2D

BRAIN AND BEHAVIOR

Session Moderator: Steven L. Buck, Psychology

Mary Gates Hall Room 228

3:30 PM to 5:00 PM

* Note: Titles in order of presentation.

Retrograde Neuronal Tracing to Map Serotonergic Neurons Projecting from the Dorsal Raphe Nucleus to the Dorsal Striatum

Evan Carlos, Junior, Biology (General), Communication
Mentor: John Neumaier, Psychiatry
Mentor: Daniel Eskenazi, Psychiatry & Behavioral Sciences

The dorsal raphe nucleus (DRN) lies in the midbrain and provides serotonergic innervation to multiple areas in the forebrain. One of these areas is the caudate-putamen complex or dorsal striatum (DS) which current research suggests is further divided into distinct subregions. The DS has been implicated in the obsessions that characterize obsessive-compulsive disorder and other addictive behaviors. Since some of these disorders respond to medicines that target the serotonin system, we investigated the serotonergic innervation of the rat DS by stereotaxically injecting retrogradely transported red (excitation at 605 Hz) and green (excitation at 515Hz) fluospheres. We used 35 Sprague Dawley rats ranging in weight from 300-360g. The red and green fluospheres were injected at three different coordinates: anterior dorsal medial, posterior dorsal medial and dorsal lateral striatum. After a five day waiting period, to allow the tracers to reach the DRN, rats were transcardially profused and 40μm coronal sections prepared on a vibratome were mounted on slides to be viewed under a fluorescent microscope. Preliminary data show fluosphere injections in the forebrain successfully transport retrogradely to discrete regions within the DRN and we are performing stereological analysis to quantify these results. Additionally, we will be using immunohistochemistry to verify the identity of these neurons as serotonergic. As an anatomical control, fluorescent signal was detected in the substantia nigra (SN) and signal was strongest in the rostral sections of the DRN corresponding to previous literature. The visualization of discrete subregions of DRN projecting to discrete subregions of the DS provide a rationale for further analysis of this circuitry.

Validation of shRNA-Induced 5-HT1B Knock-Down Expression in Rat Reward Circuitry

Shinn Yi (Cindy) Chou, Senior, Applied Music (Orchestral Instruments), Biology (Physiology), Neurobiology
Mentor: John Neumaier, Psychiatry
Mentor: Amy Furay, Psychiatry and Behavioral Sciences

Serotonin receptor type 1B (5-HT1B) plays an important role in addictive behavior. Specifically, it has been shown to regulate the rewarding properties of drugs of abuse such as cocaine and alcohol. These receptors, present in the brain's reward pathway, are expressed on the terminals of nucleus accumbens shell (NAcSh) GABAergic neurons that project to dopamine neurons in the ventral tegmental area (VTA). These receptors modulate dopamine tone in the NAcSh via disinhibition of dopamine release from VTA neurons. To date, there is no regionally selective method for targeting this population of neurons. We explore a novel method for region-specific knockdown of 5-HT1B receptors using short hairpin RNA (shRNA) interference to degrade 5-HT1B mRNA. ShRNA constructs were designed, cloned, and tested for mRNA knockdown efficacy using HeLa cells engineered to express 5-HT1B. The most promising construct, as indicated by quantitative PCR (qPCR) data, was packaged with herpes simplex virus and injected locally to the targeted area of interest. Here we present data for the validation of the construct using various techniques, including qPCR, immunohistochemistry, and behavioral models.

Topography of the ERP Response to Faces and Objects in Infants at High and Low-Risk for Autism Spectrum Disorder

Ashley Allison (Ashley) Danies, Senior, Art (Photography), Psychology
EIP Scholar
Mentor: Sara Webb, Psychiatry & Behavioral Sciences, Seattle Children's Research Institute

Individuals with autism spectrum disorder (ASD) have symp-

toms that fall into three key domains: social, communication, and restricted or repetitive behaviors. Facial recognition may also be an area of early impairment in young children with ASD. These impairments may contribute to the difficulties with social interaction and communication found in people with ASD by disallowing normal development of early social understanding and empathy. Work with event-related potentials (ERP) has indicated that individuals with ASD may process faces more slowly than neurotypical adults, but do not have a delayed processing speed for objects. Typical development of facial recognition involves development of a special status for faces over objects, resulting in a distinguished means of processing and perceiving faces. It is my hypothesis that faces are processed similarly to objects for individuals with ASD. It is important to understand the onset of this impairment in children to better realize the progression of ASD and the implications for social impairment at the developing neurological level. One way to study the early development of face recognition in ASD is to prospectively follow younger siblings of children with ASD, who have a higher risk of developing ASD themselves. In my research I have been analyzing the differences in amplitude and topography of ERP components of electroencephalography (EEG) recordings in response to pictures of objects and faces in 6-month-old infants. Two groups of participants were tested; 18 low-risk infants who have no 1st or 2nd degree relatives with ASD, and 12 high-risk infants who have an older sibling with ASD. Infants were presented with pictures of faces and objects; the ERP components which I will analyze come from an averaging of EEG response to the pictures over many trials. My prediction is that there will be significant differences between face processing components between the two groups.

Mood Disorders and Circadian Disruption

Emma Briehl (Emma) Morris, Senior, Biology (General)
Mary Gates Scholar
Mentor: Horacio de la Iglesia, Biology

Circadian disruptions are associated with mental disease, especially depression and bipolar disorder, which is characterized by alternating periods of mania and depression. Furthermore, people doing shift work, who typically show internally desynchronized circadian rhythms, have a higher incidence of mental disease. Nevertheless no clear causal link between circadian disruptions and mental disease has been established. My project utilizes a unique desynchrony protocol that produces the stable desynchronization of circadian rhythms within the same individual. The goal of this project is to exploit this protocol to establish whether genetically and neurologically intact rats with desynchronized circadian rhythms exhibit behavioral manifestations of depression, mania or alternating mania and depression. Rats with disrupted circadian rhythms were evaluated for anxiety using the marble-burying test and the open field test, as well as for depression-like behavior using the forced-swim test (FST). The FST revealed that, compared to controls, desynchronized rats alternate between depression-like behavior, characterized high immobility, and hyperactivity, characterized by increased swimming. In the last experiment, we tested the ability of lithium, one of few successful drugs used to treat bipolar disorder, to revert the FST behavioral phenotype of desynchronized rats.

Asymmetric Weight Matrices as a Method to Resolve Binocular Neuronal Activity in a Reward Time Learning Network

Victor Duc Thang (Victor) Nguyen, Senior, Neurobiology, Biochemistry, Psychology
Mentor: Harel Shouval, Neurobiology and Anatomy

The exact mechanism of where and how our neurons come to represent our conscious perception of time (of the seconds scale) is unknown. Results by Shuler and Bear show that such a process might be possible within the primary visual cortex simply through operant conditioning. Gavornik et al. have shown that it is theoretically possible for such a network to arise through changes in only synaptic weights/strengths. Their model has been shown to work in both cases of purely monocular neurons and with overlapping binocular neurons (those that respond to visual input from both eyes versus only one). However, with binocular neurons, a modified Hebbian (learning) function is required to prevent cross contamination of non-stimulated neurons from being excited. We explored how the Hebbian function affects the weights and its subsequent role on the activity of a binocular network within the Gavornik model. We heuristically found several Hebbian functions that correct for the original contamination problem and that negative cross subset weights are required to prevent non-stimulated neurons from activating.

What you See is What you Get: Does Appearance Indicate Degree of Mental Illness?

Kelly A (Kelly) Youngberg, Senior, Psychology, Scandinavian Area Studies
Joscelyn Rose Rompogren, Senior, Psychology
Mentor: Marsha Linehan, Psychology

Borderline Personality Disorder (BPD) is characterized by interpersonal problems and suicidality, symptoms that are internal and not outwardly obvious like symptoms of more external disorders like schizophrenia. There has been little research conducted on the types of subtle body language cues that might portray such a disorder, although there are data on the presence of stigma towards mental illness (Schumacher, Corrigan, & Dejong, 2003). The current research seeks to establish whether observers can correctly identify clients with BPD who are experiencing more severe symptoms. Sixteen participants have been selected from a pool of subjects who

completed Dialectical Behavior Therapy (DBT) at the Behavioral Research and Therapy Clinics. Every client was assessed at four-month intervals using the Treatment Change Scale (TCS) measuring "severity of illness;" possible scores ranged from 1 ("Normal, not at all ill") to 7 ("Among the most ill patients"). We chose clients who improved by at least three points throughout their time in the study (24-months total). We noted the time points at which the greatest difference in scores were obtained, and gathered the video assessments for these time periods. We will show these videos to observers who will be instructed to choose, based on clients' appearance, which clip was taken when the client was experiencing severe BPD symptoms and which clip was taken during a period of symptom relief. These clips will be shown on mute in random order and observers will be blind to which clip was taken at which time point. We hypothesize that the observers will be able to correctly identify clients experiencing severe symptoms of BPD versus clients who are less symptomatic. Implications from these findings may contribute to research on stigma, since people suffering from a mental illness may be treated differently based on how they appear.