BRAIN AND BEHAVIOR
Session Moderator: Sam Golden, Biological Structure
MGH 258
3:45 PM to 5:15 PM

* Note: Titles in order of presentation.

Using Radio Frequency Identification (RFID) Group-Housing Cages to Classify Substance Use in Mice
Katrina Wong, Senior, Neuroscience
Mary Gates Scholar
Mentor: Abigail Schindler, Psychiatry and Behavioral Sciences, VA Puget Sound Health Care System

Blast exposure via detonation of explosives is a major source of trauma for service members, Veterans, and civilian bystanders, resulting in mild traumatic brain injury, post-traumatic stress disorder, and chronic pain. The combination of these effects characterizes the polytrauma clinical triad and is a risk factor for increased substance use and substance use disorder (SUD). Exposure to polytrauma can result in disparate symptom trajectories. Research focused on understanding how distinct symptom trajectories map onto substance preference and SUD risk is the focus of my project. In order to understand the interactions between polytrauma and SUD risk, I use a rodent model that utilizes custom, in-house-built polysubstance self-administration chambers to measure water, alcohol, and fentanyl intake. Two types of tracking are used to monitor drinking: Radio Frequency Identification (RFID) tracking and the volumetric drinking monitor. With these two tracking types combined, we can see which mouse drinks what liquid for what period of time. For this project, I used C57Bl/6 male and female mice aged 9 weeks on arrival. These mice were then single or group-housed in the RFID cages for one week to monitor drinking patterns. Previously, I have tested 48 mice, and found that when one (fentanyl or alcohol) substance was available, mice that were single-housed drank more substance than mice that were group housed. To continue this project, I plan to test fentanyl and alcohol in the same cage, which can give us valuable insight into substance preference and polysubstance use, making it more representative of the human experience, as many people consume multiple drugs at the same time. I also plan to look into sex differences and see how that could alter substance use. These factors combined will give valuable insight into classifying substance use that can lead to more optimized treatment for Veterans with polytrauma.

Changes in mRNA Expression After Incubation of Craving
Sarah Ransom, Senior, Medical Laboratory Science
Mary Gates Scholar
Mentor: John Neumaier, Psychiatry
Mentor: Phillip Silva, Psychiatry and Behavioral Sciences

The nucleus accumbens core (NAc), among other brain regions, plays a key role in drug seeking behavior and relapse, particularly in determining incentive value as cocaine consumption escalates. Neurons in this region have two genetically-distinct output projections which form the direct and indirect pathways, D1 and D2 respectively. My experiment is based on the Incubation of Craving model, in which animals show increased drug seeking after a period of abstinence from self-administered cocaine. The behavioral side of this project seeks to better understand how these two pathways contribute to drug seeking behavior following a period of forced abstinence, and I am also investigating how RNA translation changes in and between the direct and indirect pathways following the escalation of cocaine taking and incubation of craving by forced abstinence. I used a transgenic line of rats expressing the Cre-Recombinase enzyme in the D1 and D2 medium spiny neurons (MSNs) to selectively express and manipulate MSNs in the direct and indirect pathways. I bilaterally injected either DIO-hM4Di RiboTag, DIO-hM3Dq RiboTag or a fluorescent control virus into the NAc, and the rats were catheterized during this time to allow for cocaine self-administration. The rats underwent the Incubation of Craving experiment where they experienced an acquisition and abstinence period. Once the Incubation of Craving was complete, I collected and homogenized the NAc from each subject and performed RNA purification. Then, I performed qPCR and RNA sequencing to investigate, and validate any pathway-specific changes in mRNA expression following these behaviors with the goal to discover new ther-
In the cold, the energy demands for heat production increase. My hypothesis is that ribosome-associated mRNA in synaptosomes differs from the cell bodies, with enrichment of RNAs known to be trafficked to dendrites. Additionally, I predict that incubation of craving will induce distinct patterns of RNA changes in neurons of the direct and indirect pathway.

The Contributions of the Medial Prefrontal Cortex during Spatial Reversal Learning and Spatial Probabilistic Reversal Learning
Ryan Matthew Gillis, Senior, Psychology
Mary Gates Scholar, UW Honors Program
Mentor: Sheri Mizumori, Psychology
Mentor: Kevan Kidder, Psychology, UW Psychology department

The medial prefrontal cortex (mPFC) and hippocampus (HPC) are critical structures in a network that supports spatial working memory and flexible decision making in rats. The HPC has traditionally been implicated in episodic and spatial memory, while the mPFC has been studied for roles in working memory, response inhibition, outcome evaluation, and implementation of task rules and strategies. Flexible decision making is often tested via reversal learning (RL) paradigms in rats, monkeys, and humans. However, many studies have suggested that the mPFC is not necessary for RL, and fewer studies have shown that the mPFC is crucial for specific types of RL. We elucidate the role of the mPFC in spatial RL by optogenetically disrupting the mPFC during specific task phases, or epochs, of a spatial RL task. We also perform the same epoch-specific optogenetic disruption of the mPFC during a probabilistic reversal learning (PRL) task, which is compared to RL performance data to investigate how probabilistic contingencies recruit the mPFC differentially compared to absolute contingencies. In both experiments we analyze metrics such as choice accuracy, perseverative and regressive errors, and trials per reversal. Our data suggest that RL performance is only impaired when the mPFC is disrupted during the choice epoch of our task, while mPFC disruption during any epoch of the PRL task results in performance deficits. This suggests that the mPFC is involved in decision making processes and maintenance of probabilistic reward contingencies. This study contributes to knowledge about the mPFC in reward-guided decision making and can give insight into how impaired behavioral flexibility is caused by mPFC dysfunction, which is implicated in neurological disorders including depression, schizophrenia, and others.

PVH-TH Neurons are Thermoresponsive and may be Linked to Cold Induced Hyperphagia
Rahul Kishore Chaliparambil, Senior, Neuroscience
Mentor: Jennifer Deem, Medicine

In the cold, the energy demands for heat production increase to defend core body temperature. A hyperphagic response must balance these energy costs, or body weight cannot be maintained. However, this hyperphagia may contribute to the problem of obesity in our general population, thus raising the importance of understanding the underlying neuronal mechanisms. We recently found in mouse models that agouti-related peptide (AgRP) expressing neurons located in the arcuate nucleus of the hypothalamus (ARC) are thermoresponsive and required for cold-induced hyperphagia. However, the afferent neurocircuit capable of driving AgRP neuron activity and modifying food intake drive in the cold is unknown. I recently assisted in identifying a novel population of tyrosine hydroxylase-expressing neurons located in the rostral paraventricular nucleus of the hypothalamus (PVH-TH). Using fiber photometry, we found these neurons respond similarly to AgRP neurons, increasing their activity with cold and reducing their activity in response to food-related cues. I found that hemogenetic activation of these rostral PVH-TH neurons mimics the effect of cold exposure on energy intake and elicits a modest thermogenic response. This study provides evidence for a link between thermoregulatory and food intake neurocircuitry in the mouse, setting the stage for further investigations into the role of ambient temperature on food intake drive. Because these systems are uncoupled in the setting of obesity, our findings may provide future therapeutic options for the treatment or prevention of obesity.

[Unable to Present] Sensory Integration of Olfaction and Touch in C. elegans
Rd (RD) Pant, Senior, Neuroscience
Mary Gates Scholar
Mentor: Jihong Bai, Basic Sciences, Fred Hutchinson Cancer Research Center

The goal of our research is to understand how a nervous system integrates multiple sensory inputs, such as vision, touch, and olfaction, to direct the behavior of an animal. We use the nematode C. elegans as a model system because it has a well-defined neural circuit that can process multisensory information for its survival. Here, we set up an experimental paradigm to examine how two sensory inputs interact in the living neural circuits. C. elegans is given a primary stimulus – an attractive odor – and then a secondary stimulus – a gentle touch to its body. Our hypothesis is that the reflex avoidance response to touch is modulated by the attractive drive for animals to pursue favored odor. To provide the touch stimulus, we expressed the light-sensitive ion channel ChR2 in touch receptor neurons via the mec-4 promoter and presented the worms with blue light. As a response to touch, animals reliably carry out a reversal behavior. We find that while the worm is traversing to the attractive odor, it suppresses its natural response to touch, as quantified by the proportion of worms responding to the touch. Thus, our results suggest that C. elegans is a promising system to study the integration of multiple senses. Using this system, we will determine how
neurons process complex sensory signals in living animals.

**Assessing Changes in the Strength of Corticospinal Connections After Spinal Cord Injury**

Shannon Hong, Senior, Neuroscience  
Mary Gates Scholar, UW Honors Program  
Mentor: Samira Moorjani, Physiology and Biophysics  
Mentor: Rebecca Burch, Physiology and Biophysics  
Mentor: Robert Robinson, Physiology and Biophysics

Spinal cord injuries (SCIs) produce motor impairments that have devastating consequences for the independence and quality of life of affected individuals. These impairments result from the weakening of connections between the cerebral cortex and the spinal cord. Therefore, there is an ongoing need to develop interventions that strengthen corticospinal connections post SCI. Our laboratory focuses on a hybrid intervention that combines intraspinal neuromodulator delivery with use-dependent physical rehabilitation, which increases motor performance after SCI. However, the mechanisms behind this recovery remain relatively unexplored. Our project aims to address this knowledge gap by using evoked potentials (EPs) as biomarkers to quantify the strength of neuronal connections. EPs represent electrical responses in the brain to stimuli. Following a stimulus event, measuring the EP amplitude allows us to assess the strength of neuronal connections. For our experiment, we will implant chronic cortical and spinal microwire arrays in adult rats with chronic cervical SCI and conduct weekly recording sessions before, during, and after a 6-week therapy period. We will then compare changes in the size of EPs recorded during these sessions. We will also assess motor recovery through behavioral scores on a forelimb reach-and-grasp task, which the cervical cord injury directly impairs. We hypothesize that our interventions will strengthen corticospinal connections damaged by the injury, as manifested in a correlation between an increase in EP amplitudes and changes in motor performance. Ultimately, results from our experiments will help us understand how physical rehabilitation and targeted delivery of neuromodulators mediate recovery of the damaged central nervous system. We also hope our project will inform future rehabilitation strategies targeting SCI.

**Vagus Nerve Stimulation as a Therapy for Blast TBIs**

Emma S Skillen, Senior, Psychology  
Mary Gates Scholar  
Mentor: Abigail Schindler, Psychiatry and Behavioral Sciences, VA Puget Sound Health Care System  
Mentor: Britahny Baskin, Neuroscience, Seattle Children’s Research Institute/UW

Traumatic brain injuries (TBIs) are a major cause of disability among war veterans, leading to behavioral dysfunction and post-concussive symptoms such as depression, anxiety, pain, and substance abuse. These symptoms are thought to be caused by neural inflammation combined with a malfunctioning autonomic nervous system following injury, called dysautonomia. Dysautonomia leads to changes in heart and respiratory rate, increased fatigue, and has been shown to be able to predict future behavioral outcomes such as depression. Vagal nerve stimulation (VNS) is currently being examined as a treatment for blast trauma, as the vagus nerve helps regulate the autonomic nervous system. I predict that VNS following blast exposures will reduce the neural inflammation and severity of dysautonomia following blast TBIs, in turn lessening the chronic behavioral dysfunction that normally occurs after blasts. To examine the effects of VNS on TBIs, I looked at both vital signs and behavioral dysfunction immediately and chronically following the blast. A shock tube that generates clinically relevant overpressure waves was utilized to simulate chronic (3x blast exposures (or sham exposure)) in 11-week-old C57BL/6J mice (n=5-6 per group, from two cohorts of mice). In addition to analyzing cytokine expression to determine inflammation and vital signs, several behavioral assays were run, including: operant conditioning, t-maze, y-maze, acoustic startle, and photophobia, to examine both biological and behavioral changes following blast and VNS treatment. Thus far it appears likely that the VNS treatment has lessened the severity of multiple measures of dysfunction, including pain, startle sensitization, and inflammation. This demonstrates that VNS could be a potential therapeutic for blast TBIs but further research, including running more mice to obtain a larger sample size, is necessary to draw more conclusions.