BIOLOGICAL BASIS OF BEHAVIOR PROGRAM

25th Annual

Student Research Symposium

Celebrating 41 years
1978-2019

Friday, April 26, 2019

Levin Building

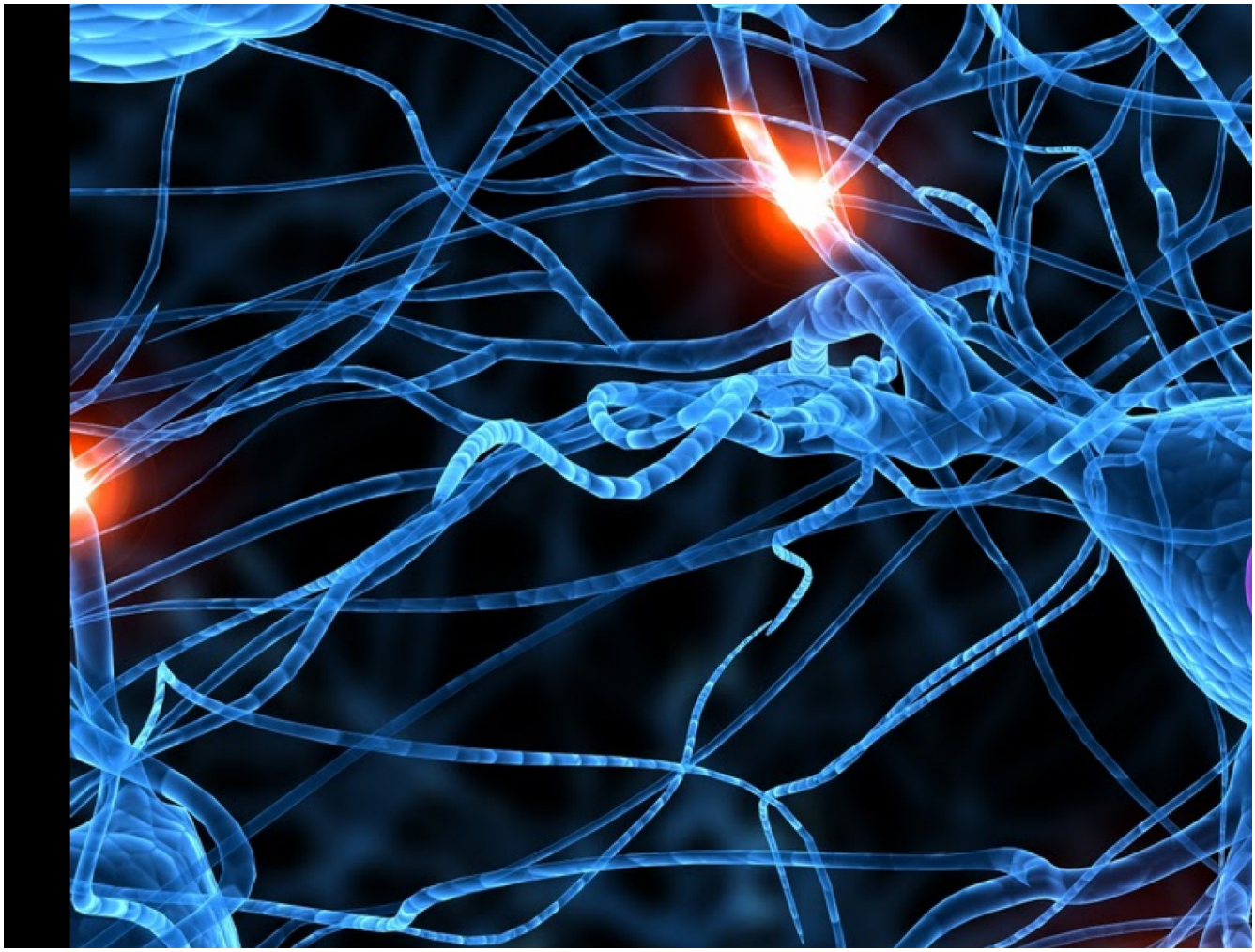
425 S. University Avenue

SCHOOL OF ARTS AND SCIENCES
UNIVERSITY OF PENNSYLVANIA

W e l c o m e

On behalf of the Biological Basis of Behavior Program. We welcome you to this very special day, our 25th Annual Student Research Symposium. It has been the goal of the program since its inception 41 years ago, to provide our BBB majors with the opportunity to work with faculty committed to multidisciplinary teaching and research. Such a commitment is clearly evident in the research accomplishments of our majors showcased today. Whether you spend the entire day with us or just a portion of it, we are sure you will be impressed.

Dr. Lori Flannagan-Cato, Co-Director
Dr. Marc Schmidt, Co-Director



Schedule of Activities

9:00 a.m.	Continental Breakfast
9:30 - 10:30a.m.	Honor Thesis Presentations Levin Conference Room 250 & 357
10:45 a.m.	Break
11:00 - 12 noon	Honor Thesis Presentations Levin Conference Room 250 & 357
12:15—1:30p.m.	Poster Session and Lunch Levin Lobby

Biological Basis of Behavior Graduation Awards Reception

Class of 2019

Saturday, May 18, 2019

11am-1pm

Levin Building Lobby

425 S. University Avenue

RSVP to mhobson@sas.upenn.edu by

Monday, May 6th

Levin Conference Room 250

9:00 Continental Breakfast

Session 1

9:30 **Frank Aguilar**
"The Attenuation of the Innate Fear Response by AgRP Neuron Projection Regions"
Supervisor: Nicholas Betley

9:45 **Shae Chambers**
"Behavioral Threat Response Following Repetitive Mild Traumatic Brain Injury in Mice"
Supervisor: Akiva Cohen, PhD

10:00 **Sandy Samuel**
"Dietary Branched Chain Amino Acids Improve Some Spatial Memory Deficits After Mild Traumatic Brain Injury"
Supervisor: Dr. Akiva Cohen

10:15 **Ivan Covarrubias**
"Identifying Sleep Active neurons in the Preoptic Area"
Supervisor: Shinjae Chung

10:30 **Ryan Leone**
"Evaluating Neurophysiological Metrics of Synchrony in Athletic Teams to Predict Performance"
Supervisors: Dr. Michael Platt and Dr. Scott Rennie

10:45 BREAK

Session 2

11:00 **Mahip Grewal**
"Exploring the Genetic Architecture of Autism: The Relationship Between Polygenic Risk Score and Quantitative Pheno types"
Supervisor: Dr. Edward Brodkin

11:15 **Courteney Ly**
"Probing the Neural Basis of Courtship Behavior"
Supervisor: Marc Schmidt

11:30 **Mackenzie Kagan**
"Investigation of Neurofilament Light Chain as a Potential Biomarker for Frontotemporal Degenerative Diseases"
Supervisor: Dr. Murray Grossman

11:45 **Gerardo Valasquez**
"Frontoparietal Network Plasticity: Individual Differences Following Working Memory Training"
Supervisor: ?

12:00 **Abigail Katz**
"The Developmental Progression of Higher-Order Statistical Learning in Children"
Supervisor: Allyson Mackey

Levin Conference Room 357

Session 1

9:30 **Samantha Stone**
"Effects of Nucleoside Reverse Transcriptase Inhibitors on Oligodendrocyte Differentiation"
Supervisor: Dr. Judith Grinspan

9:45 **Nana Acquah**
"Investigating Granule Cell Layer Volume and Cortical Microenvironment after Mild Traumatic Brain Injury in Mice"
Supervisor: Amelia Eisch

10:00 **Andrea Gomez**
"Time-Dependent Role of Gadd45b on Behavioral Flexibility"
Supervisor: Hongjun Song

10:15 **Zach Weiss**
"The Neuronal Basis of Salt Preference in Drosophila melanogaster"
Supervisor: Dr. Yali Zhang

10:30 **Vanessa Weir**
"The Role of Hindbrain Projections to the Nucleus Accumbens in Cocaine Seeking"
Supervisor: Dr. Heath Schmidt

10:45 BREAK

Session 2

11:00 **Rachel Levinson**
"Long Interspersed Element-1 Retrotransposons in Schizophrenia"
Supervisor: Wade Berrettini, MD, PhD

11:15 **Rebecca Li**
"Increased Norepinephrine Transmission from the Locus Coeruleus onto the CA1 of the Hippocampus Enhances the Acquisition of Aversive Memories"
Supervisor: John Dani

11:30 **Alexandra Croicu**
"The Role of the Chloride Transporter KCC2 in Alcohol Consumption in Mice"
Supervisor: John Dani

11:45 **Erica Rego**
"Drug Seeking Behavior Contributes to KCC2 Downregulation in the VTA"
Supervisor: Dr. John Dani

12:15 **Poster Session & Lunch**

Levin Conference Room 250

Frank Aguilar
Title: The Attenuation of the Innate Fear Response by AgRP Neuron Projection Regions
Supervisor: Nicholas Betley
Hunger and fear are two examples of competing signals that must be resolved to ensure survival. Currently, the neural circuitry responsible for integrating these conflicting survival needs has yet to be identified. Utilizing TMT as an innate predator odor stimulus, we tested if activation of AgRP neurons in the arcuate nucleus as well as AgRP neuron projection subpopulations was responsible for modulating the innate fear response. We found that activation of AgRP neurons in the arcuate nucleus not only attenuated fear due to TMT but also to other fearful stimuli like the open areas of an elevated zero maze. We also discovered that activity in AgRP subpopulations in the PVH and BNST may be implicated in prioritizing food-seeking behavior over innate fear. These findings suggest that when food is available, certain regions in the neural circuit for hunger become preferentially activated and can attenuate the neural circuit for innate fear.

Shae Chambers
Title: Behavioral Threat Response Following Repetitive Mild Traumatic Brain Injury in Mice
Supervisor: Akiva Cohen, PhD
The goal of this project was to discern the negative behavioral and neurobiological effects of repetitive brain injury in mice by implementing the lateral fluid percussion injury (LFPI) model. A secondary goal of this project was to attempt to implement the context pre-exposure facilitation effect (CPFE) paradigm, in addition to traditional contextual fear conditioning, in evaluating memory deficits. Within the repetitive mild traumatic brain injury timeline of this project, two repetitive mTBI conditions are examined: short-term (injuries delivered 5 hours apart) and long-term (injuries delivered 7 days apart). Goals for the future include examining the role of experimental branched chain amino acid (BCAA) dietary therapy in mediating these effects. Though current results from this project are inconclusive, they do have implications for the future, particularly in regard to the efficacy of the contextual fear response paradigms used.

Sandy Samuel
Title: Dietary Branched Chain Amino Acids Improve Some Spatial Memory Deficits After Mild Traumatic Brain Injury
Supervisor: Dr. Akiva Cohen
Traumatic Brain injury (TBI) results in cognitive impairment for which there is currently no approved treatment. Mild to moderate TBI can be represented via a lateral fluid percussion injury model (LFPI) which mimics the effects of clinical TBI in brain regions including the cortex and the hippocampus. The first stage of my project demonstrated that LFPI mice exhibited impaired spatial memory when performing a modified spatial object recognition task (SOR) that involves the hippocampus. Dietary consumption of branched chain amino acids (BCAAs) were previously shown to restore TBI-induced shifts in synaptic excitability in the hippocampus. Hence, dietary BCAAs were tested to examine if they can improve LFPI mice performance in the SOR task. The second part of my project aimed to assess LFPI mice performance in a new behavioral task (pattern separation task) that is known to specifically implicate the dentate gyrus- a region in the hippocampus that was shown to increase in excitability after injury.

Ivan Covarrubias
Title: Identifying Sleep Active neurons in the Preoptic Area
Supervisor: Shinjae Chung
Sleep is an essential biological function that is necessary for one's development, memory, and well-being. Several brain regions and neuron types within have been identified to play a role in sleep behaviors. The preoptic area of the hypothalamus (POA) is a brain region known to be sleep active in mice; however, it is a heterogeneous area where sleep active neurons are intermingled with other neurons. A new method has recently developed in which activity dependent neurons of *TRAP2;Ai14* double transgenic mice may permanently express tdTomato fluorescent protein when injected with 4-OHT. In this experiment, *TRAP2* mice were sleep deprived and injected with 4-OHT at the time of sleep rebound in order to identify sleep active neurons in the POA. TRAP2 mice were further tested using *in vivo* calcium imaging to confirm the POA activity's correlation to sleep, as well as optogenetics to determine whether the sleep active neurons are sleep promoting.

Ryan M. Leone
Title: Evaluating Neurophysiological Metrics of Synchrony in Athletic Teams to Predict Performance
Supervisors: Dr. Michael Platt and Dr. Scott Rennie
Physiological synchrony, represented by coupled oscillations of biological rhythms like neural activity across individuals in a group, is thought to be strongly related with group performance. However, most work on synchrony has been done outside of real-world, athletic settings. This project sought to collect electroencephalography, breathing rate, and heart rate measurements from student-athletes on Penn's Varsity Lightweight Rowing team to determine how physiological synchrony relates to athletic performance. The experiment was conducted over five trials, in which groups of four rowers participated in an erg machine workout in three workout conditions; yoked together, side-by-side but unyoked, and separated. After each condition, objective performance metrics from the machines and subjective ratings of flow from participants were collected. Preliminary findings suggest that we can predict heart rate synchrony based on the workout condition and that the degree of movement synchrony correlates with physiological synchrony. Performance and EEG data are currently under analysis.

Levin Conference Room 357

Samantha Stone
Title: Effects of Nucleoside Reverse Transcriptase Inhibitors on Oligodendrocyte Differentiation
Supervisor: Dr. Judith Grinspan
Approximately 50% HIV+ individuals suffer from HIV-associated neurocognitive disorders (HAND), a spectrum of cognitive, motor, and behavioral dysfunction. While the use of combined antiretroviral (ARV) therapy (cART) has greatly suppressed HIV replication, the overall prevalence of HAND has remained the same, suggesting that ARV compounds might contribute to the persistence of HAND. In addition to neuronal damage, astrogliosis, and microgliosis, myelin abnormalities and loss are common in HAND. Previous studies from the Grinspan and Jordan-Sciutto laboratories have demonstrated that select ARV drugs dose-dependently inhibit oligodendrocyte differentiation, possibly contributing to the persistence of myelin alterations observed in HAND patients. This study investigates the effects of nucleoside reverse transcriptase inhibitors (NRTIs), tenofovir disoproxil fumarate (TDF), tenofovir alafenamide (TEN A), and emtricitabine (EMT) on oligodendrocyte differentiation. Preliminary data suggests that TEN A and EMT exert a dose-dependent effect on oligodendrocyte differentiation once activated by endogenous thymidine kinase.

Nana Acquah
Title: Investigating Granule Cell Layer Volume and Cortical Microenvironment after Mild Traumatic Brain Injury in Mice
Supervisor: Amelia Eisch
Mild Traumatic Brain Injuries (mTBIs) are common worldwide and can disrupt cortical and hippocampal functions like cognition and memory. We sought to investigate the effect of mTBI on hippocampal granule cell layer (GCL) volume and on cortical cell proliferation in mice. We hypothesized that mTBI would decrease GCL volume and increase cortical cell proliferation. Adult male C57BL/6J mice received a lateral fluid percussion injury (LFPI) or sham injury, and brains were analyzed at 3 or 31 days post-injury (dpi). The GCL was stained for visualization, and proliferating cells were labeled with 5-bromo-2'-deoxyuridine (BrdU). GCL volume was estimated with the Cavalieri Principle. The cortices of 3dpi mice were semi-quantitatively assessed for BrdU+ cells. Sham and LFPI animals showed no differences in GCL volume at either timepoint. LFPI animals had more BrdU+ cells per cortical section. We concluded that cell proliferation is more significant than structural changes post-mTBI, and is a potential target for treating TBI-induced cognitive deficits.

Andrea Gomez
Title: Time-Dependent Role of Gadd45b on Behavioral Flexibility
Supervisor: Hongjun Song
Epigenetics describes how gene expression can be modulated by environmental factors and experience. Growth arrest and DNA damage-inducible gene 45 beta (Gadd45b) is involved in dynamic epigenetic modifications in mature neurons. Gadd45b expression increases after neural activation but returns to baseline levels after a few hours. The transient Gadd45b upregulation following neural activation suggests a time-dependent role in learning and memory processes. Therefore, we tested two different kinds of learning and memory paradigms with time-dependent components – behavioral tagging and retroactive interference – in order to adopt a behavioral assay to test the role of Gadd45b. One example of behavioral tagging is hypothesized to enhance learning by exposure to a novel environment before weak training. Retroactive interference reduces learning due to the introduction of new or conflicting information after training disrupting an existing memory. The results were variable and did not reliably show the effect of novelty exposure on learning and memory.

Zack Weiss
Title: The Neuronal Basis of Salt Preference in *Drosophila melanogaster*
Supervisor: Dr. Yali Zhang
The ability for an organism to discern between low-salt and high-salt food sources is integral for survival. Sodium Chloride (NaCl) is a necessary part of an organism's diet, but it's ingestion must be tightly regulated, as over consumption can lead to a variety of health concerns, such as elevated blood pressure and lowered cardiovascular health. This leads to an interesting dichotomy in which low-salt foods are preferred over high-salt foods. In recent years, great steps have been made to uncover some of the mechanisms underlying salt perception in the peripheral gustatory receptor neurons of various animal models. However, questions still remain as to how organisms encode this peripheral information to generate salt preference behavior. Using *Drosophila melanogaster* as an animal model, we use the GAL4/UAS-TNT system to elucidate which neurons are involved in the salt preference circuit, and the behavioral aberrations that occur when the function of these neurons are altered.

Vanessa Weir
Title: The Role of Hindbrain Projections to the Nucleus Accumbens in Cocaine Seeking
Supervisor: Dr. Heath Schmidt
Emerging literature suggests that glucagon-like peptide-1 receptors (GLP-1R) could be a potential molecular target for novel cocaine addiction pharmacotherapies. Since activating GLP-1R in the nucleus accumbens (NAc) attenuates cocaine seeking and the nucleus tractus solitarius (NTS) is the main source of central GLP-1, we investigated the role of endogenous NTSàNAc GLP-1 projections in the reinstatement of cocaine-seeking behavior, an animal model of relapse. We utilized chemogenetic techniques to selectively activate NTSàNAc projections prior to cocaine reinstatement test sessions. Our results indicate that activating these endogenous neural circuits is sufficient to reduce cocaine seeking. Next, we pretreated rats with a GLP-1R antagonist into the NAc prior to activating NTSàNAc circuits and a reinstatement test session. Blocking GLP-1R in the NAc was sufficient to prevent the suppressive effects of activating NTSàNAc circuits on cocaine seeking. Taken together, these results indicate that endogenous central GLP-1-expressing circuits play an important role in cocaine seeking.

Levin Conference Room 250

Mahip Grewal
Title: Exploring the Genetic Architecture of Autism: The Relationship Between Polygenic Risk Score and Quantitative Phenotypes
Supervisor: Dr. Edward Brodkin
Autism spectrum disorder (ASD) is a phenotypically heterogeneous neurodevelopmental disorder characterized by impairments in social communication and restricted, repetitive behaviors. In the current study, probands with ASD and/or *NRXN1* mutations as well as their extended family members, undergo whole genome sequencing and complete a battery of quantitative behavioral measures. Interested in the contribution of common genetic variants, we sought to explore the relationship between polygenic risk score (PRS), a sum of trait-associated alleles across multiple loci weighted by effect size, and scores on phenotype measures. We hypothesized that probands would have higher PRS than relatives and that higher PRS would be associated with measures of elevated autistic (SRS, BAPQ), social anxiety (LSAS), or executive functioning (BRIEF) behaviors on the SRS, BAPQ, BRIEF and LSAS. Although the sample size analyzed was small, PRS for ASD appears to be positively associated with scores on both the BRIEF and SRS.

Courteney Ly
Title: Probing the Neural Basis of Courtship Behavior
Supervisor: Marc Schmidt
The neural circuit known as the "song system" in passerines has long been studied in the context of production of male song. However, this neural circuit is found to be present in non-singing females, indicating that this circuit may be involved in more than simply song production. Recent research has shown that non-singing female cowbirds are selective in the potential male suitors they respond to, only displaying interest if the male is deemed high enough quality. Studies have been conducted showing that lesions in HVC in female cowbirds leads to a decrease in the female's mate selectivity. This study utilizes electrophysiology methods to record neurons from HVC in the female cowbird with randomized playback of male songs of varying quality. We hypothesize that HVC is involved in selectivity of song perception, and therefore that we will see differences in neural firing activity in response to differing quality of song.

Mackenzie Kagan
Title: Investigation of Neurofilament Light Chain as a Potential Biomarker for Frontotemporal Degenerative Diseases
Supervisor: Dr. Murray Grossman
FTD remains a common and debilitating form of dementia, with reliable forms of diagnostic measures lacking. Four CSF biomarkers (NFL, T-tau, P-tau, and Ab42) were measured in subjects with bvFTD, CBS, PPA, and PSP. Cross-sectional biomarker levels were compared across groups, and correlations between biomarkers ansd cross-sectional/longitudinal measures of cognitive abilities were assessed. NFL levels were higher among all diagnostic groups compared to controls. Within the bvFTD group, NFL was associated with greater decline in executive functioning as measured by changes in MMSE and fluency scores. In the PPA group, NFL was associated with greater impairment in language functioning as measured by BNT scores. MRI imaging analysis showed that NFL was correlated with cortical atrophy in regions of the brain associated with disease-specific cognitive decline. Thus, NFL may serve as an indicator of FTD onset and be associated with specific domain decline related to the brain region of likely disease.

Gerardo H. Velasquez
Title: Frontoparietal Network Plasticity: Individual Differences Following Working Memory Training
Supervisor: ?
Imaging of the frontoparietal network (FPN) has revealed several markers of plasticity following long-term training. Previous studies have shown decreases in task activation and increases in functional connectivity within the FPN following training. However, studies have yet to observe these changing following short-term learning. Many studies in animal models have found myelin to be a suppressor of plasticity. The present study will utilize a ratio of T1-weighted/T2-weighted structural images to measure individual differences in myelination within the frontoparietal network. This measure of myelination will be used to predict plasticity changes following training on an auditory n-back task. Participants have demonstrated significant decreases in task activation within the FPN following working memory training. Individuals with lower myelination in the FPN also had greater decreases in task activation, and greater improvements on the n-task following training.

Abigail Katz
Title: The Developmental Progression of Higher-Order Statistical Learning in Children
Supervisor: Allyson Mackey
Humans as early as infancy can learn statistical regularities between pairwise objects and in adulthood, humans are sensitive to higher order network structure. However, it is unknown how humans go from simple pairwise associations learned during childhood to understanding complex network structures, and if this ability progresses with development. We used a modular network structure with 10 nodes in two communities to determine if children can learn an underlying network. Children were exposed to a random walk of 150 steps on this graph (of degree $k=3$), where each trial consisted of pairwise elements presented together. Participants then completed two assessments of higher-order learning. Results suggest that children detected community transitions during exposure to the graph. Higher-order learning was weakly associated with age but did not display relationships with working memory nor SES. Future work will analyze the developmental trend of network learning with a larger sample size across sites.

Levin Conference Room 357

Rachel Levinson
Title: Long Interspersed Element-1 Retrotransposons in Schizophrenia
Supervisor: Wade Berrettini, MD, PhD
Schizophrenia (SZ), a psychiatric disorder characterized by hallucinations, delusions, and cognitive impairments, affects 0.5-1.0% of the population worldwide. Despite the high heritability of SZ, estimated at 64%, the genetic etiology of SZ is poorly understood. This project investigated the role of neuronal long interspersed element-1 (L1)-induced germline mutations in increasing the risk for schizophrenia. Genomic DNA from post-mortem brain samples in the dorsolateral prefrontal cortex (DLPFC) of schizophrenic patients and controls were amplified into L1 enriched next generation sequencing libraries. L1 insertions were detected using REBELseq, a novel sequencing and analysis technique. High priority insertions, such as in genes known to be associated with schizophrenia, will be independently confirmed by PCR to determine the potential role of L1 mutations in the pathophysiology of SZ. Future analyses will examine how gene expression may be altered by these insertions and the potential role of somatic L1 mutations.

Rebecca Li
Title: Increased Norepinephrine Transmission from the Locus Coeruleus onto the CA1 of the Hippocampus Enhances the Acquisition of Aversive Memories
Supervisor: John Dani
The locus coeruleus (LC) is the main noradrenergic nucleus in the brain and has connections to a variety of structures. There has been research into the effects of LC neurotransmission on hippocampal dependent novelty memory consolidation and retrieval, but not much current data regarding its effects on aversive memory acquisition. This study aimed to investigate these effects through optogenetic activation of the LC release onto the CA1 of the hippocampus in ChR2 positive mice during contextual fear conditioning, which demonstrated that LC signaling was able to enhance aversive memory formation. The next experiment demonstrated that infusion of propranolol (β-adrenergic antagonist) into the CA1 did not result in a deficit in aversive memory when given to mice that did not receive optogenetic LC activation, but reduced the enhanced memory to control in mice that did receive LC activation.

Alexandra Croicu
Title: The Role of the Chloride Transporter KCC2 in Alcohol Consumption in Mice
Supervisor: John Dani
Alcohol use disorder (AUD) is a major public health issue and is one of the leading causes of preventable death worldwide. Our investigation into factors contributing to increased alcohol consumption revealed that the chloride transporter, KCC2, showed decreased functionality in the ventral tegmental area (VTA), a reward area of the brain, after chronic ethanol consumption. Here, we examine the effect of a KCC2-activating drug, CLP290, or serotonin 2A receptor (5-HT_{2A}R) agonist, TCB-2, in increasing KCC2 function and thereby reducing ethanol consumption in mice. CLP290 (10mg/kg, i.p.) produced no significant alteration in ethanol consumption (g/kg/2hr) or preference for ethanol relative to the vehicle-treated control group in a binge drinking model. In contrast, treatment with the 5-HT_{2A}R agonist, TCB-2 (1mg/kg, i.p.), during chronic heavy alcohol consumption, decreased preference and intake of alcohol (g/kg/24hr). Further experimentation is needed to examine potential effects of KCC2-activating drugs on VTA KCC2 after ethanol drinking.

Erica Rego
Title: Drug Seeking Behavior Contributes to KCC2 Downregulation in the VTA
Supervisor: Dr. John Dani
Currently, the exact neural mechanisms of drug addiction remain largely unknown and there are no effective pharmacologic treatments. Identifying neuronal adaptations caused by prolonged drug exposure is crucial for understanding the pathophysiology of addiction and identifying potential targets to treat substance abuse. We used rodent models of cocaine and morphine self-administration to identify drug-induced neuronal adaptations within the ventral tegmental area (VTA), a critical brain region that is involved in drug addiction. We found that cocaine and morphine self-administration dysregulates midbrain inhibitory circuitry via decreased expression of KCC2, a chloride transporter that maintains low intracellular chloride concentrations in neurons. Driven by these preliminary data, further research will measure cocaine and morphine self-administration while manipulating KCC2 activity in the VTA.

Poster Presentations

Elizabeth Feindt-Scott

Title: Validation of Impaired Fear Learning in Vulnerable Rats Following Exposure to Stress
Supervisor: Seema Bhatnagar
Stress and impaired fear extinction are defining features in the onset of posttraumatic stress disorder (PTSD). This research aimed to develop an animal model of impaired fear extinction to study extinction deficits in PTSD. It has been shown that Sprague Dawley rats subjected to chronic stress show PTSD-like deficits characterized by short-latencies (SL) to social defeat, whereas rats more resilient to stress exhibit long-latencies (LL) to the defeats (LL/resilient). However, it is unclear whether fear extinction is altered in vulnerable rats (SL/vulnerable). Both social defeat and contextual fear conditioning experiments were used to examine impairments. We hypothesized that SL/vulnerable rats would show impaired fear extinction compared to the LL/resilient. Collectively these experiments demonstrated that SL/vulnerable rats exhibit impaired extinction overtime following exposure to stressful stimuli. Further, the contextual fear experiment demonstrated that pre-determined SL/vulnerable rats exhibited increased freezing behavior at baseline, suggesting elevated fear-processes.

Maya Ganeshan

Title: Necrostatin Decreasing Cell-Death in Neuronal Organoids
Supervisor: Isaac Chen
Neuronal organoids are an integral part of neurosurgical research, and on the frontier of this research they are being used regenerate neural tissue and could be used as models of disease. A current issue with the generation of neuronal organoids, is that there is a necrotic core and it is an incredibly delicate process where cell death is common. Necrostatin and ROCK small molecule inhibitors, are tools used to inhibit cell death, and have been shown to work in other spinal cord injury and stroke cases to stop necroptosis, so it was used in this project to examine whether or not it could inhibit cell death, and increase cell health in neuronal organoid generation. Necrostatin and ROCK was applied to three different conditions: organoids that were developing, physically manipulated organoids and organoids exposed to bloods toxicity. These organoids were frozen, sectioned and stained for a variety of markers including neuronal markers, progenitor zones, and necroptosis. The efficient generation of these organoids still remains in its nascent stages, and that is why is necessary to study the most efficacious ways to promote the structure, function and health of the organoids.

Anh Cao

Title: The effect of high fat diet on DVC astrocytes and microglia in a rodent model of obesity
Supervisor: Dr. Matthew Hayes
Obesity is a public health crisis that increases the risk of illnesses such as cardiovascular diseases. Therefore, it is important to investigate the underlying mechanisms of obesity and develop better treatment. The majority of studies focused on the neuronal aspect in energy balance and hypothalamus as a critical site. However, extra-hypothalamic regions, such as the dorsal vagal complex (DVC), contribute as well and are largely understudied. My experiment aims to examine the effects of diet on DVC gliosis. Rats were maintained on either a standard chow or 60% high fat diet (HFD) followed by immunohistochemical analysis of DVC astrogliosis and microglia infiltration. Exposure to a HFD resulted in a significant decrease GFAP integrated density for both male and female rats. Conversely, HFD resulted in an increase in microglia density in solely female rats. These findings provide additional information regarding energy balance regulation, and highlight a potential sex-dependent effect of diet.

Ananya Chandra

Title: VTA and NTS oxytocin receptor activation reduces motivated aspects of feeding behavior
Supervisors: Dr. Harvey Grill and Hallie Wald
Defining the neural circuits underlying feeding regulation is important in developing effective treatments for obesity. Oxytocin (OT) is a neuropeptide that plays a role in feeding inhibition and has received attention as an obesity treatment. However, the contribution of OT receptors (OT-Rs) to motivational aspects of feeding is unknown. This study used pharmacological techniques to investigate the effects of OT-R signaling on motivational aspects of feeding. Results indicate that OT-R activation in the nucleus tractus solitarius (NTS) and the ventral tegmental area (VTA) reduces motivation to obtain sucrose. This data highlights a novel role for NTS and VTA OT-R signaling on food reward and motivation, but does not determine the endogenous role of OT-R signaling in these behaviors. Ongoing studies are exploring the endogenous role of OT-R signaling by injecting a specific oxytocin receptor antagonist to acutely block OT-Rs, as well as using an AAV shRNA to chronically knock down OT-Rs.

Poster Presentations

Jack Chen
Title: Amplification of Satiation Signaling by Melanocortin-4 Receptors (MC4Rs) in the Nucleus Tractus Solitarius (NTS)
Supervisors: Dr. Matthew R. Hayes and Postdoc: Samantha M. Fortin
Obesity has become a major public health concern since the start of the 21st century. The melanocortin system, specifically via melanocortin-4 receptors (MC4Rs), is known to regulate energy balance. Our research in rats demonstrates pharmacological modulation of food intake and body weight using MC4R agonists and antagonists delivered directly to the nucleus tractus solitarius (NTS). We aimed to next determine if MC4Rs in the presynaptic vagal afferents and/or postsynaptic NTS neurons contribute to regulation of feeding behavior and body weight control. We used an adeno-associated virus delivering Cre Recombinase to the nodose ganglia or NTS of $MC4R^{lox/lox}$ mice to knockdown pre- and post-synaptic MC4Rs, respectively. Our studies have shown that neither population is necessary for food intake and body weight control. However, ongoing work is necessary to validate our viral approach and confirm viral placement. Collectively, these studies will provide insight for the development of obesity pharmacotherapies.

Lizette Grajales
Title: Do Susceptibility to Peer Influence and Subjective Social Status Influence Drinking Behavior and Neural Reward Sensitivity in College Students?
Supervisor: Emily B. Falk
Risky alcohol consumption behaviors in college students have become a public health concern given that they are associated with decreased academic performance and negative health outcomes. Although students drink for a variety of reasons, peer pressure and social influence are known to play an important role in regulating drinking habits. The ability to resist peer influence (RPI) and perception of subjective social status (SSS) can moderate the effects of social influence such that high RPI and low SSS predict engagement in risky drinking habits. Additionally, variations in brain activity predict conformity, specifically valuation of stimuli in the ventral striatum (VS) and ventral medial prefrontal cortex (VMPFC) can change to conform to social norms. To that extent, this project utilizes self-report measures and functional magnetic resonance imaging (fMRI) to determine how susceptibility to peer influence and perception of social status shape drinking behaviors and influence reward sensitivity in the VS and VMPFC.

Arica Shepherd
Title: Brain Response to Emotionally Salient Tobacco Warning Labeling and Packaging
Supervisor: Dr. Daniel Langleben
Currently, in the United States, each package of cigarettes is accompanied by a text-only Surgeon General's warning about the health risks connected to smoking. It has been proposed that text accompanied by emotionally-salient images will be more effective in delivering these health warnings. This on-going study serves to ascertain what areas in adult daily smokers' brains respond to first-time and long-term exposure to graphic warning labels surrounding smoking (GWLs). The GWLs exist in low and high emotional salience. This study will be looking into possible correlations between brain response in areas of interest (amygdala, prefrontal cortex, etc.) and the emotional salience level of the label, low or high, and grey matter density in areas of interest in the brain.

Grace Lee
Title: Age, Sex, and Repeated Measures Effects on the Validity and Reliability of NASA's "Cognition" Test Battery in STEM-Educated Adults
Supervisors: Ruben C. Gur, Ph.D.
Cognition is a neurocognitive test battery created at the University of Pennsylvania Department of Psychiatry and adapted by the National Aeronautics and Space Administration (NASA). It comprises ten neurocognitive tests that examine multiple domains, and has previously been validated in a normative sample of STEM-educated adults and compared to NASA's previous operational battery, WinSCAT. This study follows the original sample to assess Cognition's test-retest reliability and age, sex, and time effects on performance. Results from the second time point largely matched predictions; performance on both Cognition and WinSCAT decreased with age but increased with repeated administration due to practice effects, and males had higher scores than females on tasks that required vigilant attention, spatial reasoning, and risk-taking behaviors. Assessment of test-retest reliability showed a higher mean intra-class coefficient for Cognition accuracy than that of WinSCAT, supporting Cognition as a broader yet reliable measure of spaceflight-relevant cognitive performance.

Poster Presentations

Levin Lobby - 1st Floor, 12:15 – 1:30pm

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1. Elizabeth Feindt-Scott
2. Maya Ganeshan
3. Anh Cao
4. Ananya Chandra
5. Jack Chen
6. Lizette Grajales
7. Arica Shepherd
8. Grace Lee
9. Emma Rodney
10. Christeen Samuel
11. Brigette Baella
12. Dejana Cotton-Samuel
13. Nikita Shadani
14. Celine Cumming

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15. Ryan Leone
16. Vanessa Weir


Penn
Arts & Sciences

Poster Presentations

Emma Rodney
Title: Induction of the Earliest Effects of Alzheimer's Disease through Mitochondrial Damage and Oxidative Stress
Supervisor: Dr. Sigrid Veasey
Sleep deprivation is a common issue that is becoming more prevalent. We know lost sleep results in injury to specific neurons and induces consequences in the brain similar to the earliest consequences of Alzheimer's disease (AD). Our previous work suggests that mitochondrial metabolic stress, specifically induced by sleep loss, is responsible for these consequences. However, it is unknown whether this stress can temporally advance significant neurodegeneration and AD. We hypothesized that mitochondrial metabolic system damage mimics our findings in chronic short sleep. For this study, we developed a mouse model combining APP^{NL}, a knock-in model of AD that increases Ab42 peptide, with NDUFS4, a genetic knock-out that mimics human mitochondrial Complex I disorders. We examined memory, Ab42, and glial responses in young adult mice. Compared to mice with just one mutation, we found that mice with both mutations fail memory tests, demonstrate more Ab42 aggregation, and experience more glial compromise.

Christeen Samuel
Title: Neurocognitive Signature of Resilience in Youth
Supervisors: Dr. Ruben Gur & Dr. Ran Barzilay
Exposure to traumatic stress in early life is common and poses a major challenge to an individual's psychological and physiological homeostasis. Nevertheless, many children and adolescents who have experienced substantial life stressors do not develop significant psychopathology. These individuals are often characterized as resilient. While many studies on resilience focus on the psychosocial and behavioral phenotypes, a rigorous picture of the role that neurocognitive function may play in resilience continues to be elusive. In our study, we examined whether trauma exposure may trigger a response that interacts with an individual's neurocognitive function to potentially protect against or precipitate the development of psychiatric symptoms of mood and anxiety. Using a 2x2 design of High/Low Traumatic stress exposure; High/Low Psychopathology, we aimed to identify neurocognitive measures that are associated with resilience in youth from the Philadelphia Neurodevelopmental Cohort. We used Penn's Computerized Neurocognitive Battery (CNB), which assesses a host of cognitive abilities: 1) executive function; 2) episodic memory; 3) complex cognition; (4) social cognition.

Brigitte Baella
Title: Corazonin expression and dominance behavior in *D. melanogaster*
Supervisor: Roberto Bonasio
Neuropeptides are short-chain polypeptides that act as messengers between neurons and help regulate social and reproductive behaviors. The neuropeptide corazonin alters social and reproductive behaviors, such as hunting and egg laying in the eusocial insect *Harpegnathos saltator*. Overexpression of corazonin increases hunting behavior and decreases egg-laying, while knockdown induces the opposite effects. The model organism *Drosophila melanogaster* also displays the same behavior changes with both overexpression and knockdown of corazonin. In addition to these behavior variations, *Drosophila* show different levels of dominance behavior between mated and virgin organisms, with mated flies showing increased aggression. However, corazonin levels in mated and virgin flies as it relates to aggression behavior has not been determined. Using behavioral assays and qPCR, we will compare behavior in wild-type flies between virgin and mated and correlate it to expression levels of corazonin.

Dejania Cotton-Samuel
Title: Conformation-selective tau monoclonal antibodies as a potential therapeutic strategy for Alzheimer's disease (AD) and other tauopathies
Supervisor: Virginia M.-Y. Lee
Accumulations of the microtubule stabilizing protein, tau, are characteristic of multiple neurodegenerative tauopathies including Alzheimer's disease (AD), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), and Pick's Disease (PiD). In these diseases, tau becomes hyperphosphorylated and dissociates from microtubules which leads to accumulations and tangles of the protein in the brain. Studies suggest that the pathological tau protein also acts as a seed that initiates the aggregation of tau protein when it is transferred to previously unaffected cells. The use of anti-tau monoclonal antibodies (mAbs) is a promising approach to prevent the spread and aggregation of tau protein, however, the mechanisms of tau mAbs have not been thoroughly categorized. We have conducted assays to optimize two conformation-selective tau antibodies, DMR7 and SKT82, have quantified their ability to block the uptake of tau fibrils and to inhibit seeded tau aggregation in primary mouse neurons.

Poster Presentations

Nikita Shadani
Title: Pharmacological Activation of the Potassium-Chloride Cotransporter KCC2 as a Potential Therapeutic for Alcohol Use Disorder
Supervisor: Dr. John Dani
Alcohol use disorder (AUD) is a neuropsychiatric disease characterized by habitual, uncontrollable alcohol use that can ultimately lead to alcohol dependence. There are many risk factors for AUD, including stress and prior alcohol abuse. Identifying the neural substrates of these risk factors will aid in treating AUD. Among these, downregulation of the neuron-specific potassium-chloride cotransporter 2 (KCC2) in the brain's mesolimbic pathway regulates alcohol intake in rodents that have experienced stress and may promote chronic consumption of alcohol. Thus, correcting KCC2 function could serve as a novel form of AUD therapy. I am studying the effects of a KCC2-activating drug known as TCB-2 during ongoing heavy alcohol consumption in mice. TCB-2 is an agonist for the serotonin 2A receptor (5-HT_{2A}R), and 5-HT_{2A}R activation has been shown to increase KCC2 function when it is impaired. As such, targeting this receptor could be a future intervention for treating people suffering from AUD.

Celine Cumming
Title: Investigation of Mechanisms for Ghrelin's Action in the Hindbrain
Supervisor: Harvey Grill
Hindbrain Ghrelin Receptor activation increases willingness to work for food
Obesity, a major epidemic in the U.S., is largely caused by increased food intake, making the study of intake control important for treatment development. Food intake is mediated by neural systems processing signals of energy availability, including the peptide, ghrelin. Fourth (hindbrain) ventricle ghrelin receptor (GHSR) activation induces hyperphagia. However, it is unknown whether this is driven by inhibition of satiation signals and/or heightened motivational drive. To investigate how GHSR activation increases food intake, we tested whether hindbrain GHSR activation attenuates the intake inhibitory effect of a satiating preload and increases sucrose self-administration under a fixed ratio 5 (FR5) operant paradigm. We found that hindbrain GHSR activation did not attenuate the intake inhibitory effects of a preload, however, did significantly increase willingness to work for food in FR5, suggesting that the intake stimulatory actions of hindbrain GHSR activation are mediated in part by an increase in appetitive or motivational drive.

Ryan M. Leone
Title: Evaluating Neurophysiological Metrics of Synchrony in Athletic Teams to Predict Performance
Supervisors: Dr. Michael Platt and Dr. Scott Rennie
Physiological synchrony, represented by coupled oscillations of biological rhythms like neural activity across individuals in a group, is thought to be strongly related with group performance. However, most work on synchrony has been done outside of real-world, athletic settings. This project sought to collect electroencephalography, breathing rate, and heart rate measurements from student-athletes on Penn's Varsity Lightweight Rowing team to determine how physiological synchrony relates to athletic performance. The experiment was conducted over five trials, in which groups of four rowers participated in an erg machine workout in three workout conditions; yoked together, side-by-side but unyoked, and separated. After each condition, objective performance metrics from the machines and subjective ratings of flow from participants were collected. Preliminary findings suggest that we can predict heart rate synchrony based on the workout condition and that the degree of movement synchrony correlates with physiological synchrony. Performance and EEG data are currently under analysis.

Vanessa Weir
Title: The Role of Hindbrain Projections to the Nucleus Accumbens in Cocaine Seeking
Supervisor: Dr. Heath Schmidt
Emerging literature suggests that glucagon-like peptide-1 receptors (GLP-1R) could be a potential molecular target for novel cocaine addiction pharmacotherapies. Since activating GLP-1R in the nucleus accumbens (NAc) attenuates cocaine seeking and the nucleus tractus solitarius (NTS) is the main source of central GLP-1, we investigated the role of endogenous NTSàNAc GLP-1 projections in the reinstatement of cocaine-seeking behavior, an animal model of relapse. We utilized chemogenetic techniques to selectively activate NTSàNAc projections prior to cocaine reinstatement test sessions. Our results indicate that activating these endogenous neural circuits is sufficient to reduce cocaine seeking. Next, we pretreated rats with a GLP-1R antagonist into the NAc prior to activating NTSàNAc circuits and a reinstatement test session. Blocking GLP-1R in the NAc was sufficient to prevent the suppressive effects of activating NTSàNAc circuits on cocaine seeking. Taken together, these results indicate that endogenous central GLP-1-expressing circuits play an important role in cocaine seeking.