with the scent of bedding an unfamiliar cage). Very preliminary analyses show no significant differences in approach time between 22q11.2DS mice (both treated and untreated with D-cycloserine) (M=106.75s and 114.61s, respectively) and the wildtype control (M=51.24s) ($p>0.05$, n=15) for the familiar string. The amount of time to approach the social conspecific string also showed no significant differences between 22q11.2DS mice (treated M=42.23s, untreated 133.40s) and the wildtype control (M=35.16s) ($p>0.05$, n=15). On the average pull time of the familiar or social strings there were also no significant differences observed between groups ($p>0.05$, n=15). Overall, these data encourage ongoing and future analyses of motor coordination in this dataset with an increased group size and additional measures related to the string-pulling (e.g., amount of time pausing between string pulls and differences in time of baited strings versus the familiar/social presented strings). This study may stimulate interest to investigate therapeutic interventions that may be involved in social-cognitive domains, such as NMDAR activation within 22q11.2 deletion syndrome.

Funding Support: Taconic Biosciences (JAB); Provost Office CNU (JAB)

FUN Member Sponsor: Jessica Burket

Theme A: Development

Poster #7 **Poster Board: XX88**

CONNECTING MITOCHONDRIAL DYNAMICS TO THE FATE OF RADIAL GLIAL NEURAL PROGENITOR CELLS IN THE XENOPUS LAEVIS OPTIC TECTUM

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Radial glial neural progenitor cells (NPCs) are the heterogeneous proliferating stem cell population that gives rise to all cells in the brain. These slender cells span the developing brain making contact with the ventricle and the outer pial surface. Early on, these highly polarized cells divide symmetrically to expand this progenitor pool, but as development continues the NPCs begin to asymmetrically divide to produce neurons. Intrinsic and extrinsic cues guide this irreversible and critical fate switch. If regulated inappropriately, a premature shift to neurogenesis limits brain development and contributes to neurodevelopmental disorders. A feature of many stem cells is their reliance on non-mitochondrial ATP production. Yet, these cells contain dynamic and motile mitochondria. In some stem cells it has been shown that the metabolically mature older mitochondria are segregated during cell division so that they are preferentially inherited by the progeny that differentiate. It is not known whether NPCs also compartmentalize mitochondria leading up to division and how that distribution influences the fate of the progeny. To address these questions, we use in vivo time-lapse confocal microscopy to image fluorescent protein-labeled NPCs and their mitochondria in the optic tectum of albino Xenopus laevis tadpoles. This approach preserves the surrounding neural circuitry of the developing visual system and allows us to monitor and track the NPCs, their mitochondria, and their progeny over days in their natural environment. We find that mitochondria in the NPCs are motile and undergo fusion and fission. Our data suggest that mitochondria are not equally inherited when the NPCs divide. Using photo-activatable GFP to label subpopulations of mitochondria in NPCs within the 24 hours before cell division reveals high levels of mitochondria fusion and organelles that migrate >100 μms. Together our data show that mitochondria dynamics and distributions are biased as the NPCs prepare for cell division, suggesting that the position of the mitochondria may regulate the type of division.

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FUN Member Sponsor: Jennifer Bestman

Theme A: Development

Poster #8 **Poster Board: XX87**

REGULATION OF RETINAL CELL PROLIFERATION AND NEUROGENESIS BY INTEGRATED BMP, FGF/MAPK, AND RA PATHWAYS

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Both extrinsic and intrinsic cues regulate whether cells continue to proliferate or proceed to differentiation during embryo development. Within the developing zebrafish retina, the neurogenic marker atoh7 shows that differentiation of retinal progenitor cells into retinal ganglion cells is slower in the dorsal retina between 36-48 hpf. However, due to a missense mutation within the bmp13 gene in a gdf6au768 mutant, a delay in differentiation onset as marked by atoh7 is not observed. Both BMP and FGF have been observed having increased activity within the dorsal retina between 36-48 hpf, suggesting that they play a role in the onset of differentiation into retinal ganglion cells. If BMP is upstream of FGF and activates it, when BMP is downregulated then FGF expression would also be affected. Experimental trials used a combination of FGFR receptor inhibitors, PD166866 and BGJ398 to downregulate FGF/MAPK expression from 22-34 hours post fertilization (hpf). When this trial was replicated but using instead a BMP inhibitor, DMH1, similarly decreases in FGF/MAPK activity were observed. Furthermore, disrupting the FGF pathway using PD-BGJ from 22-34 hpf within the wild-type embryo suggests a decrease of active mitotic cells within the dorsal retina, while within the gdf6au768 mutant an increase in active mitotic cells has been observed. A MAPK inhibitor, LY32, acts similarly to PD-BGJ, causing decreases in dusp6, a gene activated by FGF expression, and when used to disrupt development from 26-44 hpf, expression of the neurogenic marker, atoh7, is strongly decreased. Retinoic acid (RA) activity is also present within the dorsal retina, and while being downstream of FGF/MAPK activity appears to downregulate FGF activity, as suggested by experimental trials activating RA activity from 22-34 hpf leading to the downregulation of dusp6 activity. This delay in differentiation in the dorsal retina may occur in order to allow a dorsal retinal blood vessel to descend, because in the gdf6au768 mutant the formation of this vessel is disrupted. However, treating the gdf6au768 with the FGF upregulator BCI, partial rescue of the dorsal vessel formation occurs, suggesting that this delay is crucial for vasculature development. Further research is needed to fully understand why the dorsal retina differentiates later into retinal ganglion cells, and what signals cause this, and how those signals affect proliferation.

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FUN Member Sponsor: Kara Cerveny

Theme A: Development

Poster #9 **Poster Board: XX86**

EMOTION ESSENTIALISM IN DEVELOPMENT

Abbygail Michel, Chantal Valdivia, Erik Nook.

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Essentialism is a psychological phenomenon that involves the use of categorizing information to help us make sense of the world. It refers to the idea that things in a category are stable over time, are innate, and are distinctive. Those with essentialist beliefs tend to think that members of a category share an underlying "essence" that leads to the production of the features that define that category. Developmental research on essentialist beliefs has been focusing on how essentialism impacts social categories, such as race and gender. All existing research on emotion essentialism, the belief that different emotion types are defined by a latent "essence" that produces their defining features, has been done on adults. Recent studies have shown that adults do display essentialist views of emotions, though these findings have not been explored in a developmental context. As such, the change in essentialist views from childhood to young adulthood will be investigated in this study. We will explore how essentialist beliefs about emotions, cognition, and bodily states change across development in youth ages 7 to 15 as well as in young adults between the ages of 20 and 25. In this study, we will also collect data on other affective phenomena, like emotion differentiation and emotion abstraction, to test hypotheses about relations between emotion essentialism and these affective processes in youth.

FUN Member Sponsor: Erik Nook

Theme A: Development

Poster #10 **Poster Board: XX85**

ASD PATHOGENESIS: THE EFFECTS OF EARLY LIFE CEPHALOSPORIN ANTIBIOTIC EXPOSURE ON HIPPOCAMPAL NEUROGENESIS AND BEHAVIOR IN 16P11.2 MICRODELETION MICE

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Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental disorder that affects approximately 1 out of 36 children in the United States. Neuroimaging, neuropathology, and gene enrichment studies have rigorously implicated altered neurogenesis, the generation of brain cells, as a phenotype commonly observed in ASD. This process is highly sensitive to genetic and environmental risk factors, warranting investigation of a gene x environment (GxE) model. A recently identified environmental factor that has been linked to increased ASD outcomes is exposure to cephalosporin antibiotics during the first two years of life. Importantly, not all infants exposed to antibiotics are later diagnosed with ASD, suggesting a contributing role of genetic vulnerability. To incorporate a genetic risk basis in our model, we use the 16p11.2 deletion copy number variation (16pDel CNV) mouse. This CNV is highly penetrant and accounts for ~1% human ASD cases. Infant antibiotic exposure was modeled by exposing WT and 16pDel mice to saline (control) or 10mg/kg cefdinir (cephalosporin antibiotic) from postnatal (P) days 5-9. We hypothesized that early life cefdinir exposure would alter postnatal neurogenesis and behavioral outcomes, with an exacerbated phenotype in the 16pDel mice. We quantified total numbers of neuronal precursors in the postnatal hippocampus at P13, a timepoint and brain region where robust proliferation occurs. We found a 40% reduction in S-phase cell numbers (EdU+) in cefdinir-exposed 16pDel males compared to the saline exposed 16pDel males, whereas no differences were observed in other groups. To complement these data, we also quantified general stem cell marker, Ki67, in the hippocampal dentate gyrus. Remarkably, we detected a parallel 31% reduction in Ki67+ cells only in cefdinir-exposed 16pDel males, further supporting our hypothesis. To determine if this reduction at P13 persists to the postmitotic neuronal population, we quantified numbers of Prox1+ cells in the hippocampal dentate gyrus at P21 using stereology. Our preliminary findings reveal a decrease in Prox1+ cells in cefdinir-exposed male mice, regardless of genotype. To examine behavioral differences, we performed the juvenile social task for mice at P21 and found that cefdinir-exposed mice had reduced sociability at P21 compared to saline-exposed mice, with an exacerbated phenotype in 16pDel mice, supporting our hypothesis. These observations suggest that early-life antibiotic exposure in genetically vulnerable mice may impact hippocampal dentate gyrus neurogenesis, a possible basis for altered neurodevelopment and juvenile behavioral functions.

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FUN Member Sponsor: Emanuel DiCicco-Bloom

Theme A: Development

Poster #11 **Poster Board: XX84**

CORTICOLIMBIC NEURAL RECRUITMENT AND BEHAVIORAL CHANGES IN RESPONSE TO EARLY LIFE ADVERSITY ARE SEX-SPECIFIC IN RATS

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Excessive stress at any stage of life increases the likelihood that a person may develop mental health problems in the future. However, extensive stress during developmental periods such as juvenility or adolescence predisposes individuals to develop mental health disorders such as anxiety and depression in the future, and disproportionally impacts women. The early-life adversity (ELA) caused by extensive stress can contribute to maladaptive outcomes through the disruption of the development of brain regions directly related to stress and emotional regulation such as the circuit linking the prefrontal cortex (PFC) and basolateral amygdala (BLA). Sex works as a biological variable in the development of these regions in both humans and model systems. In response to ELA, the connections from the BLA to the PFC develop at sex-specific rates, with females experiencing precocial maturation of axonal innervation earlier than their male counterparts. However, the overall local functionality and cell-type specific integration of this maturation – as well as concomitant behavioral manifestation – is unclear and remains to be investigated. Using stereotaxic electrical stimulation via bipolar electrode, we introduced physiologically relevant stimulation to the BLA of adolescent rats (postnatal day 28) to activate the region and enable the quantification and characterization of downstream circuit-specific effects. Within the PFC, we use immunohistochemistry to label cells recruited by this activation through upregulation of the immediate early gene, c-Fos, and leveraged cell-specific markers for inhibition (i.e., parvalbumin; PV) as a proxy to determine changes in local excitatory: inhibitory balance. Immunohistochemistry results suggest differences in overall neural, as well as cell-type, recruitment across sex and rearing condition within the PFC. To connect the neurological results to larger scale changes, rat behavior in response to an aversive social stimulus (22kHz ultrasonic vocalization (USV) alarm calls) were assessed. Rats were placed in the open field for a total of 10 minutes, with a 5 minute baseline followed by 5 minute exposure to 22kHz rat USV playback to assess environmental vigilance within the context of potential threat. Center duration, latency to center, average velocity, and maximum velocity were compared for all conditions across both 5-minute time bins. Sex and rearing condition differences in these measures suggest an impact of sex on behaviors. Overall, these findings provide compelling evidence that point to a sex-specific effect of ELA on the neural circuitry responsible for behavioral regulation during ambiguous threat.

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FUN Member Sponsor: Jennifer Honeycutt

Theme A: Development

Poster #12 **Poster Board: XX83**

ALTERED SENSITIVITY TO COCAINE IN ADOLESCENT SPONTANEOUSLY HYPERTENSIVE RATS, A RODENT MODEL OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

Ingrid Schoenborn, Aili Ramsden, Miriam Kirylo, Luis Martinez

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Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder impacting approximately six percent of all adolescents. Although initiating substance use early in life (e.g., during adolescence) is generally associated with an increased risk of developing a substance use disorder (SUD), there is reason to believe that adolescents with ADHD are at particular risk for SUDs. Indeed, adolescents with ADHD initiate substance use at an earlier age and have higher prevalence rates of SUDs for cocaine and other illicit substances, compared to those without ADHD. Given that (1) the psychoactive effects of cocaine are mediated (in part) by increases in dopamine signaling in the brain, and (2) psychostimulant-induced dopamine release is higher in spontaneously hypertensive rats (SHRs; a rodent model of ADHD) compared to controls, here we sought to determine whether behavioral responses to cocaine are enhanced in SHRs. To begin to address this question, 5-week-old male and female SHRs and Sprague Dawley (SD; a control strain) rats underwent a series of behavioral tests. Rats were first assessed for inattentiveness in an 8-min y-maze test, during which the percentage of spontaneous alternations was measured. They were then examined for hyperactivity (as indexed by total distance traveled) in a 10-min open-field test. Rats were then assessed for behavioral sensitization to cocaine. On each of the first four test days, rats were habituated to a locomotor activity chamber for 30 min, injected intraperitoneally with cocaine (10 mg/kg) or saline vehicle (1 ml/kg), and then returned to the locomotor activity chamber for one hour. The number of ambulations, fine movements, and the time spent rearing were determined via analysis of beam break data. Rats subsequently experienced a 48-hour forced abstinence period, during which the degree of inattention and hyperactivity was reevaluated. On the final (challenge) day of behavioral sensitization testing, rats with a history of repeated cocaine injections and those with a history of repeated saline injections all received a final cocaine injection and were tested for cocaine-induced locomotor activity. We found that SHRs exhibited increased distance traveled (open-field test) and increased ambulations (habituation phase of challenge day test) compared to SD rats, verifying that SHRs exhibit the expected hyperactivity ADHD phenotype. Furthermore, behavioral sensitization to cocaine on the challenge day, as indicated by greater cocaine-induced ambulation and fine movement responses in rats with a history of cocaine vs. those with a history of saline injections, was enhanced in female SHR vs. SD rats; these effects were not observed in male rats. Assessment of the inattentive ADHD phenotype of SHRs is ongoing. Our results indicate that adolescent females with ADHD may be particularly sensitive to the effects of cocaine, and consequently may be at greater risk for developing addiction to this drug.

FUN Member Sponsor: Luis Martinez

Theme A: Development

Poster #13 **Poster Board: XX82**

HIPPOCAMPAL ENLARGEMENT EMERGES IN ADOLESCENCE IN THE VALPROIC ACID MODEL AND PARALLELS HUMAN FINDINGS

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Hippocampal enlargement is commonly observed in adolescents with autism spectrum disorder (ASD). fMRI studies indicate that this enlargement may compensate for dysfunctions in the posterior medial network utilized for memory tasks. The valproic acid (VPA) model was used to model ASD in rodents. Our previous work found VPA exposure increased cerebellar pathology in adulthood and enlarged anterior cingulate cortex (ACC) in female adolescent rats. Furthermore, some of these enlargements were associated with impaired cognitive performance on an attentional set-shifting task. The current work examined volumetric dysregulation in the cerebellum and hippocampus throughout adolescence.

Pregnant Long-Evans dams were given intraperitoneal injections of 600 mg/kg sodium valproate (VPA) or vehicle control at gestational day 12.5. Rats were reared and aged to postnatal day (P) 28 or P40, which correspond to early and middle adolescence, respectively. At P28 or P40, animals were euthanized by phenobarbital overdose and transcardially perfused with saline followed by PFA. Heads were postfixed in PFA prior to MRI acquisition. MRI images were segmented in ITK snap for total hippocampus and cerebellum volumes by blind-to-condition researchers. Cerebellar lobules Crus I and Lobule VI were also segmented. Structure volumes were normalized to total brain volume and total cerebellar volume for cerebellar lobules. Data were analyzed by region as normalized volumes in a mixed effects model with litter as a random effect to control for the litter effect when collapsed across sex.

The hippocampus was not enlarged in VPA animals relative to controls at P28, but significant enlargement was observed bilaterally in VPA animals at P40. When separated by sex, both sexes had enlarged left hippocampi and right hippocampi. No significant volumetric changes were observed in the cerebellum, but a trend-level increase in left Crus I, which is functionally connected to the left hippocampus, was observed. These results show that the VPA model captures specific brain volumetric changes and pathology that are paralleled in humans with ASD.

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FUN Member Sponsor: Bethany Plakke

Theme A: Development

Poster #14 **Poster Board: XX81**

EFFECTS OF CLOZAPINE ON LOCOMOTOR BEHAVIOR IN ZEBRAFISH EMBRYOS

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Clozapine is an atypical antipsychotic drug that is used to alleviate symptoms for patients with schizophrenia. Clozapine's impact on dopamine receptors involves a temporary occupation of the dopamine D2 receptors in the human striatum. The effectiveness of antipsychotics, including clozapine, is closely tied to their interaction with the dopamine D2 receptor. Although clozapine offers substantial benefits to patients due to its ability to treat core symptoms such as hallucinations and delusions, more studies on the drug are required as its effects on embryonic development are not fully understood. Previous research on clozapine in zebrafish larvae revealed that swimming activity is impaired by clozapine exposure in a dose- dependent manner. However, the effects of clozapine exposure on early locomotor behaviors, such as spontaneous tail coiling and touch-evoked tail coiling, have not been fully investigated. To address this, we treated zebrafish embryos with 0 μM, 10 μM, and 50 μM clozapine and investigated spontaneous tail coiling and touch-evoked behavior. We found that clozapine reduced early locomotor behaviors in a dose-dependent manner. These findings suggest that clozapine's effect on locomotion begins early in development, and can be used to inform decisions about the potential safety of this drug.

Funding Support: George Mason University, Neuroscience

FUN Member Sponsor: Gwendolyn Lewis

Theme A: Development

Poster #15 **Poster Board: XX80**

SEX DIFFERENCE IN THE CEREBELLAR VERMIS DUE TO GONADAL SEX BUT NOT SEX CHROMOSOMES

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The cerebellum is generally not included in lists of sex differences in the brain. Nonetheless, sex differences due to both gonadal sex or sex chromosomes have been detected in cerebellar vermis using MRI scans in a 4-core mouse model (Corre et al., 2014). Here we 1) extend research on the cerebellar vermis to a rat model, 2) look for differences at a cellular level, & 3) describe Purkinje cells across lobules and see if they differ with either gonadal sex or sex chromosomes. The density and size of Purkinje cells in the cerebellar vermis were compared among XY male rats (n = 5), XX female rats (N = 10), and transgenic XX male rats (N = 6), who had testes due to the insertion of the Sry gene into an autosome. Forty-micron cerebellar sagittal sections were thionin stained, and between 2-6 pictures of a line of Purkinje cells spanning 330μm were taken of each lobule of the vermis. Cell counts (densities) were made blind and only included cells where the nucleus was not touching the edge of the field of view and a nucleolus was visible. Counts were averaged within a lobule for each animal. Also, 3 to 12 Purkinje cell sizes were measured in each lobule and averaged per lobule for each rat. Purkinje cell densities varied significantly across groups, $F(2,18) = 7.509$, $p < 0.01$ $\eta 2 = 0.455$. A Holm test revealed Female XX had fewer cells than Male XX ($p < 0.01$) or Male XY ($p < 0.05$). This result suggests that gonadal steroids are responsible for the difference.There was no interaction between lobule measures and genetic/gonadal sex, but we did find density differences across lobules, $F(10,170) = 7.776$, $p < .001$, $\eta 2 = 0.314$, as well as cell size differences $F(10,200) = 3.620$, $p < .001$, $\eta 2 = 0.153$. Posthoc Holm tests showed density differences were primarily due to lower densities in lobules 6b and 7; size differences were due to cells in Lobules 2 and 6b being smaller than those in Lobules 8 & 9. Our data show 1) Similar to the mouse model, there are gonadal sex differences in the rat cerebellar vermis 2) these differences exist at the cellular level, at least in Purkinje cell density 3) There are differences among lobules in the Purkinje cell density and size, which have not been well described before.

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FUN Member Sponsor: William Grisham

Theme A: Development

Poster #16 **Poster Board: XX79**

EFFECTS OF DENERVATION ON OPTIC TECTUM CELL DEATH DYNAMICS IN ZEBRAFISH LARVAE

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Cell death is essential for brain development, neural plasticity, injury responsiveness, and regeneration. We are interested in understanding how neuronal connections influence cell survival in the developing vertebrate brain and are using the zebrafish visual system to address how the nervous system copes with cell death during development and injury. Previous work has shown that the zebrafish retina and optic tectum (OT), the retinorecipient area of the brain, grow continuously, with both tissues concordantly adding new neurons that integrate into existing circuitry. Recent work from our lab has also shown that both cell survival and proliferation in the OT is stimulated by optic nerve innervation. When retinal innervation is lost or fails to form, the OT experiences reduced proliferation and increased cell death. Using both genetic and surgical approaches, we observe elevated levels of TUNEL+ cells in non-innervated and denervated OT lobes. Specifically, we find that lakritz (lak) mutants that lack optic nerves exhibit elevated levels of cell death in their OT starting at 7 dpf. In contrast, cell death in the OT of wildtype larvae peaks 2 days later at 9 dpf. When one-eyed larvae are generated by removing an eye at 5 dpf, dying cells are initially observed throughout the OT but then are concentrated on the denervated side. It is currently unknown which types of OT cells are undergoing apoptosis, how quickly the cells die, and how rapidly and effectively dying cells are cleared.

To begin to address these questions, we are using time-resolved fluorescence light sheet microscopy to observe cells labeled by secreted annexin A5 (SecA5)-GFP, a fluorescent reporter that labels phosphatidylserine on the outer membrane of dying cells. This allows us to observe apoptotic cells as they bleb, fragment, and get cleared. In combination, we are also observing the dynamics of microglia, the phagocytic immune cells of the brain, which patrol the brain and engulf dying cell debris throughout the central nervous system.

In both one-eyed and lak larvae, we find that fluorescently labeled microglia are preferentially recruited to the denervated and non-innervated OT lobes, and appear to engulf and clear degenerating fluorescently labeled RGC axons in the OT neuropil. In addition, our recent preliminary data show that SecA5-GFP+ cells in the OT are engulfed and cleared away by microglia, and that more cells appear to be labeled with SecA5-GFP in the denervated versus innervated OT lobe.

Now that we know this system of live-cell imaging of apoptosis works, further trials and analysis of this time-lapse data could give us a wealth of information about cell death localization, time, amount, and impact in the non-innervated OT, as well as information about how microglia clean and shape the developing OT without the presence of innervation. Additional future directions involve analyzing clonal relationships between apoptotic cells and visualizing differences in neuron calcium flux between the innervated and non-innervated OT. These results can provide new insights into the mechanisms of brain degeneration as well as neural plasticity and regeneration in response to injury/loss of neural input.

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FUN Member Sponsor: Kara Cerveny

Theme A: Development

Poster #17 **Poster Board: XX78**

A NOREPINEPHRINE-ASTROCYTE TO DOPAMINE-NEURON AROUSAL PATHWAY: A FURTHER LOOK AT THE ALPHA1-ADRENERGIC RECEPTOR (α1AR)

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The locus coeruleus (LC) is the area of the brain at the helm of norepinephrine (NE) production. This neurotransmitter has been indicated in wakefulness and is projected from the LC to another area of the brain, the ventral periaqueductal gray area (vPAG). NE then interacts with dopaminergic neurons located in the vPAG, which have previously been shown to be heavily involved in the sleep/wake cycle. Current studies have found that the α1ARs that respond to NE in the rostral vPAG were primarily found on astrocytes, cells that formerly were known primarily as supportive structures. When the astrocytes containing α1ARs were stimulated in prior studies, the dopaminergic neurons in the vPAG became more active and suppressed sleep behaviors. Despite the general understanding of sleep mechanisms, the location of the α1ARs has yet to be thoroughly investigated. This localization is critical to fully grasp how NE and DA interact to balance sleep and wake. Once the location has been established in normal brains, it can be studied under other conditions, including alcohol dependency. Therefore, the goal of this current research was to study the location of α1ARs and the type of cells they are found on in the caudal vPAG via immunohistochemistry and electron microscopy. Thus far, single labeling for the α1AR determined that α1ARs have the heaviest presence in unmyelinated axons and glial elements. Double labeling studies are ongoing in order to definitively say the type of neural cells the α1ARs are found on within the caudal vPAG.

FUN Member Sponsor: Darlene Mitrano

Theme B: Neural Excitability, Synapses, and Glia

Poster #18 **Poster Board: XX77**

SEIZURES IN A BANG-SENSITIVE MUTANT IMPACT SOME FORMS OF LEARNING IN A DROSOPHILA LARVAL ASSOCIATIVE LEARNING MODEL

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The seizures associated with epilepsy may impact learning and memory and are associated with early cognitive decline, however the mechanism of how the seizures themselves lead to the deficiency is not clear (Duncan et al., 2006; Palop et al. 2009; Vingerhoets, 2006). Drosophila has been used effectively as a model for human epilepsy by using mutant flies that have seizure phenotypes (Fisher et al 2023). In this study, we tested whether seizures induced in Drosophila parabss mutants, a mutation in the fly sodium channel gene, affect learning. We used both rewarding and aversive stimuli to test associative learning in Drosophila larvae, similar to the methods developed by Apostolopoulou et al. (2010) and Pauls et al. (2010). Third instar larvae were collected from CS (wildtype), dunce (a mutant that doesn't learn), and parabss lightly laid bottles. For the rewarding stimulus task, larvae were trained 3x by pairing a neutral odor with a reward (sugar). The larvae were then tested for movement towards the odor without the reward. For the aversive learning task, a brief shock was paired with the reward as training and then movement away from the reward was determined. We found that we could demonstrate associative learning using larva and that parabss learned well as compared to wildtype using both rewarding and aversive stimulus tasks. To test the impact of seizure, the three groups of larvae were exposed to the cold between the training and testing trials, which cause the parabss mutant larvae to seize. Seizure in the mutant flies disrupted the rewarding associative learning but not the aversive learning task. Similar to results we obtained previously in an adult courtship assay, seizures in parabss mutants can disrupt learning but may impact only some types of learning tasks.

FUN Member Sponsor: Elaine Reynolds

Theme B: Neural Excitability, Synapses, and Glia

Poster #19 **Poster Board: XX76**

NEUROPEPTIDE-DEPENDENT SPIKE TIME PRECISION AND PLASTICITY IN CIRCADIAN OUTPUT NEURONS

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Circadian rhythms are biological processes that follow an approximately 24-hour cycle and are regulated by an internal biological clock. These rhythms influence various physiological and behavioral processes such as sleep-wake cycles, hormone secretion, and metabolism. Circadian output neurons are a group of neurons that receive input from the central circadian clock located in the suprachiasmatic nucleus of the mammalian brain and transmit timing information to different regions of the brain and body, coordinating the circadian rhythms of various physiological processes. In Drosophila, the circadian output neurons are called pars intercerebralis (PI) neurons, which receive input from specific clock neurons called DN1. The neuropeptide diuretic hormone 44 (DH44) is the insect homolog of the mammalian corticotropin-releasing factor. In Drosophila, DH44 is known to activate PI neurons to control activity rhythms and is activated by the detection of nutrient sugars. However, the neurophysiological basis of how DH44 affects the neural coding of PI neurons is not well understood. Here we identify DH44-dependent spike time precision and plasticity in PI neurons. We first find that the application of synthesized DH44 affects membrane potential dynamics such as the precise timing of neuronal firing of PI neurons through calcium-activated potassium channel conductance. Further, we characterize that DN1 and PI neurons interact bidirectionally, and DH44 affects the bidirectional interaction between that DN1 and PI neurons through synaptic plasticity. Finally, we find increased glucose metabolism in DN1 in sleep-deprived flies, and artificial activation of DH44 innervates gut motility as measured by EMG recordings in the Drosophila crop. We are also investigating how another neuropeptide, DH31, is involved in this DH44-dependent process. Together, these results suggest a link between metabolism and circadian neural coding that affects sleep and the gut-brain axis in Drosophila.

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Theme B: Neural Excitability, Synapses, and Glia

Poster #20 **Poster Board: XX75**

KETOGENIC DIET IMPACT ON LONG-TERM POTENTIATION IN THE DORSAL CA1 HIPPOCAMPAL REGION IN YOUNG AND ADULT RODENTS

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The ketogenic diet (KD) has gained notoriety over the last few decades, originally for its potential to treat epilepsy. In recent years, the diet has resurged as a weight loss aid, though its effects on the neurological system are not completely understood. We examined the cognitive effects of the KD on behavior and synaptic plasticity, employing CA1 hippocampal long-term potentiation (LTP) as a measure in young (3-8 weeks) Sprague-Dawley rats, as well as young (2-8 weeks) and adult (7 months) C57 mice. For each of these groups, two treatment methods were employed including a 3-4 week high lipid diet to increase ketone bodies in vivo, or bathing hippocampal slices in a controlled amount of ketone beta-hydroxybutyrate (BHB)-enriched artificial cerebrospinal fluid (ACSF) to produce a higher concentration of ketones than was produced in rodents in vivo. Rodents on the lipid diet only reach ~2mM levels of blood ketones on this diet, less than what can be attained in humans. To ensure scientific rigor researchers were blinded as to which treatment group they were analyzing. Experiments were conducted using field electrophysiology. In both young and adult animals, there were no statistically significant differences in LTP between animals on KD and animals on a control diet. However, in 3-8 week old female rats, we noted that those exposed to 7.5 mM BHB with 2.5 mM glucose for >2 hours demonstrated significantly ($p<0.05$) increased LTP (190 ± 13%; n=13) compared to controls of 0 mM BHB and 11 mM glucose (150 ± 9%; n=13). In contrast, in trials of slices from 2-8 week old mice, we did not observe a difference in LTP between slices exposed to 7.5 mM BHB and 2.5 mM glucose for >2 hours (n=13) compared to controls of 0 mM BHB and 11 mM glucose (n=15). There were no statistically significant differences in the magnitude of LTP between slices from young male and female mice that were exposed to BHB or control ACSF. We plan to repeat BHB-enriched ACSF experiments in adult mice. Additionally, in experiments involving young mice given 3-4 weeks of the KD, behavioral Morris water maze experiments, which involve training an animal to find a submerged platform and test spatial memory, showed no significant ($p>0.05$) difference in time to platform or time in correct quadrant comparing mice treated with the high-fat diet chow (n=11) compared to control chow (n=12). We are currently analyzing Morris water maze data for adult mice given 3-4 weeks of the KD. Overall, our data suggest examining KD for impact on neurological function such as LTP and memory behavior warrants further investigation.

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FUN Member Sponsor: Jeffrey Edwards

Theme B: Neural Excitability, Synapses, and Glia

Poster #21 **Poster Board: XX74**

INVESTIGATING ROLES FOR EXTRACELLULAR MATRIX IN NEURONAL SYNAPSE FORMATION

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Synapse formation is orchestrated through interactions between both pre- and postsynaptic molecules and the extracellular matrix (ECM). While our understanding of synapse development and maintenance has significantly progressed, our knowledge of ECM contributions remains relatively limited. Here, we investigate potential roles for the ECM in synapse formation by studying the outgrowth of dendritic spines from GABAergic neurons of the nematode Caenorhabditis elegans. We found that the endogenously GFP-tagged ECM molecule CLE-1/ collagen XVIII is localized with and surrounding dendritic spines. Additionally, we observed a significant reduction in the number of spines in animals carrying a deletion mutation that produces a truncated CLE-1 lacking the NC1 domain. These results suggest the CLE-1 NC1 domain may be important for dendritic spine development. Surprisingly, the decrease in dendritic spines in cle-1(cg120) mutant animals was rescued by GABAergic, but not pan-neuronal, expression of wild-type cle-1. These results demonstrate that GABAergic expression of cle-1 is sufficient for GABAergic spine formation; however, the lack of rescue with pan-neuronal expression may indicate that ectopic CLE-1 localization inhibits spine outgrowth.
To investigate the role of the ECM in dendritic spine formation, we asked if integrins, a family of receptors that bind to collagen and other ECM molecules, are required for proper spine formation. Integrins are heterodimeric receptors, containing one alpha and one beta subunit, vertebrates have over 24 different integrin subunit combinations. Fortunately, C. elegans has only two alpha integrin subunits (ina-1, pat-2) and one beta integrin subunit (pat-3). Null integrin mutants are lethal; however, we found that hypomorphic alpha integrin ina-1(gm144) mutants have fewer dendritic spines, suggesting a requirement for ina-1. To investigate the role of the sole beta subunit, pat-3, we used 3 CRISPR engineered pat-3/beta integrin alleles where the NPxY phosphotyrosine motif in the cytoplasmic tail of PAT-3 is mutated1. Interestingly, we found that dendritic spines were significantly decreased in only one of these pat-3/beta integrin mutant alleles, kq8042 that encodes a Y>E substitution which mimics tyrosine phosphorylation of the NPxY motif. The NPxY motif is important for interactions with intracellular binding partners such as kindlins, and tyrosine phosphorylation is predicted to prevent these interactions. Unexpectedly, we found ~20% of dendritic spines in pat-3(kq8042) mutants were dorsally directed, whereas all dendritic spines are ventrally directed in wild-type animals. We are currently investigating the location of presynaptic cholinergic terminals in these mutants to determine if presynaptic sites are also located dorsally. In summary, our research suggests the ECM molecule collagen XVIII/cle-1 and ECM binding receptors, integrins, are required for dendritic spine outgrowth and neuronal synapse formation.

FUN Member Sponsor: Michele Lemons

Theme B: Neural Excitability, Synapses, and Glia

Poster #22 **Poster Board: XX73**

VISUALIZING RETINOIC ACID SIGNALING IN DENTATE GYRUS GRANULE CELLS AND SPATIAL RELATIONSHIPS WITH PARVALBUMIN-POSITIVE INTERNEURONS

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All-trans retinoic acid (ATRA), the brain's bioactive metabolite of Vitamin A, plays a pivotal role in oxidative stress, mitochondrial function, and amyloid beta (A□) production. Our goal is to establish that a depletion of ATRA, a major antioxidant and hormone-like transcription factor, contributes to the progression of Alzheimer's Disease (AD). Originally developed to map embryonic ATRA signaling using X-Gal staining, RARE-lacZ mice express E. coli beta-galactosidase (lacZ) under the control of retinoic acid response elements (RAREs). We acquired homozygous RARE-lacZ (Jax Tg(RARE-Hspa1b/LacZ)12Jrt/J) mice, a reporter model that could be crossed with AD mouse models. Our first goal was to successfully visualize lacZ-positive cells. Drawing on a previous study demonstrating X-Gal staining in the hippocampal dentate gyrus (Luo et al. 2004), we employed anti-LacZ immunohistochemistry in free-floating 40 μm-thick hippocampal slices, counterstained with NeuroTrace 435/455. We discovered that virtually all lacZ-positive neurons in the dorsal and ventral hippocampus were an unidentified subset of dentate gyrus granule cells (DGGCs). LacZ staining was present not only in the somatic compartment but also in dendritic compartments, axons, and mossy fiber terminals in the hippocampal CA3 region. To identify the maturation state of LacZ-positive DGGCs, we performed LacZ double-labeling with calbindin or doublecortin antibodies. LacZ colocalized with calbindin but not doublecortin, confirming the identity of LacZ-positive cells as mature DGGCs. Fast-spiking parvalbumin (PV) interneuron impairment has been linked to neuronal network dysfunction and cognitive decline (i.e. Hijazi et al. 2023), but the spatial relationship to ATRA signaling remains unclear. Therefore, we also performed LacZ double-labeling with an anti-PV antibody in both hippocampal and medial septum (MS) slices. PV expression was robust in both hippocampus and MS, though we observed no obvious colocalization of lacZ in hippocampal or MS PV interneuron types. However, PV-positive synaptic puncta were frequently observed in apposition with LacZ-positive DGGC soma and dendrites, suggesting innervation by DG PV interneurons. Finally, we examined possible sex differences in PV and LacZ expression in male and female RARE-lacZ mice. We observed that both PV and lacZ staining were weaker in female than male mice, consistent with an earlier study on sex differences in PV neurons related to stress (Nahar et al. 2021). In conclusion, we find that ATRA signaling is restricted to a subset of calbindin-positive DGGCs which may be innervated by PV-positive synaptic terminals. As PV neuron dysfunction and ATRA deficiency have been implicated in AD, these results provide new insights into spatial relationships between this newly discovered DGGC subtype and PV neurons, which provide new avenues of exploration in the context of cognitive decline, excitation/inhibition balance, and neurological disease. Overall, this study provides important foundational data for future studies using single-nucleus RNA sequencing to further examine relationships involving ATRA signaling and PV interneurons in AD mouse models.

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FUN Member Sponsor: J. Josh Lawrence

Theme B: Neural Excitability, Synapses, and Glia

Poster #23 **Poster Board: XX72**

FAST-SPIKING AND REGULAR-SPIKING INHIBITORY PERISOMATIC SPINULE-BEARING BOUTONS ARE THE LARGEST PERISOMATIC BOUTONS AND ENVELOP DISTINCT SPINULE SUBTYPES WITHIN CA1 HIPPOCAMPUS

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Fast-spiking (FS) and regular-spiking (RS) inhibitory perisomatic synapses in CA1 hippocampus play crucial and distinct roles in regulating network timing and behavior, whereas disruptions in their development or activity can result in disease states. Thus, a complete understanding of FS and RS perisomatic synaptic function is critical to elucidating their roles in regulating behavioral output and neurological disorders. Recent work investigating excitatory synapse ultrastructure in CA1 found that 75% of these synapses contain mysterious structures called synaptic spinules. Synaptic spinules are thin, finger-like projections from one neuron that are embedded within the presynaptic or postsynaptic compartments of another neuron. While the function of synaptic spinules remains enigmatic, recent data suggests they may act as novel forms of neuronal communication and/or increase the strength and stability of spinule-bearing synapses. Yet, the prevalence and types of synaptic spinules within FS and RS inhibitory perisomatic boutons remains unclear. Here, we performed a 3D analysis of FS and RS perisomatic presynaptic boutons within a focused-ion beam scanning electron microscopy image volume from CA1 hippocampus of an adult male mouse. We sought to determine the prevalence, types, and sizes of spinules within these two distinct subsets of perisomatic inhibitory boutons. Using conservative criteria to analyze hundreds of perisomatic synapses, we found that approximately 50% of all inhibitory perisomatic boutons contained spinules, and that the majority of these spinules emanated from their postsynaptic pyramidal soma partners. In addition, we found that RS and FS spinule-bearing boutons (SBBs) were significantly larger than their non-spinule bearing bouton counterparts, comprising the largest perisomatic boutons in CA1. Yet, while a majority of both FS and RS SBBs contained spinules from their postsynaptic soma(s), they also contained distinct percentages of spinules from other neurites. Together, these findings suggest that the presence of a spinule within FS and RS boutons is a marker for synaptic maturity and stability, and that FS and RS boutons may participate in distinct forms of spinule-driven neuronal communication and circuit remodeling.

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FUN Member Sponsor: Marc Nahmani

Theme B: Neural Excitability, Synapses, and Glia

Poster #24 **Poster Board: XX71**

THE ROLE OF NEUROTROPHIC FACTORS IN THE ABILITY OF EXERCISE TO FACILITATE EXTINCTION OF METHAMPHETAMINE CONDITIONED PLACE PREFERENCE AND ATTENUATION OF DRUG-PRIMED REINSTATEMENT.

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Over 60 million people worldwide report using amphetamine-type stimulants, especially methamphetamine (METH), and use is endemic in the western United States. METH use is particularly problematic due to the well-documented long-term consequences on the structure and function of the brain. Exposure to multiple high doses of METH produces damage to central monamine systems. Long-lasting decreases in markers of dopamine (DA) innervation of the striatum have been reported in both human METH users and rodent models of binge METH use. Importantly, this METH-induced damage is accompanied by impairments in cognition in both humans and rodent models. These cognitive deficits include impairments in memory, decision making, and executive function and significantly impact the ability of METH users to engage in and ultimately benefit from treatment. Reported relapse rates for METH users are as high as 61% during the first year post-treatment and 25% during the 2-5 years post-treatment. Conditioned place preference (CPP) is a widely used paradigm used to study the impact of cue and stress triggers on relapse to drug seeking behavior. While exercise has been reported to attenuate the rewarding effects of drugs of abuse, no studies to date have directly investigated the effects of exercise on extinction and reinstatement of methamphetamine-cue memory. Here we show that voluntary exercise led to facilitated extinction of methamphetamine-cue memory and attenuated reinstatement to a priming injection of the drug. We also investigated the role that neurotrophic factors, such as BDNF, might play in the ability for exercise to impact methamphetamine-cue memory. Together these results demonstrate the potential for exercise to serve as a non-pharmacological treatment for METH addiction by protecting against risk of relapse.

FUN Member Sponsor: Ashley Fricks-Gleason

Theme C: Neurodegenerative Disorders and Injury

Poster #25 **Poster Board: XX70**

COMBINING AN α7 NACHR ALLOSTERIC MODULATOR AND ENVIRONMENTAL ENRICHMENT IMPROVES SUSTAINED ATTENTION AND CHOLINERGIC NEUROTRANSMISSION AFTER CONTROLLED CORTICAL IMPACT INJURY IN MALE AND FEMALE RATS

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Introduction: Traumatic brain injury (TBI) is a leading cause of disability and pharmacological strategies that enhance acetylcholine (ACh) transmission may ameliorate cognitive deficits. Enhancing acetylcholine (ACh) transmission after TBI may ameliorate cognitive deficits, especially combined with noninvasive rehabilitation, mirroring clinical approaches. Hypothesis: We predicted that chronic NS-1738, a novel α7 nicotinic ACh receptor (α7-NAChR) positive allosteric modulator (PAM), will improve sustained attention post-TBI, alone and in combination with environmental enrichment (EE). Blocking α7-NAChRs with methylycaconitine (MLA) will attenuate the effects of NS-1738, confirming its mechanism of action. Methods: Adult male and female rats were trained in the 3-choice serial reaction time task (3-CSRT) prior to right parietal controlled cortical impact (2.8 mm cortical deformation depth) or sham injury. Rats were randomized to NS-1738 (5 mg/kg) or vehicle (saline), as well as daily EE (6h) or standard housing for 28d starting post-injury day (PID) 1. Male subgroups also received daily α7-NAChRs blockade via MLA (3 mg/kg) injections. 3-CSRT retrials occurred on PID 14-24. Medial prefrontal cortex (mPFC) and basal forebrain Western blots assessed cholinergic markers [acetylcholinesterase (AChE), choline acetyltransferase (ChAT), and α7-NAChR]. Microarray analysis examined serum inflammatory gene expression. Statistical analysis utilized ANOVAs with Newman-Keuls post hoc tests. Results: TBI rats of both sexes exhibited impaired sustained attention ($p<0.05$) and ChAT disruptions in both mPFC and basal forebrain, which were improved by chronic NS-1738 ($p>0.05$). Moreover, NS-1738+EE rendered an additive effect on lowering omissions and improving inflammatory markers ($p<0.05$), including TREM-1 f(triggering receptor expressed on myeloid cells-1) and IL-1 RA (interleukin-1 receptor antagonist). TBI groups that received MLA demonstrated a reinstatement of performance deficits, as hypothesized. Conclusions and Significance: Our findings support benefits of α7-NAChR PAM and/or EE treatment after experimental TBI on sustained attention and cholinergic neurotransmission.

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FUN Member Sponsor: Anthony Kline

Theme C: Neurodegenerative Disorders and Injury

Poster #26 **Poster Board: XX69**

INSIGHT INTO SYNUCLEINOPATHIES: MOLECULAR DISSECTION OF β- AND γ-SYNUCLEIN FOR POTENTIAL TOXICITY IN A YEAST MODEL

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The family of synucleinopathies are linked to the misfolding and aggregation of proteins within the family of the synucleins (α-, β-, and γ-), include Parkinson's Disease (PD), the second most prevalent neurodegenerative disease. While α-synuclein is well-studied for its direct contribution to PD, less is known about the role in neurodegeneration and toxicity potential of β- and γ-synuclein. Two β-synuclein mutants (P123H and V70M) were recently linked with Dementia with Lewy Bodies (DLB), and recently, γ-synuclein inclusions were reported observed with ALS pathology. Lessons from α-synuclein pathogenicity demonstrate that it is not only enhanced by point mutations within it, but modified by post-translational modifications and altered cellular environments linked with mitochondrial dysfunction, altered lysosomal pathways, nitrative stress, and lipid metabolism. Here, we further evaluated the toxicity potential of β- and γ-synuclein in these various neurodegeneration-related cellular environment strains, using our Saccharomyces cerevisiae (budding yeast) PD model system. Additionally, we evaluated substitution mutants for V70M and P123H β-synuclein, where the original amino acid was mutated to representatives of all four amino acid classes (A, R, N, E), for whether loss of the original amino acid (V70, P123) or gain of the new mutant (70M, 123H) is key to toxicity. Finally, we swapped several known familial mutations in α-synuclein and β-synuclein onto each other and onto γ-synuclein as assessed their toxicities. We report that: 1) V70M and P123H β-synuclein mutants aggregate and are more toxic than WT β-synuclein, in a strain- and expression-dependent manner. 2) Evaluation of β-synuclein substitution mutants demonstrate that that gain of histidine is key to P123H-β-synuclein toxicity. 3) The V70M β-synuclein mutation when swapped into α-synuclein makes the latter differentially more toxic than swapping in the P123H mutation. 4) WT and mutant β-synuclein toxicities are differentially aggravated by altered nitrative stress. Overall, this study expands the evaluation of β- and γ-synuclein, as well as genetically modified mutants in a yeast model, to understand mechanisms of toxicity for these two nervous system proteins and illuminates mutant toxicity in β-synuclein.

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Theme C: Neurodegenerative Disorders and Injury

Poster #27 **Poster Board: XX68**

NEUROBEHAVIORAL AND PHYSIOLOGICAL EFFECTS OF TRAUMATIC BRAIN INJURY IN SPONTANEOUSLY HYPERTENSIVE RATS

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Approximately 2.8 million people sustain a traumatic brain injury (TBI) yearly, with many experiencing long-term disabilities often exacerbated by pre-existing comorbidities. In the United States, an estimated 45-50% of adults suffer from hypertension, which may lead to blocked or damaged arteries, heart attacks, strokes, and premature death. There is a critical need to investigate TBI in hypertensive rats to better characterize neurological, physiological, and cognitive impairments, and to enhance clinical translatability of the TBI models. This study explores the effects of TBI on Spontaneously Hypertensive Rats (SHR) via a battery of behavioral assays, such as motor coordination/balance, hippocampal-dependent learning, sustained attention, and anxiety-like symptoms. Firstly, a novel pathophysiological study was conducted on SHR rats compared to normotensive Wistar Kyoto (WKY) rats. Adult male rats (17 weeks of age) were assigned to receive a controlled cortical impact (CCI; 2.8mm cortical deformation depth, 4 m/s) or a sham injury. Both sham and TBI rats underwent the Beam Walking Task (motor) as well as the Morris Water Maze (MWM; spatial learning). Open field testing (OFT) was performed to examine anxiety, while Shock Probe Defensive Burying Task (SPDB) inspected passive/active coping behavior. 3-Choice Serial Reaction Time Task (3-CSRT) was employed in a separate cohort of SHR rats to examine sustained attention and distractibility. Before surgery, rats underwent 3-CSRT training for 1-2 months to a 2 s cue in operant chambers. Starting on post-op day 14, rats underwent 10 days of 3-CSRT re-testing. Data were analyzed using ANOVAs followed by Newman Keuls post hoc tests. Adult male SHR TBI rats exhibit 10% higher heart rate and 30% higher mean arterial pressure than injured WKY counterparts. Moreover, injured SHR rats display impaired beam-walking capability, as well as reduced spatial learning compared to SHR shams ($p<0.05$). SHR TBI rats presented more immobility and anxiety-like behavior in comparison to SHR shams, seen as reduced center area exploration in OFT and less time approaching and burying the shock probe in SPDB ($p<0.05$). SHR TBI rats also displayed markedly reduced percent accuracy and increased omissions during 3-CSRT suggesting impairments in sustained attention ($p<0.05$). Results indicate that TBI in rats with a hypertensive phenotype renders neurobehavioral deficits across a variety of behavioral tasks. Understanding the impact that underlying conditions such as hypertension may have on TBI pre-clinically is critical to further developing clinically-relevant therapies.

FUN Member Sponsor: Corina Bondi

Theme C: Neurodegenerative Disorders and Injury

Poster #28 **Poster Board: XX67**

LIVE CELL IMAGING SINGLE MRNAS USING AN MS2V7-MCP SYSTEM

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Studying regulation of gene expression through live imaging of single mRNAs in their native environment may provide valuable insights into the dynamic processes and intricate mechanisms governing gene expression. The MS2-MCP system enables specific tagging of mRNAs with 24 repetitive MS2 stem loops incorporated into the target 3'UTR. These MS2 loops have high affinity for MCP protein and allow visualization of puncta MCP-GFP interacting with the RNA. To achieve this, three plasmids,Suntag MS2V5, MCP-GFP, and MS2V7,were acquired from Addgene. Due to the improved performance for live mammalian cell imaging, the MS2V5 sequence in the Suntag plasmid was replaced with the MS2V7. The Suntag plasmid was digested with enzymatic restriction enzymes for removing the MS2V5 sequence and purified on agarose gel. Two PCRs were required to reconstitute the Suntag plasmid with the new MS2V7 sequence. The cloning was performed through a Gibson assembly and the product of assembly was transformed into E.Coli. Single clones resistant to ampicillin were amplified and plasmids were purified by miniprep. The intergrity of the plasmid was verified by enzymatic digestion. We obtained several successful clones which were sent for DNA sequencing. The plasmids containing the desired sequences were amplified through a midi prep for further transfection experiments. HeLa cells were co-transfected with the modified Suntag-MS2V7 and MCP-GFP plasmids using the lipofectamine 3000 transfection reagent. Wide-field fluorescence microscopy was then utilized to track the dynamic transport and stability of individual mRNA molecules within the transfected HeLa cells. The successful cloning and transfection of the modified plasmids, coupled with the application of wide-field fluorescence microscopy, have the potential to reveal valuable insights into mRNA dynamics and localization within the cellular context.

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Theme C: Neurodegenerative Disorders and Injury

Poster #29 **Poster Board: XX66**

SEX DIFFERENCES IN THE EFFECT OF EXERCISE ON THE COGNITIVE CONSEQUENCES OF METHAMPHETAMINE ABUSE.

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Methamphetamine (METH) is a widely used psychostimulant drug, and its use in the United States has reached a near-epidemic in the past 15 years, due to the ease with which METH can be manufactured, as well its highly addictive properties. METH use costs the government billions per year through crime, foster care, lost workplace productivity, and other social problems, in addition to causing destructive effects in the lives of users. In humans, METH abuse has been shown to result in long-lasting brain injury as well as significant cognitive impairments. METH interacts with the catecholamine nerve terminals in the brain, inducing non-exocytotic transmitter release, which results in the initial euphoria after taking the drug but then leads to long-lasting brain injury for the user. The neurotoxic effects of the drug are responsible for inducing the cognitive consequences associated with abuse, which include impairments in memory, attention, executive functioning, and decision making skills. The memory impairments caused by METH are seen as the most prominent and persistent cognitive problems, because they interfere with the user's ability to adhere to and benefit from addiction treatment. Therefore, it is of utmost importance to find ways to attenuate these cognitive deficits and thereby improve treatment outcomes for METH users. The impacts of exercise on the rodent brain, such as induction of synaptic plasticity, increased production of neurotrophins, and enhanced neurogenesis, have been extensively characterized, and the beneficial effects of exercise on cognition are well-documented. Here we investigated whether exercise can improve performance on cognitive tasks known to exhibit METH-induced deficits. The studies described herein focused on two well-validated tests of memory in an animal model: object recognition and odor recognition. Notably, work on this question has historically left out a critical portion of the population – females. Women are just as likely as men to develop substance use disorder, but women often use and respond to drugs differently. Research in both humans and animals suggests that women may be more vulnerable to the reinforcing effects of stimulants, potentially making them more susceptible to craving and relapse. Here we demonstrate critical sex differences in the ability for exercise to attenuate METH-induced cognitive deficits, as evidenced by variability in scores on object-in-place and odor recognition tasks.

FUN Member Sponsor: Regis College

Theme C: Neurodegenerative Disorders and Injury

Poster #30 **Poster Board: XX65**

DIFFERENTIAL EXPRESSION OF THE PIM KINASE PROTO-ONCOGENES IN THE BRAIN RESPONSE TO INJURY IN FISH

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In response to injury, the brain repair capability of mammals is severely limited due to an inability to replace lost cells. In contrast, fish have tremendous brain repair capacity, which is thought to be associated with their continual production of new brain cells. We examined the acute (1hr) brain response to injury of the mummichog (Fundulus heteroclitus), with a focus on the midbrain/diencephalon (MB/DI), using RNAseq. Among the most highly differentially expressed genes (DEGs) were the serine/threonine pro-survival Pim kinase proto-oncogenes. Because Pim kinases promote cell proliferation and, in response to injury, the fish brain undergoes a tremendous amount of cell proliferation, the goal of this work was to examine the temporal expression profiles of the Pim kinase genes, pim-1, pim-2, and pim-3, in the fish brain over the course of two days post-injury (2DPI). To follow cell proliferation concomitantly, we also examined the temporal expression profile of the proliferating cell nuclear antigen (pcna) gene, a marker of cell division, as well as that of neurod2, a marker of neurogenesis, to examine the state of neural differentiation. Finally, because Pim kinases promote the proliferation of cells in tumors by inhibiting the expression of the cyclin-dependent kinase inhibitor 1 (cdkn1) gene, we examined the temporal expression pattern of cdkn1(bb). Over the course of two days, relative pim kinase expression continually increased, while pcna levels increased at 2DPI and neurod2 levels decreased. Prior to pcna expression levels increasing, cdkn1(bb) expression levels decreased at 1DPI. Differential expression patterns of all three pim kinase genes and pcna suggest that that Pim kinases may influence cell proliferation in the brain repair process of fish by inhibiting the transcription of cdkn1(bb).

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Theme C: Neurodegenerative Disorders and Injury

Poster #31 **Poster Board: XX64**

IMAGING PHYSIOLOGICAL DEFICITS IN A SPINOCEREBELLAR ATAXIA TYPE 1 CELL MODEL

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Spinocerebellar Ataxia Type 1 (SCA1) is a progressive neurodegenerative disease primarily affecting cerebellar Purkinje neurons, characterized by an abnormal expansion of CAG repeats within the coding region of the ataxin-1 (ATXN1) gene. Recent published work supports the interaction between mutant polyQ-expanded ATXN1 and mitochondrial proteins involved in apoptosis, oxidative phosphorylation (OXPHOS), membrane composition, and mitochondrial gene transcription. Work in our lab has further found that mitochondrial dysfunction is associated with SCA1 in mice models and in vivo application of the OXPHOS substrate succinic acid ameliorates Purkinje cell neurodegeneration and cerebellar behavioral deficits. Human cerebellar-derived cellular models of SCA1 reveal gross mitochondrial morphological, locational and compositional abnormalities, along with increased oxidative stress and metabolism. In these models, succinic acid treatment and mitochondrial-specific antioxidants reduce the effects of oxidative stress. Here we characterize in vitro physiological deficits in our cellular models through live cell imaging of mitochondrial membrane potential and calcium signaling. Since high energy-demanding cerebellar Purkinje cells bear the brunt force of the pathology, mitochondria emerge as potential targets for therapeutic intervention to alleviate the symptoms and pathology of the disease.

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FUN Member Sponsor: Sarita Lagalwar

Theme C: Neurodegenerative Disorders and Injury

Poster #32 **Poster Board: XX63**

SEX DIFFERENCES IN THE ABILITY OF EXERCISE TO ATTENUATE METHAMPHETAMINE-INDUCED MONOAMINERGIC NEUROTOXICITY

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Methamphetamine (METH) use continues to be a major public health concern. Upwards of 14.7 million people in the U.S. report having tried METH. The use of METH is highly problematic, not only due to the acute effects of the drug which can include psychosis and aggressive behavior, but also due to the long-term consequences including neurotoxicity, cognitive deficits, and addiction. METH-induced monoaminergic neurotoxicity has been modeled in numerous species. One well-known rodent model of METH use utilizes binge administration, where repeated doses of METH are given in a single day. This dosing regimen has been shown to cause long-lasting damage to monoaminergic nerve terminals in the striatum and prefrontal cortex similar to that seen in human METH users. In fact, individuals who use METH are more likely to develop Parkinson's disease, suggesting enduring and possibly progressive dopamine loss as a consequence of METH use. Exercise is well known for its beneficial physiological effects and cognition-enhancing properties and has long been investigated in the context of neurodegenerative disease; only recently has exercise gained traction in the treatment of drug use and addiction. Here we demonstrate a critical sex difference in the ability of exercise to attenuate METH-induced neurotoxicity. Previously, we've shown that 3 weeks of voluntary running after a METH binge protects against METH-induced dopaminergic neurotoxicity. Critically, delaying the start of exercise for 7 or 30 days also results in attenuated neurotoxicity, suggesting that post-METH exercise isn't simply disrupting the mechanisms that lead to neurotoxicity, but is reversing the neurotoxic effects post-hoc. While METH-induced neurotoxicity has been modeled in many species, these studies have largely excluded female subjects. The goal of this project was to replicate our previous work in females. Female Sprague Dawley rats were dosed with a comparable neurotoxic regimen of (+)-METH-HCl (4 x 3 mg/kg, s.c. at 2-hr intervals) or saline (4 x 1 ml/kg, s.c. at 2-hr intervals) as used in preclinical studies of male rats. Beginning 1, 7, or 30 days after injections, animals were then subdivided into one of two exercise conditions, voluntary exercise (rats were given continuous access to a running wheel for 3 weeks) or sedentary control (rats were housed with a locked wheel for the same duration). Our results demonstrate critical sex differences in the ability for exercise to attenuate METH-induced neurotoxicity, as evidenced by variability in degree of damage to dopaminergic nerve terminals. These results highlight the necessity of including sex as a biological variable in methamphetamine neurotoxicity studies going forward.

FUN Member Sponsor: Regis University

Theme C: Neurodegenerative Disorders and Injury

Poster #33 **Poster Board: XX62**

THE EFFECTS OF BILATERAL ENTORHINAL CORTEX LESIONS ON SPATIAL WORKING MEMORY AND SEPTODENTATE INNERVATION IN RATS

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The central nervous system is capable of remarkable functional reorganization to compensate for the loss of brain tissue by neurodegeneration or injury. The entorhinal cortex is among the first regions to show signs of deterioration in Alzheimer's disease, a neurodegenerative disease characterized by significant memory loss. This study investigated how bilateral lesions of the entorhinal cortex impacts rats' performance in a spatial working memory task and how synaptogenesis might contribute to behavioral recovery. Ablation of the entorhinal cortex disrupts the flow of information throughout the hippocampal formation, as the hippocampus no longer receives this information from this prominent source of cortical input. A delayed-alternation task conducted on a Y-maze was used to measure the rats' spatial working memory performance. Male, Sprague-Dawley rats were assigned to an entorhinal-surgery (n = 8) or control (n = 7) group where they either received the bilateral entorhinal cortex lesions or a craniotomy, respectively. Their working memory was subsequently assessed using an acquisition alternation task on the Y-maze with an intertrial interval (ITI) of 30 seconds (11 trials per day for a possible 10 alternations). Their performance was evaluated based on the number of total and perseverative errors in the task across a 6-week testing period (5 consecutive days per week; Monday through Friday). A histological stain for acetylcholinesterase (AChE) was used to study the sprouting response from the AChE-containing, septodentate pathway to compensate for the loss of the entorhinal cortex's input to the dentate gyrus of the hippocampal formation. The AChE stain density is used as a marker for cholinergic septodentate sprouting, and in the current experiment it was quantitatively assessed using a BioQuant Image Analysis System. Animals that received bilateral lesions to their entorhinal cortices committed more errors on the delayed alternation task compared to the sham-operated group throughout the testing period, including the first week of testing and the last week of testing. The entorhinectomized rats also committed significantly more perseverative errors than the sham-operates; however, by week 6 the differences in perseveration between the lesion group and the control group were not significant. These behavioral outcomes highlight the importance of the entorhinal cortex for spatial working memory. Additionally, histological results revealed a significant sprouting response in the middle molecular layer of the dorsal dentate gyrus. Despite the AChE-containing septodentate sprouting response, rats with bilateral entorhinal lesions performed poorly as measured by total errors throughout the testing period. Thus, heterotypic septodentate sprouting failed to significantly mitigate the loss of the entorhinal inputs for total errors committed. However, the lesioned rats committed fewer perseverative errors by the end of the 6-week testing period and were no longer significantly different from the sham-operated rats by week 6. Whether the latter improvement in perseverative errors production is related to septodentate sprouting is worthy of further exploration.

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FUN Member Sponsor: Julio Ramirez

Theme C: Neurodegenerative Disorders and Injury

Poster #34 **Poster Board: XX61**

HIPPOCAMPAL SUBICULUM VOLUME IS ASSOCIATED WITH MEMORY PERFORMANCE IN OLDER ADULTS WITH DOWN SYNDROME

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Individuals with Down syndrome (DS) are at a high risk of developing Alzheimer's disease (AD), which is thought to be due to the overexpression of the amyloid precursor protein on chromosome 21 and associated early age of onset of beta-amyloid plaque accumulation. AD progression in the neurotypical population is associated with hippocampal volume loss and a decline in memory. Additionally, there is a relationship between decreases in hippocampal subfield volumes, particularly the cornu ammonis 1 (CA1) and subiculum, and cognitive decline. Here, we assess the relationship between CA1 and subiculum volumes and memory performance in older adults with DS who progressed clinically to mild cognitive impairment (MCI) and dementia compared to those who remained cognitively stable (CS).

We used 1mm3 T1-weighted MRI scans from 74 cognitively stable individuals with DS (mean age 48 +/- 6.18, 45% female) enrolled in the Alzheimer's Disease in Down Syndrome (ADDS) study that included 3 sites. Hippocampal subfields were segmented using Deep Fusion Labeling for Automated Segmentations for the Hippocampus (DeepFLASH) software, and were normalized by total intracranial volume. Memory performance was assessed with the modified cued recall test (mCRT). Participants who converted to dementia or MCI in the follow-up visit, approximately 18 months later, were deemed as converters (n=11 or 15% of sample). We assessed the relationship between regions of interest and memory using linear regression analysis and evaluated the differences between sub-groups using linear regression analysis. Sex and site were used as covariates.

Lower memory scores were associated with reduced subiculum volume across all participants (R^2=.084, p=.032). No association between memory performance and volume was found in the CA1 (R^2=.007, p=.329). Additionally, we found no differences in subiculum and CA1 volumes between the converter and non-converter groups.

Our results suggest that decreased subiculum volume is associated with worse memory scores in older adults with DS who converted from CS to MCI or dementia. Future analysis will investigate the effect of structural changes in the hippocampus on longitudinal memory decline in this cohort and in younger adults with DS.

FUN Member Sponsor: Michael Yassa

Theme C: Neurodegenerative Disorders and Injury

Poster #35 **Poster Board: XX60**

HEADSTRONG: ANALYZING THE CORRELATIONS BETWEEN SUB-CONCUSSIVE HEAD INJURY AND BALANCE, DEPRESSION, AND COGNITION IN COLLISION AND CONTACT SPORTS

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Athletes are susceptible to head injuries that could potentially lead to alterations in cognitive function. Of particular concern for many professional athletes is the risk of developing chronic traumatic encephalopathy (CTE). CTE is a neurodegenerative brain condition in which patients show cognitive impairment and emotional dysregulation as a result of repeated head injuries. The National Football League (NFL), for example, has acknowledged that playing football can and does lead to brain damage. Recent evidence, however, suggests that it is not just the professionals that are at risk. Repeated sub-concussive events (head trauma that does not cause observable concussions) at any level of sport play are harmful to the brain because of the damage it causes to white matter. An athlete's previous sport history, position, team, and activity plays a role in the exposure to head trauma. It can be assumed that white matter damage begins to accumulate early in an athlete's career, which has the potential to later develop into chronic traumatic encephalopathy. To test this hypothesis, we recruited college students with a history of playing either a collision or contact sport. We tested their cognitive function and compared it to that of control participants who had no history of playing sports. It was found that the no sports condition group performed significantly better in numerous cognitive tasks compared to the collision and cognitive sports group.

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FUN Member Sponsor: Echo Leaver

Theme C: Neurodegenerative Disorders and Injury

Poster #36 **Poster Board: XX59**

WITHDRAWN

Poster #37 **Poster Board: XX58**

ACITRETIN, AN UPREGULATOR OF α-SECRETASE (ADAM10), STRENGTHENS HIPPOCAMPAL LONG-TERM POTENTIATION IN Aβ-TREATED SLICES AND IN THE 5XFAD MOUSE MODEL OF ALZHEIMER'S DISEASE

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Secreted APP alpha (sAPPα) is a product of non-amyloidogenic APP processing that has neurotrophic and neuroprotective properties and enhances hippocampal long term potentiation (LTP) in vivo and in vitro. In addition, over-expression of sAPPα can prevent deficits in spatial memory seen in the APP/PS1 mouse model of Alzheimer's Disease. Recently, acitretin, an FDA-approved synthetic retinoid, has been demonstrated to increase the concentration of sAPPα in an α-secretase (ADAM-10)-dependent manner. In addition, nine-day intraperitoneal treatment with acitretin reverses behavioral deficits in 4-month-old 5XFAD mice. In the present study, we examined the impact of acitretin treatment on hippocampal long-term potentiation (LTP) in vitro in both C57BL/6 and 5xFAD mice by extracellularly recording EPSPs at CA3/CA1 Schaffer collateral synapses. We predicted that acitretin treatment would raise CNS sAPPα levels and thereby enhance LTP in slices prepared from treated mice. We found that acitretin treatment of C57BL/6 mice (five days of treatment; 10 mg/kg i.p.) can produce LTP induced by an otherwise sub-threshold theta burst stimulation (TBS). Application of a half theta-burst stimulation (half-TBS: 5 trains (5 Hz) of 5 pulses (100 Hz)) induced post-tetanic potentiation (PTP), but not LTP, in slices from mice treated with vehicle. In contrast, slices from mice treated with acitretin showed significantly enhanced PTP and stable LTP (148.16 ± 19.51% of baseline, vs 100.73 ± 2.85% of baseline in vehicle-treated mice; $p<0.01$). The 5-day acitretin treatment also prevented the deficits in LTP seen following treatment of slices with Aβ25-35 (200nM), an active fragment of β-amyloid. LTP induced by two full TBS (10 trains (5 Hz) of 5 pulses (100 Hz); 148.04 ± 11.89% of baseline) was significantly reduced in slices treated with Aβ25-35 (119.7 ± 9.8 of baseline), but these deficits were prevented by the pretreatment of mice with acitre;n (177.57 ± 42.99% of baseline). In a parallel investigation in 8-month-old 5xFAD mice, we also observed that deficits in LTP were prevented by acitretin treatment ($p < 0.05$, 5xFAD: LTP = 127.05 ± 15.03% of baseline; 5xFAD + Acitretin: LTP = 167.39 ± 10.50%). Taken together, these results offer preliminary evidence supporting the utility of acitretin as a novel therapeutic target for AD, paving the way for possible drug repurposing of retinoids for AD treatment.

FUN Member Sponsor: Karen Parfitt

Theme C: Neurodegenerative Disorders and Injury

Poster #38 **Poster Board: XX57**

PLCG2 HYPERMORPHIC VARIANT RESULTS IN TARGETED INFLAMMASOME ACTIVATION AND UPREGULATED MICROGLIA INTERACTION WITH AMYLOID PLAQUE

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Alzheimer's disease (AD) is a devastating neurodegenerative disorder and the most important cause of dementia worldwide. Recent studies have identified that many genes associated with AD are involved with immune function, including TREM2, INPP5D, and PLCG2. Microglia, the resident macrophages of the brain parenchyma, are mediators of the innate immune response in the central nervous system (CNS), and mutations in these genes are associated with altered microglial function and responses to amyloid-β (Aβ) plaques in AD. Phospholipase C gamma 2 (PLCG2) is an intracellular phospholipase and an important transducer of many upstream immune receptors, including TREM2, and, in the brain, is only found in microglia. PLCG2 activation results in many downstream actions, including increased intracellular calcium and diacylglycerol (DAG) production. Two mutations of PLCG2 that result in divergent effects on AD risk have recently been identified. PLCG2P522R enhances microglial functions and reduces AD risk, while PLCG2M28L impairs microglial functioning and increases AD risk. The mechanisms underlying these effects remain unclear. PLCG2 activation directly leads to NLRP3 inflammasome activation and subsequent production of the cytokines IL-1β, IL-18, and gasdermin-D, and PLCG2 hyperactivity is known to increase NLRP3 inflammasome activity. The NLRP3 inflammasome is an intracellular assembly composed of three proteins: NLRP3, ASC, and caspase-1. Once caspase-1 is cleaved into its active form, ASC can subsequently polymerize and enhance cytokine production via cleaved caspase-1. Assembly and activation of the NLRP3 inflammasome can be induced by many signals associated with PLCG2 activity, including increased calcium, DAG accumulation, or other unknown pathways. We sought to identify whether the PLCG2 variants impact NLRP3 inflammasome activation in the SAA mouse model of AD. Cortices of 12-month-old SAA mice harboring the PLCG2 variants were analyzed by immunohistochemistry and immunoblotting to investigate the processes through which the variants work and to establish if altered NLRP3 inflammasome activation contributes to the rescuing effects of PLCG2P522R and the detrimental effects of PLCG2M28L. Immunoblotting revealed an increase in ASC and cleaved caspase-1 in PLCG2P522R compared to PLCG2M28L. Additionally, increased immunoreactivity of ASC was found inside microglia around X34+ plaques in PLCG2P522R compared to PLCG2M28L, indicating increased NLRP3 inflammasome activation in microglia associated with plaques, despite reduced plaque burden. While previous studies have identified NLRP3 inflammasome activation as damaging in neurodegeneration, our findings have suggested that the beneficial, hyperactive PLCG2P522R may increase activation, and the detrimental PLCG2M28L may reduce activation. Altogether, these findings implicate a paradoxical role of the NLRP3 inflammasome in enhancing microglial function and improving AD pathology resulting from altered PLCG2 activity.

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Theme C: Neurodegenerative Disorders and Injury

Poster #39 **Poster Board: XX56**

LOVE IT OR LEAVE IT: BEHAVIORAL EFFECTS OF ESSENTIAL OILS IN HOUSE CRICKETS, ACHETA DOMESTICUS

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Insects have a well-developed sense of smell. Their distinct antennae which bear a multitude of sensory organs (sensilla) allow them to detect odor cues in their environment, triggering behaviors such as orientation toward food, locating mating partners, and avoiding predators. House crickets, *Acheta domesticus*, make excellent models in neuroscience research, as these insects have moderately complex nervous systems and display a rich behavioral repertoire. Since they are omnivorous feeders and can feed on a vast array of food sources, they can become nuisance pests by entering human dwellings and contaminating food sources with their fecal matter. The focus of this study was to determine if essential oils had any effect in evoking a repellent behavior from the odorant. Several essential oils have been reported to be effective repellents in mosquitoes. We tested a vast array of essential oils on the house cricket to determine if a similar repellent effect was noted in this species. We hypothesized that some of the essential oils that we tested would serve as moderate to strong repellents, while others would serve as weak repellents or not repel house crickets at all. As we continue with these studies, we are investigating concentration effects and hope to determine which chemical derivatives may be responsible for the repellent behavior noted in this species.

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Theme D: Sensory Systems

Poster #40 **Poster Board: XX55**

THE AWC NEURON IS REQUIRED FOR ATTRACTION TO 1-BUTANOL IN CAENORHABDITIS ELEGANS

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Caenorhabditis elegans is a free-living nematode found commonly in compost, rotten fruit, and other environments rich with bacteria, its major food source. *C. elegans* uses olfaction to discriminate among odorants released by its bacterial food. In *C. elegans* specific neurons have been shown to be required for detecting specific odorants. However, the neuronal basis of detection of many odorants is not known. In this study, our goal was to determine which neuron or neurons are responsible for the detection of the attractive chemical odorant 1-butanol. Using a chemotaxis assay in which the *C. elegans* can choose between the odorant diluted in ethanol and ethanol, the chemotaxis index of the nematode was calculated to reflect its attraction to the odorant at various concentrations. The wild type (N2) strain is attracted to 1-butanol. The odr-7 mutant strain lacking the AWA neurons is also attracted to 1-butanol, indicating the AWA neurons are not involved in the attraction to 1-butanol. The ceh-36 mutant strain lacking the AWC neuron showed no preference for the 1-butanol odorant, denoting that the AWC neurons are involved in 1-butanol detection. The che-1 mutant strain lacking the ASE neurons is attracted to 1-butanol, indicating the ASE neurons are not involved in the attraction to 1-butanol. Therefore, we conclude that the AWC neuron is likely required for the detection of 1-butanol by *C. elegans*.

FUN Member Sponsor: Elizabeth Glater

Theme D: Sensory Systems

Poster #41 **Poster Board: XX54**

CHARACTERIZATION OF THE ROLE OF THE VAGUS NERVE PATHWAY IN VISCERAL PAIN PERCEPTION

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Visceral pain (VP) is a prevalent symptom of multiple diseases and among the leading causes for seeking medical help. This referred pain is difficult to localize and even more difficult to treat. VP occurs when nociceptors of internal organs become activated, leading to sensations of discomfort in areas like the gastrointestinal (GI) tract or chest area. Current analgesics, particularly opioids, can worsen VP symptoms, especially GI-related symptoms, due to side-effects like constipation. Thus, characterization of the underlying circuitry for VP could inform better treatment strategies, and the vagal nerve (VN) pathway, which delivers parallel ascending signals with spinal projection pathways from the GI tract to the brain, serves as a potential target.

To characterize how ascending pathways encode GI pain, we used a chemogenetic approach to label and contextually activate visceral nociceptive neurons for behavioral paradigms. The parabrachial nucleus (PBN) is a known sensory relay for interoceptive inputs. Thus, we injected Cre-dependent AAV vectors to express activating-DREADDs in the PBN of FosCreERT2 mice. We then subjected the mice to 3% Dextran Sodium Sulfate (DSS) drinking solution to induce colonic inflammation. We injected 4-OHT to induce Cre to express the DREADD actuators. After this, we surgically ablated the VN pathway by a subdiaphragmatic dissection in a group of these mice (VGX). A second group of these mice underwent a SHAM procedure (SHAM), which is the same surgical procedure except the vagus nerve is left intact. As a further control, a third group underwent VN ablation before the DSS trapping. After a CNO injection to recall the visceral-pain associated neurons (VPANs), we performed a von Frey behavioral assay, which assessed the sensory dimension of VP through mechanical sensitivity testing, and a conditioned place aversion (CPA) assay, which assessed the affective and motivational dimension of pain by measuring the changes of their preference for darkness after pairing with VPAN reactivation over a two-day conditioning paradigm.

Our results show a non-significant difference between VGX and SHAM cohorts for the von Frey assay; however, we found a significant difference between the two cohorts for CPA. These findings demonstrate that the VN pathway is likely not directly involved in the sensory processing of GI VP, but rather mediates the affective dimension of VP perception. These findings can inform exploration of circuit-based treatments to modulate those VPANs that specifically govern the affective dimension of VP and direct attention to the spinal cord projection pathway as a potential arbiter of sensory VP perception.

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Theme D: Sensory Systems

Poster #42 **Poster Board: XX53**

THE IMPACT OF INNOCUOUS TASTE EXPERIENCE ON LONG-TERM TASTE LEARNING AND MEMORY PERSISTENCE

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The five senses allow for the interpretation of experiences that are crucial for survival. For example, one wrong food choice can lead to detrimental repercussions-including death. Taste experiences are a risky process that pave the way for strong and robust taste learning. Rats can learn to associate a negative consequence, like malaise with a taste after only one negative experience. This type of learning is called conditioned taste aversion (CTA), and the strength of association between the taste and the consequence is known to be modulated by experience. For example, familiarity with a taste protects that taste from future associations with an aversion. The fact that benign familiarity can impact learning towards a known taste raises the question of how our everyday inconsequential taste experiences can impact learning towards a novel taste. Our lab has shown that animals who have had prior inconsequential experience with an array of tastes learn stronger aversions towards novel tastes. Here, we hypothesize that aversions formed after inconsequential taste experience are more adeptly stored in long term memory as compared to taste naïve rats due to enhanced plasticity. Long Evans rats experienced inconsequential tastes (water, salty, and sour) followed by an conditioned taste aversion (CTA) to novel sucrose. Aversion memories were tested 24 hours, 72 hours, 1 week, or 2 weeks later. Thus far, our results show that experienced rats retain aversion memories longer than taste naïve rats. We measured synaptic plasticity behind this retention through the immediate early gene Npas4 which is specific to long term potentiation. We hypothesize that incidental taste experience will also enhance the expression of Npas4 within primary taste cortex; a region known for taste processing. These results are the first to demonstrate the impact of inconsequential taste experience on synaptic plasticity and long-term memory retention.

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FUN Member Sponsor: Veronica Lee Flores

Theme D: Sensory Systems

Poster #43 **Poster Board: XX52**

CHARACTERIZING THE SIGNALING PATHWAY FOR INTRINSIC PHOTORESPONSES IN THE MAMMALIAN IRIS

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Purpose: The iris is a muscular tissue in the anterior of the eye that controls the amount of light entering the eye. Iris muscle activity such as pupillary light reflex (PLR) is driven by a neurological signal in response to changes in ambient light. This neurological signal is initiated in the retina and transmitted to the brain which directs the neuronal input to drive PLR via the oculomotor nerve. In non-primate vertebrates, iris tissue constriction can also be driven by an intrinsic light-response pathway in the iris tissue. Both retinal-driven and intrinsic light-responses are driven by photoreceptor cells that require the melanopsin photopigment for initiating constriction. It has also been shown that the intrinsic iris light-response pathway also requires the Gq G-protein, PLC**β**, and the Trpm1 cation channel to drive light-dependent constriction. Currently it is still unclear how photoreceptive cells in the iris are transmitting light-dependent signals to the iridial muscle cells. Some studies investigating this intrinsic mechanism have indicated that cholinergic chemical synapses are not involved in signal transmission.

Based on these studies, we hypothesize that connexin protein electrical synapses are responsible for the transmission of the intrinsic light signaling within the iris.

Methods: We have designed tests to identify the location and morphology of melanopsin expressing photoreceptors and to identify the expression of connexins in the iris tissue.

Results: We used RT-PCR to probe mouse iris tissue for the presence of 5 connexin proteins that have previously been demonstrated to be expressed in the eye. Our results show the presence of Connexin 43 and Connexin 45 in wild-type mouse iris tissue.

Conclusion: Presence of these proteins suggests that connexins may be responsible for the light signaling transmission, and support the need for further studying the role of these proteins in the iris.

FUN Member Sponsor: Marquis Walker

Theme D: Sensory Systems

Poster #44 **Poster Board: XX51**

DISCRETE CELL ASSEMBLY STRUCTURE IN THE MOUSE VISUAL CORTEX

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As we increase our capacity to record large-scale neural data, interest in defining the suitable units with which to study brain activity and connectivity has equally grown. In this study, we show that Hebbian cell assemblies provide a better description of both the activity correlation and the structural connectivity among neurons than a continuous embedding of the system. We extract these assemblies in large-scale multi-modal data recorded from the mouse visual cortex through the application of Similarity Graph Clustering (SGC), an advanced clustering algorithm shown to reliably derive assemblies from calcium imaging data. We find that the extracted assemblies exhibit strong spatial organization while possessing extensive overlap with other assemblies. We compute a low-dimensional representation of the correlation space through the application of Isomap, a non-linear technique, and conclude that a model with discrete assemblies and a continuous variation in the assemblies provide the best fit. We analyze the connectivity and find a significant overabundance of higher-order chain motifs with respect to the non-assembly set, while the difference in the number of inbound and outbound connections between the two sets remains insignificant. We also assess the assembly response to acute visual stimuli, including their receptive fields, orientation preference, and reliability of response. The assemblies respond more reliably to repeated natural movies than the average cellular response. Altogether, our results strongly indicate that assembly organization is important to understanding the units of activity and connectivity in cortical microcircuits.

FUN Member Sponsor: Kathleen Quast

Theme D: Sensory Systems

Poster #45 **Poster Board: XX50**

INVESTIGATING CHANGES IN STRIATAL ACTIVITY AND MOTOR BEHAVIORS AS A FUNCTION OF LEARNING

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From eating spaghetti to executing a near-perfect tennis serve, our capacity to learn new behaviors for a given task is remarkable. However, it remains unclear how activity in motor circuits dynamically changes to support the learning or execution of new behaviors. Prior work has identified that the cortico-basal ganglia-thalamic-cortical loop is critical for this process, with recent studies showing that the sensorimotor input layer of the basal ganglia, termed the dorsolateral striatum (DLS) in rodents, is uniquely required for the acquisition and execution of newly learned movements (Dhawale et al., 2021). Specifically, DLS seems to 'store' the neural instructions for the execution of a learned movement, with DLS activity tightly linked to the kinematics of learned movements. Naturally, a central question arises: how does DLS activity change as a function of learning to incorporate this information?

To probe this question, we leverage a new experimental paradigm to track DLS activity while a rat shapes a new motor skill from an innately-expressed behavior. This paradigm is novel as it enables us to monitor and directly shape the rat's movements in closed-loop. For example, we can shape a new variant of an innately-expressed rearing behavior, which allows us to easily track the entire learning process, unlike in other paradigms that involve a complicated several-step learning curriculum, such as lever-pressing tasks (Kawai et al., 2015). To track behavior, we use four cameras to record videos of the rat's movements and a machine vision algorithm called 3-Dimensional Aligned Neural Network for Computational Ethology (DANNCE) to track 14 key points on the animal over time, creating a detailed representation of movement (Dunn et al., 2021). An inertial measurement unit (IMU), equipped with an accelerometer and gyroscope, is attached to the rat's head and transmits a continuous signal throughout each session. A water reward is then delivered while a tone plays if a pre-selected 'template' IMU signal matches the current IMU signal. Simultaneously, 32-tetrode microdrives record neurons from the DLS. We process signals from these neurons in a way that lets us track the same 50-100 neurons through multiple sessions. Together, these datasets contain high-dimensional descriptions of behavior and neural activity that allow observation of many stages of learning.

To describe the behavioral data, we use a pipeline called MotionMapper, which employs principal component analysis (PCA) and t-distributed stochastic neighbor embedding (t-SNE) to project the key point trackings to two-dimensional space (Berman et al., 2014). Building on these descriptions, we apply an algorithm to systematically extract and visualize quantitative descriptions of successful and unsuccessful attempts at achieving the desired behaviors. We also expect that learning is characterized by a decrease in behavioral variance, which we can detect using these behavioral descriptions. Collectively, these analyses give us the ability to quantify changes in behavior, and thus changes in learning, and will allow us to more rigorously test hypotheses about how DLS activity changes throughout learning.

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FUN Member Sponsor: Kristina Penikis

Theme E: Motor Systems

Poster #46 **Poster Board: XX49**

CHARACTERIZATION OF THE NOCICEPTIVE WITHDRAWAL RESPONSE IN THE RAT TAIL BASED ON CONCURRENT ELECTROMYOGRAPHIC AND HIGH SPEED VIDEO RECORDING

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Movement planning by the central nervous system is computationally difficult. To decrease computational load, the CNS must use strategies that simplify computations. Previous kinematic studies from our laboratory have shown that the movement of the hyper-redundant 28 segment tail can be largely explained by four components – tail base rotation, local bend, bend progression, and whole tail stiffing. Based on isometric electromyography (EMG), we preliminarily determined that the patterns of extrinsic and intrinsic muscle activity are consistent with the four components of movement. However, our studies were conducted in absence of tail movement. Consequently, a more definitive evaluation should incorporate a trial-to-trial analysis of both EMG and the resulting nociceptive withdrawal response (NWR) movement. The specific aim of our study was to determine the contributions of extrinsic and intrinsic tail muscles of the tail to movement during a heat-evoked NWR by utilizing concurrent EMG recordings and tail kinematics based on high speed video (500 fps) records. In adult, Sprague-Dawley rats, eight bipolar fine-wire EMG electrodes were inserted percutaneously and bilaterally, four of which targeted the extrinsic dorsal lateral muscle in the pelvis, and four of which targeted the dorsal intrinsic muscles in the tail. Placement of electrode location in target muscles was verified by electrical stimulation and postmortem dissection. The NWR was evoked by lateral noxious heat (980 nm infrared laser diode) at five stimulus locations on both sides of the tail. Lateral tail movement was quantified by software tracking of overhead high-speed video (325 fps). Based on a preliminary results, we have identified 3 correlations connecting EMG and tail movement. Magnitude and duration of the extrinsic agonist muscle EMG showed a positive correlation with tail movement. EMG also showed that agonist activation preceded antagonist activation, and the time delay was broadly correlated with lateral tail deceleration. Finally, intrinsic muscle activity, which followed extrinsic muscle activity, was temporally correlated with stiffening of the distal tail. Our preliminary results suggest that the extrinsic muscles contribute to tail movement and braking, while intrinsic muscles, possibly through synergies, contribute to tail stiffening.

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Theme E: Motor Systems

Poster #47 **Poster Board: XX48**

REPETITION-BASED MOTOR SKILL LEARNING IS PRESERVED WITH AGE

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The biological aging process leads to impairments in both cognitive and motor function. While the impacts of aging on cognitive function have been well-documented, its effects on motor function decline remains unclear. Existing literature suggests that aging influences motor learning in a task-specific manner: older adults may perform on par with younger adults in certain tasks after learning, while performance disparities widen in others. To further elucidate this task-specific relationship, we investigated motor learning in mice across 4 different age groups (ranging from 3 to 22 months old; N=81; female and male) performing a novel stimulus-response association task. In this task, mice learn to maneuver a visual stimulus (a Gabor patch) to the center of the screen by turning a wheel leftward or rightward. When a Gabor patch appeared on the left of the screen, moving it to the center via a rightward wheel turn constituted a correct response, and vice versa. A correct response was reinforced with a water drop reward. We analyzed their motor function attributes including reaction time, peak velocity, and trial-to-trial movements correlations over 40 training sessions. Our data revealed that older mice exhibited the longest reaction and slowest peak velocities during early training sessions. However, despite this disadvantaged performance, older mice demonstrated unexpectedly rapid learning rates in these two attributes, thus offsetting the performance disparities. By the conclusion of the training period, no motor function attributes significantly differ between younger and older mice. The trial-to-trial movement correlation that measures the consistency of motor execution improved at a similar rate regardless of age. Our results suggest that although aging impairs the motor performance of older mice, it does not degrade their learning capacities. Thus, with training, older mice improved their motor performance to a comparable level to younger mice. This finding is in stark contrast to the finding that older mice were significantly impaired in cognitive functions (i.e., correct choice rate) in the same task. In summary, our results indicate no significant differences in motor performance between younger and older mice after extensive training in this specific task, underpinned by the preservation of motor learning ability in older mice. This highlights the potential for continued learning and adaptation for the elderly, thereby offering valuable insights for interventions aimed at mitigating age-related motor function decline.

FUN Member Sponsor: Ryan Selleck

Theme E: Motor Systems

Poster #48 **Poster Board: XX47**

HYPOTHESIZED MODELS OF INTERACTION BETWEEN THE DORSOMEDIAL STRIATUM AND THE ANTERIOR CINGULATE CORTEX DURING AN EVIDENCE ACCUMULATION TASK

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Accumulation of evidence is a central component of decision-making. Prior work suggests that the dorsomedial striatum (DMS) and anterior cingulate cortex (ACC) are important in the decision-making process for action selection and decision evaluation, respectively, so elucidating the mechanisms of interaction between these regions in the corticostriatal loop (Foster 2021) is crucial to better understand how these regions contribute to decision making. Recent experiments show that inhibiting activity in either the direct or indirect pathway in DMS leads to opposing effects on choice in an evidence accumulation task (Bolkan 2022). We propose two possible mechanisms for the roles of the direct and indirect pathways that could explain these opposing influences: position gating and evidence gating. In position gating, signals from the indirect and direct pathway act as a spatiotemporal scaffold to populations representing ipsilateral and contralateral evidence respectively, with the inhibition of one pathway leading to inhibition of the choice-selective sequence in the corresponding population and choice biases. In evidence gating, the two pathways asymmetrically gate incoming evidence to each side and evidence is only integrated if the corresponding pathway is active, leading to biased representations of accumulated evidence and biased choices. We employ mathematical models to compare these hypothesized mechanisms. Specifically, we model ACC as two chains that integrate evidence through choice-selective sequences and that receive input from the striatal pathways as either a position or evidence gate. We simulate the effects of inhibition on performance and neural sequences to make predictions that can be further tested experimentally.

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Theme E: Motor Systems

Poster #49 **Poster Board: XX46**

THE NOCICEPTIVE WITHDRAWAL RESPONSE IN INTACT, UNANESTHETIZED RATS EXHIBITS STRONG DEPENDENCE ON INITIAL POSTURE BUT WEAK DEPENDENCE ON STIMULUS LOCATION

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Animals adopt numerous survival behaviors in response to aversive stimuli. One of these behaviors, the nociceptive withdrawal response (NWR), consists of the removal of an animal's limb from the affected site when presented with a noxious stimulus. Preliminary studies in our laboratory have identified three distinct components of the NWR – early extension, rapid flexion, and rapid extension. These studies have suggested that posture may be critical in influencing the animal's NWR when the animal is in a weight-bearing stance. Despite these findings, how the NWRs of intact, non-human mammals rely on stimulus location and how this pattern may be influenced by the animal's initial posture and stimulus location remains unclear. The specific aim of our research was to investigate the NWR in intact, unanesthetized rats in a weight-bearing posture when presented with noxious heat stimuli at various locations on the sole of the foot and circumferentially around the leg. We hypothesized that as stimulus location changed, the direction of the NWR direction of the rat's hind limb would depend on both stimulus location and initial posture. To accomplish this, adult Sprague-Dawley rats were anesthetized and marked with 2 mm circles at six locations on the left hind leg, which defined rotation around the toes, ankle, knee and hip. Following recovery, the rats were then presented with localized heat stimuli that targeted specific rostra-caudal locations on the plantar surface of the foot and anterior and posterior surfaces of the lower leg. Hind limb movement was tracked laterally using a high-speed (500 fps) video. Rotation of the toe, ankle, knee, and hip joints was calculated based three adjacent marks. Based on preliminary results, we found that there was limited effect of stimulus location on the three phases of response but a clear dependence on the initial location of the foot prior to stimulation. Overall, the NWR appears designed to preserve postural stability and sufficiently remove the leg from the noxious stimuli, rather than accurately direct withdrawal movements away from the stimuli.

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Theme E: Motor Systems

Poster #50 **Poster Board: XX45**

INVESTIGATING POSTINHIBITORY REBOUND IN ELEVATED EXTRACELLULAR POTASSIUM IN THE PYLORIC CIRCUIT OF THE CRAB, CANCER BOREALIS

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Central pattern generators (CPGs) are critical for producing and maintaining essential motor patterns, such as sleeping, walking, and breathing; the pyloric circuit of the crab Cancer borealis is an example of such. The pyloric rhythm is driven by the anterior burster (AB) neuron and the two pyloric dilator (PD) neurons. When perturbed with an increase in extracellular potassium concentration, the pyloric rhythm initially loses its bursting activity, then quickly adapts to its new environment and resumes close to normal activity (He et al., 2020). In previous research, the pyloric rhythm lost its bursting activity initially in elevated extracellular potassium as a result of the lateral pyloric (LP) neuron releasing neurotransmitters to shut off the circuit. The mechanism by which the pyloric rhythm is restored is unknown. In neurons, the hyperpolarization activated inward current (IH) is known to induce a postinhibitory rebound (PIR) that allows the cell to depolarize so that it can fire a subsequent action potential. The recovery of the bursting activity may be modulated by IH and PIR. The stomatogastric nervous system (STNS) was superfused with picrotoxin (PTX) to isolate the PD and LP neurons from reciprocal inhibition and 2.5x[K+] saline. While the STNS is superfused with PTX and 2.5x[K+] saline, steps of hyperpolarizing current pulses were injected into the PD and LP neurons to observe the PIR of the cells. Preliminary results indicate a decrease in the sag potential in LP neurons (n=4) in elevated extracellular potassium. This suggests a regulation of IH that causes neurons to adapt to the increased potassium perturbation. However, in the PD neuron, there was an increase in the sag potential (n=2), which suggests, while LP is responsible for shutting the rhythm off after exposure to elevated extracellular potassium, PD may be involved in returning the network to near normal activity after a period of time. This also suggests there may be a shift in the IH activation curve. Future directions include investigating the cryptic memory of the circuit in response to elevated extracellular potassium. Previous research has shown the network retains a memory of prior high [K+] after multiple washes (Rue et al. 2022). Determining whether the change in sag potential persists in control conditions will more comprehensively describe the changes in potassium currents during the adaptation period. These data will provide insights into the mechanisms and sources of variability of rapid adaptation to the changes in extracellular potassium concentration.

FUN Member Sponsor: Eve Marder

Theme E: Motor Systems

Poster #51 **Poster Board: XX44**

CEREBELLAR INVOLVEMENT IN REM SLEEP

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The cerebellum is well known for its classical functions in motor planning and coordination, but recent investigation has begun to reveal its numerous non-motor functions. Among these is the cerebellum's contribution to various aspects of sleep-wake regulation. Sleep disorders are prevalent among patients with cerebellum-related disease, such as ataxias, dystonia, and autism spectrum disorder. Cerebellar dysfunction is most strongly correlated with REM sleep behavior disorder, which involves abnormal expression of REM sleep characteristics. Features of normal REM sleep include cortical activation, muscle atonia, eye movements, and pontine P-waves generated by the sublaterodorsal nucleus (SLD). Given the impact of cerebellar dysfunction on REM sleep, cerebellar activity overall may influence the expression of such REM features. Additionally, this cerebellar contribution to sleep may come about in part through its connections to the brainstem. Recent work has discovered neuronal populations in the nucleus prepositus (PRP) of the dorsomedial medulla that contribute to REM sleep initiation and maintenance as well as P-wave generation. Electrophysiological recordings were used to demonstrate the existence of cerebellar Purkinje cells (PCs) with functional connections to the PRP. These PRP-projecting PCs were localized with retrograde tracing. PC and PRP activity, as well as SLD P-waves, were recorded in vivo during sleep and wake periods. EEG and EMG recordings and eye- and body-movement tracking were used to measure REM sleep parameters and delineate waking, non-REM and REM phases. These behavioral and physiological results, along with further investigation, will better illuminate the involvement of the cerebellum in sleep regulation.

FUN Member Sponsor: Christopher Chen

Theme E: Motor Systems

Poster #52 **Poster Board: XX43**

INTERDEPENDENCE OF THE COMPONENTS OF THE NOCICEPTIVE WITHDRAWAL RESPONSE IN INTACT RATS

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Animals depend on withdrawal responses to noxious stimuli for their survival, such as the nociceptive withdrawal response (NWR), which can be evoked in rats by noxious stimulation of the skin. The NWR has been primarily thought of as one singular movement with the sole purpose of protection, but recent studies emphasize that the NWR consists of multiple components that may contribute to posture and locomotion. Our laboratory preliminarily found that in response to a noxious stimulus in intact rats, there were three distinct sequential phases of movement: early extension, rapid flexion, and rapid extension; however, little is known about their interdependence. The goal of this study was to characterize the three phases of NWR movement and to determine the extent to which they are interdependent. The NWR in male Sprague-Dawley rats (n=8, 10-30 weeks) was evoked using localized noxious heat stimulation (980 nm infrared laser) delivered to the left hind limb and foot, either briefly (0.5 s) and near threshold, or continuous at various intensities. The two-dimensional response was captured using high-speed video (500 fps). The iliac crest, trochanter major, knee joint, lateral malleolus, fifth metatarsophalangeal joint, and distal phalanx of the 2nd toe were marked and tracked over time, to provide the magnitude and direction of movement for each anatomical landmark and allow for calculation of hip, knee, ankle, and toe joint angles. In response to brief stimuli near threshold, rats moved the stimulated hind limb (37%) or failed to respond entirely (63%), consistent with stimulating near threshold. Importantly, there were no occurrences of the early extension phase without the succession of the rapid flexion phase, and the rapid flexion phase rarely (3%) occurred without the early extension phase. Further, the third rapid extension phase always followed the rapid flexion phase. In response to continuous stimulation, there was no significant correlation between latency and time difference ($p=0.3$) for the first two phases, suggesting that they cannot be temporally dissociated. Additionally, there was a strong, positive correlation ($p<0.001$) between the magnitudes of these phases, further suggesting their association. Preliminary results demonstrate that the three phases of the NWR could not be disassociated, indicating that these phases are not independent but rather integrated into a singular response. Our results support a more complex understanding of the NWR, suggesting that the NWR is a multiphasic response that incorporates postural adjustments, preparatory responses, and withdrawal from the noxious stimulus.

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Theme E: Motor Systems

Poster #53 **Poster Board: XX42**

REGULATING NEURONAL ACTIVITY VIA ATP-SENSITIVE POTASSIUM CHANNELS IN THE C. BOREALIS STOMATOGASTRIC GANGLION

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The ability of neurons to transmit electrical impulses is modulated by the amount of energy available to them in the form of intracellular ATP. ATP demands fluctuate with changing neuronal activity levels as ATP is essential for maintaining the hyperpolarization of neuronal membranes. A neuron can shift its activity level depending on the amount of ATP available to it through the action of K-ATP channels. ATP-sensitive K+ channels are known to maintain glucose homeostasis in mammals, provide neuronal protection from excitotoxicity, promote neurotransmitter release, and prevent epileptic activity in response to hypoxia in the substantia nigra. These channels open in conditions of low intracellular concentrations of ATP, leading to K+ outflow and resulting in membrane hyperpolarization. They close in conditions of high intracellular ATP concentrations allowing for membrane depolarization and uninterrupted firing. Here we explore the role of K-ATP channels in generating and maintaining pacemaker activity in the C. borealis pyloric circuit and the cellular contributions of K-ATP in these neurons. The stomatogastric nervous system (STNS) of Cancer borealis is a commonly used model to study the neural function of small circuits. The stomatogastric ganglion (STG) contains about 26 large neurons that produce two central pattern generating rhythms--the gastric mill rhythm and the pyloric rhythm. These neurons in the STG have all been characterized, are easy to record from, and continue to produce motor patterns in vitro, making the STNS an ideal model to study circuit function. In these experiments, pharmacological methods were used to test the contribution of K-ATP channels in generating and maintaining pacemaker activity in the neurons of the C. borealis pyloric circuit. We characterized the dose response curves of both K-ATP channel agonists and antagonists in the STG. The K-ATP agonist, diazoxide, was superfused over the preparation and network output was measured to quantify the effect of opening K-ATP channels on network function. The preparation was then decentralized with tetrodotoxin (TTX) and superfused with the K-ATP antagonist, glibenclamide, to quantify the effects of the closing of the channel in a network in the absence of neuromodulatory inputs. The following concentrations of diazoxide and glibenclamide were superfused over the preparation: 50uM, 100uM, 200uM, and 400uM. It was found that the K-ATP channel agonist inhibited bursting of the PD neuron at concentrations greater than 100uM in the intact preparations (n=4). The extent of inhibition varied across preparations with the most extreme response being a complete shut-down of spiking and slow wave oscillations. Preliminary results with K-ATP channel antagonists showed an initiation of bursting in PD neurons in a preparation that was silent upon decentralization at concentrations higher than 200uM (n=1). Future directions include performing additional dosage response curves with drug concentrations within the limits specified, performing dosage response curves with diazoxide on decentralized preparations, and performing dosage response curves with glibenclamide on intact preparations.

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Theme E: Motor Systems

Poster #54 **Poster Board: XX41**

CHARACTERIZING NORMAL FLUCTUATIONS OF THE CARDIAC AND PYLORIC RHYTHMS OF C. BOREALIS THROUGH LONG-TERM IN VIVO RECORDINGS

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The Stomatogastric Nervous System (STNS) and heart of the Jonah Crab, C. borealis, have been extensively studied in vitro to understand neuromodulation and circuit dynamics. However, there are fewer recordings in vivo. Studies show that in intact animals, with sensory feedback, the frequency range for the pyloric rhythm is more restricted in vivo than in vitro with change in temperature (Soofi et. al. 2014). These experiments were recorded using implanted extracellular electrodes, while we use Photoplethysmography (PPG) which records using light reflection to detect muscle rhythms non-invasively. PPG used in previous experiments to record from cardiac and pyloric muscles indicated that cardiac frequency ranges from 0.3 to 2.3 Hz, and pyloric frequency ranges from 0.2 to 1.6 Hz, consistent with our data seen thus far (Kushinsky et. al. 2019). This set of experiments recorded from cardiac and pyloric muscles in altered tank temperatures over 60 minute periods. Even in periods of controlled temperature, there were strong inhibitory bouts during which the heart decreased in frequency or became quiescent or the pyloric rhythm decreased in frequency. Long term in vivo data allow observation of normal fluctuations like inhibitory bouts or quiescence that occur over extended periods of time. Due to the short-term nature of in vitro experiments, it has not been shown before whether there is fluctuation in rhythm at different time points during the day or night. The STG neurons in the Jonah Crab are light-sensitive as there is change in rhythmic activity with blue light perturbation, so it is possible that the muscle rhythms could be light-sensitive (Kedia, S. et. al. 2022). Our current aim is to observe normal fluctuations and determine whether there is any circadian component to the cardiac or pyloric rhythms. Experiments thus far focused on altering the light that the animals are exposed to. We assessed the presence of a circadian component through 72 hour recordings in complete darkness. In day periods (8 am - 8 pm), cardiac muscle frequency ranges from 0.4 - 0.6 Hz, and during night periods (8 pm - 8 am), the frequency still ranges from 0.4 - 0.6 Hz. In day and night periods, pyloric muscle frequency ranges from 0.5 - 0.7 Hz. Preliminary results suggest there is not a prominent circadian component to the rhythms as the frequencies remain constant (N = 5). We then attempted to induce fluctuation by altering light in a 12 hours on/12 hours off cycle. Frequencies varied significantly compared to recordings in complete darkness. Cardiac frequencies varied from 0.1 to 0.8 Hz throughout the day and night periods, and pyloric frequencies varied from 0.2 Hz to 0.9 Hz (N = 5). These frequency ranges are larger than those prior in darkness. The change in frequency does not appear to change at the same instance light is altered, so the change in fluctuation is likely an interaction between light and other factors. Data suggest light alteration does evoke fluctuation in both the cardiac and pyloric muscle rhythms.

FUN Member Sponsor: Kurt Illig

Theme E: Motor Systems

Poster #55 **Poster Board: XX40**

THE INFLUENCE OF AGE ON THE GUT-BRAIN AXIS AND BEHAVIORAL CHANGES FOLLOWING RECOVERY FROM AN INTESTINAL INSULT

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A growing body of evidence links dynamics in the intestine to behavior and sociability, thus highlighting an inter-organ connection referred to as the gut-brain axis. Mechanisms that establish the gut-brain axis are poorly understood, particularly as they pertain to behavioral changes that may be linked to advanced age. Here we tested the influence of age on behavioral changes associated with recovery from an acute intestinal insult. Intestinal insults, either from enteric pathogens or non-specific mediators of inflammation, are a normal component of mammalian life and our overarching hypothesis was that age would play a role in behavioral outcomes after recovery from an intestinal insult. To model a non-specific intestinal insult we used the acute dextran sodium sulfate model (DSS) of colitis in young (8-week-old) and aged (60-week-old) male mice. DSS-treated mice were allowed to fully recover from the insult and are hereafter referred to as DSS-recovered mice. Age-matched, control mice were used as comparisons. Sociability, evaluated by the three-chamber sociability apparatus, demonstrated that DSS-recovered mice had increased social interactions, with measurable increases observed in both young and old mice, as compared to their age-matched controls. In contrast, anxiety-like behavior measured by the elevated plus maze revealed age-associated disparities in behavior wherein increased anxiety was exclusive to DSS-recovered young mice, with no significant changes in anxiety behaviors in DSS-recovered old mice. This study was a collaboration between a neuroscience lab and a mucosal immunology lab, and future studies are planned to identify the gut-localized immune response (Hammer lab) and the brain-localized microglial response (Freeman lab) in DSS-recovered mice that underpin age-specific outcomes in anxiety following recovery from an intestinal insult.

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Theme F: Integrative Physiology and Behavior

Poster #56 **Poster Board: XX39**

USING BEHAVIORAL ANALYSIS AND MATHEMATICAL MODELING TO PROPOSE A MECHANISM FOR LIGHT ENTRAINMENT OF CIRCADIAN RHYTHM IN SPIDERS

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The circadian clock regulates the timing of a large number of biological functions. Many physiological processes such as locomotion and temperature regulation exhibit a clear cycle, even in the absence of environmental cues. The duration of this cycle is called a free-running period. While circadian regulation is an internal process, environmental cues, or zeitgebers, can modify the timing and duration of circadian phases. Light is the strongest zeitgeber, being able to sync an individual's circadian rhythm with a light-dark cycle; this synchronization is known as entrainment. Most animals have a free-running period close to 24-hours. In contrast, spiders have a wide range of periods while possessing the unique ability to entrain to a 24-hour cycle. It is well-documented that the circadian clock is a result of gene interaction; however, the set of genes responsible for a spider's clock and light entrainment is not yet determined.

To identify a potential mechanism of spider entrainment, we employed mathematical modeling and behavioral analysis. We used previously published locomotor activity data of Metazygia wittfeldae (n=25) collected every minute for 14 days (5 days LD, 9 days DD). We determined the free-running period in DD with the Lomb-Scargle method, revealing free-running periods ranging from 18.01 to 24.68 hours (μ=22.14, σ=1.56). To analyze the activity within one cycle, we split the DD data of each individual into intervals spanning the duration of its free-running period. To conduct a phase comparison, we split both the DD free-running periods and the LD days into 24 equal segments and measured the average activity during each of the segments. Our analysis revealed a period of little to no activity (dead zone) in both conditions. Further, we observed a similar rate of activity onset and offset in LD and DD (STATS?). However, the variation in the duration of the dead zones and the rate of activity onset/offset was much higher in DD compared to LD.

We combined our locomotion analysis with mathematical modeling to identify a potential mechanism for the variation between light conditions. We conducted several modeling experiments to simulate the effect of light on circadian genes. Since the Drosophila fly is well-studied, we based our numerical experiments on Ueda & Kitano's 2001 circadian clock model. This model focuses on inter-gene interactions where one set of genes inhibits the production of the other. To simulate the effect of light, we altered several parameters to modify the rate of mRNA transcription. Our model reproduced the range of free-running periods observed in our locomotion analysis. We also identified several parameters which enable 24-hour entrainment for the model despite a wide range of free-running periods. Therefore, we hypothesized a potential genetic mechanism for light entrainment in spiders.

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Theme F: Integrative Physiology and Behavior

Poster #57 **Poster Board: XX38**

MODELING A RARE GENETIC DISEASE IN CAENORHABDITIS ELEGANS

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Our lab is interested in using the nematode Caenorhabditis elegans to model rare genetic diseases. We are focused on a rare genetic human disorder that consists of seizures in childhood, developmental delay, autism spectrum disorder, as well as a wide variety of heterogenous symptoms. Current mouse and stem cell models for the disease have provided some information about the mechanism by which genetic mutations lead to the accompanying symptoms but very little is currently known. We used CRISPR-Cas9 and STOP-IN cassette method to insert a stop codon early in the coding sequence of the homologous gene in C. elegans. Thus, creating a presumed null mutant of the gene. We are beginning to study this genetic mutant strain both behaviorally and molecularly. We have found preliminary differences in locomotion behavior. The development of this strain opens the door to a variety of new approaches to understand this disease better in order to develop more effective treatments.

FUN Member Sponsor: Pomona College

Theme F: Integrative Physiology and Behavior

Poster #58 **Poster Board: XX37**

ACUTE AND SUBCHRONIC EFFECTS OF ORAL CBD ON ANXIOLYTIC AND SOCIAL BEHAVIOR IN MALE AND FEMALE RODENTS

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Cannabidiol (CBD) and delta9-tetrahydrocannabinol (THC), derived from the hemp plant, are widely used for medical and recreational purposes. While the psychoactive properties of THC are well studied, less is known about the therapeutic potential of CBD. In both controlled human and animal studies CBD interacts with many neural circuits influencing pain, inflammation, stress, and mood. Further, the pharmacokinetics of CBD can be influenced by bioavailability, exposure lengths, lipophilicity and more. Taken together we sought to examine an acute versus sub-chronic administration of oral CBD exposure in both male and female rats in anxiety-like and social behaviors. CBD, in liquid form, was administered in food and contained a rich diversity and balance of cannabinoids by using a novel method to extract CBD from smoke. We measured open and closed arm time on an elevated plus maze (EPM) after 24 hours and 12 days of 20mg/kg/day CBD administration. We found sex differences with both acute and chronic administration in anxiety-like behavior. For social testing, we examined subchronic effects of oral CBD administration and found females displayed novelty-seeking social preference. Further, we examine CB1 receptor expression in the hippocampus. This is important for a translational approach and examining effects in both males and females will further our understanding of CBD therapeutic potential.

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Theme F: Integrative Physiology and Behavior

Poster #59 **Poster Board: XX36**

DISTINCT NEURAL CIRCUITS UNDERLIE REWARD AND PERSISTENCE OF MATING BEHAVIOR IN DROSOPHILA MELANOGASTER MALES

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Mating is a goal-directed behavior that involves brain circuits to motivate an animal to pursue a mate over time and reward circuits that reinforce successful copulations. Understanding the neural mechanisms that underlie reward and motivation has important relevance to human health, as drugs of abuse can cause maladaptive changes in these brain systems. In Drosophila, successful male mating has been shown to induce a long-lasting appetitive memory, suggesting that mating is rewarding in fruit flies. As an entry point into the neural circuits underlying reward and motivation associated with mating behavior in flies, we focused on P1 neurons, which act as central regulators of male courtship behavior. P1 neurons are activated by female sensory cues and their artificial stimulation is sufficient to elicit immediate courtship behavior. Furthermore, transient P1 stimulation also evokes an internal state that prolongs the male's motivation to court for several minutes after activation. This persistent behavior requires the ongoing activity of downstream pCd neurons. In this study, we investigated whether P1 and pCd neuronal populations promote reward or motivational states associated with mating. Firstly, optogenetic activation of P1 neurons in a 2-chamber place preference assay promotes preference for the chamber paired with neuronal activation. Secondly, P1-induced place preference is sufficient to override a robust innate behavior, negative geotaxis, in which flies climb up against gravity. Optogenetic stimulation of P1 neurons in the bottom half of a chamber prevents males from climbing into the top chamber for several minutes after neuronal activation. Thirdly, P1 neuronal activation imparts a conditioned preference for a neutral odor. In contrast, optogenetic activation of pCd neurons is not sufficient to promote place preference, prevent negative geotaxis, or induce appetitive odor conditioning. Together, these results suggest that P1 neurons promote a reward state associated with mating that involves distinct neural circuits from those that mediate persistent behavior through pCd neurons.

FUN Member Sponsor: Sarah Meerts

Theme F: Integrative Physiology and Behavior

Poster #60 **Poster Board: XX35**

NICOTINE PREFERENCE IN C. ELEGANS

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Nicotine use has become prevalent in many countries, particularly the United States. In day to day life most people encounter someone who smokes tobacco products within the community. Within recent decades research has turned to the effect that nicotine has on people and their community. It has been estimated that 40% of children will be exposed to nicotine products in their childhood and that there is a relationship that contributes to them using nicotine products later in their life. There is also a heritability factor of addiction in humans, which ranges from .4-.6. This has led to increased research in animal models to provide insight to the mechanisms and pathologies behind addiction to provide future directions and interventions for work in humans. C. elegans can be used in chemotaxis assays and various behavioral experiments to determine the impact of nicotine on model organisms. In this research C. elegans were tested for transgenerational inheritance of nicotine preference when the F0 generation was exposed to nicotine during the L4 stage of development for 24 hours. After analyzing data, it was found that there was no significant difference in nicotine preference between those exposed during the prenatal development phase and controls. However, follow-up experiments with mir-232, mir-235, alg-1, and alg-2 mutants demonstrated effects on nicotine preference. This allows insight on how gene mutations can play an integral role in nicotine use.

FUN Member Sponsor: Angy Kallarackal

Theme F: Integrative Physiology and Behavior

Poster #61 **Poster Board: XX34**

GENETIC APPROACHES TO UNDERSTANDING IMMUNOSUPPRESSANT-INDUCED INHIBITION OF BINGE ALCOHOL DRINKING

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We have shown that calcineurin-inhibiting immunosuppressants act in brain to reduce excessive alcohol intake in mice. Calcineurin (CN) is a phosphatase that is abundant in brain and plays a key role in the transcription and signal transduction of neuroinflammatory and stress/reward signaling molecules. As an immunosuppressant, cyclosporine-A (CsA) works to inhibit the CN pathway in T cells, preventing the dephosphorylation of the transcription factor nuclear factor of activated T-cells (NFAT) and the production of inflammatory cytokines. In brain, glial CN plays a central role in neuroinflammatory responses. It also acts in many neuronal transduction pathways, including those regulating stress and reward. Excessive ethanol consumption and withdrawal induces both neuroinflammation and activation of many CN mediated reward and stress related pathways associated with withdrawal and excessive drinking, such as corticotropin releasing factor (CRF). We have previously shown that stress-induced activation of CRF and a host of neuroinflammatory signaling molecules in both the central nucleus of the amygdala (CeA) and paraventricular nucleus of the hypothalamus (PVN) are attenuated by the immunosuppressant CsA. The goal of this project was to characterize and test various transgenic models to determine the relative contribution of CN in various neuronal and glial cell populations to both binge alcohol consumption and the inhibitory actions of CsA on drinking. To determine the contribution of neuronal and glial CN in binge alcohol drinking, conditional transgenic and focal CN knockout models are being used. Transgenic conditional CN knockout mice were created using the Cre-loxP method. Relatively, pan-brain neuronal knockout mice (CamKII□-Cre x floxed CN) were subjected to our limited access, binge alcohol drinking model ("Drinking in the Dark"). We have also created another line of mice in which CN is knocked out in CRF producing neurons. Corticotropin releasing factor is known to drive drinking behavior and CN plays a key role in CRF transcription. These mice are now being run through our drinking model. A second approach utilizes focal CN knockouts utilizing AAV-Cre microinjections into floxed CN mice to induce regionally and cell-type specific CN knockouts. We have characterized our transgenic knockouts using immunohistochemistry and reporter mice. We have also characterized numerous AAV serotypes and promoters to enable us to achieve proper spread and cell type specificity in various brain regions. Knockout of CN in the CamkII□-Cre x floxed CN line had no effect on baseline drinking levels over the course of 6 weeks or on the ability of CsA to inhibit alcohol consumption: CsA still significantly attenuated drinking in these mice. Together, the conditional and focal CN knockout strategies will help us decipher proximal pathways mediating the immunosuppressant effect on drinking.

FUN Member Sponsor: Patrick Ronan

Theme F: Integrative Physiology and Behavior

Poster #62 **Poster Board: XX33**

THE D3 RECEPTOR AND PTSD IN THE C57 MOUSE

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Post Traumatic Stress Disorder is a psychiatric condition characterized by anxiety behaviors, such as hypervigilance and flashbacks, after exposure to a trauma. In this study, we measured the effects of a D3 receptor antagonist (SB-277011A) on the expression of hypervigilance in C57 mice. The D3 receptor is important to the expression of PTSD because it is associated with stress behaviors and memory, and it is active in brain regions such as the hippocampus and amygdala. A modified version of the Single Prolonged Stress (SPS) model was used, which induces PTSD-like behaviors (i.e. hypervigilance). In this modified version, foot shocks were used in place of ether. We tested the mice for hypervigilance in an open field maze prior to SPS to obtain baseline times. The mice were tested again 7 days later to obtain post SPS hypervigilance times. The female control group exhibited a significant increase in hypervigilance following SPS (Paired T-test $t(9)=-6.3151$, $p=0.0001$), and both the control and experimental male groups acquired PTSD following SPS, as their hypervigilance times significantly increased from baseline to post testing (experimental Paired T-test $t(9)= -5.58$, $p=<0.001$ and control Paired T-test $t(9)=-4.62$, $p=0.001$). On the day of post testing, both the male and female experimental groups were administered 6 mg/kg of SB intraperitoneally. There was no significant difference between the baseline hypervigilance times and the 7 days post SPS test times in the female group who received the antagonist. This shows that the SB blocked the expression of the PTSD-like behaviors. The male experimental group hypervigilance times did not decrease following the administration of SB, as the difference in hypervigilance times between the control and experimental post tests were not significant. These results suggest gender differences in the blocking of the D3 receptor following the acquisition of PTSD, however replication experiments will need to be done with various dosages of SB to confirm.

FUN Member Sponsor: Onarae Rice

Theme F: Integrative Physiology and Behavior

Poster #63 **Poster Board: XX32**

EFFECTS OF ACUTE STRESS DURING ADOLESCENCE IN FEMALE RATS ON DEPRESSION-LIKE BEHAVIORS

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Adolescence is a sensitive period marked by multiple physiological and behavioral changes. Stress that occurs during this sensitive time period may lead to increased risk for development of depression later in life. Rodent studies have primarily focused on identifying the effects of stressors during adolescence without using age comparison groups and have often excluded female subjects from developmental studies, making it hard to understand sex differences in stress responses (Gerhard et al., 2021). Thus, our goals is to study the stress-induced susceptibility to depression for females at different stages of adolescence. In the present study, 48 female Sprague-Dawley rats were used to examine the differences between acute stress exposure at two ages, postnatal day 28 (P28) representing early-adolescence and postnatal day 36 (P36) representing mid-adolescence. Within each age group, half of the rats (n=12) were exposed to immobilization stress paired with exposure to a predator odor. Animals underwent the singular 3-hour stress-inducing event to determine the effects of stress at a specific point during adolescence. Control animals (n=12) experienced no manipulations. The weights of each animal were measured for one week following the stress protocol. For each age group, the percentage of daily weight gain for animals in stress conditions was significantly lower than of those in the control condition for up to a week. After exposure to the stressor, animals underwent behavioral testing: the Sucrose Preference Test (SPT), 12 days post-stress, and the Forced Swim Test (FST), 14 days post-stress. The percentage of sucrose consumed in the SPT when compared to consumption of water reflected the animal's levels of anhedonia. Additionally, swimming, climbing, and immobilization in the FST were measured to represent learned helplessness after stress. Multiple two-way ANOVAs were performed to analyze the effects of age and condition on the subjects' performance at the STP and the FST. We found an interaction between age and condition that was approaching significance for the latency to immobilization ($F(1,45) = 3.82$, $p = 0.07$). Surprisingly, the P36 animals in the stress condition exhibited heightened latency to immobilization compared to the control P36 animals, as well as the P28 animals in the stress condition. Additionally, we observed a similar trend in depressive symptom expression for the group means of immobilization duration. No significant interactions were found between age and condition for the sucrose preference, swimming and climbing duration. Our findings suggest that female rats in different stages of adolescence may be differentially affected by acute stress, with mid-adolescent animals exhibiting less depression-like behaviors compared to early-adolescent animals. We propose that stressful experiences in mid-adolescence may help build resilience and better coping mechanisms when exposed to stressors later in life. Overall, our results show that females show different patterns of susceptibility to depression after exposure to acute stress in early and mid-adolescence than after chronic stress exposure throughout multiple stages of puberty, suggesting that future studies should focus on identifying the factors that contribute to these disparities.

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FUN Member Sponsor: Nancy Rempel-Clower

Theme F: Integrative Physiology and Behavior

Poster #64 **Poster Board: XX31**

BOOSTING VASOPRESSIN IN A SEXUALLY DIMORPHIC CIRCUIT: IMPLICATIONS FOR SOCIAL AND EMOTIONAL BEHAVIOR.

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The neuropeptide arginine-vasopressin (AVP) system has long been implicated in the regulation of social behavior and communication. AVP-producing cells within the bed nucleus of the stria terminalis (BNST), which represent one of the largest sex differences (male-biased) in vertebrate brains, affect social behavior differently in males and females. Indeed, removing or suppressing the activity of these cells, as well as knocking down AVP production in this cell population, all reduce social approach and investigation in male, but not female, mice. Consequently, we hypothesize that the BNST AVP cell population normally drives male-typical social interest. If so, then artificially boosting AVP in the BNST of females should increase their levels of social interaction in a male-typical way. To test this, we take advantage of the fact that AVP is colocalized with the neuropeptide galanin (GAL) in the BNST to target BNST GAL cells for viral-mediated, cre-dependent overexpression of AVP (or control GFP virus) in GAL-cre male and female mice. After viral expression, we will measure the subject's interest, ultrasonic vocalizations, and scent marking responses to male and female conspecifics as well as measuring their copulatory, aggressive, and anxiety-like behaviors. As a first step, we have confirmed that injections of cre-dependent AVP-expressing viral vectors into the BNST of GAL-cre+ male and female mice substantially increase immunohistochemical detection of AVP in these animals, but not in their GAL-cre- littermates. Testing of social behavior following viral infection is ongoing. This research will contribute to our understanding of how sexually dimorphic brain systems, such as AVP, are organized and function and may ultimately lead to better therapeutic interventions for psychiatric disorders characterized by social deficits that are sex different in their prevalence and severity.

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Theme F: Integrative Physiology and Behavior

Poster #65 **Poster Board: XX30**

EVALUATING SONG MODIFICATION TO AVERSIVE FEEDBACK FOLLOWING FOXP2 OVEREXPRESSION IN ADULT MALE ZEBRA FINCHES

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The acquisition and maintenance of complex sensorimotor skills require sensory feedback to optimize motor output. In songbirds such as male zebra finches, an essential animal model for human speech, sensorimotor learning is required throughout the lifespan to control song behavior. Juveniles imitate a tutor song during initial song acquisition whereas adults correct vocal errors during daily song maintenance. Similar to sensorimotor learning in mammals, vocal plasticity in songbirds is controlled by a basal ganglia thalamo-cortical loop. Speech impairments arising from mutations in the FOXP2 transcription factor underscore the importance of understanding how individual genes or suites of genes may influence vocal learning. Within the song-dedicated region of the avian basal ganglia, Area X, FoxP2 is dynamically regulated based on the type and quantity of song. In juvenile zebra finches, dysregulation of FoxP2 disrupts vocal learning. Additionally, overexpression of Area X FoxP2 in deafened adult birds hastens song degradation, which links FoxP2 and auditory feedback processing. To further establish a connection between FoxP2 and sensorimotor error correction, we used disruptive auditory feedback to evoke learning in adult finches. Briefly, a bird received a short burst of white noise when he performed a specific syllable in his song above (or below) a specified pitch threshold. We hypothesize that FoxP2 overexpression will interfere with sensory-guided learning in adult birds. To test this hypothesis, we identified birds that successfully modified their song over three to five days of incremental learning. These birds were then injected with a herpes simplex virus (HSV) to drive overexpression of FoxP2 or GFP (control construct) in Area X. We calculated the magnitude of change in pitch between the “Silence” and “White Noise Feedback” conditions before and after HSV injection. Preliminary data suggests that adaptive song modification is impaired following FoxP2 overexpression, which impacts a bird’s ability to avoid an aversive stimulus. Our results implicate FoxP2 in song evaluation, establishing a molecular basis for auditory processing that guides reinforcement-based learning.

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FUN Member Sponsor: Nancy Day

Theme F: Integrative Physiology and Behavior

Poster #66 **Poster Board: XX29**

THE EFFECTS OF TAURINE SUPPLEMENTATION ON SPATIAL MEMORY AND ANXIETY- AND DEPRESSIVE-LIKE BEHAVIORS IN SOCIALLY ISOLATED RATS

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Previously, our lab has shown that social isolation beginning in adolescence increases anxiety-like behaviors and impairs spatial memory in male and female Long Evans rats. Taurine is a semi-essential amino acid and dietary supplement shown to produce beneficial effects on behavior in several animal models, including rats that have been exposed to lead during development. However, the effects of taurine supplementation on social isolation have not yet been explored. Therefore, the present study examined whether chronic low-dose taurine administered in water bottles would improve anxiety- and depressive-like behaviors and spatial memory in socially isolated rats. Long Evans rats arrived on post-natal day(P) 22, and were assigned to housing at the start of adolescence (P28): either socially isolated (SI: 1 rat per cage) or group housed (GH: 3 rats per cage) conditions. Rats also received either 1% (0.08 M) taurine supplementation or water throughout the study. This resulted in four groups for each sex: SI + taurine, SI + water, GH + taurine, and GH + water. Beginning 5 weeks later, weekly behavioral tests began, including the open field test and elevated plus maze to measure anxiety-like behaviors, the forced swim test to assess depressive-like behaviors, and the Morris water maze to test spatial memory. Preliminary data from males suggest that social isolation significantly increased anxiety-like behaviors, with SI males traveling less distance in the open field test and spending less time in the open arms of the elevated plus maze than GH males. In the Morris water maze, SI males took significantly longer than GH males to reach the hidden platform, suggesting cognitive impairments. In SI males, taurine supplementation had no effect on anxiety-like measures but moderately improved spatial learning. Data from female rats are currently being collected and will be reported. These findings have important implications given the large number of adolescents that experienced social isolation during the COVID-19 pandemic.

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FUN Member Sponsor: Dr. Shannon Harding

Theme F: Integrative Physiology and Behavior

Poster #67 **Poster Board: XX28**

AN EXAMINATION OF THE MOLECULAR AND BEHAVIORAL FACTORS SUPPORTING SIGN AND GOAL TRACKING

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During Pavlovian conditioning, a predictive cue (CS) for a reward will often produce a dichotomy in behavior; one where subjects approach and interact directly with the CS (sign-tracking/ST), while others simply orient to the CS but directly approach the reward (goal-tracking/GT). Sign-trackers, but not goal- trackers, have been shown to attribute incentive salience (motivational value) to the CS rather than the reward itself. Using an eight-day noncontingent variable-time Pavlovian Conditioned Approach (PCA) paradigm, rats were assigned a phenotype based on their response behaviors to an appetitive CS. PCA index scores were calculated that incorporated all physical interactions with the CS. Hand scored behavioral measurements were included with computerized scoring for a more comprehensive assessment of PCA. To elucidate the mechanism regulating these phenotypes, the brains of animals from ST and GT phenotypes were harvested, dissected, and total RNA extracted from the dissected tissue. Transcriptomic analyses of several genetic markers were conducted on the samples to determine possible mechanisms underlying the ST and GT phenotypes and how these may relate to substance use and anxiety disorders. The genetic markers included genes that regulate monoamine neurotransmission, as dysregulation of this process is involved in both substance use and anxiety disorders. In addition, the expression of calcium channel and channel regulator genes (e.g. Transient Receptor Potential, ORAI and STIM) were analyzed in these samples, as they play a critical role in modulating monoamine neurotransmission. Identifying novel targets that alter monoamine neurotransmission and lead to the ST and/or GT phenotypes may help to elucidate the mechanism that causes substance use and anxiety disorders.

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FUN Member Sponsor: Sheralee Tershner

Theme F: Integrative Physiology and Behavior

Poster #68 **Poster Board: XX27**

THE EFFECTS OF CHRONIC MILD STRESS ON SEX DIFFERENCES IN SPATIAL LEARNING AND MEMORY AND SYNAPTIC PLASTICITY

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The development of depression is tightly linked with stress. The prevalence of depression among women is approximately twice that of men, yet research has exclusively focused on results from males. There are studies that show males are better than females in spatial memory, others show superior spatial performance in females, and some research shows no sex differences. There are limited behavioral and electrophysiological studies examining chronic mild stress (CMS) in both males and female rats. We used CMS to examine sex differences in weight, sucrose preference, Barnes maze, the novel location recognition (NLR) task and long-term potentiation (LTP). Our results show that CMS differentially affected weight gain in both CMS male and CMS female groups. For the CMS female group, there was a lower percent increase in weight over time when compared to the control females and CMS males. There was no significant difference in sucrose preference between groups. However, the control female group consumed less sucrose than the CMS female group and male CMS group during earlier weeks. For the Barnes maze, the CMS male group committed more errors than control males, control females, and CMS females in trial 1. Additionally, CMS males took significantly longer to find the escape hole during trial 1. For strategy of efficiency, CMS males utilized random rather than serial strategy during later trials. In the NLR task, there was a trend of a higher exploration time during the STM phase for the male CMS group. Electrophysiological results show that CMS males had the largest reduction in LTP compared with control males, and overall had the largest reduction in LTP compared with female control and CMS female groups. Overall, CMS appears to differentially affect male over female rats in behavioral assays and electrophysiological experiments. Additional behavioral assays and a longer period of CMS are needed to further examine potential sex differences in behavior and synaptic plasticity.

Funding Support: Pomona College SURP

FUN Member Sponsor: Jonathan King

Theme F: Integrative Physiology and Behavior

Poster #69 **Poster Board: XX26**

EFFECTS OF ACUTE IMMOBILIZATION STRESS IN FEMALE ADOLESCENT RATS ON ANXIETY TASKS

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Adolescence, a developmental stage marked by drastic changes and hormonal level variations, is associated with heightened stress reactivity and responsiveness. Acute stress imposed during adolescence could result in changes in behavioral responses for both male and female rats. However, the effects of an acute exposure to stressful experience during different phases of adolescence on anxiety-like behaviors are less explored. Psychiatric disorders, like anxiety, are more prevalent in females than in males, but the impact of adolescent stress on females is less studied than males. In our current study, half of the female Sprague-Dawley rats (N = 24) were subjected to a three-hour single combination stressor of immobilization and predator odor (fox urine) during either early adolescence (PND 28) or mid-adolescence (PND 36). For both age groups, we observed the percentage gain in body weight was lower for the animals in the stress condition than the animals in the control condition one day and a week after stress exposure. Two common anxiety assays, elevated plus maze (EPM) and open field task (OFT), were performed 15 days after the stress protocol. The rats completed the EPM before completing the OFT and both tasks had a testing period of 5 minutes. 2 x 2 ANOVA was used to evaluate the effect of condition and age on anxiety behaviors. We observed an increase in anxiety behavior in rats after acute stress exposure on the EPM. Specifically, animals in the stress condition spent less time in open arms ($F(1, 45) = 9.76$, $p = 0.003$), had fewer entries into open arms ($F(1, 45) = 7.06$, $p = 0.01$), and had fewer head dips ($F(1, 45) = 6.44$, $p = 0.02$) than animals in the control group. No main effect of condition was found in the OFT. Animals in the stress condition exhibited no difference in locomotion activity compared to animals in the control condition in both tasks. We also found that early adolescent rats displayed higher velocity than mid adolescent rats on EPM ($F(1, 46) = 12.82$, $p < 0.001$) and OFT ($F(1, 46) = 43.47$, $p < 0.001$). Our results indicated that a novel combinatorial stressor of acute immobilization and predator odor during early adolescence and mid adolescence can induce anxiety-like behavior later in life. These findings imply that both early adolescence and mid adolescence could be sensitive developmental windows during which a single severe stress exposure could shape anxiety-like behaviors and become a risk factor for anxiety disorders.

Funding Support: Grinnell College

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Theme F: Integrative Physiology and Behavior

Poster #70 **Poster Board: XX25**

THE IMPACT OF STRESS EXPOSURE ON COCAINE DRUG DISCRIMINATION IN MALE AND FEMALE RATS

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Across a number of paradigms, various stress modalities alter the behavioral effects of cocaine. Previous studies in male rats have indicated that under some conditions stress can affect the interoceptive effects of cocaine. In order to further this research, we trained male and female Long-Evans rats to discriminate the interoceptive effects of cocaine from saline. Two training doses of cocaine (5.6 mg/kg and 10 mg/kg) were used in the drug-discrimination procedure in which responses on the injection-appropriate lever were reinforced with delivery of a 45mg grain pellet on a Fixed-Ratio 10 schedule of reinforcement. Following training, rats were exposed to 15 minutes of acute restraint stress or control and then tested in a multi-component discrimination session. Each component lasted 10 min immediately followed by an injection of the next dose. Cumulative doses tested were 0 (saline), 1.0, 3.0, and 10 mg/kg.

Funding Support: Fairfield University Science Institute

FUN Member Sponsor: Karl Schmidt

Theme F: Integrative Physiology and Behavior

Poster #71 **Poster Board: XX24**

UNCONDITIONED DEFENSIVE RESPONSE TO PREDATOR ODOR IN SYRIAN HAMSTERS

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Biologically relevant odors, including those related to predators, will induce fear and anxiety-like behaviors, including risk assessment, avoidance and freezing in laboratory animals as well as elicit avoidance to the odorant. In addition, animals previously exposed to predator odors will show conditioned place avoidance. In contrast, animals exposed to aversive, non-biological odors, such as formaldehyde, will also show defensive behaviors, but importantly, they do not exhibit conditioned place avoidance. While there are many studies examining the effect of predator odors on defensive responding in rats and mice, there is currently a dearth of information using hamsters as test subjects. In this study, biological and non-biological odors were used to evaluate both unconditioned and conditioned defensive responses in male Syrian hamsters. Specifically, we examined whether coyote predator odors will elicit unconditioned avoidance behaviors in hamsters using a novel runway box. We compare these effects to formaldehyde, a non-biological odor. We hypothesized that while coyote odor exposure will elicit unconditioned and conditioned avoidance, animals exposed to formaldehyde will only show unconditioned avoidance. These results not only add to the existing literature regarding the neurobiological basis of innate avoidance behavior, it also be the first to examine predatory avoidance behaviors in hamsters.

FUN Member Sponsor: Shanglin Tommy Lee

Theme F: Integrative Physiology and Behavior

Poster #72 **Poster Board: XX23**

EFFECTS OF DIFFERENT BLUE LIGHT INTENSITIES ON SLEEP IN DROSOPHILA MELANOGASTER

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Despite the crucial role of sleep in promoting health, well-being, and the detrimental effects of sleep disturbances on daily functioning, there is limited research investigating the influence of specific environmental factors on sleep. The recent surge in electronic device usage now exposes our population to potential sleep disturbances caused by exposure to specific light colors, given that many common electronic devices are known to emit a significant amount of blue-rich light. Previous research from our lab has indicated that transitioning flies from white light to blue light reduced their daytime and nighttime sleep. The lighting utilized in those original studies had a relatively lower maximum brightness. Consequently, to address this limitation, we developed a custom-made LED grid box where we can control color and intensity (low, medium, and high). Our experiments consist of exposing flies to two baseline days (light:dark, 12:12 h) and then four experimental days (blue light:dark, 12:12 h). We performed experiments on wild-type flies (Canton-S (CS)) and white-eyed mutants (w1118). In low, medium, and high blue light, there were similar trends of decreased nighttime sleep in male CS flies, and no effect on w1118. These data suggest that regardless of low or medium intensity, decreased nighttime sleep is present, while the high intensity demonstrated the same effect but more intensely. Future studies should continue experiments on flies with mutations to different light sensor molecules to determine how the detection of light color affects sleep regulation.

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Theme F: Integrative Physiology and Behavior

Poster #73 **Poster Board: XX22**

EFFECTS OF SLEEP DEPRIVATION ON THE RAT FRONTAL CORTEX: A META-ANALYSIS

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Sleep is a biological process that is fundamental to animal life, with its disruption leading to marked negative physiological and psychological effects. The effects of sleep deprivation (SD) on the brain can be studied by using transcriptional profiling, a technique for quantifying gene expression in tissue. In this study, we examined the effects of SD on the rat frontal cortex using a systematic meta-analysis of transcriptional profiling studies. Meta-analyses are powerful tools that allow us to increase statistical power even when individual studies have small sample sizes. For this meta-analysis, we pulled an initial set of studies (n=106) from the Gemma database using a variety of search terms related to rodent SD paradigms. We used a documented set of exclusion criteria, including removing studies that lacked differential expression results in the Gemma database, an SD study paradigm, and a sample from the murine frontal cortex. This criteria allowed us to narrow down the studies used in our final meta-analysis to 8 relevant studies (n=18 contrasts), all of which used rats and had SD paradigms varying between 3-12 hours. For each gene that was represented in at least 13 statistical contrasts derived from the 8 studies (n=23387), we ran a meta-analysis of the effects of SD on gene expression (log2 fold change) across studies. Our meta-analysis revealed 182 differentially expressed genes (FDR<0.05). Of the 182 genes, 104 were upregulated and 78 were downregulated, which suggests that SD in mice reliably alters gene expression bidirectionally. Gene-set enrichment analysis (GSEA) revealed that genes that were differentially expressed as a function of SD were implicated in stress-related neurobiological pathways, including Nr3c1and Gmeb1, which are involved in the glucocorticoid pathway. GSEA showed other interesting biological pathways that were enriched with downregulated genes, such as cell death, including gene Ppp1r10, and neural cell differentiation, which includes Nr2e1 and Exosc4. Additionally, we ran a follow-up exploratory meta-analysis to examine whether our differential expression results could be explained by the duration of SD or the addition of recovery sleep to a paradigm, where recovery sleep was defined as the period between an SD treatment and the sacrifice of the animal during which time the animal is freely allowed to sleep. Out of the final set of 8 studies (n=18 contrasts), 3 (n=6 contrasts) included some duration of recovery sleep ranging from 2 hours to 18 hours. Our exploratory meta-analysis indicated that the duration of SD did not significantly alter differential expression results. The addition of recovery sleep, however, induced a reversal of the direction of differential expression seen after SD in a small set of diversely functioning genes. Those genes are Mup3, Pawr, Dclk1, and Slc23a3, which were upregulated with SD and downregulated with recovery sleep, and Aadat, which was downregulated with SD and upregulated with recovery sleep. In conclusion, our study demonstrates a diverse impact of SD on the transcriptional profile of the rat frontal cortex, affecting a wide variety of functional pathways.

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FUN Member Sponsor: Megan Hagenauer

Theme F: Integrative Physiology and Behavior

Poster #74 **Poster Board: XX21**

EFFECTS OF UNRESTRICTED SWEET ACCESS ON SUCROSE |CUE REACTIVITY IN ADULT FEMALE AND MALE RATS

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We previously found that unrestricted access to sucrose solution (“satiation”) reduces sucrose cue-reactivity in male rats, but only in early abstinence from sucrose self-administration. The purpose of the present study was to examine whether this relationship generalizes to the non-nutritive sweetener, saccharin, and to female rats. Adult rats lever pressed for 0.2 mL 10% sucrose in 10, 2 h daily sessions. A tone+light cue was presented along with every reinforced response. Rats were then randomly assigned to be tested in either early (2 days) or late (32 days) abstinence from their 10th day of sucrose self-administration. For the 46 h prior to testing, rats were satiated in home cages with either drinking water, 10% sucrose, or .3% saccharin. As described in previous works, female rats responded at a higher rate for sucrose and for the sucrose-paired cue. In addition, sucrose cue-reactivity was greater in late vs. early abstinence ("incubation of craving"). Both male and female rats consumed more sweet solution (sucrose or saccharin) than water during the 46-h satiation manipulation. This sweet satiation reduced subsequent sucrose cue-reactivity in early but not late abstinence. These findings replicate our previous findings where prolonged access to sucrose had no effect on the incubation of sucrose craving. Furthermore, this effect generalizes to the non-nutritive sweetener saccharin and to female rats. Essentially, the ability of a primary reinforcer or similar (sucrose, saccharin) to reduce conditioned responding is diminished after a period of abstinence from chronic intake. That is, in prolonged abstinence a sucrose-paired cue will continue to guide behavior even after the individual has consumed a large amount of sweet fluid. One implication is that unrestricted access to sweet will not satiate conditioned craving for sucrose following several weeks of abstinence from sucrose.

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Theme F: Integrative Physiology and Behavior

Poster #75 **Poster Board: XX20**

PROTRACTED INTAKE INCREASES ALCOHOL ENGAGEMENT IN THE 5 CHOICE SERIAL REACTION TIME TASK

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Alcohol use disorder (AUD) is characterized by excessive drinking which can lead to a dependence on alcohol. Approximately 15 million Americans are affected, and more than 88,000 Americans die annually from alcohol related deaths. Those with AUD and higher rates of alcohol drinking are more likely to have health issues, such as liver problems, cognitive dysfunction, psychiatric disorders, and a more frequent rate of illness. Several factors contribute to the development and progression of AUD, including impulsivity, motivation, and attention. Previous studies have investigated these behavioral facets using the 5-Choice Serial Reaction Time Task (5-Choice) with a sugar-based reward. Recently, our lab published a study using alcohol as a reward and identified alcohol preference, as determined by a 2-bottle choice paradigm, as a predictor to 5-Choice performance for alcohol, not sugar. In the current study, we reapproached this data in a novel way that describes a stronger relation between groups of mice based on engagement. We recategorized 48 male C57BL/6 mice into high-engaged (HE) and low-engaged (LE) as determined by a median split of their average number of correct responses during the last week of training. Early- and Late-stage behavior showed a clear difference in overall standard performance measures. Interestingly, over half of HE mice had an alcohol preference greater than 80 percent while LE had only a third. Additionally, alcohol preference correlated average correct responding across Early- and Late-stage training in the HE mice, but not for LE. After training, these mice underwent two bottle choice intermittent access (IA2BC), where they received 20 percent alcohol three days per week for three weeks. Following IA2BC, LE mice significantly increased overall performance for the alcohol reward, while HE mice did not. In comparison to the preference and consumption analyses in the previous study, engagement presented a clearer description of individuals that will work for alcohol and suggests that low alcohol engaged individuals may be at greater risk of AUD development after protracted drinking.

FUN Member Sponsor: Frederic Woodward Hopf

Theme F: Integrative Physiology and Behavior

Poster #76 **Poster Board: XX19**

ALCOHOL BEHAVIORS AND CORTICAL MAPT-GFP LOCALIZATION IN A TAU-KNOCKOUT MOUSE.

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Millions of people every year are affected by alcohol use disorders, with genetics being found responsible for about 60% of the variation in alcohol use disorder (AUD) phenotypes. A prior study found that over 1,000 of the ~31,000 genes in rodents and primates are ethanol responsive or regulate ethanol behaviors, and one of these genes is Mapt. Mapt is involved with the development, placement, and maintenance of the cells in the brain through the reorganization of microtubules via its gene product, Tau protein. To study the involvement of this gene in the neurobiological effects of alcohol (ethanol), mice were obtained that had the Mapt gene knocked out and replaced with GFP. Loss of righting reflex, light-dark box, and a two-bottle-choice drinking study have been performed on the mice, and their brains have been collected for analysis in this experiment. 4 hours prior to perfusion, the mice were given a 4 g/kg injection of 20% ethanol, and immunohistochemistry and confocal microscopy for cell-type markers were later performed. We propose to examine the types of cells in which Tau protein is expressed in the prefrontal cortex and whether the density and morphology of these brain cells can change in Mapt knockouts that received an ethanol injection versus those who received a saline injection. Data collected so far are showing an increased abundance of MAPT-GFP positive neurons in ethanol treated animals compared to saline treated animals. These results may reveal a connection between Mapt and the genetics underlying AUD, to hopefully open the door for more in-depth alcohol studies involving the human MAPT gene and Tau protein.

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FUN Member Sponsor: James Bogenpohl

Theme F: Integrative Physiology and Behavior

Poster #77 **Poster Board: XX18**

INVESTIGATING THE BEHAVIORAL EFFECTS OF OPTOGENETIC ACTIVATION OF LEUCOKININ NEURONS IN DROSOPHILA MELANOGASTER

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Sleep and feeding are both universal physiological processes that impact an organism's health and homeostasis. Additionally, starvation can suppress sleep, but the mechanisms by which these processes influence each other are unknown. This project investigated leucokinin (Lk), a neurotransmitter associated with feeding and sleep suppression in starved states, and how Lk's activation affects behavior and sleep in Drosophila melanogaster. In conditions of total darkness, Lk's effect on sleep was analyzed after optogenetically activating Lk neurons using Chrimson, an ion channel excited by red light, for one hour in the subjective daytime or evening. It was found that Lk activation at circadian time (CT) 7 caused a short increase and subsequent decrease in sleep, whereas control flies experienced an abrupt decrease and gradual increase in sleep. In contrast, Lk activation at CT13, a time point when flies were starting to fall asleep naturally, did not cause a difference in sleep patterns between control and experimental flies. This suggests that Lk's influence on sleep is dependent on the time of day of stimulation. Additionally, we activated Lk neurons optogenetically in individual flies for 30 seconds in the subjective midday, and walking, resting, grooming, and proboscis extensions were measured afterwards for 5 consecutive 30-second bins. It was found that during and throughout the post-stimulation period, experimental flies repeatedly extended their proboscis, a behavior rarely observed in controls. It remains to be seen whether this proboscis extension behavior contributed to the changes in sleep observed in our longer-term activation studies. Future studies should also examine how Lk interacts with other signaling pathways in the brain, especially those that regulate sleep and feeding.

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FUN Member Sponsor: Christopher Vecsey

Theme F: Integrative Physiology and Behavior

Poster #78 **Poster Board: XX17**

IMPACT OF VIRTUAL REALITY (VR) SIMULATIONS AND WRITTEN PROMPTS ON STRESS RESPONSES AND ATTITUDES TOWARD SCZ

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Stigma and misunderstanding often surround schizophrenia (SCZ), leading to challenges in patient care and social integration. We aimed to address this problem by investigating the efficacy of virtual reality (VR) simulations and written prompts in fostering empathy and attitudes towards SCZ, with an emphasis on how stress levels (measured with salivary cortisol) could influence in empathy change.

There were 7 male, 34 female, and 3 non-binary participants, randomly assigned to 1 of 4 conditions for a 2 (VR with and without sound) x 2 (SCZ prompt and no SCZ prompt) mixed ANOVA design. The VR conditions were 2 episodes of individuals experiencing SCZ episodes from a 1st person perspective, including auditory hallucinations. The control condition contained the same videos without sound. Empathy levels were measured with the Attitudes Toward SCZ Questionnaire (ATSQ) and the Multidimensional Emotional Empathy Scale (MDEES). Stress was assessed via cortisol pre and post-intervention by ELISA. Written prompts depicted challenges for an individual with SCZ vs. a control individual experiencing daily stressors.

A borderline significant difference in in the ATSQ was observed in the SCZ ($M = 67.60$, $SD = 8.35$) compared to the control prompt condition ($M = 62.05$, $SD = 11.29$), [$F(1,36) = 3.920$, $p = .055$]. Cortisol remained stable across time points and conditions ($ps > .05$). MDEES scores were consistent across all conditions ($ps > .05$). However, when we included proximity to someone with SCZ as a variable, that created significant differences for the MDEES and the ATSQ independent of manipulation ($ts > 2.16$, $ps < .037$), where both were higher in participants who knew someone with SCZ.

The findings suggest that, contrary to expectations, VR did not significantly alter cortisol levels. Written prompts, however, demonstrated the potential to increase ATSQ scores. The findings with personal relationships underline the value of real-life experiences in shaping attitudes. These observations have considerable implications for VR based training approaches. Specifically, while VR can provide a safe and controlled environment for healthcare professionals, they likely cannot replace lived experiences connecting with real people. A significant limitation in the present study was the user could not interact with the environment of the simulation. However, advancements in virtual and augmented reality may provide more visceral methods for experiencing diverse individual perspectives. Therefore, while these strategies can and should be adapted in tandem with developing technologies, integrating real person interaction could significantly boost empathy development.

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FUN Member Sponsor: Keith Feigenson

Theme F: Integrative Physiology and Behavior

Poster #79 **Poster Board: XX16**

A TASK-BASED MODEL OF UNCERTAINTY'S IMPACT ON REINFORCEMENT LEARNING: A FOCUS ON SOCIOECONOMIC STATUS

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Early life stress (ELS) has been highlighted as a risk factor for psychopathology throughout the lifespan, namely through alteration of the brain reward circuitry. One such source of ELS is low socioeconomic status (SES). One mechanistic reason limited financial resources may cause significant stress is due to feelings of uncertainty; relatively marginal losses may lead to insecurity in maintaining one's survival resources. Thus, we hypothesized that individuals from a lower SES background will have greater sensitivity to rewards and losses, particularly in terms of promoting survival and risk-aversion. Despite there being empirical support for this notion among samples from low-SES groups specifically, work on general ELS and adversity fall short of addressing uncertainty and insecurity in reward processes. To assess this gap, this study proposes a task to model reinforcement-learning of rewards and losses in contexts of uncertainty. In a simulated environment, computational agents undergo a critical phase, wherein they are placed in one of two environments which differ in how rewarding they are. Each of these critical periods is designed to reflect the reward statistics of real-life aversive and positive experiences. Following the critical phase, all agents undergo the same post-critical phase, wherein they respond to stimuli to receive rewards and losses. Based on the agent's learning in the critical phase, we expected differing behavior in the post-critical phase on the basis of the agent's critical environment—with greater uncertainty leading to greater sensitivity to rewards, and thus stronger belief updating following received feedback. This study demonstrates how simulation can be used to assess hypotheses about early life stressors and later life reward and loss sensitivity.

FUN Member Sponsor: Edwin Clayton

Theme G: Motivation and Emotion

Poster #80 **Poster Board: XX15**

EXAMINING THE EFFECTS OF SOCIAL HIERARCHY ON SOCIAL REWARD

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While social interaction is generally thought to be rewarding, social withdrawal and avoidance are key symptoms in many psychiatric disorders such as autism spectrum disorder, social anxiety, depression, and substance use disorder. Insight on the factors that contribute to variations in social reward behaviors is fundamental, and one such factor may be social hierarchies. Demonstrated by humans and animals, social hierarchies are used to determine resource access, health, and ultimately survival. The proposed study examined the effects of social hierarchy on social reward preference in male and female C57BL6/J mice (n = 10 per sex). The social dominance tube test was used to determine the social hierarchy of pair-housed mice (socially dominant vs submissive). Social conditioned place preference (CPP) was used to determine social preference. Social CPP consisted of 10 days, with an initial Day 1 chamber preference test, followed by 8 days of conditioning (alternating between conspecific social interaction and isolation). On Day 10, another chamber preference test was conducted, and social preferences was calculated as the time spent in the social-paired side on Day 10 minus Day 1. A two-way between subjects ANOVA was used to determine the effect of sex and social hierarchy on social preference. There was a significant main effect of sex, with females displaying more preference for social interaction than males. There was a significant main effect of social hierarchy, with socially dominant mice displaying more preference for social interaction than submissive mice, and the interaction between sex and social hierarchy was significant, indicating that social hierarchy had a larger effect on social preference in females. Dominant females displayed a greater preference for social interaction compared to all other groups. Understanding the sex-effects of social hierarchy on social preference/aversion may help improve treatments for social deficits and inform researchers working with pair-housed mice.

FUN Member Sponsor: Gina Caucci

Theme G: Motivation and Emotion

Poster #81 **Poster Board: XX14**

BEHAVIORAL EFFECTS OF NICOTINE AND ETHANOL EXPOSURE IN ADOLESCENT RODENTS

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Concurrent rates of alcohol and nicotine use are rising, especially given the increasing popularity of electronic nicotine delivery systems. Previous literature indicates that drug exposure during early developmental stages can have detrimental effects on learning and memory, as well as emotional regulation during adulthood. Our current study examines the behavioral effects of nicotine and ethanol exposure in adolescent rats on drug reward and anxiety-like behavior. Starting on post natal day 28, male and female Sprague Dawley rats were exposed to either a subcutaneous injection of 0.4 mg/kg nicotine at a dose of 1 ml/kg and an intraoral gastric gavage of 20% ethanol at a dose of 5 g/kg, or combined saline injections and water gavage. All rats received a total of 12 exposures on an intermittent, 2 day on/ 2 day off schedule. Repeated exposure to nicotine and ethanol did not have a significant effect on the percent of time spent in the open arm of an elevated plus maze in male or female rodents. Similarly, adolescent nicotine and ethanol exposure did not differentially affect reward related behavior using a single trial nicotine conditioned place preference protocol. While our studies did not yield significant interactions, future studies will examine development related effects by including an adult exposure group, and compare spine density changes in the rodent prefrontal cortex.

FUN Member Sponsor: Gina Fernandez

Theme G: Motivation and Emotion

Poster #82 **Poster Board: XX13**

MAPPING DOPAMINERGIC NEURAL SUBSTRATES OF ALCOHOL-ASSOCIATED BEHAVIORS IN DROSOPHILA

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Dopamine has an established role in a variety of processes including motivation, reward, and regulation of goal-directed and motor-related behavior across species. Furthermore, dysregulation of dopamine is thought to underlie the effect of alcohol and other drugs of abuse resulting in modified reward circuits. Given the heterogeneous role of dopamine, it is essential to gain a better mechanistic understanding of dopamine regulation and how its regulation is disrupted in maladaptive states, like those associated with alcohol. Drosophila melanogaster is a powerful model organism to investigate the neural dynamic changes that create persistent drug-related memories for alcohol intoxication and underlie alcohol-associated behaviors because of the excellent genetic tools that provide unprecedented spatial and temporal resolution. Previous work in Drosophila identified distinct dopamine circuits that underlie alcohol-associated memories and defined their temporal requirements (Scaplen et al., 2020). More recent evidence suggests that subsets of dopamine neurons (DANs) also mediate alcohol-induced locomotor activity. Here we use a multipronged approach that combines behavior, thermogenetic, and high-content behavioral analysis and take advantage of the precise circuitry of the mushroom body to investigate whether distinct DANs implicated for alcohol reward are also important for modulating locomotor responsiveness to alcohol. Preliminary data demonstrated that different subsets of DANs innervating the Mushroom Body play dynamic roles in modulating alcohol induced locomotor activity. Inactivation of DANs has the most substantial effects in late stages of alcohol exposure at high doses. We hypothesize more DANs are recruited during later stages of alcohol intoxication to counteract the sedating effects of alcohol. High-content behavioral analysis using Flytracker and Ctrax, post-processing computer vision software, suggests that distinct subsets of DANs modulate alcohol associated behavioral features characterized by fly activity, coordination, interaction, and social clustering. Interestingly, DAN subsets that are required for retrieval of alcohol reward memories do not appear to be required for alcohol-induced locomotor activity. We also describe the influence of DANs on locomotor activity in the absence of alcohol. Overall, this study clarifies the dose-dependent manner DANs mediate locomotor activity in Drosophila and is a starting point for further investigation of the mechanism in which drugs of abuse coops natural reward pathways and contribute to addiction.

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FUN Member Sponsor: Kristin Scaplen

Theme G: Motivation and Emotion

Poster #83 **Poster Board: XX12**

PREVENTING ΔFOSB-MEDIATED GENE TRANSCRIPTION IN THE NUCLEUS ACCUMBENS IMPACTS SOCIAL MOTIVATION FOLLOWING A HORMONE SIMULATED PREGNANCY

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In placental mammals, estrogens rise steeply during pregnancy then drop quickly at birth, leading to a hypothesized “estrogen withdrawal” state that correlates with deficits in motivation. Specificallyprevious work in our lab has demonstrated that following a hormone simulated pregnancy (HSP), estrogen-withdrawn mice show decreased social motivation. Additionally, estrogen-withdrawn mice show an increase in ΔFosB, a transcription factor related to stable and long-term neuroplastic changes, in the nucleus accumbens (NAc). We therefore investigated whether ΔFosB in the NAc is required for these social motivation deficits. Adult female mice were ovariectomized and injected with an adeno-associated virus containing either ΔJunD, which prevents ΔFosB-mediated transcription, or a GFP control, into the NAc. Using the HSP model, mice were split into withdrawn and sustained conditions. Social motivation behavior was assayed, which replicated social motivation deficits in withdrawn animals. There was minimal effect of ΔJunD on social motivation, although withdrawn GFP mice spent more time investigating a non-social stimulus, while withdrawn ΔJunD mice did not. This suggests ΔFosB in the NAc is generally not required for social motivation deficits.

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Theme G: Motivation and Emotion

Poster #84 **Poster Board: XX11**

THE ROLE OF THE ORBITOFRONTAL CORTEX TO VENTRAL PALLIDUM CIRCUIT IN DECISION-MAKING WITH DELAYED PUNISHMENT

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Decision-making requires evaluation of the benefits and consequences of each available choice. When a choice leads to immediate punishment, people and animals typically avoid this option. However, delayed punishment is often underestimated, leading to maladaptive decision-making. Currently, there are no animal models that consider delayed punishment regulation of decision-making. To address this, my lab developed the delayed punishment decision-making task (DPDT). In this task, rats chose between two levers, with one delivering one sugar pellet with no punishment, and the other delivering three pellets with a mild shock. As the task progresses, the shock is shifted to occur after a delay (4,8,12,16 seconds). DPDT reveals that rats, like humans, are more likely to select options when punishment happens after a delay.
Previous data from our lab showed that the orbitofrontal cortex (OFC) regulates decision-making with delayed punishment. However, the OFC does not operate independently, but forms circuits with other brain regions. One such region that receives dense connections from OFC is the ventral pallidum (VP), which is involved with motivation and sensitivity to punishment. Here, we investigated the role of LOFC-VP circuitry in sensitivity to delayed punishment in male and female rats. First, we determined the effects of VP inactivation with baclofen/muscimol on DPDT, then used inhibitory Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) to suppress activity in LOFC-VP circuit during DPDT. VP inactivation (n=5) produced a trend toward reduced choice of punished rewards regardless of punishment delay. Chemogenetic inactivation of the LOFC-VP circuit (n=5) led to inability to adapt to changes in delay, possibly a result of impaired behavioral flexibility. Understanding the role of specific brain circuits in sensitivity to punishment may lead to novel circuit-level treatments to improve aberrant decision-making in substance use disorders and other disorders.

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Theme G: Motivation and Emotion

Poster #85 **Poster Board: XX10**

INVESTIGATING THE ROLE OF GCG IN THE VENTRAL TEGMENTAL AREA IN MORPHINE BEHAVIORS

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Although opioid dependence and addiction continue to constitute a major health and economic burden, our limited understanding of the underlying neurobiology limits better diagnostics and interventions. Dysregulation of the mesocorticolimbic reward circuit is acknowledged to contribute to various aspects of drug addiction, with alteration in the activity and output of dopamine (DA) neurons in the ventral tegmental area (VTA) known to contribute to the rewarding aspects of drug use. However, the molecular mechanisms underlying these changes in VTA DA function remain relatively unexplored. Thus, we used translating ribosome affinity purification (TRAP) to identify gene expression changes in mice that specifically occur in VTA DA neurons following chronic morphine exposure. We found that expression of several neuropeptides not traditionally described in the VTA are robustly induced by morphine exposure. Glucagon-like peptide-1 (GCG) was of particular interest as it was enriched in VTA DA neurons and its expression was robustly increased following chronic morphine exposure. These data support increased GCG expression in the VTA following multiple types of opioid exposure and form a strong premise for studying GCG function. Thus, we hypothesize that activity of VTA GCG neurons contributes to morphine-elicited behaviors. To test this, we have begun to characterize the expression and functional impact of VTA DA neurons that co-express GCG using GCG-Cre mice and Cre-dependent viral vectors. Specifically, we are using DREADDs, designer receptors exclusively activated by designer drugs, to selectively activate or inhibit VTA-GCG neurons. We stereotaxically injected the excitatory DREADD hM3Dq (AAV-DIO-hM3Dq-mCherry) into the VTA of male and female wild-type and GCG-Cre mice and found that acute activation of VTA-GCG neurons via i.p. injection of clozapine-N-oxide (CNO, 0.3 mg/kg) does not affect general locomotor activity or elicit conditioned place preference or aversion (n = 5,9). We are now assessing whether activation of VTA-GCG neurons alters morphine-elicited behaviors (conditioned place preference, locomotor sensitization). Our preliminary data suggest there's a decrease in morphine-induced locomotion and morphine CPP in animals whose VTA-GCG neurons were activated. Studies are currently underway to assess these behaviors in a second cohort of mice. Together, these studies are expected to set the stage for future work investigating the role of specific VTA-DAGCG circuits, their activity during behavior, and their potential as targets for therapeutic intervention.

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Theme G: Motivation and Emotion

Poster #86 **Poster Board: XX9**

EXPLORING THE INVOLVEMENT OF THE DCN-PBN PATHWAY IN DIFFERENTIAL FEAR CONDITIONING USING CALCIUM IMAGING

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Surviving in a changing environment depends on an animal's ability to learn and predict danger, as well as respond adaptively. Equally importantly, animals must learn to stop responding to stimuli that no longer signal danger. These forms of learning rely on the ability of the nervous system to predict imminent threat or safety and depend on structures that can execute such evaluations, such as the cerebellum.

The cerebellum has extensive anatomical connections to a network of threat- and fear-relevant brain centers, either directly or indirectly through the use of intermediary nodes. An important node that connects the cerebellum to this network is the parabrachial nucleus (PBN). Projections from deep cerebellar output nuclei (DCN) to PBN are known to modulate the acquisition of learned defensive behavior. However, little is known about the pattern of neuronal activity in PBN-projecting DCN axons that underlies threat assessment, fear and safety signaling. At which stages during this processing are the DCN-PBN projections active? Is the DCN-PBN circuit functionally homogeneous or are different DCN neuronal populations activated during different phases of fear and safety processing? We hypothesize that DCN-PBN projections are activated during the extinction of learned defensive behavior, which we will test using calcium imaging, a proxy for neuronal activation, through fiber photometry in conjunction with a differential fear conditioning paradigm in mice.

Our work will build upon the findings of anatomical experiments in Ai14 reporter mice, in which DCN neurons that project to PBN will be identified through injection of a fDIO-Cre virus into the DCN and a retro-Flp virus into the PBN. The circuit specificity of this technique will allow us to identify sizable cell populations in the DCN suitable for fiber photometry recordings. To image calcium dynamics, we will inject a retro-Cre virus bilaterally into the PBN and a Cre-dependent, floxed-GCaMP6 (calcium sensor) virus into the DCN. Guided by our anatomical findings, optical fibers will be implanted bilaterally either in the PBN (to image DCN projections) or in the DCN (to image different neuronal clusters). After 4-6 weeks of expression, we will measure fear-related defensive behavior (% freezing) in a differential fear conditioning paradigm, followed by 2 days of extinction paradigm.

Throughout every stage, calcium signaling in DCN-PBN pathway will be recorded. At the end of each experiment, mice will be perfused, and their brains sliced, imaged, and analyzed to evaluate viral expression, injection specificity, and fiber placement.

Based on previous literature, I expect there to be no change in calcium signaling during the acquisition of learned defensive behavior or fear recall during context. If there is calcium activity during the CS+ in the extinction paradigm, this would suggest that the DCN-PBN pathway encodes extinction-relevant information, which could signal salience or prediction in anticipation of an aversive stimulus. Our work has the potential to elucidate the role of the DCN-PBN pathway in threat prediction and safety signal assessment.

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FUN Member Sponsor: Diasynou Fioravante

Theme G: Motivation and Emotion

Poster #87 **Poster Board: XX8**

THE EFFECTS OF REPEATED RESTRAINT AND SOCIAL STRESS ON ANXIETY RELATED BEHAVIOR IN C57BL/6J AND DBA2/J MICE

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Stress is a contributor to poor health outcomes. Repeated stress and chronic activation of the HPA axis can cause dysregulation of neurobehavioral systems and is associated with increased risk of psychopathology. The environmental context of stress plays a major role in the outcomes associated with stressful experiences; however, little is known about how different stressors contribute to individual differences in behavioral responses to stress. This project examined how physical (restraint) and social (dirty bedding of stranger) stressors affect behavior in C57BL/6J and DBA2/J mice. Males and females were exposed to 5 days of either physical or social stress. Following 2 days of rest, mice were tested in the Elevated Zero Maze (EZM), Open Field (OF), and Light/Dark (LD) tasks to measure behaviors associated with activity, exploration, and anxiety. In all 3 measures, B6 mice were more active and less anxious than D2 mice. For B6 mice, restraint stress decreased anxiety without affecting activity levels in the EZM and increased exploration in the OF without affecting center time. In contrast, social stress increased anxiety in the EZM in B6 mice. In the D2 strain, social stress increased activity in the OF and decreased anxiety related behavior in the OF and EZM. No stress effects were observed in the LD task and no sex effects were observed across all tasks. In sum, restraint and social stress differentially affect B6 and D2 mice and these effects varied by task.

Funding Support: University of Memphis

FUN Member Sponsor: Chris Hartless

Theme G: Motivation and Emotion

Poster #88 **Poster Board: XX7**

INVESTIGATING RELATIONSHIP BETWEEN DEPRESSION AND ANXIETY SYMPTOMS AND INTENT TO SEEK TREATMENT IN LARGE ONLINE POPULATION

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Depression and anxiety are disorders that impact one's personal and social life in a detrimental manner; with symptoms such as feelings of hopelessness, lack of interest in activities, and increased feelings of worry. The prevalence of depression and anxiety has increased in recent years and along with it the need for treatments (Goodwin et al., 2022). Due to the debilitating symptoms patients experience it is oftentimes assumed that symptoms are a driving force behind a patient seeking treatment. However, not all patients experiencing symptoms seek out treatment. Our study aims to examine the relationships between depression and anxiety symptom severity and a patient's willingness to seek treatment. We collected data from a large online population through a survey that includes items from the Patient Health Questionnaires (PHQ-9), General Anxiety Disorder 7 (GAD-7), the WHO Quality of Life measurement (WHO-QoL), along with questions asking about intent to seek treatment and recent treatment-seeking behaviors. Statistical and descriptive analyses will be conducted using RStudio. We hypothesize that there will not be a significant correlation between anxiety and depression symptom severity and the patient's intent to seek treatment as a patient's motivation to seek help is separate from their symptoms. The findings from this study will provide valuable information regarding factors that impact a patient's desire to get treatment which is more important than ever considering the increasing prevalence.

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Theme G: Motivation and Emotion

Poster #89 **Poster Board: XX6**

EXAMINING THE EFFECTS OF SOCIAL HIERARCHY ON MESOLIMBIC DOPAMINE RELEASE IN MICE

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The mesolimbic dopamine system plays a critical role in reinforcement learning by attributing significance to important environmental cues and subsequently driving action to obtain these rewards. Altered functioning of this system is associated with several psychiatric disorders, including substance use disorder and depression. Understanding factors that influence the way this system functions is crucial for improving the prevention and treatments of these disorders. Both human and animal studies have shown social experiences can alter mesolimbic dopamine functioning, but few studies have examined the effects of social hierarchy. The current study used in vivo fixed potential amperometry to measure dopamine release in the nucleus accumbens of mice characterized as either socially dominant or submissive. To measure the effects of a dopaminergic drug, mice were administered an injection of cocaine (10 mg/kg, ip) during dopamine recordings. In males, the dominant mice displayed similar baseline (pre-cocaine) dopamine release but significantly increased percent change in dopamine release following cocaine compared to the submissive mice. We are in the process of acquiring and analyzing data for female dominant vs submissive mice and will present this at the conference also. To our knowledge, these are the first experiments to compare phasic dopamine release in dominant vs submissive mice. Such studies are important for informing future animal studies and understanding social factors that alter mesolimbic dopamine functioning.

FUN Member Sponsor: Helen Sable

Theme G: Motivation and Emotion

Poster #90 **Poster Board: XX5**

THE EFFECTS OF DOPAMINERGIC AND NORADRENERGIC DRUGS ON DECISION-MAKING WITH DELAYED PUNISHMENT

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During decision-making, it is necessary to weigh all risks and rewards to make choices that maximize benefits while minimizing harm. A critical factor that influences decision-making is the occurrence of delayed negative consequences. For example, you may complete a purchase with a credit card despite not being financially stable, knowing that the debt will not be incurred until the next bill. Critically, this can also affect decision-making in substance use disorder, as substance users get instant drug reinforcement then face consequences later.

Very little research is available on delayed punishment. To tackle this problem, our lab created the Delayed Punishment Decision-making Task (DPDT; Liley et al., 2019). In this task, rats choose between a lever that dispenses one pellet and another that dispenses three but also delivers a shock. As the task progresses, the shock occurs after a delay, enabling assessment of sensitivity to delayed punishment. Rats are more likely to choose the punished option when shock is delayed, suggesting that rats, like humans, underestimate delayed punishment.

Little is known about the neurotransmitters that regulate this form of decision making. To address this, I tested the impact of three drugs on DPDT: cocaine, a common street drug that acts as a dopamine/norepinephrine reuptake inhibitor, quinpirole, a D2 agonist, and atomoxetine, a norepinephrine reuptake inhibitor. Cocaine reduced choice of delayed punishment without affecting choice of immediate punishment, and this effect was greater in females. Quinpirole caused near-complete avoidance of punished options in both males and females. Finally, atomoxetine reduced choice of the delayed but not immediate punishment in both males and females. The goal of this project is to help create pharmaceuticals to better treat dangerous decision-making without altering other aspects of cognition.

FUN Member Sponsor: Nicolas W. Simon

Theme G: Motivation and Emotion

Poster #91 **Poster Board: XX4**

MATERNAL SEPARATION INDUCES ANHEDONIA-LIKE BEHAVIOR IN MALE AND FEMALE RATS

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Early life adversity is a known risk factor for the development of anxiety and depression Maternal separation (MS) is an early life stressor used to model early life adversity, such as childhood neglect, and can reliably induce depression-like and anxiety-like behaviors in rodents. MS-induced depression-like behavior is commonly assessed in rodents with the forced swim test, which is thought to measure behavioral despair, a core feature of depression. Anhedonia, another diagnostic criterion for depression, is displayed as a lack of motivation for rewards which are typically sought to be pleasurable, and is not accurately modeled with the forced swim test. Thus, the degree to which motivational behavior and anhedonia are impacted by MS is not known. Here, male and female rats underwent MS, and were then tested in an effort-related choice task to assess anhedonia-like behavior. In this task, rats are given a choice between exerting effort by pressing a lever to obtain a desirable reward (a chocolate pellet), or consuming freely available, standard laboratory food. Over the course of the study, it was observed that male and female rats that experienced MS pressed the lever less than control peers who did not experienced MS. It was also observed that male rodents in the control condition consumed significantly less laboratory food on some test sessions, possibly due to their activity with the active lever. Importantly, the number of entries into the magazine where the chocolate pellets were delivered did not differ across sex or condition, suggesting there is no locomotive differences between groups. Overall, the effort-related choice paradigm displayed the anhedonia-like behavior of male and female rats who experienced early life adversity, as well as a sex difference in chow consumption in MS groups. Further testing will be done to determine if early life adversity, coupled with a second stressor, has an exaggerated effect on anhedonia-like behavior later in adulthood.

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FUN Member Sponsor: Joshua Haight

Theme G: Motivation and Emotion

Poster #92 **Poster Board: XX3**

REPEATED RESTRAINT STRESS INDUCES SEX-DEPENDENT ACTIVATION OF BNST AND ANXIETY-LIKE BEHAVIOR

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Anxiety disorders are among the most prevalent psychiatric disorders, with women being twice as likely as men to be diagnosed. This suggests underlying sex differences in the neural circuitry may contribute to the prevalence of anxiety disorders in females. The bed nucleus of the stria terminalis (BNST) is sexually dimorphic, stress-sensitive, and activated during anticipatory anxiety or anticipation of a threat. Prior studies show that female rodents extinguish conditioned freezing to anticipatory anxiety faster than males. However, the extent to which stress modulates anticipatory anxiety in parallel with BNST activation is unknown. Since females are more sensitive to stress and the stress hormone, corticotropin releasing factor (CRF), we hypothesized that anticipatory anxiety would facilitate greater BNST activation in stressed females compared to stressed males and control animals. To test our hypothesis, we used male and female rats exposed to repeated restraint stress (20 min/day for 7 out of 9 days) or control handling. Following treatment, rats underwent prolonged cued fear conditioning (5 random foot shocks during an 8-minute tone). In a separate context 4 days later, rats underwent extinction to the tone. Afterwards, we immunostained the BNST for c-Fos expression and CRF. There was no difference in time spent freezing during extinction, therefore, we also quantified active behaviors (e.g., darting, scanning, etc.). We found significant interactions between stress and sex with stress females rearing (*p=0.0234) and scanning (*p=0.0272) less than control females, whereas stressed males reared and scanned more than controls during the tone. Preliminary data further suggests that these stress-induced sex differences on anxiety-like behaviors may be related to c-Fos expression in the BNST. We found increased c-Fos expression in the BNST of stressed rats compared to controls (p=0.0544). Additionally, we found BNST CRF expression was higher in females (*p=0.0324) and affected by stress in a sex-dependent manner (*p=0.0452) with CRF expression increased in stressed females but decreased in stressed males. Together, these studies show how stress influences anxiety-like behaviors in a sex-dependent fashion, possibly through differences in activation of the BNST.

FUN Member Sponsor: Naomi Wentworth

Theme G: Motivation and Emotion

Poster #93 **Poster Board: XX2**

ENVIRONMENTAL ENRICHMENT VERSUS ISOLATION EFFECTS ON ANXIETY-LIKE AND DEPRESSION-LIKE BEHAVIOR AND ETHANOL SELF-ADMINISTRATION IN MALE AND FEMALE MICE

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A small proportion of individuals that drink alcohol become dependent or develop alcohol use disorder. We are investigating this susceptibility versus resilience to addiction-related, anxiety-like, and depression-like behaviors using the animal model environmental enrichment. Enriched mice are group-housed in a large environment with several conspecifics and plastic objects that are regularly changed and rearranged while isolated mice are single housed in standard cages. Previous work has found that enriched rodents are resilient to anxiety-like and addiction-related behaviors. Here we examined whether environmentally enriched mice compared to isolated mice showed alterations in anxiety-like, depression-like behavior, and ethanol self-administration. Male and female mice were housed in enriched or isolated conditions from weaning for a minimum of 30 days before behavioral testing including sucrose neophobia, sucrose preference, elevated plus maze, forced swim test, open field test, and ethanol self-administration. Environmental enrichment did not significantly alter body weights after differential rearing, although females had lower body weights compared to males. When exposed to a novel taste in the sucrose neophobia test, there were no differences in sucrose solution intake between enriched and isolated male and female mice after 30 minutes and 24 hours of exposure. Environmentally enriched females showed a trend towards a decrease in preference of a sucrose solution over water compared to isolated females with no changes in males. We also examined environmental enrichment versus isolation on ethanol self-administration using a two-bottle choice paradigm. Mice were given access to water and ethanol (20% v/v) for 24 hours on a M-W-F schedule for a total of 20 drinking days with free access to water on intervening days. Females overall drank more ethanol compared to males, however there was no effect of environmental enrichment or isolation. We also found a significant effect of ethanol drinking day over the intermittent access protocol, suggesting changes in intake over time in all groups. There were no significant main effects of sex or enrichment on water intake and preference for ethanol. Ongoing assessments will evaluate differences in anxiety-like behavior with elevated plus maze, depression-like behavior with forced swim test, and activity levels with open field testing. Overall these data suggest increases in anhedonia-like behavior in environmentally enriched females and show that female mice self-administer more ethanol compared to males, regardless of differential rearing environments.

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FUN Member Sponsor: Elizabeth Crofton

Theme G: Motivation and Emotion

Poster #94 **Poster Board: XX1**

PERSISTENCE OF BEHAVIORAL SENSITIZATION AFTER A SINGLE METHAMPHETAMINE INJECTION IN MICE

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The Pavlovian excitatory conditioning account of behavioral sensitization suggests that the sensitized response reflects both associative (i.e., classical conditioning) and non-associative processes. That is, the sensitized response reflects the summation of the classically conditioned response (i.e., CR) with the pharmacological unconditioned response (i.e., UR). This experiment, using an animal model of drug addiction (i.e., behavioral sensitization), evaluated the Pavlovian excitatory conditioning account by examining the temporal persistence of conditioned hyperactivity and sensitization after a single methamphetamine injection in male, Swiss Webster mice (N = 80). Following 6 weeks of acclimation, mice received either a single injection (intraperitoneal, i.p.) of physiological saline (vehicle) or methamphetamine (2.0 mg/kg) prior to a 30-minute locomotor activity session (Conditioning Day). Following the conditioning day, tests for conditioned hyperactivity (CR Test) and behavioral sensitization (Methamphetamine Challenge Test) occurred after a delay of 2 and 3 days (Immediate), 6 and 7 days (Short), 14 and 15 days (Moderate), or 27 and 28 days (Long), respectively. An injection of physiological saline or methamphetamine (1.0 mg/kg) occurred on the CR Test and Methamphetamine Challenge Test, respectively. Distance traveled and vertical counts served as the dependent measures of locomotor activity. The 2.0 mg/kg methamphetamine dose produced robust, acute locomotor activity on the conditioning day in all groups. In addition, both dependent measures of locomotor activity revealed that conditioned hyperactivity was detected at all time points, and the robustness did not decline over time. In contrast, behavioral sensitization was robust early (Immediate- and Short-Delay time points) and only detected by the vertical count measure but weakened over time and was not evident later (i.e., Moderate-Delay). Collectively, these results suggest that the 1) the pharmacological UR diminishes over time whereas the CR does not, and 2) the conditioned and pharmacological components of behavioral sensitization are dissociable following a single methamphetamine injection. These observations speak against a simple Pavlovian excitatory conditioning account.

FUN Member Sponsor: Anthony Rauhut

Theme G: Motivation and Emotion

Poster #95 **Poster Board: YY1**

IMPACT OF ADOLESCENT OXYCODONE EXPOSURE ON MOTIVATION FOR A SUCROSE REWARD

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Adolescent opioid exposure is experiencing a growing prevalence in the United States, as between just 2019 and 2021, the number of adolescent overdose deaths quadrupled to 2,155 deaths. Adolescent opioid exposure has been connected to an increased risk of developing substance-use disorders, which is attributed to dysregulation in the mesolimbic dopamine system. Other research studies have focused around the effects of opioids on the system in adult mice, however our lab was interested in understanding the effect going into adulthood after an adolescent exposure. Beginning at 5 weeks old, male C57/BL6 mice were exposed to bi-daily escalating doses of oxycodone (9 mg/kg - 33 mg/kg) or saline for a period of 5 days (n = 10/group), followed by one week of abstinence. During the abstinence period, an open field test was performed at 8 hrs, 24 hrs, 48 hrs, 72 hrs, and 1 week following the last injection of oxycodone or saline to evaluate if any anxiety or lethargy phenotypes were present. The total distance traveled and the time spent in the inner and outer zones was measured using Anymaze software. A repeated measures ANOVA demonstrated a significant time x drug interaction ($p=0.0008$) in the total distance traveled and a multiple comparisons analysis revealed that the oxycodone mice were more lethargic than saline controls at 48 hrs ($p=0.0482$) and 1 week ($p=0.0095$) after the last injection of oxycodone. There also was a significant time x drug interaction ($p =0.0343$) in the amount of time spent in the inner zone, but the analysis yielded no statistically significant multiple comparisons. After 1 week of abstinence, all mice underwent an operant food reward task in which they had to learn to nose-poke at an active port to receive a sucrose pellet reward using a progressive ratio schedule. Oxycodone-exposed mice performed more active nosepokes during the progressive ratio timepoint (in which there are exponentially increasing requirements for a single pellet) compared to saline treated mice, demonstrating an increased motivation for a sucrose reward ($p<0.001$). Future experimentation will evaluate the role of neural plasticity in modulating increased motivation for a sucrose reward in the mesolimbic pathway. The mRNA expression of BDNF, CREB, and GABA receptor alpha-subunit 1 will be measured in the ventral tegmental area, nucleus accumbens, and the prefrontal cortex using quantitative real-time polymerase chain reaction.

FUN Member Sponsor: Shivon Robinson

Theme G: Motivation and Emotion

Poster #96 **Poster Board: YY2**

EXAMINING THE RELATIONSHIP BETWEEN DOPAMINE AUTORECEPTOR FUNCTIONING AND THE DOPAMINERGIC EFFECT OF COCAINE

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Despite continuous research, drug abuse continues to be a growing problem around the world. All drugs of abuse target the mesolimbic pathway either directly or indirectly, and, as a result, this pathway becomes activated, increasing the motivation to use drugs again. Emerging research has explored the importance of dopamine autoreceptor functioning related to drug use. Autoreceptors sit on the presynaptic membrane and regulate the amount of dopamine being released in the presynaptic terminal. When a dopamine agonist is introduced into the system, autoreceptors work to stabilize the amount of dopamine in the synapse by controlling dopamine release. This study aimed to determine how autoreceptor functioning is related to the dopaminergic response to cocaine. Mice were anesthetized with urethane (1.5g/kg) and placed in a stereotaxic frame. Fixed potential amperometry was used to assess dopamine autoreceptor functioning and aspects of dopamine release in the NAc. During the dopamine recordings, mice were given an injection of cocaine (10 mg/kg, ip), and dopamine measurements continued for 1 hour. A pearson correlation was used to determine the relationship between autoreceptor functioning and percent change in dopamine release following the cocaine injection. There was a significant negative correlation between autoreceptor functioning and dopamine release post cocaine, meaning that as autoreceptor function increased the dopaminergic effect of cocaine decreased. These findings improved our understanding of the relationship between autoreceptor functioning and the dopaminergic response to a drug of abuse, aiding in new advancements in preventing or limiting the effects of drug abuse.

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FUN Member Sponsor: Deranda Lester

Theme G: Motivation and Emotion

Poster #97 **Poster Board: YY3**

ESTROGEN-MEDIATED MECHANISMS INFLUENCING RECENT AND REMOTE FEAR EXTINCTION MEMORY IN FEMALE RATS

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Anxiety and stress-related disorders are reported to be more prevalent in women. However, the neurobiological mechanisms underlying sex differences in these disorders remain unclear. Neural circuits involved in fear responses are altered in individuals affected by stress-related disorders and can be modulated by sex steroid hormones such as estrogen. Prior research has demonstrated that higher estrogen levels during extinction training facilitates extinction recall 24 hours later. The current project examined how long the enhancing effects of estrogen on extinction recall last and how this effect might be regulated by the ERK pathway and gut microbiome. Naturally cycling adult female Sprague-Dawley rats underwent a 3-day fear conditioning/extinction paradigm. On Day 1, animals completed habituation and fear conditioning. Extinction training took place on Day 2 while subjects were in metestrus. 30 minutes prior to extinction training, 7 rats were administered estradiol (15ug/kg), and 7 rats were administered a sesame oil vehicle. Recent extinction recall test took place on day 3. Remote extinction recall test took place 7-15 days after extinction training. An independent-samples t-test revealed that estrogen-treated rats showed significantly lower freezing behavior compared to vehicle-treated rats during the recent recall memory test ($t(12) = -2.568$, $p = .012$), but not remote recall ($t(12) = -1.054$, $p = .156$). Estrogen treatment resulted in short-term facilitation of fear extinction memory consolidation but not long-term facilitation. Further analyses focus on how the gut microbiome and activation of the ERK pathway within the fear circuitry contribute to the effect of estrogen on fear extinction recall.

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FUN Member Sponsor: Dr. Lisa Maeng

Theme G: Motivation and Emotion

Poster #98 **Poster Board: YY4**

DISSECTING THE ROLE OF DISTINCT INPUTS TO THE NUCLEUS ACCUMBENS IN REWARD SEEKING BEHAVIOR

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Signals from the hippocampus to the nucleus accumbens(NAc) have often been associated with reward, pleasure, reinforced learning and addiction. Dopamine afferent signals to the NAc are believed to be responsible for the central hub for reward prediction and facilitate reward seeking cues. Abstract visual cues are present in many faucets of our daily life, including negative ones such as drug paraphernalia and unhealthy food for drug addiction and food disorders. This paper attempts to locate and identify differing signal strengths and frequencies through in vivo fiber photometry and neuropixels on DAT-Cre Mice implanted with optic fibers and transfected with dLight in the Nac and gCAMP in the ventral hippocampus. The mice are then given a task where a white bar descending down a black screen is given a value based on its distance to the bottom of the screen. The reward for the behavioral task is water given to dehydrated mice. We were able to identify ramping signal strength and frequency in anticipation of reward distribution, as well as varying signal strength when the reward prediction error was varied in different experiment types. The results show the physiological differences in dopamine and calcium signaling during varying motivational states, and can help us to associate behavioral differences and motivational states are represented in the mouse brain physiology.

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FUN Member Sponsor: Robin Ball

Theme G: Motivation and Emotion

Poster #99 **Poster Board: YY5**

ORAL L-DOPA DISRUPTS BEHAVIORAL SELF-CONTROL IN MALE SIAMESE FIGHTING FISH (BETTA SPLENDENS)

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In their natural habitat, B.splendens demonstrate sex differences in foraging; males are territorial and feed primarily as ambush predators using a “sit-and-wait” strategy while females are non-territorial and feed primarily as opportunistic foragers. This ecology suggests that males, but not females, may be capable of delaying gratification, at least for food. Previous research has examined impulsive choice in a variety of species; no previous research has explored preference between Larger-Later (LL) and Smaller-Sooner (SS) rewards in B.splendens. The current study consists of two experiments. Experiment I addressed sex differences in instrumental choice behavior in male and female B.splendens. Using a submerged T-maze, thrice-daily instrumental-choice trials were conducted in which subjects were presented with a choice between a SS reward (1 food pellet delivered immediately) and a LL reward (3 pellets delivered after a 15-s delay). 70 percent of males displayed a stable preference for the LL reward option over the SS option, whereas females were just as likely to stabilize on the SS option as the LL option (48% vs 52%, respectively). These results indicate that a majority of the males in Exp. I displayed spontaneous behavioral self control for food reward without any specialized training, while females were collectively indifferent. Reward valuation is determined, in part, through mesolimbic dopaminergic activity, and previous research has demonstrated that orally-administered L-dopa increases impulsivity in humans; again, no such research exists regarding B.splendens. Experiment II investigated the potential for L-dopa to disrupt self-control in male B.splendens. The same instrumental-choice procedures from Exp.I were used for Exp. II, but with only male subjects. Subjects in the treatment group received oral L-dopa (60mg/kg) in a customized “fish pill” 30-minutes prior to each trial, while subjects in the control group received an inert “fish pill”. Male subjects in the control group were as likely to stabilize on the SS option as they were to stabilize on the LL option (48% vs 52%, respectively). Furthermore, only 30% of subjects receiving oral L-dopa demonstrated stable preference for the LL reward, with 70% of male subjects in the treatment group demonstrating stable preference for the SS. Administration of L-Dopa prior to instrumental choice between a LL reward and a SS reward increased the likelihood of impulsivity in males. Future researchers could examine dopamine agonists or antagonists (rather than a dopamine precursor) in males and/or females to further explore the role of dopamine in immediate/delayed reward valuation in B.splendens.

Funding Support: Christopher Newport University

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Theme G: Motivation and Emotion

Poster #100 **Poster Board: YY6**

LOCUS COERULEUS MODULATION OF HIPPOCAMPAL FEAR MEMORY TRACES: HIPPOCAMPAL FLEXIBILITY AND CONTEXT GENERALIZATION

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Post-traumatic stress disorder (PTSD) is a mental health condition (with a lifetime prevalence of 7.8% in the US) that is triggered by experiencing a traumatic event. It is unknown why certain subsets of individuals are more vulnerable to developing PTSD than others, with women a"ected twice as much as men. This disorder is often characterized by flashbacks, nightmares, rumination, and intrusive thoughts related to the event. A hallmark symptom of PTSD is fear generalization where acquired fear responses are expressed in non-threatening environments. Memory updating is an adaptive mechanism, which allows an organism to access the most relevant information from memory. We hypothesize that fear generalization may stem from memory updating impairments involving a failure to remap trauma-related memory traces in the presence of novel information (e.g., safety signals), and the persistent recall of these traces in the presence of non-trauma related contexts or stimuli. To examine the effects of stress on the stability and flexibility of contextual representations in the dorsal dentate gyrus (DG), we used a viral-based neuronal tagging strategy (AAV9-c-Fos-tTA-TRE-eYFP) to label cells involved in encoding a strong fear conditioning experience in male and female Th-Cre mice. Reconsolidation, where previously consolidated memories are recalled, can serve as a mechanism to update memories, specifically in the presence of new information. Previous evidence shows that the norepinephrine (NE) system is dysregulated in PTSD, and we have shown that the pathway from the locus coeruleus (LC) (site of NE synthesis) to the hippocampus is involved in remapping hippocampal contextual representations and may constitute an important pathway in memory updating. To assess whether optical activation of LC terminals in the DG (20Hz) during reconsolidation (in either the fear context or a safe context) would promote remapping of DG engrams and reduce generalization, we also infused these mice with AAV5-Ef1a-DIO-(ChR2)-mCherry in the LC and implanted an optical fiber over the DG. We hypothesized that this optical neuromodulatory manipulation would enhance discrimination and facilitate extinction restoring cognitive flexibility. Mice were tested for recall in either the fear context or the safe context. Our future goal is to also identify genetic factors that may contribute to these impairments and the way in which they interact with experience to confer susceptibility or resilience to stress.

FUN Member Sponsor: Stephanie Grella

Theme H: Cognition

Poster #101 **Poster Board: YY7**

THE ROLE OF COCAINE AND EXTINCTION-ASSOCIATED ENGRAMS IN DRIVING/PREVENTING DRUG-SEEKING BEHAVIOR USING CONDITIONED PLACE PREFERENCE

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Addiction is characterized by a continual propensity to relapse. Relapse-prevention strategies aimed at reducing the likelihood and severity of relapse following abstinence, focus on reducing cravings that lead to drug-seeking. Factors precipitating drug-seeking include exposure to drug-related cues, to the drug itself, and to stress. One factor not yet directly investigated is the contribution of drug-related memories. Conditioned place preference (CPP) has been used to study the rewarding aspect of drugs and the reinstatement model has been used to study relapse. To investigate the role of memories in promoting relapse, we tagged dorsal dentate gyrus (DG) cells involved in encoding a cocaine-related memory (the first conditioning session) using the doxycycline-inducible, tet-tag system driven by the c-Fos promoter, in male and female c57BL/6 mice. Mice underwent cocaine (15 mg/kg, i.p.) CPP training where they learned to associate cocaine with one side of the chamber and saline with the other. Following conditioning, preference for the cocaine side was extinguished and then reinstated using either a priming injection of cocaine (7.5mg/kg) (or saline) compared to optical reactivation of the tagged cocaine-related memory (20Hz, ChR2 or eYFP), thus exploring whether reinstatement can be primed via the memory of a drug in comparison to the drug itself and whether these effects may be additive. In the second experiment, we again tagged the first CPP conditioning session and then either administered cocaine (15 mg/kg) or optically reactivated the tagged memory (20 Hz) (these mice received saline) for each cocaine conditioning session thereafter to assess whether reactivation of the first drug-related experience was sufficient to drive a place preference. Finally, in the third experiment, following cocaine CPP, we ran extinction training and tagged the last extinction session. We then reactivated the cells that were involved in encoding this extinction session during a drug-primed (7.5mg/kg, i.p.) reinstatement test to assess whether this would interfere with cocaine-induced reinstatement.

FUN Member Sponsor: Steve Ramirez

Theme H: Cognition

Poster #102 **Poster Board: YY8**

IS FORGETTING OF SENSITIZATION AN ACTIVE PROCESS: TESTING THE ROLE OF FMRFAMIDE

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Although long-term memories can be very long-lasting, most are forgotten, becoming progressively less likely to be recalled. While there is some evidence that forgetting is due to simple decay of the memory trace, studies in fruit fly have suggested that forgetting is an active process, involving specific mechanisms that work to decrease expression of stored memories. We have recently found evidence suggestive of active forgetting for long-term sensitization in the marine mollusk Aplysia californica. Specifically, we have found that sensitization training produces a long-lasting increase in the expression of transcripts related to signaling for FMRF-amide, a peptide transmitter that causes synaptic depression at some of the synapses related to encoding sensitization. This suggests the possibility that sensitization is forgotten due to a global increase in FMRF-amide signaling that erodes the synaptic changes induced at the time of learning. We are conducting a high-powered, rigorous test of this hypothesis by observing the effects of pharmacological manipulation of FMRF-amide on the time course of forgetting for sensitization. Animals were given long-term sensitization training (4 painful shocks to one side of the body). This produced a robust sensitization memory, expressed as a sharp increase in the duration of the tail-elicited siphon-withdrawal reflex on the trained side of the body 1 day after induction. Animals were then given whole-body injections of either FMRF-amide (5 injections, 10uM), an antagonist to FMRF-amide signaling (4 injections of 4-bromophenacyl, 10uM) or vehicle (5 injections). Finally, the time course of forgetting was observed by monitoring reflex duration at 4, 6, and 13 days after training. We have now completed this protocol for 12 animals per group (from a pre-registered sampling goal of 18 per group). Analysis of this interim data shows that while all animals show a reduction of sensitization over time, antagonizing FMRF-amide signaling slows forgetting, with considerably higher reflex responses 6 days after training compared to the vehicle condition ($d = .86$ 95% CI[.04, 1.7]. This is interesting preliminary corroboration of the hypothesis that FMRF-amide signaling is part of an activate forgetting process for sensitization.

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Theme H: Cognition

Poster #103 **Poster Board: YY9**

ACQUISITION AND USE OF SINGULAR GENDER-NEUTRAL PRONOUNS IN ENGLISH

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As society becomes more accepting of gender diversity, the language we use must evolve to be more inclusive of varying gender identities. It is becoming more common to use gender neutral pronouns, but many people report difficulty with adjusting to their use. In an online study, we recruited 30 adult participants to learn and practice using the gender-neutral pronouns they/them. Participants were asked to complete Go/No-Go and sorting tasks before and after practice using they/them pronouns to refer to a non-binary target. Practice tasks included verbal storytelling, written responses, and rating sentences about the target. To test the efficacy of training, we measured their response time and accuracy pre- and post-training. The large majority of participants became faster in their response time for both tasks over time. Participants significantly improved on their accuracy for non-target non-binary celebrities and cisgender women celebrities, but did not improve on their accuracy of using they/them pronouns for the target non-binary person. Future work will expand on the tasks in this study through the development of a pronoun-learning app to support the practice of gender-neutral pronouns for non-binary people.

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Theme H: Cognition

Poster #104 **Poster Board: YY10**

THE RELATIONSHIP BETWEEN CHILDHOOD TRAUMATIC BRAIN INJURY AND INTERNALIZING SYMPTOMS IN YOUNG ADULTS: A PRELIMINARY STUDY OF THE MECHANISTIC ROLE OF THE N400 ERP

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The presence and increase of internalizing symptoms (withdrawal, loneliness) are associated with higher rates of mental illness, such as anxiety and depression. Young adults who survive early childhood traumatic brain injuries (TBI; head injuries caused by an external force) experience elevated internalizing symptoms compared to their peers. Furthermore, children and adolescents with more internalizing symptoms tend to have poorer verbal comprehension and language processing. However, there is a limited understanding of the cognitive mechanism for why survivors of childhood TBI are more likely to experience these elevated internalizing problems into adulthood. Therefore, the hypothesis of this study is that altered lexical-semantic processing is an underlying mechanism behind the relationship between internalizing symptoms and early childhood TBI. Participants in this preliminary study included five young adults who survived childhood TBI and age- and gender-matched controls (18-40 years of age). Electroencephalogram (EEG) recorded the N400 event-related potential (ERP) component, a neural correlate of lexical-semantic processing, during a visual sentence comprehension task. During the 128-electrode EEG recording, participants read 140 sentences that ended either with a semantically incongruent or congruent word (e.g., It was windy enough to fly a kite/treat). The sentence-final word elicited the N400 ERP. N400 component amplitudes were averaged within each condition (incongruent, congruent) and measured for each participant as the mean amplitude of the N400 difference wave (incongruent minus congruent conditions) at Cz and CPz electrode clusters. Data were processed using EEGLAB and ERPLAB toolboxes in MATLAB. Participants completed the Achenbach Adult Self-Report Form which assessed their internalizing symptoms.

As expected, statistical analyses showed that the incongruent condition elicited a significantly more negative N400 irrespective of group ($F(1,9) = 26.31$, $p < .001$) which demonstrates that this task properly produced the N400 ERP. N400 amplitudes were not significantly different between groups at this preliminary stage. A Kendall's tau correlation identified a positive correlation between N400 amplitudes and internalizing symptoms in the TBI group ($\tau b = .738$, $p < .05$). Specifically, TBI participants with a less negative (smaller) N400 tended to have greater internalizing symptoms. This positive correlation suggests that deficits in lexical-semantic processing may play a role in the level of internalizing symptoms present after childhood TBI. The connection between internalizing problems through deficits in language processing as a mechanistic explanation for elevated symptoms is a point of further investigation that this ongoing study will continue to research.

FUN Member Sponsor: Patrick Ledwidge

Theme H: Cognition

Poster #105 **Poster Board: YY11**

EYE SEE WHAT YOU MEAN: HUMAN TEACHING STRATEGIES REVEALED THROUGH EYE-TRACKING

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Passing knowledge through mentorship allows humans to acquire skills from those who came before them without starting from scratch. However, mentors need to be strategic while inferring the mindset of their mentees, also known as Theory of Mind, to only give their mentees knowledge relevant to their situation. In this study we investigate the strategies of mentors when teaching hypothetical students how to earn the maximum points in a Graph Teaching task. Mentors are shown a directed deterministic graph where a hypothetical student with limited knowledge of the graph has traversed across four nodes using three edges. The mentors assume that the student has chosen the path that gives them the most points and have the opportunity to help the student gain more points by teaching them a new edge. Previous work with this task has shown that a subset of mentors use heuristics, such as the reward values of the nodes, to teach. Through the use of eye tracking we will investigate the mentor's attention through their eye gaze when presented with the mentees' path of choice. This knowledge will inform us of what immediate strategy they intend to use whether through heuristics or Theory of Mind. We predict that mentors' behavioral strategies will be reflected in their eye gaze such that those using a reward heuristic will focus on the higher value edges.

FUN Member Sponsor: Princeton University

Theme H: Cognition

Poster #106 **Poster Board: YY12**

SEX AND STRAIN DISPARITIES AFFECT VISUAL TOUCHSCREEN DISCRIMINATION IN RATS.

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Stimulus discrimination, the skill to differentiate between distinct stimuli, and reversal learning, a measure of cognitive flexibility and inhibitory control, play pivotal roles in maintaining healthy cognitive functioning. Inhibitory control is required to break from unhealthy patterns of behavior and to reduce unwanted or improper actions. Both visual discrimination and reversal learning have been demonstrated to rely on the proper functioning of the prefrontal cortex. One objective of this experiment was to establish ideal training parameters to have rats to acquire visual discrimination in an operant touchscreen task. We also assessed the learning capabilities of male and female rats from Sprague Dawley and Long Evans strains. In this study, twelve rats of each strain (six females and six males) underwent training to distinguish between two stimuli with varying visual frequencies. During training, the two visual stimuli were presented to a rat on a touchscreen. If a rat touched one stimulus (designated as the "correct" stimulus) a food reward was given, however, if the rat touched the other stimulus (designated as the "incorrect" stimulus), no reward was given. Thus, the rats had to learn the correct response-reward association between the two visual stimuli in order to obtain the reward. Following initial discrimination, rats were given a discrimination reversal task. That is, the previously "correct" stimulus was no longer reinforced and the previously "incorrect" stimulus was now reinforced. Our results revealed a notable difference in initial discrimination learning between the rat strains. Specifically, out of the 12 Sprague Dawley rats, only 2 managed to learn visual discrimination over a span of 22 days of training. In contrast with the Long Evans strain, all but one rat succeeded in acquiring the initial discrimination. Noteworthy, the male rats, on average, reached the learning criterion within 11.5 sessions, whereas female rats required an average of 20.8 sessions to meet the same criterion. These findings support the use of Long Evans rats in future touchscreen experiments that investigate the behavioral and neural mechanics of discriminatory learning. In our future investigation we will test sex and stress effects on the rats' ability to complete the reversal learning task, and explore the role of the female gonadal hormones in the rat's ability to acquire initial discrimination.

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Theme H: Cognition

Poster #107 **Poster Board: YY13**

MEMORY CONSOLIDATION DURING OFFLINE STATES OF WAKING REST AND SLEEP: UNDERGRADUATE RESEARCH AT THE FURMAN SLEEP LAB

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Sleep is important for human memory. Past studies have demonstrated that memories can be strengthened and solidified after longer periods of sleep. Recently, however, our laboratory and others have demonstrated that even a brief period of eyes-closed waking rest after encoding can provide a similar benefit to memory. Because of these observations, our laboratory is trying to better understand the similar yet unique effects that both sleep and rest have on the memory consolidation process. In two ongoing studies we are asking the questions: 1. If waking rest can improve memory, can it also alter or distort these memories?, and 2. How do memories processed during sleep appear in dreams?

Study 1

Like sleep, post-learning rest qualitatively transforms memories during the consolidation process. Because of this, like sleep, rest might promote the formation of false memories. Previous literature has established that sleep can increase false memory formation (when using a recall testing method). Study 1 tests whether this effect holds true when waking rest is substituted for sleep. In a within-subjects design, participants will either rest or complete a distractor task following encoding Deese-Roediger-McDermott false memory task word lists. Afterwards, participants will be tested on their memory for the word lists, via both recall and recognition tests. We hypothesize that not only will false memory formation increase following a period of eyes-closed rest, but that this rest period will facilitate the consolidation of studied words as well.

Study 2

Completing a learning task just before sleep often induces learning-related dreams. Still, little is known about how this works, and the literature to date has focused almost exclusively on how recent experiences from just before sleep are incorporated into dreams. It is unknown whether and how remote memories may also be reactivated during sleep and incorporated within dreaming. In this study, we aim to experimentally trigger participants to dream about remote, long-past experiences. Participants will complete an Autobiographical Emotional Memory Task just before an experimental nap, in which they must respond to a prompt asking them to recall a remote negative emotional memory. Observing the effect of this procedure on subsequent dreams will help us to understand how new experiences may cause related remote memories to become activated and appear in subsequent sleep.

Together, this and other ongoing work in our laboratory will help to disentangle the unique ways in which sleep and waking rest promote memory consolidation.

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FUN Member Sponsor: Erin Wamsley

Theme H: Cognition

Poster #108 **Poster Board: YY14**

MTOR-MEDIATED TRANSLATION AFTER ACUTE AND CHRONIC SLEEP LOSS

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Memory formation requires protein synthesis, which is dependent on several signal transduction pathways, including mammalian target of rapamycin (mTOR) signaling. Previous research has shown that five hours of acute sleep deprivation attenuates mTOR-mediated protein synthesis in the hippocampus of male mice; however, it was not known whether this effect was limited to males or the hippocampus. Interestingly, we found that mTOR activity was also significantly reduced in the cerebellum of acutely sleep deprived male mice. A chronic sleep restriction of 20 hours of REM sleep loss per day for seven days also significantly reduced mTOR activity in the hippocampus and cerebellum of male mice. In female mice, five hours of acute sleep deprivation only significantly reduced mTOR activity in the hippocampus, and not the cerebellum, and chronic sleep restriction did not impact mTOR activity in either brain region, which differs from findings in males. Further, we determined that fluctuating levels of hormones during the female estrous cycle did not affect mTOR activity in control conditions, or after acute sleep deprivation. In both sexes we also found that 5 hours of acute sleep deprivation significantly reduced hippocampal protein synthesis and impaired spatial memory, as measured in the object place recognition task. To rescue these deficits, we injected an adeno-associated virus containing a mutant form of eukaryotic initiation factor 4E-binding protein 2 (4EBP2) under a CaMKII alpha promoter into the hippocampus of male mice. This virus contained four alanine point mutations at phosphorylation sites, rendering this “phospho-mimetic” 4EBP2 (M4EBP2) constitutively inactive and preventing 4EBP2-mediated inhibition of protein synthesis. We found that expression of M4EBP2 in excitatory hippocampal neurons of male mice rescued the spatial memory impairments observed after sleep deprivation. Work is ongoing to determine whether this result is sex-specific. Our results show that while sleep loss affects mTOR activity in the hippocampus of male and female mice similarly, other brain regions may be differentially affected based on sex.

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FUN Member Sponsor: Jennifer Tudor

Theme H: Cognition

Poster #109 **Poster Board: YY15**

EXPLORING THE INTERPLAY OF PERCEPTION OF GOD AND RELIGIOUS SOCIAL INVOLVEMENT: A STUDY ON FORGIVENESS AT INDIVIDUAL AND GROUP LEVELS

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Religion is typically defined as a set of ideals, values, and belief systems that an individual uses to interpret the world. It often plays a critical role in decision-making and behavior related to politics, social issues, and religion. For many people, religion acts as a moral framework through which they navigate various aspects of their lives, impacting their attitudes, values, and actions on a day-to-day basis. Due to its significance, much work has focused on how religion's role
on higher-level, individual, and group-level behavior. In this study, our focus lies in exploring the interplay between religious social involvement and the perception of God on forgiveness.
Forgiveness, deeply intertwined with religion, holds a central position not only within Western religious traditions but also across diverse cultural contexts. Within religious communities, forgiveness holds a significant social value, with religious individuals often attributing higher significance to forgiveness. Investigating forgiveness as a religiosity-related factor is crucial, for its role in mitigating negative emotional states, promoting mental health, and enhancing relationship well-being.
In this study, we plan to recruit a total of 200 individuals to take part in a self-report survey assessing various constructs, including the perception of God, religious social connectedness, religious motivation, ideological beliefs, and forgiveness. We hypothesize that the interaction between religious social involvement and perception of God will have a moderating effect on forgiveness toward oneself and others. Further, we predict a positive perception of God along with high social involvement will be associated with increased self-forgiveness. Regression models will be utilized to analyze the data and test the hypotheses. The findings of this study will provide valuable insights into the influence of religious factors on forgiveness processes in various contexts.

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Theme H: Cognition

Poster #110 **Poster Board: YY16**

EVALUATING CHANGES IN MOUSE VISUAL CONSCIOUSNESS

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Several theories regarding the physical basis of consciousness exist, although many of them have yet to be fully experimentally validated. One such theory is called Integrated information theory (IIT), and it is the only mathematically precise theory for consciousness. The theory is promising, but the only neurophysiological data applied to IIT thus far comes from melanogaster drosophila (Leung et al. 2019). The initial results of experimental testing demonstrate that the amount of consciousness (Φ) increases from anesthetized to awake states as expected. We were interested in evaluating if Φ could change within awake subjects by looking at neuronal firing in mice viewing different categories of visual complexity e.g. static gratings to natural movies. We also calculated Φ for 6 different brain areas: the dorsal lateral geniculate (LGd), primary visual area (VISp), rostrolateral visual area (VISrl), lateral visual area (VISl), anteromedial visual area (VISam), the posteromedial visual area (VISpm) to evaluate changes across visual areas. The data that we used was from an open-source dataset collected by the Allen Institute with 6 simultaneously penetrated Neuropixel probes: DANDIset 000021. From the dataset, we used 52 electrode recordings spanning the six visual areas. We selected three random channels within each visual area and used local field potential data (LFPs) to calculate Φ. We filtered the LFPs for gamma by using a Butterworth filter, and a zero-phase filter, and then performed full-wave rectification by taking the absolute value. After filtering the LFPs, we binarized the data around the median to discretize the data; a step necessary for calculating Φ. Our system was thus composed of three nodes (the three LFP channels) and 8 possible states (2n=3). We then created a transition probability matrix that contains the probabilities of transitioning from a state t to another state at time t+1 for all states and time points. From this, we calculated Φ using the PyPhi toolbox (Mayner et al., 2018). Analysis of our results found that Φ increases with visual stimulus complexity across all visual areas resulting in repeated measures ANOVA p-value of <.001. However, we found no difference across brain areas, even between lower visual areas such as the LGd and higher cortical areas. These results suggest that conscious experience can change with different stimuli in awake viewers and that lower brain areas might have more causal power over the informational system than previously considered.

Leung, A., Cohen, D., Swinderen, B. van, & Tsuchiya, N. (2021). Integrated information structure collapses with anesthetic loss of conscious arousal in Drosophila melanogaster. PLOS Computational Biology, 17(2), e1008722. https://doi.org/10.1371/journal.pcbi.1008722

Mayner, W. G. P., Marshall, W., Albantakis, L., Findlay, G., Marchman, R., & Tononi, G. (2018). PyPhi: A toolbox for integrated information theory. PLOS Computational Biology, 14(7), e1006343. https://doi.org/10.1371/journal.pcbi.1006343

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Theme H: Cognition

Poster #111 **Poster Board: YY36**

INVESTIGATING THE DYNAMICS OF TASK-SWITCHING IN ONLINE SAMPLES

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Cognitive flexibility allows people to switch between different tasks. A recent task-switching experiment proposed a new paradigm for studying the dynamics of task-switching. In this experiment, participants switched between auditory and visual tasks. The experimenters parametrically manipulated how much time participants had to prepare for the upcoming task. Consistent with previous work, they found that participants performed worse when they switched, but these switch costs were reduced with more preparation time.

To date, this paradigm has only been tested on a non-representative sample of Princeton undergraduates. Showing that these effects are replicable across the broader population in the United States is necessary to support their generalizability. We tested this task in a broad US sample by translating the existing paradigm to a web-based task. This translation required accommodating the constraints of web-based experiments while retaining the rich audiovisual stimuli and millisecond-precision timing required to study attentional dynamics. We recruited participants across the US using the online platform Prolific (N=29). Our online sample showed strikingly similar behavior to our college sample. Participants showed switch costs in both reaction time ($p < 0.001$) and error rate ($p < 0.01$). Moreover, preparation time reduced these switch costs in RT ($p < 0.001$). Our findings replicate the previous study, suggesting that these effects are robust and generalizable, and can be measured using online samples.

The replication study showed that it is possible to measure task-switching dynamics in an online sample, so we wanted to investigate a new facet of task-switching. Research in motor control has explored how people can quickly readjust their movements in response to perturbations. We were curious whether people also readjust their cognitive state when perturbed while switching tasks. To investigate this, we added an audiovisual distractor (noise stimulus) that occurred during the preparatory period on a subset of trials. In an online sample (N=106), we again replicated switch costs (ps < .001) and preparation effects (RT: $p < .001$). When participants were perturbed during switching, they had slower reaction times ($p < 0.005$). A longer duration after the perturbation reduced this slowing ($p < 0.001$), controlling for the total preparatory period. Surprisingly, participants also had higher accuracy when they were disrupted ($p < 0.05$). A possible explanation for this is that participants are bracing themselves for the distraction thus exhibiting more caution by responding slower and more accurately. Future work will include cognitive modeling to better understand attention and caution and a neuroimaging study (EEG or MEG).

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Theme H: Cognition

Poster #112 **Poster Board: YY35**

EFFECTS OF CHRONIC VAGUS NERVE STIMULATION ON COGNITIVE PERFORMANCE IN AGING

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Disruptions in both excitatory and inhibitory signaling within the prefrontal cortex (PFC) are implicated in age-related impairments in executive functions. Electrical vagus nerve stimulation (VNS) is an approved treatment for intractable epilepsy and certain neuropsychiatric disorders, and anecdotal reports suggest improvements in cognitive function as a side effect. This study aims to investigate the effects of chronic VNS on working memory in aging. Male and female FBN rats (24 months old) underwent surgical implantation of a cuff electrode around the left vagus nerve. They were subjected to daily testing on a delayed response working memory task in operant chambers, requiring them to learn and remember the left/right position of a response lever over short delays. In the afternoons, the rats received VNS sessions using parameters previously demonstrated to enhance cortical plasticity and other forms of PFC-dependent learning (100 stimulus trains/ 1 hour session at 30Hz, 700 μA, 120 μs biphasic pulse width, 0.8 s train duration). Data to date indicate that after 25 sessions, rats receiving VNS exhibited improved working memory compared to control rats. These findings suggest that chronic VNS may have the potential to address age-related impairments in working memory, possibly through reducing excitatory/inhibitory signaling dysregulation associated with aging.

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FUN Member Sponsor: Barry Setlow

Theme H: Cognition

Poster #113 **Poster Board: YY34**

ASSESSING COGNITION IN INFANT MARMOSETS (CALLITHRIX JACCHUS) WITH EYE-TRACKING TECHNOLOGY

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Across many species, looking time paradigms allow for investigation into different cognitive traits of interest, including social preference or comprehension of physical properties. By measuring how long an animal looks at an object or scene, and where the animal looks, violation of expectation tasks are used to determine what is surprising to an animal, revealing the animal's understanding of social or cognitive information. Eye-tracking technology allows for precise quantification of looking times in these paradigms and has been used in a variety of species including humans, canines, and non-human primates. The common marmoset (Callithrix jacchus) is of particular interest in cognitive research due to the similarity in aging patterns between marmosets and humans. Eye-tracking technology provides another method through which the cognitive capabilities of marmosets may be measured with potential use in aging studies. We developed a protocol for testing marmosets with eye-tracking technology to assess their cognitive performance on preferential looking and violation of expectation tasks. We piloted these tests with adult marmosets and began testing infant marmosets in Fall 2023; specifically, we are examining infant marmosets' understanding of physical properties by measuring looking time when viewing different physical scenarios with either expected or unexpected outcomes.

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Theme H: Cognition

Poster #114 **Poster Board: YY33**

TRANSCRIPTIONAL CORRELATES OF LONG-TERM SENSITIZATION MEMORY IN APLYSIA: DOES LONG-TERM STORAGE HAVE A LONG-TERM TRANSCRIPTIONAL COST?

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The formation of a long-term memory requires transcriptional changes in the nervous system. What happens, though, as the memory is then stored for weeks and months: Do initial transcriptional changes fade or is there an ongoing transcriptional cost for each stored memory? We are addressing this question by tracking transcriptional changes in the nervous system of Aplysia californica following long-term sensitization training, a form of pain memory that is conserved across the animal kingdom. Aplysia (n = 8 per group) received a 4-day sensitization protocol, with each day's training consisting of 4 presentations of a painful electrical stimulus to one side of the body. This was sufficient to induce a strong sensitization memory for at least two weeks, expressed as a sharp increase in reflex duration on the trained side of the body. We are now conducting microarray and qPCR to analyze the transcriptional changes occurring 1, 5, and 11 days after training, focusing on the pleural ganglia which contain nociceptive neurons that help store the sensitization memory. Preliminary qPCR results show that training produces strong increases in the expression of several learning-related transcripts, but that these decay within 11 days, much earlier than the behavioral expression of the memory.

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Theme H: Cognition

Poster #115 **Poster Board: YY32**

MISMATCH REPAIR PROTEIN-MEDIATED REPAIR OF 8OXOG:A MISPAIRS

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Loss of functional alleles of the DNA repair gene MUTYH are linked to hereditary colorectal cancer risk syndromes. MUTYH is responsible for repairing 8oxo-guanine (8oxoG) to adenine mispairs, thus an accumulation of this DNA damage in the genome increases risk for cancer. However in the absence of MUTYH, 8oxoG:A mispairs can be repaired. In yeast, the mismatch repair (MMR) complex MutS-alpha is used to initiate this repair. The aim of this study is to determine if MMR can repair 8oxoG:A mispairs in humans. CRISPR/Cas9 genome editing was used to create frameshift mutations in the two MMR genes that make up MutS-alpha: MSH2 and MSH6. This was done in both wildtype HEK293 cells and in cells with deleterious mutations in MUTYH and OGG1, which together restore 8oxoG:A mispairs to G:C base pairs. The ability of these cell lines to repair 8oxoG:A mispairs will be tested with a novel GFP-off reporter assay. In this assay, GFP expression is turned on if 8xoxG:A mispairs are repaired. Thus, if the MUTYH, OGG1, and MMR triple knockout cell lines repair less GFP-off than the MUTYH, OGG1 double knockout cell lines, then MMR is capable of repairing 8oxoG:A mispairs.

FUN Member Sponsor: Greg Gage

Theme I: Techniques

Poster #116 **Poster Board: YY31**

CHARACTERIZATION OF IMMEDIATE-EARLY GENE REPORTERS FOR MAPPING THE SOCIAL BEHAVIOR CIRCUITS IN DROSOPHILA MELANOGASTER

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Courtship and aggression are two closely linked social behaviors that are essential for an animal's survival and reproduction. Drosophila melanogaster males display a complex repertoire of courtship and aggressive behaviors. While previous studies have identified central neural circuits involved in these behaviors, our understanding of the circuits that regulate them remains incomplete. Conventional techniques such as electrophysiology and calcium imaging are challenging to implement for social behaviors in flies because they require free movement, which is necessary for the complete repertoire of social behavior. In mammals, the immediate early gene (IEG) expression is a common and non-invasive technique to map neuronal populations underlying behavior. However, until recently, IEG expression strategies were not available in Drosophila. In this study, we characterize the Hr38-GAL4 transcriptional reporter system, which utilizes the regulatory region of the Drosophila Hr38 IEG to drive GAL4 expression in an activity-dependent manner. Firstly, we examine the time course Hr38-GAL4 expression in male flies in response to social interactions with a female. Consistent with previous findings, we observed Hr38-dependent labeling of P1 neurons, which are central regulators of male courtship, in male flies housed with females for 24 hours compared to solitary controls. Secondly, we used optogenetic stimulation to activate P1 neurons and characterize the strength, duration, and time course of P1 activity required to induce Hr38-GAL4 expression. Collectively, our data demonstrate that the Hr38-GAL4 system is suitable for labeling neurons associated with courtship behavior. Future investigations will explore whether this method can also identify neurons involved in aggressive behavior.

FUN Member Sponsor: Eric Hoopfer

Theme I: Techniques