Online Proceedings

SESSION 1E

SENSORIMOTOR NEUROSCIENCE

Session Moderator: Eric Chudler, Bioengineering
234 MGH
1:15 PM to 2:45 PM

* Note: Titles in order of presentation.

Background Luminance Alters Tracking Performance of Freely Flying Hawkmoths Revealing Rariable Delays in Optomotor Processing
Robert William Hall, Senior, Biology (General)
Initiative for Maximizing Student Development Scholar, Mary Gates Scholar, Undergraduate Research Conference Travel Awardee
Mentor: Simon Sponberg, Biology
Mentor: Tom Daniel, Biology

Hawkmoths, *Manduca sexta*, feed mainly during early morning and late evening in low light conditions by hovering and tracking moving flowers. The variable lighting conditions in which the hawkmoths feed in nature allow for the perfect setting to examine how visual signal acquisition can affect the performance of motor controlled tasks. By varying the luminance levels, it could result in a change in the amount of time it takes for hawkmoths to react to visual stimuli. In other words, motion-sensing tasks, like tracking a moving flower while feeding, may vary with the background sensory environment. We tested our hypothesis with freely flying moths feeding from a robotically actuated artificial flower at a low luminance level of .3 lux and a high luminance level of 300 lux. Because the flower motion was composed of the superposition of multiple sine waves (0.2-20 Hz), we were able to examine how moths responded at different frequency levels, making it possible to reconstruct a performance pattern. The flower's movement was done in both the vertical and horizontal axes. By calculating the coherence at each frequency, gain, and phase delay, we discovered that moths reliably track at frequencies exceeding 5 Hz. As predicted, we perceived much larger processing delays from the moth's response to the flower's movement at lower luminance levels than higher. This processing delay corresponds to moths being able to perceive and react to visual stimuli 16ms faster at high luminance levels than low luminance levels. At low luminance levels, moths actually overcorrected by overshooting the flower's position at peak tracking frequencies (1-2Hz), possibly due to longer integration delays. Future experiments involve integrating two degrees of freedom by combining multiple axes. Background sensory environment significantly alters the performance of an ecologically-relevant tracking behavior as predicted from sensory neurophysiological mechanisms.

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Neuroprosthetic Rehabilitation on Rodents
Tejas Ranade, Senior, Biology (General), Political Science
Mary Gates Scholar
Mentor: Steve Perlmutter, Physiology and Biophysics

Spinal cord injury is currently only treatable to a limited extent and often involves the partial or full loss of motor function. Spinal cord injury is also believed to be a strong factor in muscle loss and motor disorientation in mammals. Recent research has suggested that electrical stimulation of affected areas of the central nervous system can play a role in restoration of the ability to control paralyzed muscles in certain model organisms. Our Neuroprosthetic Rehabilitation project is focused on improving the ability of adult Long-Evans rats to make forelimb movements, via electric microstimulation, after localized spinal cord injury. The subject rats will first undergo behavioral training to achieve aptitude at a repeated task such as using one forelimb to reach for pellets at a certain distance. Following this, suitable candidates will be subjected to unilateral, cervical spinal cord contusions and will once again attempt to reach proficiency at pellet retrieval while micro-stimulation is routinely administered during training sessions. Functional improvement in rats stimulated during the pellet retrieval task will be compared with improvement of those stimulated independently of their behavior, and those not receiving stimulation. It is hypothesized that the improvement in the former group will be more significant than that of the latter groups, but will not generalize as well to other behaviors. Significant results will be instrumen-

tal to further understanding of how a damaged spinal cord can be repaired – or the effects of injury mitigated – in people suffering from related conditions.

POSTER SESSION 2

Commons East, Easel 61

12:45 PM to 2:15 PM

Spinal Cord Injury Rehabilitation Using Stimulation and Chondroitinase to Enhance Forelimb Function

Jan Andrew (Jan) Jimenez, Freshman, Pre-Sciences
Mentor: Chet Moritz, Physiology & Biophysics

Research in our lab has demonstrated that stimulation of the spinal cord may enhance rehabilitation and restoration of forelimb function after spinal cord injury. Building on previous experiments, the goal of this project is to see how the combination of Chondroitinase (a treatment of enzymes) and spinal stimulation could promote the recovery of forelimb function in rats with chronic spinal cord injury. We trained animals on a skilled forelimb reaching task and determined their dominant hand. Once trained to proficiency, animals received a contusion injury to the lateral aspect of the 4th and 5th cervical segments resulting in paresis of their dominant forelimb. Animals were then randomly assigned to groups receiving stimulation, Chase treatment, or the combination of the two treatments. We are conducting a battery of forelimb functional tests, including skilled forelimb reaching, each week for the duration of the study in order to record their progress and observe their improvement using the injured forelimb. It is the anticipated result that the addition of Chonroitinase during rehabilitation will result in an increase of the formation of synapses in circuits bypassing the lesion, which may be investigated using neuroanatomical tracing techniques. If successful, our results can be utilized in human medicine to improve the healing of a spinal cord-related injury and promote rehabilitation.

POSTER SESSION 2

Commons East, Easel 60

12:45 PM to 2:15 PM

Synergistic Effect of Combining Chondroitinase and a Novel Peptide Treatment with Intraspinal Microstimulation in Adult Rat Spinal Cord Injury

David Alexander (David) Boe, Senior, Neurobiology
Mentor: Chet Moritz, Physiology & Biophysics

Cervical spinal injury can result in a loss of function in the hands and arms. Restoration of hand and arm function is nearly 5-fold more important to patients than restoration of other functions. A major difficulty in restoring function lies in overcoming the formation of perineuronal nets (PNNs) and the accumulation of chondroitin sulfate proteoglycans (CSPGs), which contribute to the scar around the lesion site. The disruption of CSPGs in both the scar and PNNs is possible with Chondroitinase ABC (ChABC), and more chronically, through the use of a novel intracellular sigma peptide (ISP). The inhibition of CSPGs allows for axonal regeneration, which may be guided through the use of intraspinal microstimulation (ISMS). Preliminary results shows that the combination of these approaches act synergistically, leading to much greater recovery than through ChABC and ISMS alone. Functional recovery is assessed through a series of behavioral tests, including a trained forelimb reaching task and the Irvine, Beatties & Bresnahan test (IBB). These behavioral tasks are designed to measure attributes that are important for upper limb rehabiliation, such as spasticity, ability to grasp, movement in the wrist and digits, and plantar contact. If successful, this treatment may be used to rewire spinal circuits around a lesion and restore function below the site of the lesion.

POSTER SESSION 3

Balcony, Easel 117

2:30 PM to 4:00 PM

Detection and Quantification of Nicotinamide Adenine Dinucleotide (NAD) by Method of NMR Analysis

Amir Safi (Amir) Ali, Junior, Biochemistry
Initiative for Maximizing Student Development Scholar, McNair Scholar
Mentor: Kevin Conley, Radiology
Mentor: Eric Shankland, Radiology

Nicotinamide adenine dinucleotide (NAD) is used in many biological processes such as metabolism and cellular signaling. Recently NAD is found to have an important role in many signaling pathways. As NADs role in cellular pathways is being discovered, it is important to be able to detect and quantify the amount of NAD in vivo and in vitro by nuclear magnetic resonance (NMR) analysis. NAD is found in cells at low concentrations and its peak intensity in a phosphorus spectrum is much smaller than that of other phosphorus containing molecules like ATP. By decoupling and Insensitive Nuclei Enhanced by Polarization Transfer (INEPT) experiments we hope to isolate and increase the signal of the characteristic phosphorus nuclei found in NAD molecules. Isolating and increasing the signal to noise of the NAD peak will prove that we have the right peak and allow us to quantify the amount of NAD in vivo. This will provide information about health risks of a subject.

POSTER SESSION 4

MGH 241, Easel 166

4:15 PM to 5:45 PM

Operant Conditioning using Deep Brain Stimulation of the Medial Forebrain Bundle to Modulate Brain Activity to Receive a Dopamine Reward

Siobhan Elizabeth (Siobhan) Brosnan, Senior, Biology (Physiology)
Mentor: Eberhard Fetz, Physiology & Biophysics

Many individuals with severe depression experience chronic symptoms despite the aid of pharmacological interventions. This population may benefit from further interventions such as deep brain stimulation (DBS). Indeed, promising studies have illustrated the antidepressant effects of DBS on brain reward centers in patients with severe depression. However, these studies are limited by a lack of regulation of DBS delivery. We proposed that stimulation may be more effective if it is not delivered continuously, but only when needed. For example, DBS could be given when some physiological measure of depression increases. Therefore, we sought to provide proof-of-concept that an animal could learn to volitionally modulate a specific neural signal in order to receive DBS. To accomplish this goal, we used an operant conditioning paradigm wherein a rat gradually learns to volitionally modulate brain activity recorded from the surface of the cerebral cortex. The reinforcement consists of electrical stimulation in an area of the brain known as the medial forebrain bundle (MFB). When activated by electrical stimulation, neurons coursing through the MFB release dopamine, creating a strong reward sensation. We associated activity-dependent stimulation with a green light which served as an external cue to the rat. DBS was delivered only during times in which this light was on. Initially, results revealed that the production of the intended behavior was not correlated with the external cue. Over the course of repeated experimental sessions however, the desired neural activity became dramatically elevated during periods of activity-dependent stimulation. This finding suggests that through repetitive conditioning, the animal did in fact learn to volitionally control the neural signal to receive MFB stimulation. Despite these encouraging early findings, future work to determine the long term effects of DBS, as well as the optimal stimulation parameters, will be critical to the ultimate clinical implementation of this technology.

POSTER SESSION 4

MGH 241, Easel 150

4:15 PM to 5:45 PM

Mapping *Kiss1* Gene Expression in the Mouse Brain

Paige Haas, Sophomore, Biology (Molecular, Cellular & Developmental)
Mentor: Robert Steiner, Obstetrics And Gynecology
Mentor: Don Clifton, Obstetrics And Gynecology
Mentor: Simina Popa, Molecular and Cellular Biology
Mentor: Caroline Cho, OB/GYN

The *Kiss1* gene encodes a neurotransmitter whose expression in the brain is essential for reproduction. Previous studies with *in situ* hybridization and immunocytochemistry have identified *Kiss1* expression in several hypothalamic nuclei, including the arcuate. To determine whether *Kiss1* expression is limited to the hypothalamus, we developed a transgenic mouse that expresses a marker gene (*tdTomato*) if and only if *Kiss1* expression is turned on. *tdTomato* encodes a red marker protein that is constitutively expressed, labeling the cell forever as having once expressed *Kiss1*. We looked for tdTomato labeling in brain sections to identify areas that reveal expression of *Kiss1* at some time during development. Surprisingly, we found tdTomato labeling outside of the hypothalamus. Possible causes include *Kiss1* expression early in development or low-level *Kiss1* expression in adulthood. Distinguishing between these possibilities has important implications for developing tools to genetically manipulate Kiss1 neurons in adult animals. We will test the hypothesis that *Kiss1* is widely expressed at low levels in the adult brain. *Kiss1* transcription will be mapped in two ways. First, brain sections will be examined for the presence of green fluorescent protein (GFP). GFP is expressed under the *Kiss1* promoter, but it may not mark low levels of *Kiss1* transcription. Therefore, *Kiss1* expression in adulthood will also be tested by *in situ* hybridization. *In situ* hybridization radioactively marks *Kiss1* mRNA, illuminating even low levels of transcription. Comparing *in situ* hybridization between wild-type and Kiss1 knockout mice may reveal low levels of *Kiss1* mRNA outside the adult hypothalamus— and open new possibilities for a physiological role of *Kiss1* signaling that extends beyond reproduction.

POSTER SESSION 4

MGH 241, Easel 168

4:15 PM to 5:45 PM

Characterizing Neuronal Cell Survival of the Anteroventral Cochlear Nucleus in a Unique Mouse Model of Deafness

Samantha Joyce (Sam) Motley, Senior, Biology (General)
Mary Gates Scholar
Mentor: Edwin Rubel, Otolaryngology, Head and Neck Surgery
Mentor: Melissa Strong, Otolaryngology

In the auditory system the first site of neuronal auditory processing occurs in the cochlear nucleus (CN). All vertebrates studied to date depend on afferent sensory input during a critical period of young life for the normal development of the CN. We are investigating the intercellular and intracellular signaling pathways that lead to neuronal cell death (or survival) following the elimination of sensory input to the mammalian CN using a unique mouse model for deafness. The mouse variant (DTR) has a gene that codes for diphtheria toxin (DTx) sensitivity inserted behind the promoter that con-

trols sensory hair cells. Wildtype mice will have no response to DTx but the DTR mice will have their sensory hair cells destroyed after an injection of DTx. The mice are injected with DTx at 5 days and 30 days of age. At 2 days post injection the majority of the sensory hair cells in the cochlea are destroyed. At the appropriate survival times, 6 and 10 days, the mice will be anesthetized and perfused with paraformaldehyde. Brain tissue will be collected and stained and we will be employing several visualization techniques to quantify and characterize different cell populations in the tissue. We predict that the DTR mice receiving DTx injections will show significantly more neuronal death in the CN as compared to any of the control groups. The amount of cellular death shown will depend on the age at which the mouse received the DTx injection, with younger mice showing increased cell death and the mice of 14 days and older showing less cell death with the neuronal survival rates being dependent on the age at which they received the DTx injection. And thus we will be able to specify more exactly the critical period regarding neuronal survival in the CN of this mouse variant.

POSTER SESSION 4

MGH 241, Easel 171

4:15 PM to 5:45 PM

Spinal Cord Injury Treatment: ECoG-Based Spinal Stimulation with Activity-Dependent Physical Therapy

Alison Yik Hei (Alison) Chan, Senior, Sociology, Biology (Physiology)

Mary Gates Scholar

Mentor: Steve Perlmutter, Physiology and Biophysics

Mentor: Jacob McPherson, Physiology and Biophysics

In Perlmutter lab's ongoing study, a combination of activity-based motor training and EMG-triggered electrical spinal stimulation is used as therapeutic intervention for rats with spinal cord injuries (SCI). In addition to the reach training being a form of physical therapy, electromyogram (EMG) electrodes are implemented into rat's impaired arm and on the spinal cord area that receives related motor commands from the brain. By detecting electrical potentials produced by the skeletal muscle, the electrodes then carry out electrical stimulation on the spinal cord. In response to repetitive and consistent transmission from a presynaptic neuron to a postsynaptic neuron, the connection between two neurons is reinforced as a result of Hebbian "plasticity" or the ability to strengthen or create new synaptic connections with the associated neurons. Although preliminary data suggested greater functional recovery in this novel intervention, many rats did not recover fully. This may be due to discrepancies in the timing between the EMG and the descending command arrival in the spinal cord, preventing optimal timing of the electrical spinal stimulation. In my proposed experiment, I hypothesize that triggering the electrical stimulation from the source of the descending motor commands, the brain, rather than from residual muscle activity will enable better synchronization of the stimulation, hence optimizing the intervention. Instead of EMG electrodes, electrocorticographic (ECoG) electrodes that are designed to detect brain electrical activity will be implanted on the surface of the brain. During the 12-week intervention along with the reaching exercise, a device called the Neurochip will record and trigger the stimulation of spinal cord. The ECoG technique may provide a less noisy signal by recording directly from the brain and enable a better estimate of the occurrence of spinal stimulation, thus maximizing the therapeutic potential of the intervention.