First Author: Heather Acuff (Graduate)	Poster Session: am
Presenting Author: Heather Acuff (Graduate)	Location: 1
Mentor/Lab: Dr. Mary Phillips	Category: Imaging Techniques
Department: Psychiatry	

Title: Determining Relationships between White Matter Structure and Function in Offspring at Risk for Bipolar Disorder: The Bipolar Offspring Study

Summary: Bipolar Disorder is a serious psychiatric disorder that is difficult to distinguish from other psychiatric disorders particularly in children. We examined relationships between brain structure and function in order to identify relationships that distinguish children at risk for Bipolar Disorder compared to children at risk for other disorders. We found that the relationship between forceps minor structure and activity in the cingulate cortex significantly distinguishes these two groups and may be a marker of risk for developing Bipolar Disorder.

Abstract: Early detection of Bipolar Disorder (BD) risk is critical for targeting interventions to delay or prevent illness onset. Yet the absence of objective BD biomarkers makes accurately identifying at-risk youth difficult. Recent studies have identified abnormalities in white matter (WM) structure and activity in emotion processing neural circuitry in BD at-risk youth. We aimed to elucidate WM-activity relationships in BD at-risk youth and determine how they differentiated youth at genetic risk for BD from youth at risk for other disorders. Offspring (ages 8-17) of parents with BD (OBP n=32) and offspring of parents with non-BD disorders (OCP n=30) underwent diffusion tensor and functional magnetic resonance imaging while performing an emotional face processing task. Elastic net regression analyses included GROUP(OBPOCP)xWM interactions as main independent variables and emotion processing activity as dependent variables to determine significant group differences in WM-activity relationships. 14 variables explained 16.5% of the variance in amygdala and prefrontal cortical activity to happy faces including 8 GROUPxWM interactions. Significant group differences in slopes (inverse for OBP positive for OCP) were found for relationships between right cingulum length-caudal anterior cingulate activity ($p=0.024$) and forceps minor radial diffusivity-rostral anterior cingulate activity ($p=0.014$). Only the between-group difference in forceps minor-activity remained significant in unmedicated youth without psychiatric disorders ($p=0.017$). WM-activity relationships significantly distinguish BD at-risk youth from youth at risk for other disorders and may reflect vulnerability mechanisms predisposing to future BD and biomarkers to facilitate identification of BD at-risk youth.

First Author: Arish Alreja
(Graduate)

Poster Session: am

Presenting Author: Arish Alreja
(Graduate)

Location: 55

Mentor/Lab: Christopher J. Rozell (Georgia Tech - Sensory Information Processing Lab) Ilya Nemenman (Emory University - Department of Biology)

Category: Brain Models and Systems

Department: Electrical Engineering (Georgia Tech) Biology (Emory University)

Title: Optimal E:I cell ratios in efficient coding models of V1 under volume constraints

Summary: Two different classes of neurons (those which excite other neurons and those which inhibit) are found in the brain. They account for different fractions of the neural population in different species (10-25% Inhibitory Neurons). The computational role of each type of neuron and factors governing this proportion remain an open question. In this work we use a biologically plausible model of vision and place it under a neural constraint (size of the neural population) to understand the computational principles that govern the balance between Excitatory and Inhibitory Neuron sub-populations in cortex.

Abstract: The inhibitory interneuron population plays an important role in shaping cortical activity but much remains unclear about its specific role in neural coding. While some theoretical models postulate the need for balanced excitatory and inhibitory activity we lack an understanding of why cortical E:I cell ratios in different species are consistently in a range from 2:1 - 9:1. Understanding the principles underlying E:I ratios may help illuminate the role of inhibition in cortical circuits. Recent efficient coding models of vision include explicit inhibitory interneurons with biologically observed E:I ratios and interneuron tuning properties. While similar models show that increasing the number of excitatory and inhibitory cells improves the quality of stimulus representation current models do not account for the fact that volume is a heavily constrained resource. Though both excitatory and inhibitory cell types are valuable for neural coding a fixed volume constraint means that increasing the size of one neural subpopulation necessitates decreasing the size of the other. We implement an efficient coding model of vision under a volume constraint that fixes the total population size while varying the E:I ratio. We show that the quality of the stimulus representation is optimal at biologically observed E:I ratios which can be interpreted as balancing the trade-off between computational accuracy and representation capacity for natural stimuli. This potentially provides a normative account for observed cell type distributions in sensory cortex as optimizing coding fidelity under a volume constraint. Further our model suggests that specific optimal E:I ratios within biophysically observed ranges are proportional to population sparsity with higher optimal E:I ratios observed for sparser population activity. This prediction is supported by recent electrophysiology recordings of large populations in V1 under natural scene stimuli for multiple species.

First Author: Yashar Aucie (Graduate)	Poster Session: am
Presenting Author: Yashar Aucie (Graduate)	Location: 15
Mentor/Lab: PittMotion Lab / Gelsy Torres-Oviedo	Category: Brain-Machine Interfaces
Department: Bioengineering	

Title: Innovative shoes induces locomotor learning correcting step asymmetry

Summary: we have developed a pair of portable shoes that enables the adaptation of step length asymmetries during over ground walking. This can help us improve the gait of post-stroke patients more efficiently.

Abstract: There is a clinical interest to correct step length asymmetry post-stroke (i.e. limp) because it impairs patients' mobility. Promising studies have shown that stroke survivors recover gait symmetry after walking on a split-belt treadmill that augments their step asymmetry by moving the legs at different speeds. However the transfer of gait improvements to over ground walking is limited. We hypothesize that gait improvements would be more general if we could induce locomotor learning by augmenting step asymmetry like split- belt treadmills while walking over ground. Thus we developed a portable device called Nimbus which are motorized shoes that can move the legs at different speeds while walking over ground. In this study we determined if the Nimbus shoes could induce similar gait adaptation effects to those observed on the split-belt treadmill. Thus we compared walking kinematics between subjects wearing the Nimbus shoes on a regular treadmill (n=7) vs. walking on a split-belt treadmill (n=7). Both groups experienced an adaptation period when the legs move at different speeds. Positions from the ankle and the hip were collected bilaterally and used to compute step length step position and step time asymmetry which are known to adapt during split-belt walking. These parameters were used to contrast between groups 1) the extent of adaptation (i.e. changes in gait from early to late adaptation) and 2) the magnitude of after-effects (i.e. changes in gait before and after the adaptation period). Overall the Nimbus group exhibited locomotor adaptation and after-effects like the split-belt group. Both groups had same extent of adaptation ($p>0.153$ for all parameters) and same after-effects ($p>0.071$for all parameters). In sum our results indicate that the Nimbus shoes are portable devices that can induce error-based locomotor learning as split-belt walking which is holds the great promise of inducing locomotor learning in patients that will improve their gait during real-life situations beyond the clinic.

First Author: Brett Bankson (Graduate)	Poster Session: am
Presenting Author: Brett Bankson (Graduate)	Location: 4
Mentor/Lab: Laboratory of Cognitive Neurodynamics Avniel Ghuman	Category: Imaging Techniques
Department: Psychology	

Title: Temporal Evolution of Abstract Visual Representations

Summary: Visual object recognition occurs rapidly in humans with perceptual and conceptual knowledge available in the first several hundred milliseconds of viewing an object. Novel analysis techniques allow us to view on a millisecond basis these patterns of neural activity from MEG data and make predictions about how temporal information evolves from purely visual to conceptual in nature. Using complex representational models derived from behavior and deep neural nets we plot the emergence of object concept representations that are behaviorally relevant and share information with other similar concepts.

Abstract: Object recognition in the human visual system is a dynamic process that evolves rapidly from representations of low-level visual features to behaviorally relevant concepts. Previous work characterizing the temporal progression of object representation has incorporated predictions from category structure semantic feature norms and fMRI-MEG fusion to identify recurrent processing stages during visual object recognition. We consolidate and resolve this previous work by comparing MEG signals from two independent data sets predictions from semantic and neural network models and behavior to elucidate the extent to which representational structure for object concepts can generalize across time and between exemplars. Critically the application of decoding methods and representational similarity analysis (RSA) to our data affords an unparalleled temporal resolution to the investigation of fine-grained representational structure inherent to patterns of neural activity during visual object recognition. Time course data from temporal decoding RSA and variance partitioning analyses show several latencies before 300 ms at which rapidly accessed perceptual and semantic features iteratively contribute complementary information to the emergence of abstracted conceptual representations for concrete objects. Together these methods and results highlight the emergence of conceptual representations for concrete objects within the first 250 ms of visual recognition.

First Author: Sergei Baranov (Postdoctoral)	Poster Session: pm
Presenting Author: Sergei Baranov (Postdoctoral)	Location: 35
Mentor/Lab: Friedlander R.F.	Category: Neurology & Neurodegenerative Diseases
Department: Neurological Surgery	

Title: Mitochondria controlled local caspase-3 activation in neuronal processes. Single-cell analysis

Summary: Under the stress mitochondrial failure in distal neuronal compartments induce activation of caspase-3 in neuronal processes

Abstract: Human studies reveal synaptic dysfunction decades before predicted clinical diagnosis in neurodegenerative diseases. Loss of dendrites and synapses requires activation of apoptotic terminal protease caspase-3 but does not always lead to immediate cell death. Loss of synapses is a characteristic of Alzheimer's and Huntington's diseases. Activation of caspase-3 is mitochondria dependent. Damage to mitochondria results in release of cytochrome c and activation of caspase-3. We hypothesized that Huntington's disease associated synaptic loss among other factors caused by mitochondria- dependent local caspase-3 activation without immediate cell death. Using single cell analysis approach we assessed modulation of local caspase-3 activity in the primary neurons from mouse model of Huntington's disease. We found that activation of caspase-3 in axo-dendritic neuronal compartments was associated with mitochondrial depolarization under excitotoxic conditions. We showed that found elevated activity of caspase-3 in distal compartments of neurons of Huntington's disease model was correlated with a decreased mitochondrial membrane potential increased level of oxidized/damaged mitochondrial protein content and an increased production of reactive oxygen species by mitochondria found in the same compartments. We explained our data in the framework of mitochondria-dependent cytochrome c-associated activation of caspase-3 in distal neuronal compartments where mitochondria are more vulnerable to stress associated with the neurological disorder.

First Author: Kelly Barko (Faculty)	Poster Session: pm
Presenting Author: Kelly Barko (Faculty)	Location: 59
Mentor/Lab: Logan/Dr. Ryan Logan	Category: Psychiatry
Department: Translational Neuroscience Program Department of Psychiatry	

Title: Circadian Rhythms and Opiates: Role of the Circadian Transcription Factor NPAS2 to Regulate Morphine Conditioned Reward

Summary: Acute and chronic substance use such as morphine can cause disruptions in circadian rhythm. The molecular mechanism behind drug-related behavior with respect to circadian rhythm remains uncertain. Thus our current research focuses on exploring a putative cell-specific type mechanism post morphine administration.

Abstract: Background There is evidence supporting substance use such as psychostimulants or opiates can cause disruption in endogenous circadian rhythms. However the molecular mechanism behind the pathophysiology of mood and addiction disorders with respect to circadian rhythm remains uncertain. Located within the striatum of the mammalian forebrain is the reward center of the brain known as the nucleus accumbens (NAc). NPAS2 an integral basic helix-loop-helix (bHLH)-PAS transcription factor of the molecular clock found throughout the NAc is expressed in medium spiny neurons (MSNs) that contain dopamine subtype receptors 1 (D1+) or 2 (D2+). According to our previous studies an increase in NPAS2 expression was observed when D1+ MSNs were activated post psychostimulant administration. Thus our current research focuses on manipulating NPAS2 within the NAc of D1+ or D2+ MSNs to explore a potential cell-type specific role in the behavioral response to morphine. Methods Wild-type and NPAS2-bHLH-deficient male and female mice underwent unbiased morphine CPP. We also designed a Cre-inducible shRNA virus (AAV2) to knockdown Npas2 (or Scramble control) specifically in D1+ or D2+ MSNs by stereotaxic injection into the NAc of D1-Cre or D2-Cre mice. The NAc of extracted brains were punched and used for molecular assays including qPCR Western blots and protein IP. Results Acute and chronic morphine administration altered the expression of NPAS2 in the NAc. Wild-type male and female mice showed an expected preference for the morphine-paired side. NPAS2 KO male mice displayed a significantly attenuated development of morphine CPP. Cell-type specific knockdown of Npas2 in D1+ MSNs of the NAc also significantly attenuated morphine CPP in male mice with moderate effects in D2+ MSNs. Concluding Statement Although a definitive singular cellular mechanism remains unclear we will continue to investigate the role(s) of NPAS2 within the NAc in relation to substance use and the circadian pathway.

First Author: Darius Becker-Krail (Graduate)	Poster Session: pm
Presenting Author: Darius Becker-Krail (Graduate)	Location: 56
Mentor/Lab: Colleen McClung	Category: Psychiatry
Department: Psychiatry (TNP)	

Title: Circadian transcription factor NPAS2 and metabolic redox sensor SIRT1 interact in the mouse nucleus accumbens (NAc) to regulate cocaine reward-related behavior

Summary: Cocaine's effects on the metabolic state of the cell may feed into the circadian molecular clock and in turn alter reward regulation.

Abstract: Cocaine addiction is a widely prevalent substance use disorder in the United States. With a lack of successful therapeutic options it is important to investigate the cellular and molecular level changes following cocaine use and how these changes establish and/or reinforce addiction. As its mechanism of action cocaine increases mesolimbic dopaminergic signaling via inhibition of dopamine transporter. This increased activity is energy taxing for the cell and can cause both severe oxidative stress and altered mitochondrial function. Interestingly metabolic changes associated with cocaine use may directly regulate the circadian molecular clock and its output genes through associated metabolic redox sensors. More specifically the circadian transcription factors CLOCK/NPAS2 and the NAD+ dependent deacetylase SIRT1 have all been shown to directly respond to changes in levels of the mitochondrial coenzyme NAD+. Previous work in the lab has shown CLOCK and NPAS2 differentially regulate cocaine reward; e.g. mutations in the Clock gene increase cocaine preference and self-administration while mutations in Npas2 yields an opposite phenotype. Moreover our data suggest NPAS2 regulates reward through its enriched expression in the nucleus accumbens (NAc). Interestingly SIRT1 modulators have also been shown to regulate cocaine preference in that SIRT1 agonists increase cocaine preference and vice versa. In addition to NPAS2 and SIRT1 modulation altering cocaine reward chronic cocaine exposure has been shown to preferentially alter expression of these proteins in the NAc. Given these observations we investigated how changes in cellular metabolic state may feed into the circadian molecular clock and alter regulation of cocaine reward and whether an interaction between NPAS2 and SIRT1 in the NAc mediates this regulation. Through co-immunoprecipitation studies our preliminary findings suggest that NPAS2 and SIRT1 do interact in a shared complex in the NAc and chronic cocaine may alter this interaction. Furthermore utilizing high-performance liquid chromatography to assess NAD+ concentration we observed a diurnal variation of NAD+ levels in the striatum that is disrupted following chronic cocaine exposure. Finally in mice with a NAc specific viral-mediated knock-down of NPAS2 we determined NPAS2 to be necessary for the increase in cocaine preference seen with a SIRT1 agonist. Ultimately our findings highlight a mechanism by which chronic cocaine’s metabolic changes can directly alter circadian molecular clock function and how this interaction mediated by NPAS2 and SIRT1 may afford regulation of cocaine reward-related behavior.

First Author: Joanne C. Beer (Graduate)	Poster Session: pm
Presenting Author: Joanne C. Beer (Graduate)	Location: 52
Mentor/Lab: Howard J. Aizenstein Stewart J. Anderson and Robert T. Krafty	Category: Psychiatry
Department: Biostatistics Psychiatry	

Title: Predicting Social Responsiveness Scale scores of autism spectrum disorder patients from resting state fMRI data using structured sparse penalized regression

Summary: Can resting state functional connectivity predict Social Responsiveness Score in autism patients? We propose a novel penalized regression estimator that is informed by spatial and functional relationships between neuroimage voxels. We apply the estimator to resting state fMRI data from the Autism Brain Imaging Data Exchange (ABIDE) Preprocessed dataset in order to pinpoint the cortical brain regions whose functional connectivity with a subcortical seed region best predicts Social Responsiveness Score.

Abstract: Penalized regression estimators such as lasso ridge regression or elastic net are often used in neuroimaging-based prediction models. These estimators yield unique solutions when data is high dimensional (i.e. when there are more predictors than subjects) by imposing optimization constraints that result in global sparsity or shrinkage of estimated coefficients. However often more is known about the relationships between predictors. For example when neuroimage voxels are used as predictors we might expect neighboring voxels to be similar to each other and therefore expect estimated coefficients to exhibit some degree of spatial smoothness. Additionally we might expect related voxels such as those residing in the same functional networks or anatomical regions to be selected or shrunk to zero as a group. We propose incorporating information about spatial and functional relatedness of voxels into the optimization constraints by using a fused sparse group lasso estimator. Lasso fused lasso group lasso and sparse group lasso are special cases. Simulation studies demonstrate conditions under which the fused sparse group lasso penalty yields better predictions than the lasso fused lasso group lasso or sparse group lasso penalties alone. We apply the fused sparse group lasso estimator to resting state fMRI data from the Autism Brain Imaging Data Exchange (ABIDE) Preprocessed dataset in order to pinpoint the cortical brain regions whose functional connectivity with a subcortical seed region best predicts Social Responsiveness Scale score.

First Author: Carl Beringer (Graduate)	Poster Session: am
Presenting Author: Carl Beringer (Graduate)	Location: 9
Mentor/Lab: Rehab and Neural Engineering Robert A. Gaunt	Category: Brain-Machine Interfaces
Department: Bioengineering	

Title: An optimization-based approach to translate myoelectric signals to muscle activation for Hill-type muscle models

Summary: We have developed a biomimetic model of the hand using a Hill-type framework. Hill-type muscle models require activation as an input but the translation from EMG to activation has not been well-characterized. Using EMG signals from intramuscular electrodes which have many benefits to traditional superficial electrodes we are attempting to use a mathematical optimizer to validate different methods of signal processing to find the EMG-to-activation mapping.

Abstract: Myoelectric prosthetic hands rely on interpreting electromyography (EMG) signals from the residual extrinsic hand muscles to act as prosthetic command signals. Present myoelectric prosthetic hands typically use one of two algorithms for control: pattern recognition in which predetermined prosthetic hand movements or states are commanded based on recognizing previously recorded patterns of activity across multiple signals or direct control in which EMG activity directly controls output for a given degree of freedom (DOF). Both of these approaches face challenges in replicating dexterous movements capable in newer prosthetic hands and are unable to effectively scale beyond 3 DOFs. The Musculoskeletal Biomimetic Model (MBM) is a detailed dynamic model of the hand with Hill-type muscle actuators that use muscle activation as an input signal and that can estimate joint movements by solving a forward dynamic simulation of the hand. Using intramuscular EMG we are able to use up to 16 simultaneous channels of recording. However the feature extraction and signal processing methods required to translate intramuscular EMG recordings to muscle activations have not been well-characterized for this biomimetic approach. In order to identify the EMG-to-activation mapping we used an optimization approach. 14 able-bodied subjects were acutely implanted with intramuscular electrodes in the extrinsic hand muscles . Subjects were asked to perform single and multiple DOF movements of the fingers and wristwhile intramuscular EMG activity and kinematics were recorded. Following experiments the torques of the fingers wrist and thumb joints were calculated using inverse dynamics in MuJoCo simulation software using the position velocity and acceleration of the recorded movements as input. The recorded EMG activity was then converted into activation and then entered into the MBM to calculate output torques and the error between the MBM torques and calculated torques was used as the term to minimize in an optimizer. With this approach we are able to investigate different signal processing parameters (filter type order and frequency) as well as EMG-to-activation methods by comparing the minimized error of each method.

First Author: Megan Bertholomey (Postdoctoral)	Poster Session: pm
Presenting Author: Megan Bertholomey (Postdoctoral)	Location: 58
Mentor/Lab: Torregrossa	Category: Psychiatry
Department: Psychiatry	

Title: KETAMINE REDUCES YOHIMBINE+CUE-INDUCED REINSTATEMENT OF ETHANOL SEEKING AND DEPRESSIVE-LIKE BEHAVIOR IN FEMALE RATS.

Summary: Females represent a vulnerable population with respect to stress-related disorders like depression and alcoholism indicating better treatment for women is needed. Low doses of ketamine have been shown to produce antidepressant and stress-blocking effects in male humans and animals. We show that ketamine not only blocks depression-like behavior in female rats but it also blocks stress-related alcohol drinking and seeking.

Abstract: Alcohol use and major depressive disorder are frequently comorbid with individuals diagnosed with a substance use disorder being nearly three times as likely to have major depression. Poor treatment responses are found for both disorders and are further complicated when they co-occur underscoring the need for better therapies. One promising candidate is ketamine which has been shown to have rapid and long-lasting effects in individuals with treatment-resistant depression and in rodent stress models. Ketamine has also been shown to reduce ethanol drinking in male Sardinian alcohol-preferring rats. However though women are more likely to have this comorbidity few studies have examined sex-specific effects of ketamine on depressive symptoms and none have done so for alcohol drinking or seeking. Therefore the goal of the present experiment was to determine both acute and long-term effects of ketamine on both alcohol-motivated and depressive-like behaviors in female rats. Rats were injected with an antidepressant dose of ketamine (10mg/kg) an anesthetic dose of ketamine (90mg/kg) or saline at postnatal day p27 and were trained to self-administer a 10% ethanol+0.1% saccharin solution in young adulthood beginning around p70. Though adolescent pretreatment with ketamine did not alter ethanol self-administration acute ketamine (10mg/kg) treatment robustly reduced cue+yohimbine-induced reinstatement of ethanol seeking which tended to last up to 3 weeks post-treatment in subsequent reinstatement tests in rats that had received the same antidepressant dose of ketamine prepubertally. This suggests that antidepressant doses of ketamine may cause neuroadaptive changes during development that increase the sensitivity to the protective effects of acute ketamine exposure in mitigating stress-related behaviors in adulthood. During subsequent forced swim testing ketamine produced significant decreases in immobility suggesting an antidepressant effect. Thus acute ketamine treatment reduces both alcohol-motivated and depressive-like behavior under stressful conditions in female rats. These data confirm the antidepressant effects of ketamine in female rats that have been previously shown in males but also demonstrates that ketamine may be an effective treatment for stress-induced alcohol seeking. Ongoing studies are aimed at identifying the neural mechanisms underlying these effects and expanding these findings to determine the effects of ketamine on stress-related alcohol or saccharin drinking in both male and female rats.

First Author: Patrick Beukema (Graduate)	Poster Session: am
Presenting Author: Patrick Beukema (Graduate)	Location: 22
Mentor/Lab: CoAx lab / Tim Verstynen	Category: Motor
Department: Neuroscience	
Title: Decoding single finger movements versus movement sequences	
Summary: A large part of the brain is dedicated to motor control. We show what specific parts of the brain are involved in generating single finger movements like tapping versus sequential movements like playing piano.	
Abstract: Coordinated finger movements are ubiquitous in daily life. Using representational similarity analysis of BOLD data from human subjects we isolate the motor control network for individual finger movements and sets of movements during the production of cued sequences. In a second set of experiments we show that a movement sequence network and a goal sequence network involve largely distinct regions in somatomotor cortex and visual cortex respectively but partially overlap in premotor dorsal cortex.	

First Author: Matthew Boring (Graduate)	Poster Session: am
Presenting Author: Matthew Boring (Graduate)	Location: 31
Mentor/Lab: Avniel Ghuman	Category: Sensory
Department: Center for Neuroscience	

Title: Investigating the spatiotemporal dynamics of human visual category processing with intracranial EEG

Summary: Regions dedicated to visual object recognition have been studied for decades however the temporal dynamics of this processing are not well understood. Intracranial electroencephalography is a technique that excels in both spatial and temporal resolution. Machine learning was applied to this recording modality to better understand how category level object recognition evolves in the human ventral visual stream.

Abstract: It has been known for centuries that damage to circumscribed brain regions can cause category-specific deficits in perception. This has led to an extensive search to build maps of category selective regions in the brain. Less is known about the spatiotemporal dynamics of visual category processing and the stages of this information processing. To help elucidate the spatiotemporal dynamics of visual object recognition 25 patients with intractable epilepsy were presented images of faces bodies houses hammers words or scrambled objects while intracranial electroencephalography (iEEG) data was collected from a total of 2464 electrodes distributed across the cortex. Multivariate classification and time series analyses were applied to these data to produce movies of the dynamics of category sensitivity across the regions covered by these electrodes. Of these electrodes 195 showed significant decoding accuracy at a conservative statistical threshold for at least one stimulus category at some point after stimulus presentation. Onset of this sensitivity was as early as 100 ms with peak sensitivity at 220 ms and many electrodes in the ventral visual stream continued to show sensitivity beyond 600 ms post stimulus presentation. Object sensitive electrodes had a clear organization with houses represented medially while words and faces were represented laterally. In addition to this several electrodes were sensitive to more than one category and some of these electrodes had different time-courses of sensitivity between categories. Further analyses show the functional connectivity dynamics of these object-sensitive regions (time evolving graphs) and use time series modeling to assess processing stages in a data-driven manner. Taken together these results illustrate important principles regarding the neural information processing dynamics and information flow that underlie visual object processing and recognition.

First Author: Joe Brague (Postdoctoral)	Poster Session: pm
Presenting Author: Joe Brague (Postdoctoral)	Location: 24
Mentor/Lab: Rebecca Seal	Category: Neurology & Neurodegenerative Diseases
Department: Neurobiology	

Title: VGLUT3 Knockout Mice Show Increased Dopamine Synthesis Spine Density and Normal Motor Behavior in a Parkinson's Disease Model

Summary: Parkinson's Disease (PD) is characterized by a loss of dopamine which impacts structural and functional changes of neurons and ultimately leads to the debilitating loss of motor functions. Recently our lab reported that a genetically modified mouse lacking a specific excitatory transporter showed an increase in dopamine and the number of neuronal connections in PD neuronal circuitry and interestingly showed normal motor behavior in the PD model. This poster highlights these exciting findings and outlines an experimental plan to rescue the motor deficits seen in parkinsonian mice and ultimately in humans.

Abstract: Joe C. Brague Christopher B. Divito Rebecca P. Seal* Department of Neurobiology University of Pittsburgh Parkinson's Disease (PD) is a progressive and debilitating disorder of the nervous system afflicting approximately ten million people worldwide. Symptoms including postural instability and slowed gait stemming from the death of dopamine (DA) neurons of the substantia nigra pars compacta (SNpC). These DA neurons densely innervate the dorsal striatum and profoundly influence motor function through actions of medium spiny neurons (MSN) the major projection neurons of the striatum. Loss of striatal DA in PD is thought to affect motor behavior by altering direct (go) and indirect (no-go) pathway output of MSNs. Understanding more precisely how loss of DA affects basal ganglia motor circuits will greatly expand treatment options for patients suffering from PD. In this study we explore the role of the vesicular glutamate transporter 3 (VGLUT3) one of three proteins responsible for the uptake of glutamate into synaptic vesicles in DA signaling and motor behavior in healthy and Parkinsonian animals. We recently showed that mice lacking VGLUT3 (Vglut3-/-) have increased DA synthesis and release in the striatum during the waking cycle. Additionally the density of immature spines on direct pathway MSNs is also increased during this time. When tested in a 6-hydroxydopamine depletion model of Parkinson's disease Vglut3-/- showed normal motor behavior during both waking and sleep cycles suggesting rescue results from more than simply increased dopamine release but also from a form of plasticity. We hypothesize that in the KO mice dopamine depletion triggers maturation of the increased immature spines on direct pathway MSNs and that this normalizes motor behavior across the day/night cycle. We are currently testing our hypothesis by measuring whether there is an increase in the density of mature spines on direct pathway MSNs in Vglut3-/- relative to their WT littermates after DA depletion. We are also recapitulating the elevated DA release in the VGLUT3 KO by targeting an excitatory designer receptor hM3Dq to SNpC DA neurons in Vglut3+/+ mice. This paradigm will allow us test whether a transient increase in DA activity during the waking cycle is sufficient to rescue motor behavior across the day/night cycle in the Parkinson's model a concept that potentially could be applied to patients in early stages of the disease.

First Author: Jordan Brooks (Graduate)	Poster Session: pm
Presenting Author: Jordan Brooks (Graduate)	Location: 39
Mentor/Lab: Ava Puccio	Category: TBI-Concussion
Department: Department of Neurosurgery	

Title: Differential CSF Cytokine Profile of Patients with Post-Traumatic Hydrocephalus

Summary: This project compares the inflammatory response of severe traumatic brain injury patients who developed post-traumatic hydrocephalus to severe traumatic brain injury patients who did not develop post-traumatic hydrocephalus. The goal of the project was to assess whether the inflammatory reaction ensuing traumatic brain injury influenced the development of post-traumatic hydrocephalus. Ultimately this project will give us a better understanding of the cause of post-traumatic hydrocephalus which has been associated with worst outcomes in this patient population to ultimately allow for intervention.

Abstract: Post-traumatic hydrocephalus (PTH) is a secondary neurological insult resulting in the derangement of cerebrospinal fluid (CSF) dynamics ensuing moderate to severe traumatic brain injury (sTBI). Given the high risk of clinical deterioration and documented worse outcomes the identification of biomarkers indicating the onset of PTH is imperative to allow early clinical detection and improve neurological outcomes in afflicted patients. This study examined CSF cytokine profile with PTH to elucidate the pathogenesis and aide in the early diagnosis of PTH. We conducted a matched case-control study on 50 patients who sustained a sTBI at a level 1 Trauma facility from 2002-2015. All patients were treated with five days of continuous CSF drainage via an extraventricular drain. CSF research samples was collected on post-trauma days 1 3 and 5. Patients who incurred CNS infection or died within 6 months were excluded. 25 patients who incurred PTH were matched by age sex and initial Glasgow Coma Scale with 25 patients who did not incur PTH. The CSF concentrations of 36 different inflammatory markers were analyzed via a Luminex Array Scanner. There were no PTH differences detected between the groups in CSF RBC WBC. Across all time points IL-15 ($p=0.007$) IL-5 ($p=0.038$) and CX3CL1 ($p=0.031$) were significantly lower among PTH patients. CCL4 was significantly higher in the PTH group ($p=0.029$). IL-2 levels increased at a significantly slower rate in patients with PTH ($p=0.037$). No other statistically significant differences were found in any other of the cytokines assayed. Overall our data suggests potential differences in the immune responses in patients who develop PTH which may impede the clearing of debris following sTBI. Lower levels of IL-15 and IL-5 suggest the decreased recruitment and proliferation of natural killer cells T-cells B-cells and eosinophils in PTH patients. High levels of CCL4 may indicate a more macrophage rich environment. A slower increase in IL-2 may be indicative of a global impairment of immune function particularly T-cell function and B-cell differentiation.

First Author: Heather Bruett (Graduate)	Poster Session: am
Presenting Author: Heather Bruett (Graduate)	Location: 48
Mentor/Lab: Dr. Marc Coutanche LeNS Lab	Category: Brain Models and Systems
Department: Psychology	
Title: The Role of Inter-region Information Synchrony in Processing Visual Stimuli	
Summary: We examined how scenes are processed through connections between different regions of the brain.	
Abstract: The brain processes the many aspects of visual stimuli via the coordinated activity of a number of relevant regions. The processing targets of these regions can be uncovered by “decoding” multivoxel activity patterns which can represent subtle distributed information. An approach that examines the timeseries of pattern discriminability –informational connectivity– can help determine which regions contain information in the same trials - in other words which regions are acting in synchrony. I will present fMRI data that was analyzed via multivariate analysis tools and informational connectivity to determine how information synchrony plays a role in processing scenes and objects. We ask how regions within the scene and object processing networks can decode scenes and objects from “pseudo-scenes” which contain certain elements present in typical scenes but lack other visual components. We find that the strength of informational connectivity within these networks differs based on the object or scene discriminations examined.	

First Author: Finnegan Calabro (Faculty)	Poster Session: am
Presenting Author: Finnegan Calabro (Faculty)	Location: 57
Mentor/Lab: Laboratory of Neurocognitive Development	Category: Learning
Department: Psychiatry and Bioengineering	

Title: Dynamic changes in striatal dopamine predict reward learning: evidence from simultaneous PET/MR

Summary: We have used simultaneously acquired fMRI and PET imaging to assess the relationship of dopaminergic brain activity with reward learning. We found differences in both activation and dopamine release associated with the ability of subject to learn based on reward-feedback. This provides direct in vivo support for the role of striatal dopamine not only in responding to rewards but in using them as the basis for learning.

Abstract: Dopamine is strongly associated with reward processing in the striatum but its precise contribution to reward learning in humans has been difficult to characterize. Here we combined behavioral (reinforcement learning) modeling with simultaneously acquired task fMRI and PET to assess the relationship of dopamine signaling and brain activation to reward related behavior. A sample of 77 young adults (40 female ages 18-30) were scanned in a Biograph MMR combined PET/MR scanner during which subjects performed a rewarded map exploration task in which they attempted to accumulate rewards and learn reward probabilities for each map location. Performance data was characterized using a reinforcement learning (RL) model to assess learning parameters. A bolus/infusion paradigm was used to administer the D2/D3 ligand [11C]Raclopride and task-related DA was quantified as a change in binding potential (BP) using a modified version of the simplified reference tissue model (SRTM). Task fMRI data was acquired simultaneously and activation was assessed by comparing BOLD responses among high low and no reward trials. Voxelwise analysis of the PET data across the striatum showed significant decreases in BP during task in bilateral portions of the ventral striatum (nucleus accumbens NAcc) and dorsal putamen indicating task-related DA release. Notably the magnitude of DA release was greater among subjects who exhibited reward learning compared to non-learners in the NAcc but not putamen. Furthermore among learners DA release in the NAcc was positively correlated with learning rate. DA responses were highly correlated with BOLD reward responses in the NAcc and this effect was more closely related to parametric prediction error related activation than to reward expectation. Non-learners did not show any relationship between DA and BOLD. Our results provide direct in vivo support for dopamine signaling in NAcc contributing to the neural and behavioral indices of reward learning. These data confirm and extend models of reward-related dopamine signaling from rodent and primate studies.

First Author: Nicholas Card (Graduate)	Poster Session: am
Presenting Author: Nicholas Card (Graduate)	Location: 23
Mentor/Lab: Omar El-Gharbawie	Category: Motor
Department: Bioengineering	

Title: Intrinsic connections of motor cortex columns revealed with intracortical microstimulation and optical imaging in squirrel monkeys

Summary: To determine how primary motor cortex (M1) coordinates the activity of many hand and arm muscles at once we used an optical imaging technique to visualize local connections within the forelimb representation of squirrel monkey M1. We found that zones in M1 are preferentially connected to other M1 zones with similar muscle targets.

Abstract: In primary motor cortex (M1) a roughly concentric topography exists for the motor representations of the hand elbow and shoulder. Cortical columns within these representations send corticospinal projections that can influence activity in groups of arm and hand muscles. The muscle synergies needed for manual movements are therefore predicated on coordinated activity between M1 columns within the arm and hand representations. Multiple communication channels have the potential to coordinate activity in M1 columns. Intrinsic M1 connections represent the most direct channel of communication between M1 columns but are perhaps the least understood among M1 connections. The objective of the present study is to investigate the spatial organization of the intrinsic connections of M1 in columns within the arm and hand representations. In three squirrel monkeys we focused on mediolateral rows of cortical columns in M1 wherein motor output changes but other defining features are invariant. To study an individual column we first determined the output targets of that column via intracortical microstimulation (ICMS) and electromyographic (EMG) recordings. Second we identified zones in M1 that are connected to that column using ICMS (trains of 150 pulses 0.2 ms/pulse 300 Hz 1000 μm below pia) and concurrent intrinsic signal optical imaging (630 nm illumination). For all M1 columns investigated in this study the most prominent activation was a spatial cluster (~ 2.0 mm2) of contiguous columns that surrounded the stimulating microelectrode. In addition columns were preferentially connected with other clusters (~ 0.5 mm2) of columns. The muscle targets of the connected columns overlapped with the muscle targets of the microstimulation site. Our results build on tracer studies that showed that the anatomical connections of the thumb representation in monkeys (Huntly and Jones 1991) and the wrist representation in cats (Keller 1993) are widely distributed across the entire forelimb representation. Here we show that the functional connections of M1 columns within the forelimb representation are spatially biased towards M1 columns that target the same muscle groups. Thus our results to date suggest that functional connections within M1 may be primarily concerned with coordinating matched columns. In this framework other communication channels (e.g. thalamic inputs intra-areal connections) may be responsible for coordinating nonmatched M1 columns. We are currently testing the effects of ICMS in one column on the activity of single units in connected columns to determine if interactions between connected columns are excitatory or inhibitory.

First Author: Christina Cerkevich (Postdoctoral)	Poster Session: am
Presenting Author: Christina Cerkevich (Postdoctoral)	Location: 30
Mentor/Lab: Peter Strick	Category: Motor
Department: Systems Neuroscience Institute	

Title: How primary is primary motor cortex for the control of vocalization?

Summary: These results indicate that the descending control over laryngeal muscles originates from multiple cortical motor areas. Thus the vocal motor system is characterized by multiple brain areas with the potential for sending parallel commands.

Abstract: Laryngeal muscles play a critical role in enabling vocalization in monkeys and humans. Yet we know surprisingly little about the areas of the cerebral cortex that are involved in the descending control of these muscles. Here we used retrograde transneuronal transport of rabies virus to identify the cortical areas that are most directly connected to the motoneurons of laryngeal muscles in the macaque. This approach identified five cortical areas as the major origin of output to laryngeal muscles. Two of these areas are on the lateral surface of the hemisphere and include the primary motor cortex (M1) and a region that overlaps portions of ventral area 6 (6V) and the motor proisocortex (ProM). Three of these areas are on the medial wall of the hemisphere and include the supplementary motor area (SMA) the rostral cingulate motor area (CMAr) and the ventral cingulate motor area (CMAv). We totaled the surface area of cerebral cortex that is the origin of descending control over laryngeal muscles. Then we assessed the relative contribution of each motor area to laryngeal control. This analysis showed that M1 makes the single largest contribution to laryngeal control (~40%). The next largest output originates from two areas: 6V/ProM (~20%) and CMAr (~20%). In fact taken together the output from these two areas is equal to or greater than that from M1. Significantly smaller output originates from the SMA (~10%) and the CMAv (~6%). These results indicate that the descending control over laryngeal muscles originates from multiple cortical motor areas in the frontal lobe. M1 is the single largest source of cortical control over laryngeal muscles. Even so the majority of the descending control originates from cortical areas outside of M1.

First Author: Daniel Charek (Postdoctoral)	Poster Session: pm
Presenting Author: Daniel Charek (Postdoctoral)	Location: 37
Mentor/Lab: Anthony Kontos PhD	Category: TBI-Concussion
Department: Department of Orthopaedic Surgery	

Title: Predicting Patients with Vestibular Clinical Profiles following Concussion

Summary: Concussions may involve different clinical profiles and this study sought to determine which factors best predict patients with a vestibular profile which is associated with poor clinical outcomes and recovery times. Of relevant factors included in a statistical model for predicting participants with vestibular clinical profiles a history of motion sickness and combined nausea dizziness and fatigue symptoms were positive predictors. These factors should be considered by clinicians when evaluating patients to facilitate identification of the vestibular profile so that appropriate targeted treatments can be prescribed.

Abstract: Objective: Concussions may involve different clinical subtypes or profiles including cognitive anxiety/mood migraine oculomotor and vestibular (Collins Kontos Reynolds et al. 2014). Early identification of clinical profiles is critical to inform effective and timely treatments. The vestibular clinical profile is associated with poor clinical outcomes and longer recovery times (Corwin Wiebe Zonfrillo et al. 2015; Lau Kontos Collins et al. 2011). The aim of this study was to determine which factors best predict patients with a vestibular clinical profile. Methods: Participants included 50 adolescent patients aged 12-20 years with a diagnosed sport-related concussion. Participants were divided into either: 1) vestibular or 2) other clinical profile groups based on positive findings on a vestibular screening exam clinical evaluation and subsequent follow-up testing. A logistic regression (LR) model was used to predict participants with vestibular profiles. Predictors included: gender; age; history of motion sickness migraine and concussion; dizziness at time of injury; computerized neurocognitive scores; clinical balance performance; and specific symptoms. Results: The LR was significant (p<.001 Nagelkerke R2=.51) with history of motion sickness (p=.02) and combined nausea dizziness and fatigue symptoms (p=.002) as positive predictors of the vestibular profile. Sensitivity for the model was 81.0% and specificity was 85.2%. Conclusion: A history of motion sickness and higher reported nausea dizziness and fatigue are useful predictors of patients with vestibular clinical profiles. Clinicians should focus on these factors when evaluating patients to better identify those with vestibular profiles to allow for more effective precision treatments.

First Author: Fangzhou Cheng (Graduate)	Poster Session: pm
Presenting Author: Fangzhou Cheng (Graduate)	Location: 10
Mentor/Lab: Anne M. Robertson	Category: Neurology & Neurodegenerative Diseases
Department: Mechanical Engineering	

Title: Understand the structural mechanism of cerebral aneurysm bleb: ruptured vs. stable. Report of two cases.

Summary: The rupture risk of cerebral aneurysm is strongly correlated to the appearance of aneurysm bleb. The purpose of this study is to gain insight into the structural mechanism of stable and ruptured blebs.

Abstract: Aneurysm blebs are outward surface protrusions that form on the side of aneurysm walls. They are speculated to be bulging weakened areas that reduce the tensile stress in the aneurysm wall. Even though this hypothesis suggests a protective role against aneurysm rupture a strong correlation has been found between the aneurysm blebs and rupture. However despite this established association little is known about the remodeling mechanisms within the aneurysm bleb. To gain insight into these mechanisms we analyzed blebs in two aneurysms - one stable and one ruptured. Multiphoton microscopy (MPM) was used to obtain the collagen fiber structure of the blebs and their parent aneurysm wall. Collagen fiber recruitment and orientation distribution were directly measured from the MPM images. The collagen fiber orientation distribution was mapped back to the 3D geometry obtained by micro-CT and compared with the stress distribution calculated using a customized finite element code. The relationship between wall architecture and intramural stresses were compared in the ruptured and unruptured aneurysm blebs and different structural mechanisms explained.

First Author: Michael Chiang (Graduate)	Poster Session: am
Presenting Author: Michael Chiang (Graduate)	Location: 46
Mentor/Lab: Sarah Ross	Category: Sensory
Department: Neurobiology	

Title: Neural pathways that convey separable aspects of the pain experience

Summary: Pain affect is believed to arise from the spino-parabrachial pathway via the lateral parabrachial nucleus (LPBN). However the role of distinct projections from the LPBN in the pain response is poorly understood. We use viral tracing and optogenetic methods to reveal unique behavioral roles for the different lateral parabrachial outputs in the generation of the pain experience.

Abstract: Pathological pain is a widespread condition that affects one in four Americans. Although opioids have long been used for their analgesic effects in pain management these drugs have severe adverse effects. An alternative approach with reduced adverse effects is delivering pain therapeutics to modulate neural circuitry within the brain responsible for contributing to the affective component of pain perception. Pain affect is believed to arise from the spino-parabrachial pathway via the lateral parabrachial nucleus (LPBN). However the role of distinct projections from the LPBN in the pain response is poorly understood. Here we show that the LPBN projects to six major targets in the brain: the insular cortex bed nucleus stria terminalis central amygdala hypothalamus paraventricular thalamus and periaquedutal gray. Using optogenetic approaches to target specific pathways we find that the two amygdala targets (central amygdala and dorsolateral bed nucleus stria terminals) are highly aversive as measured in a real time place preference assay. In contrast projections from the LPBN to hypothalamus mediate changes in heart and respiratory rates. Finally projections from the LBPN to the periaqueductal gray mediate the descending modulation of pain as measured by response latency to heat stimuli. These findings suggest that different components of a pain response are encoded within distinct pathways arising from the LPBN. Interestingly anatomical tracing of LPBN pathways indicate that spatially and neurochemically distinct subpopulations of LPBN neurons differentially project to subsets of recipient brain regions suggesting that LPBN subsets convey different aspects of pain perception. Identifying these will provide insight in our understanding of how the brain integrates nociceptive stimuli to generate pain perception. Furthermore this understanding can potentially contribute to the development of novel therapeutic agents that target a specific neural pathway underlying clinically relevant aspects of pain such as those neural pathways conveying the unpleasantness of pain.

First Author: Joseph-Patrick Clarke (Postdoctoral)	Poster Session: pm
Presenting Author: Joseph-Patrick Clarke (Postdoctoral)	Location: 1
Mentor/Lab: Christopher Donnelly	Category: Neurology & Neurodegenerative Diseases
Department: Neurobiology	

Title: Inducing Stress Granule Formation Using Optogenetics

Summary: The goal of this work is to generate light-induced SGs to study the role of these membraneless organelles in ALS/FTD. Our work is the first to report the formation of functional membraneless organelles using light and demonstrates spatial and temporal control in their formation in the absence of cytotoxic cell stress. Employing this method allows us to broaden our understanding of the pathobiology underlying ALS and FTD and their neuropathologies.

Abstract: Amyotrophic lateral sclerosis (ALS) and Frontotemporal dementia (FTD) are progressive fatal neurological diseases caused by the loss of upper and lower motor neurons or cortical neurons respectively. The majority of diagnosed ALS and FTD patients are classified as having a sporadic phenotype with the remaining considered familial based on patient history. A molecular similarity between both neurological diseases is the observed cytoplasmic aggregation of the RNA-binding proteins TDP-43 and FUS in post-mortem tissue samples. Current hypotheses suggest that impaired homeostasis of cell stress activated cytoplasmic granules called stress granules (SGs) may serve as sites of TDP-43 and/or FUS aggregation in disease and thus may promote disease progression. SGs form under periods of cell stress and function to prevent global protein synthesis to promote the upregulation of stress response genes until the stress is removed. Elucidating such an effect however has been problematic using current methods to form stress granules since prolonged treatment with extracellular stress is cytotoxic thus preventing the study of prolonged or repetitive stress granule formation on in the induction of ALS/FTD neuropathology. To overcome this we developed a novel method employing light-induced protein clustering to seed the core protein components. The goal of this work is to generate light-induced SGs to study the role of these membraneless organelles in the absence of toxic extracellular stressors. Employing this method we are able to broaden our understanding of the pathobiology underlying ALS and FTD and their neuropathologies. Our results demonstrate that the light induced SGs co-localize with endogenous stress granule components including G3BP1 Ataxin-2 PABPC1 TIAR and eIF3H. Additionally the light-induced SGs sequester mRNAs and translation factors to inhibit global protein synthesis similar to endogenous SGs. Light-induced SGs can be controlled to induce prolonged or repetitive SG formation and light-induced SGs sequester with the ALS/FTD proteins TDP-43 and FUS. This body of work allows us to form functional SGs with great spatial and temporal control and in the absence of cytotoxic cell stress. This is the first report of the formation of functional membraneless organelles using light. We are currently using this tool to elucidate the role of SGs in TDP-43 and FUS aggregation and in ALS/FTD pathobiology.

First Author: Jamie Cohen (Graduate)	Poster Session: am
Presenting Author: Jamie Cohen (Graduate)	Location: 2
Mentor/Lab: Kirk Erickson	Category: Imaging Techniques
Department: Psychology	

Title: Cardiorespiratory Fitness and Brain Activity During a Stroop Task

Summary: Better cardiorespiratory fitness is associated with improved cognition and brain health in older adults and children so we sought to determine if this relationship exists in young adults. Smaller differences in brain activity during two conditions of an executive functioning task were associated with better cardiorespiratory fitness in multiple brain regions. These increases in neural efficiency related to fitness levels provide important evidence that the relationship between cardiorespiratory fitness and cognition exists across the lifespan.

Abstract: Better cardiorespiratory fitness (CRF) is associated with improved executive functioning (EF) in older adults and children. However few studies examine this relationship in younger adults. The variability in EF task performance is often limited in younger samples leading to fewer studies exploring its relationship with CRF. However it is an important link to establish as increasing exercise and physical health may improve cognitive functioning in the general population. Here we sought to determine if the relationship between CRF and EF exists throughout the lifespan. 50 young adults (age=25.22+5.17; 44% male) underwent a neuropsychological assessment neuroimaging and CRF testing. CRF testing included a quantification of maximal oxygen consumption (VO2max) that controlled for body mass (VO2max/kg). Participants completed a computerized Stroop task in a magnetic resonance scanner to obtain functional neuroimaging (fMRI). Lower-level contrasts compared the incongruent (INC) congruent (CON) and neutral (NEU) conditions of the Stroop task with a fixation and against each other. Higher-level analyses controlling for sex examined the whole-brain associations between VO2max/kg and BOLD activation. Paired-sample t-tests compared the mean percent signal change for the Stroop task conditions for each activation cluster. Comparing activation during INC and CON revealed bilateral clusters in the medial prefrontal cortex superior parietal cortex and right caudate nucleus that were negatively associated with VO2max/kg. In all cases smaller differences in activation between conditions was associated with higher CRF (all r(49)<-.423 all p<.002). Higher CRF was associated with increased neural efficiency in younger adults without cognitive deficits. Areas known to be susceptible to changes following increased exercise including the prefrontal cortex showed this increased CRF-related neural efficiency. These associations have not previously been demonstrated in younger adults and provide evidence that CRF is related to EF across the lifespan.

First Author: Victoria Corbit (Graduate)	Poster Session: pm
Presenting Author: Victoria Corbit (Graduate)	Location: 51
Mentor/Lab: Susanne Ahmari Aryn Gittis	Category: Psychiatry
Department: Neurobiology	

Title: Dysregulation of specific cortical inputs to central striatum in the OCD-relevant Sapap3-KO mouse model

Summary: Imaging studies in Obsessive-Compulsive Disorder patients identify brain circuits showing dysregulated activity but the specific cell types and circuits are more easily studied using animal models. This work identifies a circuit imbalance such that a movement region has a strong influence on behavioral selection in an OCD-relevant mouse model whereas a cognitive flexibility region controls behavioral selection in healthy mice. These two regions are the best targets for brain stimulation treatment for OCD and these data provide evidence for how they may be important in OCD.

Abstract: Obsessive-Compulsive Disorder (OCD) is defined by the inability to suppress obsessive thoughts and compulsive behaviors. The exact neuronal mechanisms underlying these symptoms are unclear however hyperactivity in corticostriatal circuits is consistently observed in OCD patients. The Sapap3-KO OCD mouse model shows dysfunction in homologous corticostriatal circuits particularly those involving central striatum (CS) and lateral orbitofrontal cortex (LOFC). Specifically striatal fast-spiking interneurons (FSIs) are implicated because their aberrant regulatory influence over striatal output neurons (MSNs) is thought to play a role in abnormal behavioral selection. Both FSIs and MSNs are driven primarily by cortical inputs so investigating how specific cortical projections influence these CS cells is essential to understanding how these microcircuits contribute to compulsive behaviors. While LOFC is identified as an affected region in OCD patients CS is largely understudied. We first sought to characterize the major cortical afferents to CS. Using retrograde tracing we observed the well-known LOFC projections to CS but also unexpectedly identified a second major projection source M2. M2 has been suggested to be homologous to supplementary motor regions in humans and subregions of M2 in rodent are involved in the motor preparation while LOFC is important for cognitive flexibility. Thus both major inputs to CS are involved with behavioral selection and dysregulation in these inputs may play a role in the aberrant compulsive-like behaviors displayed by this OCD-relevant mouse model. To determine how specific cortical projections regulate microcircuits in CS we injected channelrhodopsin2 (ChR2) into cortex and recorded optogenetically-evoked excitatory post-synaptic currents (EPSCs) using acute slice physiology. LOFC-evoked EPSCs onto MSNs were weaker in KO mice relative to WTs while LOFC inputs to FSIs were unchanged. The ratio of EPSC amplitudes confirmed that LOFC input to FSIs is increased relative to nearby MSNs suggesting LOFC-evoked feedforward inhibition is stronger in Sapap3-KOs. In contrast we found that M2-evoked EPSCs were increased onto both MSNs and FSIs in the CS of Sapap3-KOs relative to WTs indicating a general increase in CS drive from M2. These data suggest that M2 rather than LOFC may be the primary source of cortical control of CS in Sapap3-KO mice potentially causing aberrant grooming behavior. This finding has particular relevance to OCD treatments as LOFC and supplementary motor area have been identified as the best targets for repetitive transcranial magnetic stimulation treatment in OCD patients. These results bring new focus to the role of supplementary motor cortical regions in the pathology of OCD and provide a foundation for future studies on M2 in compulsive behaviors in rodent models. Moreover increased relative drive to CS FSIs suggests that interneuron dysfunction may play a role in abnormal behavioral selection and initiation mechanisms relevant to OCD. Taken together these results reveal corticostriatal abnormalities that may cause compulsive behaviors in OCD.

First Author: Nicole Czachowski (Graduate)	Poster Session: pm
Presenting Author: Nicole Czachowski (Graduate)	Location: 28
Mentor/Lab: Dr. Yijen Wu	Category: Neurology & Neurodegenerative Diseases
Department: Developmental Biology	

Title: MRI Investigation of CDKL5 in Mutant Mouse Models

Summary: CDKL5 is a rare genetic disorder with symptoms that affect neurodevelopment in children. In order to uncover the mechanisms of the disorder mutant mice models were imaged analyzed and compared to unaffected mice revealing significant volume disparities in various brain regions and differing proportions of brain axes. These results suggest that CDKL5 may affect the development of specific brain regions leading to poor patient outcomes.

Abstract: Introduction: CDKL5 is a rare X-linked genetic disorder that entails of a mutation in the CDKL5 gene located on Xp22.13 which codes for the protein cyclin-dependent kinase-like 5. Symptoms of CDKL5 include epileptic encephalopathy arising prior to 3 months of age muscular hypotonia and severe developmental delay. CDKL5 is often associated with Rett Syndrome despite being a separate entity due to similar symptoms and outcomes. Little is known about the etiology or specific neurodevelopmental problems associated with CDKL5. The objective of this study is to elucidate the neurodevelopmental abnormalities associated with CDKL5 in order to better understand the neurological outcomes of the disorder. Methods: Animal model: Genetically modified mice with a mutation in the CDKL5 gene were used in comparison to wild-type (WT) control littermates. The mice were divided into three groups based on age each containing WT and CDKL5 mice. The hemizygous CDKL5 mutants and WT controls were then analyzed using MRI technology. Brain MRI analysis: Multi-modal magnetic resonance imaging (MRI) was utilized to anatomically analyze the mouse brains. Multi-slice 2D T2 WT (RARE8 78 x78 matrix 0.55 mm SLTH) and 3D Heavy T2WT (RARE10 49 x 52 x 52 matrix) were used to acquire gray matter and cerebrospinal imaging respectively. The multi-slice 2D MRI images underwent volumetric and bi-planar analysis and the 3D images underwent volumetric analysis only. Results: Volumetric analysis showed a statistically significant difference in volumes of the cerebral hemisphere corpus callosum cortex subcortex aqueduct and cerebrospinal fluid between the mutant and WT mice in all groups. Bi-planar analysis revealed a statistically significant difference in the ratio of the anterior-posterior and dorsal-ventral axes between the mutant and WT mice. Conclusion: Our results suggest that CDKL5 may cause brain dysplasia in the cerebral hemisphere corpus callosum cortex subcortex and aqueduct as well as abnormal cerebrospinal fluid and axes proportions. These findings suggest that the poor neurological outcomes of CDKL5 patients may be associated with deviations in these brain regions.

First Author: Kase Daisuke (Postdoctoral)	Poster Session: pm
Presenting Author: Kase Daisuke (Postdoctoral)	Location: 25
Mentor/Lab: Robert S. Turner	Category: Neurology & Neurodegenerative Diseases
Department: Department of Neurobiology	

Title: Movement-related activity in the basal ganglia-recipient motor thalamus (VLa) of the parkinsonian macaque

Summary: What causes the symptoms of Parkinson's disease? The principal symptoms of Parkinson's disease slowed movement rigidity and tremor have been recognized for many years. And quite a lot is known about the selective damage to dopamine neurons that is a root cause of those symptoms. Still mysterious however is why a loss of dopamine from a structure deep in the brain leads to this specific cluster of symptoms. We are working on this problem by studying how abnormal neuronal activity spreads from that deep brain structure to impair the operation of brain circuits that control movement. A better understanding of how this kind of malfunction of neural circuits leads to symptoms may lead to enhancements in therapies such as deep brain stimulation for Parkinson's disease.

Abstract: Disordered function of the VLa thalamus is thought to be a critical step in the pathophysiology of motor impairments in Parkinson's disease (PD). For example the traditional "rate model" hypothesizes that elevated discharge rates in efferents from the parkinsonian basal ganglia cause excessive inhibition of VLa neurons which may be evidenced by reduced baseline discharge rates and/or reduced magnitude of movement-related increases in activity. Little information is available however on how the activity of VLa neurons is altered in the parkinsonian state. To address this gap in knowledge we sampled single unit extracellular activities from the VLa before and after (n=99 and 96 units respectively) the induction of hemiparkinsonism by intracarotid MPTP administration in one macaque monkey. The animal performed a simple choice reaction time reaching task for food reward. The animal was able to perform the task throughout the month's-long recording period following MPTP but with markedly prolonged and more variable reaction times and movement durations (reaction time: 248±35 ms vs. 457±215 ms movement durations: 244±35 ms vs. 845±333 ms means±SEM pre- vs. post-MPTP respectively; p<0.01 for both K-S test). The baseline firing rates of VLa neurons sampled during attentive rest while the animal waited for the task's "go" stimulus were not altered by MPTP (14.0±1.2 Hz pre- vs. 12.0±1.1 Hz post-MPTP respectively; p>0.05 K-S test). Large fractions of neurons changed firing rates around the time of reach onset (92% and 83% of neurons pre- and post-MPTP; p=0.07 χ2-test) with increased firing as the earliest change in 79% (pre-MPTP) and 61% (post-MPTP) of these cells and decreased firing as the earliest change in the remainder. This shift following MPTP toward early movement-related decreases in firing was significant (p=0.01; χ2-test). In addition the magnitudes of movement-related increases in firing were reduced markedly following MPTP (20.9±2.2 Hz pre- vs. 5.0±0.7 Hz post-MPTP; p<0.01 K-S test) whereas the magnitude of decreases did not differ (6.2±0.8 Hz pre- vs. 6.1±1.0 Hz post-MPTP). Finally peri-movement activity began earlier relative to movement onset following MPTP (96.5±14.2 ms pre- vs. 176.8±19.9 ms post-MPTP respectively; p<0.01 K-S test). The shift in timing was similar for increases and decreases in firing. The observed MPTP-induced reductions in the prevalence and magnitude of movement-related increases in activity lend partial support for the traditional rate model of PD pathophysiology.

First Author: Patricia B. de la Tremblaye (Postdoctoral)	Poster Session: pm
Presenting Author: Patricia B. de la Tremblaye (Postdoctoral)	Location: 36
Mentor/Lab: Anthony E. Kline	Category: TBI-Concussion
Department: Physical Medicine and Rehabilitation	

Title: Long-term effects of adolescent chronic stress on TBI cognitive and emotional impairments in adult male rats

Summary: The most common neuropsychiatric consequence of TBI is depression. Early stress exposure has been recognized as an important mechanism for neuropsychiatric disorders in adulthood. In rodents as in humans adolescence is a transitional period between child- and adult-hood that is marked by behavioral changes heightened brain development and cognitive maturation. Therefore exposure to adverse environmental conditions during this sensitive period of development could influence TBI psychiatric outcomes. Therefore the current study examines weather repeated stress during adolescence will result in deleterious effects on emotional and cognitive functional impairments in rats subjected to a TBI as adults. Understanding the impact of environmental factors underlying post concussive symptoms will help develop effective preventive and therapeutic strategies for TBI patients.

Abstract: Exposure to early life stress has lasting effects on behavior and brain function due to dynamic plasticity occurring in the developing adolescent brain. However it is yet to be determined how stress exposure in this developmental period influences functional recovery post traumatic brain injury (TBI) induced later in life. Thus the goal of this study was to test the hypothesis that stress in adolescence would confer deleterious effects on behavioral impairments post TBI in adulthood. Adolescent male Sprague-Dawley rats (n=40) were exposed to 4 weeks (postnatal day PND 30-60) of chronic unpredictable stressors (CUS) or no stress and after a 1-month resting period (PND 60-90) were anesthetized and received a cortical impact of moderate severity (2.8 mm tissue deformation at 4m/s) or sham injury. After one week of recovery anxiety-like behavior in the open field test (OFT) and elevated plus maze (EPM) and cognitive performance in the novel object recognition (NOR) task and Morris water maze (MWM) were measured. Brains were collected 25 days after TBI for histological analysis. Preliminary results show increased time spent in the anxiogenic zones of the OFT and EPM and improved NOR memory after a 24 h delay in addition to reduced time to reach the platform in the MWM for CUS groups compared to no-stress control groups although TBI rats remained significantly more anxious and cognitively impaired compared to sham controls. These results suggest that aversive environmental conditions in adolescence induces adaptive behavioral responses in TBI rats albeit without leading to full functional recovery.

First Author: De Miranda Briana (Postdoctoral)	Poster Session: pm
Presenting Author: Briana De Miranda (Postdoctoral)	Location: 22
Mentor/Lab: Greenamyre	Category: Neurology & Neurodegenerative Diseases
Department: Neurology	

Title: Sex differences in sensitivity to rotenone reflect male-to-female ratios in human Parkinson's disease incidence

Summary: Parkinson's disease affects males approximately 1.5 times more frequently than females however the reason for this is unknown. Animal models of PD rarely take into consideration sex as a variable therefore we examined the differences between male and female Lewis rats in the rotenone model of PD. Similar to human data females were resistant to rotenone degeneration and required a higher dose to produce equivalent pathology observed in male rats.

Abstract: The male to female odds ratio for incidence of Parkinson's disease (PD) is 1.49 indicating that sex differences likely play a role in the pathogenesis of the disease. Animal modeling of PD however rarely uses sex as a variable when examining neurodegeneration possibly overlooking important etiological factors. Rotenone an organic pesticide and prototypical mitochondrial complex I inhibitor reliably reproduces parkinsonism in rats including motor behavioral deficits of postural instability rigidity and bradykinesia. In addition rotenone causes the selective neurodegeneration of dopamine neurons in the substantia nigra (SN) and their terminal projections in the striatum (ST) endogenous alpha-synuclein accumulation microglial activation and changes in iron metabolism. To date the rotenone model has primarily been utilized in adult male Lewis rats however our pilot studies in adult female Lewis rats using the same dose of rotenone (2.8 mg/kg i.p.) did not yield equivalent motor behavioral changes nor dopamine neuron loss or brain pathology. Therefore we postulated that female rats may be less vulnerable to rotenone-induced neurodegeneration and would require a higher dose of rotenone to induce the parkinsonian morbidities observed in male rats. To this end we generated a dose-response using 2.8 mg/kg 3.2 mg/kg or 3.6 mg/kg (daily i.p.) of rotenone in female Lewis rats with one additional group receiving BID dosing (1.6 mg/kg total 3.2 mg/kg) of rotenone. Female rats receiving 3.2 mg/kg 1.6 mg/kg (BID) and 3.6 mg/kg rotenone had a significant loss of dopamine neurons within the SN as assessed by stereology accompanied by a loss of tyrosine hydroxylase-positive terminals in the ST. Significant microglial activation within the SN was observed in only the 1.6 mg/kg BID and 3.6 mg.kg group compared to a marked activation of microglia in male rats given 2.8 mg/kg. The transferrin receptor (TfR1) was measured as an indicator of cell surface iron binding and was significantly increased in male rats receiving 2.8 mg/kg of rotenone but did not result in a significant increase in female rats across any dose. Ferritin an iron binding protein expressed predominately in oligodendrocytes within the SN was significantly preserved in female rats following rotenone exposure (all doses) indicating that females may have better iron storage capacity following neurotoxic insult. Taken together these data indicate that female rats require a higher dose of rotenone to produce equivalent neurodegeneration in the rotenone PD model an effect that parallels human data of a higher prevalence of PD in males and highlights the importance of using female animals when experimentally modeling PD pathogenesis.

First Author: Alan Degenhart (Postdoctoral)	Poster Session: am
Presenting Author: Alan Degenhart (Postdoctoral)	Location: 17
Mentor/Lab: Aaron Batista	Category: Brain-Machine Interfaces
Department: Systems Neuroscience Institute	

Title: A self-recalibrating brain-computer interface

Summary: Brain-computer interfaces (BCIs) can provide restoration of function for individuals with paralysis but are sensitive to instabilities in the neural activity used for control. We developed a self-recalibrating BCI system that leverages characteristics in neural population recordings to maintain performance in the presence of these instabilities. This work has the potential to increase the quality of life for individuals with paralysis by eliminating the burden of frequent BCI calibration.

Abstract: A key problem limiting the clinical translation of intracortical brain-computer interface (BCI) technology is that of stability. Over time neural signals recorded by penetrating microelectrode arrays can change due to a number of factors including glial scarring electrode micro-motion and mechanical failure. To combat these changes BCI systems typically rely on explicit daily recalibration of their decoding algorithms to recover satisfactory control. Recalibration procedures require the user's participation and may be burdensome in a clinical setting. To overcome this shortcoming we present an algorithm for decoding a continuous control signal which performs automatic recalibration by leveraging the low dimensional structure found in neural population activity. We make the assumption that the day to day relationship between a low-dimensional representation of neural activity and intended BCI movements is constant even if the set of neurons recorded and the characteristics of the signals vary from day to day. By finding the alignment between low-dimensional spaces of the population activity estimated at different points in time decoding parameters can be automatically updated based only on observation of new neural activity and without knowledge of intended movement kinematics. This allows recalibration to occur in the background and requires no time or effort on the part of the user. We assessed performance of the self-recalibrating algorithm in a series of closed-loop BCI experiments with two Rhesus macaques implanted with Blackrock arrays in primary motor cortex (M1). Experiments began with the calibration of a well-controlled "baseline" decoder. As the neural activity within a single experimental session is often stable we generated recording instabilities by perturbing the neural activity using: (1) baseline shifts where a random constant offset was added to the firing rate of each neuron (2) silencing where the firing rates of a subset of neurons was set to zero (3) swaps where the activity of a subset of neurons was replaced with that of held-out neurons or (4) combinations of baseline shifts silencing and swaps which might mimic clinically severe recording instabilities. In 41 of 42 single-day experiments we find that the self-recalibrated decoder was able to significantly improve performance in the presence of the perturbation. Furthermore we find that the self-recalibrating decoder is able to sustain BCI performance over multiple days in the presence of both natural and artificial instabilities. This work has the potential to increase the viability of BCI systems for clinical use.

First Author: Lauren DePoy (Postdoctoral)	Poster Session: pm
Presenting Author: Lauren DePoy (Postdoctoral)	Location: 57
Mentor/Lab: Colleen McClung PhD	Category: Psychiatry
Department: Psychiatry	
Title: Npas2 knockout increases intravenous cocaine self-administration	

Summary: Substance use is associated with changes in sleep/wake cycles and circadian rhythms and circadian genes appear to play an important role in regulating reward. Here a mutation in one gene Npas2 increases cocaine intake and motivation in a mouse model of drug taking. By understanding how circadian genes regulate reward we can develop novel treatments for substance dependence.

Abstract: The development of substance dependence is associated with disruptions in circadian rhythms and circadian genes. In mice a dominant negative mutation in circadian locomotor output kaput (CLOCK) increases both cocaine reward and self-administration. However the role of its homologue neuronal PAS domain protein 2 (NPAS2) in cocaine self-administration remains unclear despite Npas2 knockout contrastingly decreasing cocaine reward. We performed intravenous cocaine self-administration using male and female mice with a mutation in Npas2. Mice first acquired an operant response for food and then were implanted with an indwelling jugular catheter. After recovery mice acquired cocaine self-administration and then dose-response testing was conducted both at a fixed ratio and progressive ratio schedule. Npas2 knockout did not impact acquisition of a food response however it did accelerate acquisition of a cocaine-reinforced response as well as increase the total number of infusions earned. Furthermore Npas2 knockout increased the reinforcing and motivational properties of cocaine as evidenced by an upward shift in dose-response curve and an increase in breakpoint ratio respectively. Overall Npas2 knockout increases cocaine intake propensity to self-administer cocaine as well as the reinforcing and motivational properties of cocaine in mice across sex. This divergence from decreased cocaine reward seen in Npas2 knockout mice is likely due to the volitional control over drug intake during self-administration compared to conditioned place preference. Further research is required to understand the differences between NPAS2 regulation of cocaine reward and drug consumption.

First Author: Michael Durka (Graduate)	Poster Session: pm
Presenting Author: Michael Durka (Graduate)	Location: 11
Mentor/Lab: Anne M. Robertson	Category: Neurology & Neurodegenerative Diseases
Department: Department of Mechanical Engineering and Materials Science	

Title: Oxygen Transport in Cerebral Aneurysms

Summary: Cerebral aneurysms can be lethal or severely debilitating if they rupture but what exactly causes them to weaken to the point of rupturing is not well understood. This study utilized computer simulation techniques to analyze the transport of oxygen from the blood to the interior of the aneurysm wall - something which cannot be done clinically due to the limits of current technology. The goal of this study was to determine whether the unusual blood flow patterns in a cerebral aneurysm (relative to the normal blood flow patterns in a normal artery) diminish the amount of oxygen transported to the aneurysm wall to a point which the lack of oxygen could potentially cause damage to the wall tissues.

Abstract: Cerebral aneurysms are abnormal balloon-like structures in brain arteries which are often mechanically inferior to a healthy artery in that their yield strength is significantly reduced. This reduction in yield strength can lead to rupture which often has debilitating if not lethal consequences. Surgical intervention though a potential solution at preventing such an event carries its own risks to a patient which sometimes exceed the natural risk of rupture. It's therefore critical to be able to reliably determine the propensity for rupture; unfortunately this is not yet possible with current minimal-risk non-invasive techniques. Furthermore the exact cause(s) of this condition is not fully understood. While the impacts of fluid-influenced mechanical factors such as wall shear stress (WSS) magnitude (low high or both) and direction (temporally stable or unstable) as well as intra-aneurysmal blood flow structure on wall degradation have been heavily studied little work has been done (with cerebral aneurysms) to study the influence of fluid-influenced chemical-based factors such as mass transport of oxygen; particularly the impact of the abnormal intra-aneurysmal flow pattern (relative to a healthy artery) on the effectiveness of nourishment (or lack thereof) to the aneurysm wall. Hypoxia has already been implicated in the development of abdominal aortic aneurysms; therefore it is reasonable to explore the same effect in the context of cerebral aneurysms. We therefore conducted a computational study of oxygen transport in two cerebral aneurysms having identical parent vessels but different aneurysm geometries. The impact of geometry on flow structure and mass transport was then analyzed. Qualitative relationships between oxygen transport and WSS were also explored. The study then yielded an assessment as to the degree to which aneurysm geometry can influence the concentration of molecular oxygen within the aneurysm wall. Such information in larger future studies could aid in further understanding the disease

First Author: Kale Edmiston (Postdoctoral)	Poster Session: pm
Presenting Author: Kale Edmiston (Postdoctoral)	Location: 45
Mentor/Lab: Mary Phillips	Category: Psychiatry
Department: Psychiatry	

Title: Predicting quality of life in distressed young adults: Visual cortex and thalamic BOLD signal during reward processing

Summary: In people at risk for depression or anxiety disorders brain activity while waiting to receive a reward predicted their overall quality of life six months later. Parts of the brain related to visual processing were more active among people who had better quality of life later on. This could be related to how visually interesting or noticeable the cue for a future reward is to people with depression and anxiety symptoms; people who have more of a response to reward tend to be functioning better six months later.

Abstract: Study: Identification of neurobiological factors that predict quality of life (QoL) in mood and anxiety disorders could help identify young adults requiring more targeted treatment. Alterations in reward processing are a core component of mood and anxiety disorders. Functional MRI research indicates associations between BOLD during reward processing and mood and anxiety symptoms. However it is unclear how such alterations might predict later QoL. Methods: In this fMRI study twenty-eight young adults (ages 18-25) experiencing psychological distress completed an uncertain reward task in scanner. Participants then returned for a six-month follow-up and completed the Quality of Life Enjoyment and Satisfaction Questionnaire (QLESQ). Correlation between BOLD signal during reward expectancy or BOLD signal during prediction error and QoL as assessed by the change in QLESQ Total Scores at time one and six-month follow-up was modeled. Results: There were significant positive correlations between change in QoL at follow-up and BOLD signal during reward expectancy in the dorsomedial thalamus cuneus and left primary visual cortex such that increased BOLD was associated with improved QoL (p<0.001 uncorrected). There was also a significant positive correlation between QoL at follow-up and BOLD in the left premotor cortex during the prediction error portion of the task. Conclusion: Our findings indicate that enhanced activity of cortico-thalamic regions during reward processing is predictive of later QoL in a distressed sample of young adults. Significance: These findings may help to identify neurobiological features associated with improved outcomes in mood and anxiety disorders potentially leading towards targeted therapeutic interventions.

First Author: Robert J. Ferguson (Faculty)	Poster Session: am
Presenting Author: Robert Ferguson (Faculty)	Location: 61
Mentor/Lab: Biobehavioral Oncology Program UPMC Hillman Cancer Center	Category: Learning
Department: Medicine Division of Hematology/Oncology	

Title: Cognitive-Behavioral Treatment of Cancer-Related Cognitive Dysfunction: Treatment Dissemination and Outcomes Monitoring of Survivors

Summary: Cancer-related cognitive dysfunction (CRCD) can last for years following treatment of many different forms of cancer and can have significant negative impact on employment social and family roles. Memory and Attention Adaptation Training (MAAT) is a non-drug brief behavioral treatment of CRCD that has been found to be effective in clinical research but helping professionals such as psychologists receive training so they can offer MAAT to survivors has been a challenge. We are developing and implementing an online training program for MAAT for psychologists and others (anywhere there is an internet connection) and an online system so we can monitor memory and attention function of survivors who are treated with MAAT.

Abstract: Objective. Cancer-related cognitive dysfunction (CRCD) affects roughly half of all cancer survivors and has long-term (> 10 years) significant negative effects on social vocational and emotional function. Memory and Attention Adaptation Training (MAAT) is an evidence-based cognitive-behavioral therapy (CBT) that improves survivor quality of life patient-reported and objective neurocognitive function. However disseminating CBT's to clinical use and evaluating real-world effectiveness in cancer survivors suffering CRCD remains a challenge. We describe a treatment dissemination and outcomes monitoring system that uses internet technology to train clinicians and the Patient Reported Outcomes Measurement Information System (PROMIS) to evaluate MAAT clinical outcomes. Methods. First MAAT training utilizes a web-based videoconferencing workshop with live interactive learning with licensed qualified health professionals involved in cancer care-- regionally nationally and internationally. Second we describe an outcomes monitoring system where individual survivors enrolled in MAAT will respond to PROMIS measures of daily cognitive symptoms and emotional distress through a secured web-portal. Data security data management and analysis utilizing single case designs and aggregate analyses to evaluate MAAT effectiveness is described. Results. Information gained through the PROMIS-based MAAT outcomes monitoring system will provide greater detail of MAAT “real-world” effectiveness as a treatment of CRCD. This can include survivors who have not been carefully selected for previous MAAT randomized trials such as those with medical comorbidities that affect cognitive function (e.g. vascular disease) varying cancer treatments (e.g. hormonal therapies or immunotherapies) and history of traumatic brain injury. The proposed PROMIS outcomes monitoring system can thus help identify moderator variables that influence MAAT effectiveness and identify which survivors who are most likely to benefit. Conclusions. Using web-videoconferencing and PROMIS technology may provide a realistic method of disseminating and evaluating evidence-based treatment and translate cancer survivor research into practice. This system is currently being implemented and evaluated.

First Author: Ronald Fortunato (Graduate)	Poster Session: pm
Presenting Author: Ronald Fortunato (Graduate)	Location: 14
Mentor/Lab: Spandan Maiti	Category: Neurology & Neurodegenerative Diseases
Department: Department of Mechanical Engineering and Material Science and Bioengineering	

Title: COMPUTATIONAL STUDY OF UNIAXIAL TENSION TESTING OF SMALL SOFT TISSUE SPECIMEN

Summary: In this article we investigate the material properties used in uniaxial tensile grips that will ensure development of uniaxial stress state within a tissue sample and failure of the tissue in the region where uniaxial conditions prevail based on a finite element model. We also model failure and parametrically vary tissue strength and toughness to quantify failure mode of the tissue. Property-function relationship of the wall tissue will enhance our understanding about different clinical scenarios where some aneurysms fail catastrophically while others gradually progress towards rupture.

Abstract: Uniaxial testing is the most popular method for the evaluation of biomechanical properties of soft tissue. In this method a tissue specimen is fixed between two grips and stretched with a known displacement in one direction while the load borne by the specimen is recorded. The load-displacement data provides the constitutive behavior of the tissue. Often the specimen is also stretched until failure to ascertain the uniaxial strength of the tissue. For accurate evaluation of the material properties however uniform stress transmission within the tissue needs to be attained. The fixity at the tissue-grip interface is known to give rise to localized stress concentrations or even tissue damage that may provide erroneous uniaxial data. The standard practice to alleviate this problem is to attach the tissue to pieces of an intervening material typically sandpaper or cardboard glued to the metallic grips. However no analysis exists in the literature to ascertain whether this arrangement results in uniform stress distribution in the vicinity of the grips. For this study we present a detailed computational study of the effect of grip design and tissue shape on the stress state of the soft tissue specimen. Concurrently we studied the effect of tissue strength and toughness on failure. We developed an image derived finite element model of a dog bone shaped tissue specimen attached to steel grips through a thin layer of soft material. The grips were first clamped down on the specimen with a specified pressure and then uniaxial displacement was applied to one of the clamps. The strength and toughness was parametrically varied to observe the evolution of tissue damage that would lead to tissue failure. We computationally found that insertion of a soft rubber layer between the steel grips and cerebral artery tissue specimen resulted in uniform uniaxial stress near the midlength of the specimen while no stress concentration was observed near the grips. In addition damage was also localized in the midregion of the specimen. These results are expected to provide guidelines for proper design of grips for the uniaxial testing apparatus for testing of soft tissues in general and cerebral arterial wall tissue in particular.

First Author: Lily Francis (Graduate)	Poster Session: pm
Presenting Author: Lily Francis (Graduate)	Location: 31
Mentor/Lab: Chu Lab/ Charleen Chu	Category: Neurology & Neurodegenerative Diseases
Department: Neuropathology/ Human Genetics	

Title: Neuropathology of POLG-related mitochondrial diseases in patient-derived iPSC-neurons

Summary: We describe the use of stem cell derived neurons from patients as a model for the study of Neurodegenerative diseases.

Abstract: DNA polymerase gamma (Polg) is responsible for mitochondrial DNA (mtDNA) replication and repair. Mutations in POLG the gene encoding the catalytic subunit of Polg result in a set of clinical syndromes characterized by mtDNA depletion in affected tissues with variable organ involvement and severity. The brain and neuromuscular system are the most commonly affected organs with intractable seizures developmental delay dementia ataxia liver failure axonopathies myopathy and ophthalmoplegia comprising major symptoms. Treatment for POLG-related disorders remains mostly supportive with the majority of patients progressing to severe disability and death within a few years of diagnosis. Therefore a better understanding of disease mechanisms in the affected cell types is needed to illuminate new therapeutic options for these devastating diseases that typically affect children and teenagers. Most patients with POLG mutations are compound heterozygotes bearing a different mutation in each allele. Here we describe our work studying cortical neurons differentiated from two new patient-derived models of POLG-related mitochondrial diseases (POLG1 and POLG3). Fibroblasts from diagnostic skin biopsies were reprogrammed into induced pluripotent stem cells (iPSCs) and mutation status confirmed by DNA sequencing. While the patient-derived iPSCs did not show mtDNA depletion relative to control iPSCs both POLG1 and POLG3 failed to undergo the dramatic increase in mtDNA content observed in control lines upon differentiation to cortical neurons. Neurons differentiated from patient iPSCs exhibited simplification and shortening of the neuritic arbor with multiple abnormal neuritic swellings. POLG1 and POLG3 also exhibited abnormal mitochondrial ultrastructure by electron microscopy with accumulation of autophagic vacuoles and altered neuritic trafficking of lysosomes. Ongoing studies are aimed at characterizing mitochondrial function and dynamics in somatic and neuritic compartments and use of gene editing or other strategies to reverse these pathological neuronal phenotypes.

First Author: Harman Ghuman (Graduate)	Poster Session: pm
Presenting Author: Harman Ghuman (Graduate)	Location: 16
Mentor/Lab: Dr. Mike Modo	Category: Neurology & Neurodegenerative Diseases
Department: Bioengineering	

Title: ECM hydrogel injection for the treatment of stroke

Summary: Functional replacement of the damaged brain tissue after stroke remains a major therapeutic challenge. Here we demonstrate a long term retention of ECM hydrogel in the stroke cavity that promotes influx of host cells into the biomaterial and eventually leading to a reduction in lesion volume over 3 months.

Abstract: Stroke is the leading cause of adult disability and a significant effort is underway to develop therapies to repair the damaged tissue. One of the key challenges in treating chronic stroke is the dramatic loss of brain tissue and the formation of a cavity filled with extracellular fluid (ECF) and cell debris. Extracellular matrix (ECM) constitutes 20% of brain tissue volume. Biomaterials composed of mammalian ECM promote constructive tissue remodeling with minimal scar formation in peripheral tissue and organs. However the biodegradation and functional effect of injecting a large volume of ECM hydrogel into the brain are unknown. The current study therefore aimed to determine if biodegradation occurs and if ECM remodeling will affect the behavioral deficits of animals with stroke damage. At an 8 mg/mL concentration ECM hydrogel has rheological properties similar to brain tissue. It can be formulated in a fluid phase at room temperature while forming hydrogels at body temperature. Two weeks post-stroke Magnetic Resonance Imaging-defined lesion volume equivalents of ECM was injected into the lesion cavity of stroke rats. A battery of behavioral tests including Grip Strength Bilateral Asymmetry Test (BAT) Footfault and Rotameter were performed at pre-treatment 1 4 and 12 weeks post-treatment for control (n=14) untreated (n=11) and ECM-treated (n=11) groups. Retention gelation and biodegradation of the ECM as well as host cell invasion and phenotype were analyzed at 12 weeks post-injection using immunohistochemistry. Brain tissue deformation analysis using T2-weighted MRI scans indicated a 10% decrease in whole brain tissue volume 2-fold increase in ventricle size a 10% midline shift and 30% decrease in tissue in the stroke-affected hemispheres over 12 weeks. There was no significant difference between untreated and treated groups. Behavioral tests indicated a functional impairment that was not affected by the injection of a large volume of ECM into the cavity. ECM showed a robust gelation and retention in the lesion cavity with a 30% decrease in volume over 12 weeks. A significant host cell invasion into the ECM hydrogel was seen with an average of 72000 cells present within the hydrogel. Monocytes accounted for 55% of the total invading cells and expressed a neutral M1/M2 (CD86/206) phenotype indicating a shift from the acute inflammatory phase to an ECM remodeling phase. Significant proportions of oligodendrocyte progenitor cells (30%) and endothelial cells (4-5%) essential for repopulation of the neural tissue were also present. This characterization demonstrates that an ECM hydrogel can be readily injected and retained within the lesion cavity while promoting an acute endogenous repair response without deleterious effects. A time course study with varying ECM concentrations is necessary to determine the optimal rate of in vivo biodegradation to further improve the endogenous repair processes.

First Author: Brandon Gillie (Postdoctoral)	Poster Session: pm
Presenting Author: Brandon Gillie (Postdoctoral)	Location: 41
Mentor/Lab: UPMC Sports Medicine Concussion Program	Category: TBI-Concussion
Department: Department of Orthopaedic Surgery	

Title: Association of High-definition Fiber Tracking to Recovery Time and Clinical Outcomes in Adolescents following Concussion

Summary: Advanced neuroimaging techniques including high definition fiber tracking may help to predict recovery from concussion. Adolescents who were slow to recover from concussion showed differences in white matter tracts that were not present among those who recovered quickly.

Abstract: Objective: Findings from conventional imaging techniques such as CT scans and MRI are typically normal following concussion. Evidence of damage to white matter tracts following concussion using diffusion tensor imaging (DTI) though better than convention approaches has been equivocal. There is a need for a better approach to quantify structural damage to white matter following concussion as there are no established markers of brain injury that might identify athletes at risk for prolonged recovery and correlate with clinical findings. One such approach may involve high definition fiber tracking (HDFT). The aim of this study was to examine the association of HDFT white matter tractography metrics at 1-14 days post injury with recovery time and clinical outcomes in concussed adolescent athletes. Methods: Participants included 26 (9F/17M) adolescents aged 15.7 +/- 2.7 years with a diagnosed currently symptomatic concussion. Participants were divided into long (45+ days; n=16) and short (<45 days; n= 10) recovery groups. All participants completed HDFT scans and clinical outcome measures including self-reported post-concussive symptoms computerized neurocognitive testing and vestibular/oculomotor symptoms and impairment within 14 days of injury. Correlations and split-half comparisons of HDFT tract metrics (spread symmetry streamlines) between recovery groups were performed. Correlations adjusted for multiple comparisons were conducted between HDFT metrics and clinical outcomes. Results: Participants with long recovery times had fewer streamlines in the L optic (p=.03) and L thalamic (p=.01) radiations and less variability of streamline length in the R frontal aslant (p=.02) and uncinate (p=.04). They also had longer streamlines in L arcuate (p=.03) and L frontal-occipital fasciculus (p=.04). There were numerous positive correlations among HDFT spread symmetry and streamlines and clinical outcomes (p<.05). Conclusions: HDFT metrics were associated with both recovery time and clinical outcomes. However these associations in this sample of concussion patients at acute/sub-acute post-injury time point differ from those reported in moderate to severe TBI patients at chronic post-injury time points.

First Author: Scott Ginebaugh (Graduate)	Poster Session: pm
Presenting Author: Scott Ginebaugh (Graduate)	Location: 29
Mentor/Lab: Stephen D. Meriney	Category: Neurology & Neurodegenerative Diseases
Department: Neuroscience	

Title: A novel computational model for the development of a new therapeutic approach for Lambert-Eaton myasthenic syndrome

Summary: This research improves our understanding of and examines potential treatments for the disease Lambert-Eaton Myasthenic Syndrome which causes severe muscle weakness. We essentially built the part of the body which is effected by this disease called the neuromuscular junction in a supercomputer which allows us to examine this disease at levels which are not feasible under the microscope or in the laboratory. After building or model in the computer we will use it to estimate the proper dosage of drugs needed to effectively treat this disease which will not only allow us to learn more about the neuromuscular junction and help facilitate the development of treatment for Lambert-Eaton Myasthenic Syndrome but will also help develop a powerful new tool in the drug development process which can be applied to a variety of diseases and conditions.

Abstract: The neuromuscular junction is a reliable synapse in which reliability is derived from the summed activity of numerous unreliable elements each consisting of a synaptic vesicle and associated voltage gated calcium channels (VGCCs). Lambert-Eaton myasthenic syndrome (LEMS) is an autoimmune disease that reduces reliability leading to muscle weakness. This weakness is due to an autoantibody-mediated removal of some of the VGCCs that are critical for transmitter release an upregulation of other VGCC types and a disruption in organization of these VGCCs. LEMS patients are currently managed using a potassium channel blocker (DAP) that broadens the presynaptic action potential. However DAP provides only modest symptomatic relief for LEMS patients. We have previously reported the development of a novel first-in-class Cav2 gating modifier (GV-58) which prolongs channel deactivation effectively increasing calcium flux during an action potential by stabilizing the open state of the channel. We hypothesize that a combination of DAP plus our calcium gating modifier would work synergistically to provide a stronger and more complete relief of neuromuscular weakness. We have built an MCell computational model of the presynaptic neuromuscular active zone to examine the structure-function relationship of the healthy and LEMS disease state neuromuscular junctions. This validated model not only provides us with information about the presynaptic terminal but also allows us to computationally explore various combinations of DAP and GV-58 and study the spatio-temporal dynamics of presynaptic calcium influx and the subsequent impact on transmitter release. The ability to examine the combination of these drugs in silico is particularly important due to the difficulty of creating LEMS model mice. Within MCell we modeled DAP effects by increasing the amplitude (5-10%) and prolonging the decay time (5-15%) of the presynaptic action potential. To model the effects of GV-58 we edited our calcium channel gating scheme to include drug bound states with kinetic rates that resulted in modeled calcium current that matched our patch clamp recordings of calcium current modulation. Then we used these two modifications in both control and LEMS model active zone architecture to evaluate the effects on transmitter release. Our MCell model provides new information on the organization of the transmitter release site and gives us dose-response details for the synergistic effect of GV-58 and DAP which will help facilitate the design of pre-clinical experiments on LEMS model mice.

First Author: Amanda Gleixner (Postdoctoral)	Poster Session: pm
Presenting Author: Amanda Gleixner (Postdoctoral)	Location: 2
Mentor/Lab: Christopher Donnelly	Category: Neurology & Neurodegenerative Diseases
Department: Neurobiology	

Title: Evaluation of FG Nup deficits in C9ORF72 ALS

Summary: Proper cellular function relies on the transport of molecules between the nuclear and cytoplasmic compartments. However deficits in nucleocytoplasmic trafficking have been observed in C9ORF72-associated ALS but why this occurs in the disease remains unknown. This work exams defects in the protein responsible for nucleocytoplasmic transport the nuclear pore complex and seeks to rescue neuronal dysfunction by reversing nuclear pore complex deficits.

Abstract: Amyotrophic lateral sclerosis (ALS) is a progressive and fatal neurodegenerative disease characterized by the degeneration of the motor neurons and interneurons in the brain and spinal cord. Ninety percent of ALS cases occur sporadically (sALS) while approximately 10% of cases are linked to genetic mutations which are associated with a family history of the disease (familial ALS) (Renton et al. 2013; DeJesus-Hernandez et al. 2013). The most common genetic mutation associated with both sporadic and familial ALS is attributed to a GGGGCC hexanucleotide repeat expansion (HRE) in the first intron of the C9orf72 gene. Patients with C9ORF72 ALS may show up to hundreds or thousands of GGGGCC repeats while fewer than twenty repeats are typically observed in control patients (DeJesus-Hernandez et al. 2012). Neurotoxicity of the GGGGCC HRE in C9ORF72 ALS has been associated with the generation of toxic GGGGCC RNAs and dipeptide repeat proteins (DPRs) that are synthesized from the GGGGCC HRE by the non-canonical repeat associated non-ATG translation (RANT) pathway (Donnelly et al 2013; Wen et al 2014; Ash et al 2013). Recent studies have shown that nucleocytoplasmic transport pathways are greatly perturbed by the GGGGCC HRE (Zhang et al 2015; Freidbaum et al 2015; Jovičić A). Nucleocytoplasmic transport is driven by the nuclear pore complex (NPC). The NPC is comprised of approximately 30 different proteins that are termed nucleoporins. Nucleoporins have been shown to be modifiers of both nuclear transport defects and neurodegeneration in C9orf72 ALS Drosophila models (Freidbaum et al 2015; Boeynaems et al 2016). The permeability and selectivity barrier of the NPC is comprised in part by a class of nucleoporins with phenylalanine-glycine repeat domains (FG Nups). We performed a comprehensive analysis of FG Nups in cellular Drosophila models of C9orf72 ALS and are validating these findings in ALS patients tissue. We observed that modulation of various FG Nup levels altered neurotoxicity in C9orf72 ALS Drosophila models. Furthermore FG Nup deficits were detected in C9ORF72 ALS cellular models. Our work assessed how the GGGGCC HRE elicits downregulation of FG Nups and identified whether FG Nup deficits contribute to the cellular defects observed in C9ORF72 ALS. Furthermore we attempted to rescue cellular impairment by reversing FG Nup deficits in C9ORF72 ALS cellular and Drosophila models. Through our understanding of nucleoporin deficits we may identify novel approaches to reversing cellular impairment in C9ORF72 ALS.

First Author: Felipe Gomes (Postdoctoral)	Poster Session: pm
Presenting Author: Felipe Gomes (Postdoctoral)	Location: 53
Mentor/Lab: Anthony Grace	Category: Psychiatry
Department: Neuroscience Psychiatry and Psychology	

Title: The ability of stress during adolescence or adulthood to produce schizophrenia-like pathophysiology is dependent on the state of the critical period

Summary: Timing of the stress is a critical determinant of the pathophysiology that is present in the adult. While adolescent stress could led to changes that recapitulates schizophrenia adult stress induced changes observed in depression. Re-opening the sensitive period in the adult restores vulnerability to stress-induced pathology resembling schizophrenia.

Abstract: Title: The ability of stress during adolescence or adulthood to produce schizophrenia-like pathophysiology is dependent on the state of the critical period Felipe V. Gomes Xiyu Zhu Anthony A. Grace Departments of Neuroscience Psychiatry and Psychology University of Pittsburgh Background: Unregulated stress exposure occurring during the sensitive period of development leads to the emergence of circuit deficits consistent with schizophrenia in the adult. If accurate one would predict that re-opening the sensitive period in the adult could make it susceptible to a similar disruption. Methods: Male rats were submitted to a combination of footshock (FS) and restraint stress (RS) during adolescence (PD31-40) or adulthood (PD65-74). The activity of dopamine (DA) neurons in the ventral tegmental area (VTA) and the pyramidal in the ventral hippocampus (vHipp) were evaluated 1-2 or 5-6 weeks post-stress. We also evaluate if the administration of valproic acid (VPA; 300 mg/kg) which is known to re-instate the critical period in adults would recreate an adolescent phenotype of susceptibility to stress. Results: Our data suggest that as indicated by the increased VTA DA neuron population activity. The adolescent stress increased VTA DA population activity 1-2 and 5-6 weeks post-stress suggesting that adolescent stress induced both short- and long-term schizophrenia-like changes in the VTA DA system. These changes seem to be driven by an increased vHipp activity. On the contrary adult stress produced short-term depression-like changes as indicated by the decreased DA neuron population activity in the VTA which failed to persist after 5-6 weeks. Interestingly VPA treatment altered the impact of adult stress. When rats were treated with VPA FS+RS increased VTA DA population activity similar to that observed with adolescent stress. Conclusion: Timing of the stress is a critical determinant of the pathophysiology that is present in the adult. While adolescent stress could led to changes that recapitulates the MAM model of schizophrenia adult stress induced changes observed in animal models of depression. Re-opening the sensitive period in the adult restores vulnerability to stress-induced pathology resembling schizophrenia. Financial support: MH57440

First Author: Michael Granovetter (Graduate)	Poster Session: am
Presenting Author: Michael Granovetter (Graduate)	Location: 52
Mentor/Lab: Marlene Behrmann	Category: Brain Models and Systems
Department: Medical Scientist Training (MD-PhD) Program	

Title: Atypical task-evoked pupillary responses in individuals with autism implicate norepinephrine's contributions to imbalances in neural excitation and inhibition

Summary: We measured pupil dilations (an established approach to infer the amount of norepinephrine produced in the brain) as participants with and without autism performed a working memory task. Our preliminary analyses suggest that individuals with autism produce higher levels of norepinephrine in the brain compared to neurotypical controls.

Abstract: An imbalance in excitatory and inhibitory neural activity is postulated to be associated with features of autism spectrum disorders although the neurobiological mechanisms underlying such an imbalance remain unclear. Norepinephrine (NE) produced from the locus coeruleus (LC) globally regulates the homeostasis of neural excitation and inhibition by enhancing the signal-to-noise ratio or neural gain of circuits throughout cortex. We hypothesize that individuals with autism exhibit an imbalance in excitatory and inhibitory neural activity as a consequence of atypically elevated release of NE from the LC. To test this hypothesis we measured pupil size (an established correlate of LC activity and cortical NE production) in 15 individuals with autism and 13 age-matched neurotypical controls as they performed a one-back working memory detection task. Our preliminary analyses suggest that while both groups performed the task with similar proficiency individuals with autism exhibited lower task-evoked pupil dilations compared to controls. As the magnitude of the pupil dilation is inversely correlated with tonic cortical NE release from the LC our data suggest that individuals with autism generate higher concentrations of tonic NE relative to neurotypical individuals. Given the critical role of the LC in attention and learning an inherent difference in cortical NE production in individuals with autism could potentially contribute to cognitive deficits observed in ASD and thus warrants further study.

First Author: Junichi Hachisuka (Faculty)	Poster Session: am
Presenting Author: Junichi Hachisuka (Postdoctoral)	Location: 45
Mentor/Lab: Sarah Ross	Category: Sensory
Department: Neurobiology	
Title: Research Assistant Professor	
Summary: Wind-up is involved in pain amplification. We found a novel mechanism of wind-up that is caused by reverberating activation of the excitatory interneuron circuit in the spinal cord.	
Abstract: Wind-up is a frequency-dependent increase in the excitability of spinal cord neurons and could be involved in pain amplification of chronic pain. However the neural circuit basis for wind-up in lamina I spinoparabrachial (SPB) neurons is mostly unknown. We found a subset of these SPB neurons shows wind-up by repetitive root stimulation. We hypothesized that an excitatory interneuron network mediates wind-up. Supporting this idea we found repetitive optogenetic activation of NtsCre expressing excitatory interneurons induce increase of action potentials in lamina I SPB neurons. Root-evoked wind-up was completely blocked by silencing NtsCre neurons with activation of archaerhodopsin. In addition we found that NtsCre neurons form an excitatory network that causes reverberating activity and enhance excitatory input to the lamina I SPB neurons. These data indicate that excitatory interneuron network is involved in sensory augmentation in lamina I SPB neurons.	

First Author: Amanda Henton (Graduate)	Poster Session: am
Presenting Author: Amanda Henton (Graduate)	Location: 38
Mentor/Lab: Thanos Tzounopoulos	Category: Sensory
Department: Otolaryngology	

Title: Cell-Specific Noise-Induced Changes in the Intrinsic Properties of Auditory Cortical Projection Neurons

Summary: Tinnitus is a condition where a sound is perceived where no sound is present in the external environment we have developed a new behavioral model to test the presence of tinnitus in mice. While some subcortical mechanisms of tinnitus are known tinnitus' mechanisms in cortex are unknown. Here we found cell type-specific changes in projection neurons in auditory cortex after noise exposure.

Abstract: Tinnitus is a condition in which a sound is perceived when no sound is present in the external environment. Among its causes acoustic overexposure is thought to be the most common. Tinnitus is becoming increasingly prevalent in older adults with hearing loss and in active duty military members that may be routinely exposed to loud sound. However since tinnitus is the perception of a sound that is absent from the external environment it presents many challenges to objectively evaluate its presence or severity in humans or in animal models. Here we have developed a mouse model of tinnitus that utilizes operant training. With this model it is possible to classify noise exposed mice into two groups those that develop tinnitus and those that are resilient. While recent research has shown evidence for maladaptive changes associated with the initiation of tinnitus in subcortical areas the mechanisms underlying tinnitus maintenance in cortex the likely site of perception remain largely unknown. Here we investigated the changes in intrinsic properties of specific subpopulations of projection neurons in auditory cortex pyramidal tract (PT) which project to the inferior colliculus and auditory brainstem and intratelencephalic (IT) neurons which project to the contralateral cortex. After noise exposure whereas no changes were found in the intrinsic properties of IT neurons the resting membrane potential of PT neurons in auditory cortex is significantly lower than controls. These findings may reveal a novel cell-specific site of modulation in auditory cortex after noise exposure and in pathological conditions such as tinnitus.

First Author: Angelica Herrera (Graduate)	Poster Session: am
Presenting Author: Angelica Herrera (Graduate)	Location: 14
Mentor/Lab: Jennifer Collinger	Category: Brain-Machine Interfaces
Department: Bioengineering	

Title: Grasp force encoding in human primary motor cortex during attempted isometric grasping

Summary: Using a force match task grasp force can be accurately classified from neural recordings in human primary motor cortex.

Abstract: Brain-computer interfaces (BCIs) can restore limb function by controlling a prosthetic arm with signals recorded from primary motor cortex (M1) and recently have begun to incorporate sensory feedback through stimulation of somatosensory cortex (S1). With the ability to sense graded levels of tactile feedback we aim to extend the capabilities of BCIs to control grasp force. Here we examined whether motor cortex encoded a force signal during an attempted isometric grasp in a virtual reality environment (MuJoCo). A 28-year old male with tetraplegia was implanted with two 88-channel and two 32-channel intracortical microelectrode arrays in M1 and S1 respectively. We recorded neural data while the participant used a virtual hand to grasp spherical objects at three force levels indicated by a spoken audio cue (gentle medium and firm ranging from 4 to 12 N). He attempted to perform the task while the computer controlled the kinematics and grasp force. Graded stimulation was provided as the object was compressed based on the measured reaction force on the index finger in MuJoCo. The participant had five seconds to close the hand around the object and was required to maintain hold of it for two seconds at the specified force level. To determine whether M1 activity encoded force-related information we trained a Naïve Bayes classifier to obtain the classification accuracy of the force levels using five sets of 27 trials collected over three test sessions. A time series of accuracies was computed by averaging each channel's firing rate over a 1 second sliding window (200 ms step) for the duration of the hold phase (2 seconds). The model was validated using leave-one-out-cross validation. Classification accuracy was high at 70 +/- 5% throughout the isometric grasp phase for all six time bins tested with no significant differences in classification accuracy between the bins. In addition to the 70% of correctly classified force targets 16 +/- 13% of incorrectly classified trials were to the adjacent force level when classifying data during the first second of the isometric grasp. Our results demonstrate that grasp force can be well classified from neural recordings in M1. In the future we plan to analyze the effects of providing feedback on classification accuracy. Currently we use a linear mapping of stimulation amplitude to force levels; however this is not naturalistic. Future work will involve developing more effective ways of incorporating stimulation such as using biomimetic stimulation patterns. We will also investigate the most effective ways of implementing force decoding with BCI control to provide accurate manipulation of objects of different sizes and compressibility.

First Author: Yunhong Huang (Postdoctoral)	Poster Session: pm
Presenting Author: Yunhong Huang (Postdoctoral)	Location: 4
Mentor/Lab: Amantha Thathiah	Category: Neurology & Neurodegenerative Diseases
Department: Department of Neurobiology	

Title: In vivo inactivation of β-arrestin 2 signaling in Alzheimer's disease

Summary: Alzheimer's disease (AD) is one of the most significant medical and societal challenges of our time and yet no current intervention strategies can halt or modify the underlying disease course. Our lab identified the orphan G protein-coupled receptor (GPCR) GPR3 as a primary modulator of AD pathology. The current study investigates the in vivo therapeutic modulation of GPR3 signaling to understand disease mechanisms and open a potentially novel avenue for therapeutic intervention in AD.

Abstract: Alzheimer's disease (AD) is one of the most significant medical and societal challenges of our time and yet no current intervention strategies can halt or modify the underlying disease course. Clinically AD is characterized by progressive memory loss personality disturbances and general cognitive decline. Neuropathologically AD is characterized by the accumulation of amyloid-β (Aβ) tau and neuroinflammation. Aβ is derived from proteolysis of the β-amyloid precursor protein (APP) following sequential cleavage by the β- and γ-secretases. G protein-coupled receptors (GPCRs) are involved in key neurotransmitter systems that are disrupted in AD patients and are also associated with multiple stages of APP proteolysis indicating an intimate association between GPCRs and the molecular pathways involved in AD. We identified the orphan GPCR GPR3 as a key modulator of γ-secretase activity and determined that β-arrestin 2 (βarr2) which belongs to a small family of multifunctional GPCR adaptor proteins specifically interacts with the γ-secretase complex and critically is required for the GPR3-mediated effect on Aβ generation. These results support the hypothesis that βarr2 is a critical link between GPCR dysfunction and Aβ generation in AD. Here we sought to determine the in vivo consequence of selective abrogation of βarr2-dependent signaling on amyloid pathology which is likely essential for triggering physiological and pathophysiological outcomes in mouse models of the disease. We utilized a CRISPR/Cas9-mediated genome editing strategy to introduce defined point mutations in the C-terminus of murine Gpr3 to interfere with the interaction between GPR3 and βarr2. These studies will provide the first demonstration of the in vivo consequence of selective modulation of βarr2-dependent signaling in AD pathogenesis. Results from these studies will not only address a major challenge in understanding disease mechanisms in AD they will also provide new avenues for the development of potential therapeutic targets to mitigate and/or halt the neurodegenerative changes observed in AD.

First Author: Christopher Hughes (Graduate)	Poster Session: am
Presenting Author: Christopher Hughes (Graduate)	Location: 10
Mentor/Lab: Robert Gaunt	Category: Brain-Machine Interfaces
Department: Department of Bioengineering	

Title: The complex relationship between frequency and perceived magnitude of intracortical microstimulation in human somatosensory cortex

Summary: We are stimulating a human participant's brain with electrical currents to evoke perceived sensations on the hand. We varied the stimulus parameters (amplitude and frequency) and measured how this affected the perceived intensity of stimulation.

Abstract: It is difficult to grasp and manipulate objects without tactile feedback and yet prosthesis users must work with this limitation. To work towards a solution we implanted microelectrode arrays in primary motor (M1) and primary somatosensory (S1) cortices in a person with a cervical spinal cord injury to enable closed-loop prosthesis control. Using neural activity decoded from M1 our participant can control a dexterous prosthetic limb while sensory feedback is delivered through intracortical microstimulation (ICMS) in S1. Microstimulation on more than 60 of the 64 implanted electrodes reliably evokes sensations in the hand but the perceived intensity of the stimuli evoked can vary significantly from electrode to electrode. We have previously shown that stimulation amplitude has a linear relationship to perceived intensity but the stimulation frequency was always 100 Hz. In non-human primates increasing stimulation frequency decreases detection thresholds but has little effect on discriminability. [1] It has also been suggested that increasing stimulus frequency could increase perceived intensity. Here we explored the effects of stimulus frequency on perceived magnitude in a human participant. To test this we used a free magnitude estimation task where varying stimulus amplitudes (20 50 and 80 uA) and frequencies (20 100 and 300 Hz) were paired and presented in randomized order. For each stimulus pair the participant reported the perceived intensity on a self-selected scale. We found that that perceived intensity increased with stimulation amplitude on all electrodes at all frequencies as expected. However stimulus frequency changed the perceived intensity in idiosyncratic ways that were electrode dependent: when comparing between 20 and 100 Hz on 3 of 8 stimulated channels 20 Hz was associated with increased perceived intensity while on 5 of 8 stimulated channels 100 Hz was associated with increased perceived intensity and these relationships generally held across all stimulus amplitudes. Understanding the relationships between stimulus frequency perceived intensity and other perceptual characteristics could help us improve the perceptual quality of ICMS and develop prostheses that provide a rich sensory repertoire. Ultimately these techniques could also help us understand how inputs are processed more generally in the somatosensory cortex. [1] S. Kim T. Callier G. A. Tabot R. A. Gaunt F. V. Tenore and S. J. Bensmaia “Behavioral assessment of sensitivity to intracortical microstimulation of primate somatosensory cortex.” Proc Natl Acad Sci USA p. 201509265 Oct. 2015.

First Author: James Hyde (Postdoctoral)	Poster Session: pm
Presenting Author: James Hyde (Postdoctoral)	Location: 50
Mentor/Lab: Susanne Ahmari	Category: Psychiatry
Department: Psychiatry	

Title: In vivo calcium imaging of SKF38393 induced perseverative grooming in awake behaving mice

Summary: This study examines the neural activity in the ventral medial striatum during repetitive grooming in a pharmacological mouse model of OCD. We separated grooming behaviors into multiple types of grooming and showed that pharmacologically induced repetitive grooming selectively affects facial grooming rather than body grooming. We also showed that neural activity decreased during facial grooming during both pharmacologically induced repetitive grooming and normal grooming.

Abstract: Obsessive compulsive disorder (OCD) is characterized by intrusive obsessive thoughts and abnormal repetitive behaviors. Studies of several independent mouse models of OCD-like behavior suggest that perseverative grooming in mice is related to compulsive behaviors seen in OCD. Understanding the mechanisms leading to the development of abnormal grooming is therefore relevant to OCD pathophysiology. However the changes in cellular activity that are correlated with the development of perseverative grooming are unknown. Using miniaturized head-mounted microscopes and calcium imaging we therefore examined changes in cellular activity in the ventromedial striatum (VMS) during pharmacologically- induced perseverative grooming behavior. Drd1a-tdTomato mice were injected with the genetically encoded calcium indicator AAV9.hsyn.GCaMP6m and implanted with a microendoscope (6.1mm x 0.5mm GRIN lens) in VMS. Four weeks after virus injection mice were fitted with a microscope baseplate. Upon recovery behavioral experiments were performed. Using a cross-over within subjects experimental design mice were treated with either vehicle or the D1 agonist SKF38393 to induce perseverative grooming. Both behavior and calcium signaling were monitored continuously for 10 minutes prior to injection and 30 minutes post injection. Calcium data were extracted from processed videos to analyze event frequency and time-locked activity; both PCA/ICA and CNMF algorithms were used. As expected grooming activity increased after SKF38393 injection in VMS implanted mice. However we also found that SKF38393 selectively induces increased grooming activity only during the facial grooming steps of a stereotyped grooming chain. In vivo microendoscopy demonstrated that average calcium event rates decreased during facial grooming regardless of SKF38393 or saline treatment. However event rates selectively increased during non grooming and body grooming periods in SKF treated mice. Event rates during saline control experiments showed no differences between grooming and non-grooming time periods. These results suggest selective changes in striatal firing patterns as well as changes to initiation transition and cessation of grooming behavior after SKF38393 treatment. Ongoing analysis is delineating the precise relationship between changes in network level activity and bouts of perseverative grooming and determining whether the SKF-induced differences in event rates during non-grooming time periods are related to transitions into and out of grooming bouts.

First Author: Bistra Iordanova (Faculty)	Poster Session: pm
Presenting Author: Bistra Iordanova (Faculty)	Location: 7
Mentor/Lab: Vazquez	Category: Neurology & Neurodegenerative Diseases
Department: Bioengineering	

Title: In vivo NADH fluorescence imaging of double transgenic AD mice reveals chronic tissue hypoxia

Summary: Shedding light on the relationship between Alzheimer's disease (AD) oxygen metabolism and neurovascular deficits is the goal of this project. AD and vascular disease were traditionally considered separate conditions AD being caused by brain neurodegeneration and the vascular deficits caused by pathological changes in the blood vessels. Recently increasing evidence indicates that there is a connection between these two conditions. The relationship between AD and the neurovascular deficits is the focus of this project. The results can ultimately lead to new clinical therapies that target vascular and metabolic pathways to halt AD progression.

Abstract: Background: Vascular and metabolic dysfunctions are well known features of Alzheimer's Disease (AD) and they precede clinical dementia. Undoubtedly vascular changes are expected as amyloid accumulates in the arterial vessel walls in cerebral amyloid angiopathy (CAA) leading to the death of smooth muscle cells cerebral hypoperfusion and inadequate oxygen supply. These vascular events could also contribute to metabolic alterations in glucose homeostasis. High resolution in vivo study of the dynamic vascular and metabolic events may reveal which tissue regions and cell populations are affected and cast light on the mechanisms that contribute to AD pathogenesis. Methods: We used fluorescence imaging of nicotinamide adenine dinucleotide (NADH) as an intrinsic marker for cellular metabolic states and tissue oxygen supply in vivo. We resolved the tissue boundaries of NADH fluorescence in the cortex of transgenic AD mice (B6C3.Tg(APPswe-PSEN1de9) n=4 12-24 months old) and observed NADH pattern relative to vessels during hyperoxia and normoxia. We then used in vivo two-photon fluorescence microscopy together with cell-type specific labeling to determine the cellular origin of the intrinsic signal and the locality of CAA. Results: Reduction of oxygen supply from hyperoxia to normoxia produced no detectable changes in controls however AD mice showed characteristic NADH pattern (Figure 1A) indicative of reduced oxygen gradient and rise in glycolysis in tissues further away from the arterial oxygen supply. Areas around capillary beds showed decreased NADH signal. Two-photon imaging under the same conditions revealed numerous cells with increased signal (Figure 1B) and only some of those cells stained positive for the astrocyte marker Sulforhodamine-101 (Figure 1C). All AD mice had CAA and tissue plaques seen with Methoxy-X04 staining (Figure 1D) and there appeared to be no association of the NADH signal with the plaques location. Conclusion: In agreement with previous findings double transgenic AD mice display chronic tissue hypoxia. Our preliminary results also indicate that under those conditions a subset of cells may adapt by up-regulating glycolysis to overcome the deficient oxidative phosphorylation. The population of cells with increased NADH signal is likely a combination of neurons and glia. This work can lead to new strategies that target metabolic pathways to halt AD progression.

First Author: Pablo Iturralde (Graduate)	Poster Session: am
Presenting Author: Pablo Iturralde (Graduate)	Location: 27
Mentor/Lab: Gelsy Torres-Oviedo	Category: Motor
Department: Bioengineering	

Title: Adaptation of muscle-activity during split-belt walking predicts the extent of human locomotor learning

Summary: We studied the evolution of muscle activity during a task that required subjects to adapt the way they walk on a treadmill. We found that fast changes in walking conditions lead to feedback responses that are adapted as subjects spend more time walking in the altered environment. Further we were able to predict how subjects would react to going back to normal walking afterwards.

Abstract: Split-belt treadmill walking has been used to study the locomotor control and adaptation in humans and has been suggested as a therapeutic tool to restore gait symmetry in chronic stroke patients. While muscle activity offers direct insight into the nervous system's regulation of locomotion and learning mechanisms little is known about how muscle activity changes during a split-belt protocol. Here we present a thorough characterization of muscle activity in 15 lower limb muscles on each leg during a split-belt treadmill adaptation and de-adaptation protocol. Analysis is focused on the relation between activity during the adaptation condition and the aftereffects during the deadaptation condition. As expected muscle activity was consistent with feedback postural responses when the split-belt condition was introduced. In other words subjects where perturbed by the split-belt environment leading to reactive responses intended to maintain stability. These feedback responses are extinguished and an asymmetric muscle activation pattern emerges as subjects adapt to the split-belt condition. We observed that the adapted muscle activation patterns are inconsistent with strictly ipsilateral speed-dependent modulation which highlights the bilateral nature of walking. Interestingly we found feedback responses are modulated by the duration of the split-belt condition suggesting that they reflect changes in subjects' expectation of the environment. The extent of this adaptation was age dependent with older subjects showing less adaptation. Surprisingly aftereffects in muscle activity were dominated by feedback control responses rather than feedforward (learned) activity.Finally we fitted a linear time-invariant space-state model to characterize the temporal evolution of muscle activity during adaptation and de-adaptation. Notably our model was able to predict the aftereffects when fitted strictly to data observed during the split-belt condition providing a first description of the relation between behavior during adaptation and its consequences for normal walking (learning). Taken together our results suggest that feedback control rather than feedforward is the main driver of observed aftereffects in this task setting it apart from other modalities of motor learning such as reaching in a force field. These results need to be considered when designing split-belt treadmill protocols for therapeutic purposes.

First Author: Uday Jagadisan (Postdoctoral)	Poster Session: am
Presenting Author: Uday Jagadisan (Postdoctoral)	Location: 29
Mentor/Lab: Neeraj Gandhi	Category: Motor
Department: Bioengineering	

Title: A causal study of movement generation using multi-channel recording and patterned microstimulation

Summary: Coordinated activity of neurons is important for many brain functions and behaviours including movement generation. We show that neurons in the superior colliculus a brain region that encodes both sensory input and motor output are de-coordinated during visual processing and coordinate to produce a gaze shift. We verify this observation using causal experiments in which coordinated or uncoordinated patterns of pulses are used to stimulate this region.

Abstract: Sensorimotor transformations are mediated by premotor brain networks whose evolving activities multiplex sensory cognitive and movement-related information. A fundamental question in neuroscience is how the brain resolves activity related to movement generation from prior activity. In the gaze control system visuomotor neurons serve as appropriate substrates to study this question. These neurons are activated both by the onset of a visual stimulus in (visual burst) as well as a saccade to (premotor burst) their response field and are prevalent in the superior colliculus (SC) and frontal eye fields (FEF) critical nodes in the gaze control network. Intriguingly visuomotor neurons also have direct projections to brainstem burst generators that are involved in saccade initiation thus raising the question - why does the high-frequency visual burst not produce a saccade? In other words how does a decoder parse incoming sensorimotor information to guide movement generation? Extant models posit threshold-based gating or low-D population-based readouts as the solution to this demuxing problem. We recently showed using pseudo-population analyses that SC and FEF activity during the visual burst is temporally unstable while regaining stability during the premotor burst (bioRxiv doi: 10.1101/132514) suggesting a combination of high firing rate and population stability as a putative mechanism for movement generation. Here we test these alternative models in a causal framework. We first verified that the temporal stability hypothesis also holds on individual trials by using a linear microelectrode array to record SC population activity in monkeys performing the delayed saccade task. Differences observed in the temporal structure of visual and premotor bursts were similar to those mentioned above. Additionally a linear decoder operating on reduced-D population activity was also able to discriminate between the two bursts. We then explicitly tested the alternative population-based models by applying sub-threshold patterned microstimulation simultaneously across multiple electrode sites in SC. Stimulation patterns were designed to be either stable or unstable on different trials with matched pulse rates across the population. Stable patterns were more likely to evoke saccades and at lower latencies compared to rate-matched unstable patterns. Crucially a linear decoding mechanism was insufficient to explain the differences in stimulation outcomes. This provides a causal demonstration that the temporal structure of instantaneous population activity is the key variable determining movement initiation at least in gaze control.

First Author: Abhishek Jauhari (Postdoctoral)	Poster Session: pm
Presenting Author: Abhishek Jauhari (Postdoctoral)	Location: 33
Mentor/Lab: Dr Robert Freidlander	Category: Neurology & Neurodegenerative Diseases
Department: Department of Neurological surgery	

Title: Absence of endogenous melatonin induced immune response mediated synaptic degeneration in differentiated neurons

Summary: AANAT KO leads to absence of endogenous melatonin which in turn to results in accumulation of ROS and MMP loss of mitochondria. Elevated ROS and hypopolarized mitochondria activate immune response which results in synaptic and neuritic degeneration and finally neuronal cell death.

Abstract: Absence of endogenous melatonin induced immune response mediated synaptic degeneration in differentiated neurons Abhishek Jauhari Sergei Baranov Svitlana Yablonska Diane L Carlisle and Robert Friedlander* Department of Neurological surgery University of Pittsburgh Medical center Pittsburgh PA USA *Corresponding Author Melatonin is an endogenously occurring free radical scavenger and well documented in neuroprotection as it reduced the loss of neurons under pathophysiological conditions. Therefore to test whether endogenous melatonin is involved in regulation of neuronal development and neurodegeneration we developed CRISPR/CAS9 mediated Arylalkylamine N-acetyltransferase (AANAT) knockout (KO) N2A cells. AANAT is a rate limiting enzyme in the synthesis of melatonin from serotonin. Wild type (WT) and AANAT KO N2A cells were differentiated into mature neurons by the exposure of retinoic acid. Our studies have demonstrated that differentiated AANAT KO cells have elevated reactive oxygen species (ROS) and significant loss in mitochondrial membrane potential (MMP) in comparison to their wild type differentiated N2A cells. Further qPCR studies has shown that differentiated AANAT KO cells have increased level of inflammatory markers (IL6 TNFα IFNA IFNB). In addition our studies has revealed that differentiated AANAT KO cells have lower number of synapses decreased average length of neurites and neurite numbers. Interestingly when AANAT KO cells were treated with melatonin during differentiation the synaptic degeneration neuritic length neuritic numbers MMP and ROS were rescued similar to their WT differentiated N2A cells. In addition AANAT KO differentiated N2A cells have shown the decrease in level of inflammatory markers when grown with melatonin. In conclusion AANAT KO leads to absence of endogenous melatonin which in turn to results in accumulation of ROS and MMP loss of mitochondria. Elevated ROS and hypopolarized mitochondria activate immune response which results in synaptic and neuritic degeneration and finally neuronal cell death.

First Author: Ahmed Jorge (Graduate)	Poster Session: am
Presenting Author: Ahmed Jorge (Graduate)	Location: 8
Mentor/Lab: Jennifer Collinger	Category: Brain-Machine Interfaces
Department: Neurosurgery Physical Medicine and Rehabilitation	

Title: The Use of a Finger Exoskeleton and an Intracortical BCI in Patients Suffering from a Stroke

Summary: Many people that have suffered a stroke have problems moving their fingers. Unfortunately our current therapies for helping them are still lacking. We believe; however that a brain computer interface and an external finger robot could help these patients get back some of their ability to move their fingers.

Abstract: Stroke is the third most common cause of morbidity (4%) and the second most common cause of mortality (10%) worldwide. Despite this pronounced incidence therapies for upper limb weakness and paralysis are still limited in scope and outcomes and do not address the needs of individuals with severe and chronic weakness specifically in regards to their fingers. Conventional robotic therapy can provide individuals that have suffered a stroke with repetitive physical therapy with hopes of regaining function. It also facilitates movements that the patient would not be able to achieve otherwise. Nonetheless blind repetitive motion can impact a patient's behavior during therapy and thus affect the motor plasticity rehabilitation process. In addition robotic therapy still does not provide favorable outcomes for patients with severe deficits. A brain computer interface (BCI) system can provide the patient with the means for a meaningful therapy session and also address more pronounced deficits. BCI therapy in stroke survivors has been shown to be as effective and safe in arm rehabilitation when compared to intensive robotic assisted repetition therapy but with reduced repetitions needed. Moreover patients with chronic hand weakness that responded poorly to standard rehabilitation efforts have shown a clinically improvement in muscle function from no activity using BCI therapy. Furthermore electroencephalogram (EEG) combined with BCI has led to significantly greater functional connectivity gains when compared to robotic therapy rehabilitation further supporting BCI-induced cortical reorganization. Some of these studies were limited however to simple hand opening and closing and are therefore unlikely to show any gains in higher-level functional ability for example individual finger mobility. Currently robotic therapy for this patient population is lacking in the finger and hand dexterity realm. Nonetheless many critical activities of daily living require a coordinated quick and skillful use of individual fingers. Here we studied the addition of an intracortical BCI system combined with an exoskeleton to allow for more refined individual finger mobility during therapy.

First Author: Dana Jorgensen (Graduate)	Poster Session: pm
Presenting Author: Dana Jorgensen (Graduate)	Location: 18
Mentor/Lab: Gianaros / Rosano	Category: Neurology & Neurodegenerative Diseases
Department: Epidemiology	

Title: Racial Differences in Brain Health at Midlife and the Potential Mediating Role of Cardiometabolic Risk.

Summary: Blacks are at a higher risk of stroke and developing dementia than whites but it remains to be determined whether differences in brain health are evident at midlife. Here we found several racial differences in brain health and that cardiometabolic risk was a partial mediator for the relationship between race and cortical surface area. These results have implications for understanding the pathways by which race may impact brain health prior to the onset of stroke and other clinical outcomes later in life.

Abstract: Introduction Blacks are at a higher risk of stroke and developing dementia than whites [4 5]. However much of what is known about racial differences in brain health is exclusive to those >65 years old and it remains to be determined whether relationships between race and brain health are apparent in midlife. Here we examined racial differences in brain health at midlife and tested whether cardiometabolic risk (CMR) statistically mediated any observed differences. Methods 747 community volunteers (20.6% black) aged 30–54 years old underwent neuroimaging to assess brain morphology and cerebral blood flow (CBF). Components of a composite CMR score included: body mass index waist circumference high-density lipoproteins triglycerides glucose insulin SBP and DBP. Results After adjustment for demographics and socioeconomic status blacks exhibited a significantly smaller hippocampus less cortical surface area and a thinner cerebral cortex than whites. We observed no significant differences in CBF. Mediation models showed that CMR partially mediated the association of race with cortical surface area. Conclusions Race differences in brain health are evident in midlife. CMR partially mediated the relationship between race and cortical surface area. These results have implications for understanding the pathways by which race may impact brain health prior to the onset of stroke and other clinical outcomes later in life.

First Author: Gabrielle Kaplan (Graduate)	Poster Session: pm
Presenting Author: Gabrielle Kaplan (Graduate)	Location: 46
Mentor/Lab: Logan/McClung	Category: Psychiatry
Department: Psychiatry	

Title: Mitochondrial complex I alterations in a mouse model of bipolar mania

Summary: Our studies show that the ClockΔ19 mouse as a model for bipolar mania recapitulates the mitochondrial alterations found in human postmortem tissue and will serve as a model for future studies investigating the direct links between circadian clock machinery cellular metabolism and mitochondrial respiration.

Abstract: Study: A confluence of evidence points towards an underlying dysfunction of mitochondrial complex I in bipolar disorder (BD) which may lead to an increase in oxidative stress and inflammation. The Clock mutant mice (ClockΔ19) which has been shown to display a behavioral repertoire similar to bipolar mania serves as a model in which we can investigate both the circadian control of complex I and potential neuronal mitochondrial dysfunction in the prefrontal cortex a critical structure known to regulate mood and decision making in the brain. Methods: Live mitochondria from WT and ClockΔ19 mouse PFC brain tissue were isolated and separated via density centrifugation. Mitochondria then underwent high-resolution respirometry measures to obtain rate of oxygen consumption. RCR (respiratory control rate) was calculated by dividing State 3 (ADP-stimulated) and State 2 (substrate-stimulated) oxygen consumption rates. Frontal cortex mitochondria from WT and ClockΔ19 mice were also used for protein and gene assays to compare mitochondrial subunit expression across oxidative phosphorylation (OXPHOS) complexes. Mitochondrial protein lysates were run on a Western blot and blotted using an antibody cocktail of against critical subunits of each of the 5 OXPHOS complexes (Abcam ab110413). qPCR was run for mitochondrial genes as previously described. Results: Human postmortem studies conducted in the PFC of patients with BD have shown a decrease in mitochondrial complex I function and expression. Our data shows a similar decrease in complex I-driven respiratory rate as determined by the addition of glutamate-malate and ADP to synaptosomal mitochondria from the PFC of ClockΔ19 mice. Additionally we demonstrate alterations to protein and gene levels specific to complex I and its downstream targets. Conclusion: These results show a decrease in mitochondrial expression and respiratory function that can be attributed to alterations in complex I in the presence of a dominant negative CLOCK protein. As the “entry enzyme” of cellular respiration complex I integrity has significant implications for ATP production management of reactive oxygen species (ROS) levels and maintenance of the NAD-NADH ratio. Significance: Through these preliminary studies we demonstrate that the ClockΔ19 mouse as a model for bipolar mania recapitulates the mitochondrial alterations found in human postmortem tissue and will serve as a model for future studies investigating the direct links between circadian clock machinery cellular metabolism and mitochondrial respiration.

First Author: Scott Kennedy (Graduate)	Poster Session: am
Presenting Author: Scott Kennedy (Graduate)	Location: 24
Mentor/Lab: Schwartz	Category: Motor
Department: Bioengineering	

Title: Motor cortical encoding of arm impedance during the coordinated control of both force and movement

Summary: When we interact with an object to move it from one place to another we have to coordinate the movement of the object with the force that we exert on the object. If the relation between movement and force is not known then we can stiffen the arm to still achieve the desired movement. Here we present motor cortical signals that correlate with both force and movement; these correlates could explain the strategy of stiffening the arm to interact with objects.

Abstract: The coordinated control of both force and movement is fundamental to object interaction. However in many cases the relation between force and movement is inherently unstable or unpredictable and thus can never be learned. A framework that is robust to this inherent uncertainty is impedance control. In this study we tested a neurophysiological hypothesis derived from the framework of impedance control. We trained a monkey to pull on a handle that was locked in place until a specific force threshold was crossed. Then the handle was suddenly released to move along a track. The monkey was required to stop the handle in one of four different targets spaced along the track. We observed how the firing rates of motor cortical neurons varied with target position. For comparison we repeated this procedure across four different force thresholds. We observed that arm impedance increased as the force threshold increased. We also observed that arm impedance increased as the target moved closer to the handle's lock position. This pattern was consistent with the framework of impedance control and led to our specific hypothesis: if a neuron encodes information about impedance then that information should be consistent across thresholds and across targets. Indeed we found that 20 of 101 neurons had firing rates that were correlated with both target and threshold. In addition 18 of those neurons had correlations that were consistent with impedance encoding. Specifically the firing rates of 8 neurons were negatively correlated with target and positively correlated with threshold i.e. positively correlated with impedance. The remaining 10 neurons had the opposite correlation. These results demonstrate that the simultaneous encoding of both force and movement in the firing rates of motor cortical neurons can explain the variation of arm impedance during object manipulation. This suggests the possibility that impedance control could be implemented by the motor system and could provide a unifying framework that describes the coordinated control of both force and movement.

First Author: Sanjeev Khanna (Graduate)	Poster Session: am
Presenting Author: Sanjeev Khanna (Graduate)	Location: 33
Mentor/Lab: Matthew Smith	Category: Sensory
Department: Bioengineering	

Title: Correlated variability during eye movement planning in the frontal eye fields and superior colliculus

Summary: Planning an eye movement to a visual stimulus such as looking at a traffic light at an intersection requires the coordination of multiple cells both within and between brain regions. Here we studied how groups of cells in two brain regions responsible for controlling eye movements varied their activity in relation to each other.

Abstract: Trial-to-trial fluctuations in spiking activity which give rise to correlated variability are commonly observed between pairs of neurons in a wide variety of cortical areas. Correlation among a population of neurons has been suggested to impact the amount of information it can represent. This stored sensory information such as a visual stimulus could then be used to guide a motor output such as an eye movement. Very little is known however about the correlated activity in areas that bridge this sensory and motor divide particularly the relationship between correlated activity and behavior. The frontal eye fields (FEF) and superior colliculus (SC) are both considered to be important regions controlling eye movements as both areas contain neurons with a wide variety of response profiles (both visual and motor). This makes them ideal candidates for studying the relationship between correlated activity and the planning and execution of eye movements. We used linear electrode arrays to record from groups of FEF or SC neurons in alert rhesus macaque monkeys performing a conventional memory guided saccade task (FEF) or delayed visually guided saccade task (SC). We measured the spike count correlation (also known as noise correlation) between pairs of simultaneously recorded neurons during the delay period after the visual stimulus was present but before the animal had made an eye movement. We found correlation in this epoch leading up to an eye movement varied depending on the reaction time of the animal's subsequent eye movement in pairs of both SC and FEF neurons. Additionally the relationship between correlation and reaction time was dependent on the direction of the eye movement. This correlation structure shared a number of common features between FEF and SC populations while the observed differences may be understood by considering their different levels in the oculomotor hierarchy.

First Author: Marc Coutanche (Faculty)	Poster Session: am
Presenting Author: Griffin Koch (Graduate)	Location: 5
Mentor/Lab: Marc Coutanche	Category: Imaging Techniques
Department: Psychology	
Title: Neural Correlates for Trait Memory Differences	
Summary: We used neuroimaging techniques to investigate brain regions involved in episodic and semantic memory. Additionally we compared the relative sizes of these regions with participants' memory characteristics (episodic or semantic).	

Abstract: Humans draw on an array of neural systems in the course of learning (and later remembering) the broad range of information encountered every day. Although healthy humans all have access to the same sets of brain systems there is evidence that people differ in the extent to which they draw on one type of memory versus another. Some individuals tend to emphasize the factual components of past events (semantic) while others are more biased to forming memories that are rich in spatiotemporal and contextual features (episodic). The current study investigated the neural basis for trait differences in the relative use of semantic episodic and spatial memory systems across individuals. We scanned the brains of 20 participants using magnetic resonance imaging (MRI) and related the volume of key brain regions and systems to scores on a survey of autobiographical memory which quantifies self-reported episodic semantic and spatial memory usage. We have found that brain regions associated with different memory systems differ in relative volume across individuals in ways that systematically track individual variation in trait memory biases. Our findings include the result that individuals with stronger semantic memory characteristics have a larger percentage of cortical gray matter occupied by the temporal poles and right angular gyrus. These anatomical findings contribute additional evidence to identifying the anterior temporal lobes and angular gyrus as "semantic hubs". More generally this study provides evidence that anatomical brain differences have a relationship with an individual’s memory characteristics.

First Author: Jared Kopelman (Graduate)	Poster Session: pm
Presenting Author: Jared Kopelman (Graduate)	Location: 47
Mentor/Lab: Ahmari	Category: Psychiatry
Department: Psychiatry	

Title: The Role of Candidate Gene Slc1a1 in OCD-relevant Behaviors in Mice

Summary: Obsessive Compulsive Disorder (OCD) is a debilitating psychiatric disorder characterized by intrusive obsessive thoughts and compulsive behaviors. Many studies have indicated that genetics play a significant role in the development of OCD. Here we investigate the role of Slc1a1 a gene associated with OCD in humans on behavior in mice.

Abstract: Obsessive Compulsive Disorder (OCD) is a debilitating psychiatric disorder characterized by intrusive obsessive thoughts and compulsive behaviors. The cause of OCD is unknown but human imaging studies have consistently shown hyperactivation of corticostriatal circuit nodes in patients with OCD. In addition twin and family studies show a significant role for genetics in its etiology with multiple studies identifying association of polymorphisms in the gene SLC1A1 with OCD. The most common of these OCD-associated polymorphisms increases expression of the encoded protein– the neuronal glutamate transporter excitatory amino acid transporter-3 (EAAT3). This protein is expressed in OCD-relevant corticostriatal circuits where it plays several roles including modulating the activation of peri-synaptic glutamate receptors. The OCD-linked allele is associated with increased SLC1A1 expression in lymphoblastoid cells human postmortem brain a luciferase reporter assay and transfected HEK cells where there is also a functional increase in EAAT3 protein activity as evidenced by increased glutamate uptake. There is also increased EAAT3 protein expression in striatum of Sapap3-knockout (KO) mice a model of OCD-like behavior. To directly test the effect of manipulations of EAAT3 levels on OCD-like behavior we used the Flexible Accelerated STOP Tetracycline Operator-knockin (FAST) system which combines cre flippase and tTA technology to create mice with either ablated or increased EAAT3 expression. Slc1a1-STOP knock-in mice that have ablated EAAT3 protein expression and function show blunted responses to pharmacologically-induced repetitive behavior. These mice have attenuated increases in stereotypy and hyperlocomotion in response to amphetamine and attenuated grooming increases in response to a dopamine D1 receptor agonist (Zike et al PNAS in press). Slc1a1-Overexpressing (OE) mice were created by breeding Slc1a1-tetO mice with CamKII-tTA mice. Slc1a1-OE mice show increased striatal EAAT3 expression that can be normalized by the administration of doxycycline allowing us to study the effects of temporally-specific EAAT3 overexpression. Here we present data from the initial behavioral characterization of Slc1a1-OE mice including OCD-relevant behaviors such as perseverative grooming pre-pulse inhibition and anxiety-like behavior.

First Author: Manoj Kumar (Postdoctoral)	Poster Session: am
Presenting Author: Manoj Kumar (Postdoctoral)	Location: 35
Mentor/Lab: Thanos Tzounopoulos	Category: Sensory
Department: Department of Otolaryngology	
Title: Cell-specific gain modulation by synaptically released zinc in cortical circuits of audition	
Summary: We used widefield transcranial imaging of the genetically-encoded calcium indicator GCaMP6 to identify the effects of synaptic zinc on populations of specific neuronal types in the auditory cortex and two-photon imaging to interrogate the effects of zinc on individual layer 2/3 neurons. Our results highlight synaptic zinc as a novel modulator of cortical responses to sound.	
Abstract: In many excitatory synapses mobile zinc is found within glutamatergic vesicles and is coreleased with glutamate. Ex vivo studies established that synaptically released (synaptic) zinc inhibits excitatory neurotransmission at lower frequencies of synaptic activity but enhances steady state synaptic responses during higher frequencies of activity. However it remains unknown how synaptic zinc affects neuronal processing in vivo. Here we imaged the sound-evoked neuronal activity of the primary auditory cortex in awake mice. We discovered that synaptic zinc enhanced the gain of sound-evoked responses in CaMKII-expressing principal neurons but it reduced the gain of parvalbumin- and somatostatin-expressing interneurons. This modulation was sound intensity-dependent and in part NMDA receptor-independent. By establishing a previously unknown link between synaptic zinc and gain control of auditory cortical processing our findings advance understanding about cortical synaptic mechanisms and create a new framework for approaching and interpreting the role of the auditory cortex in sound processing.	

First Author: Daniela Leronni (Faculty)	Poster Session: pm
Presenting Author: Daniela Leronni (Faculty)	Location: 26
Mentor/Lab: Friedlander	Category: Neurology & Neurodegenerative Diseases
Department: Neurological Surgery	

Title: Melatonin Synthesis Enzyme is Misregulated in Huntington's Disease Model

Summary: HD is an autosomal-dominant chronic neurodegenerative disease due to an extended polyQ repeat in the huntingtin (HTT) protein. Mutant HTT (mHTT) protein localizes in brain mitochondria and interferes with the inner membrane mitochondrial importing complex. Mitochondria import defect precedes overt symptoms onset in R6/2 mice suggesting it is an early disease mediating event. Melatonin is a potent endogenous free radical scavenger and it is deficient in humans with HD. The cause and consequence of melatonin deficiency in HD are unknown. Our hypothesis is that AANAT the melatonin synthesis rate-limiting enzyme is actively transported across the mitochondrial membrane and that this transport is disrupted in neurons expressing mHTT.

Abstract: Melatonin is a well-known hormone secreted by the pineal gland and it is involved in circadian regulation. This hormone has several other important functions in the organism and it is shown to be neuroprotective in many neurodegenerative diseases. Melatonin can exert anti-apoptotic effects mainly targeting mitochondria but it can also enhance cell survival pathways leading to cell rescue. In some neurodegenerative diseases for example Huntington's disease (HD) melatonin plasma level is decreased. However circulating melatonin levels regulated by pineal gland activity do not reflect neuronal melatonin levels and the mechanisms for making and maintaining melatonin in neurons is unknown. High levels of melatonin have been found in mitochondria but little is known about the transport of melatonin inside the mitochondria. Our preliminary data show that Arylalkylamine N-acetyltransferase (AANAT) the rate-limiting enzyme in the production of melatonin is in the mitochondria. AANAT must actively be transported from the cytosol across the mitochondrial membranes a process known to be disrupted in HD patients. HD is an autosomal-dominant chronic neurodegenerative disease due to an extended polyQ repeat in the huntingtin (HTT) protein. Recently our group showed that mutant HTT (mHTT) protein localizes in brain mitochondria and interferes with the inner membrane mitochondrial importing complex thus inhibiting mitochondrial protein import. Our data demonstrated that the mitochondrial import defect precedes overt symptoms onset in R6/2 mice suggesting it is an early disease mediating event. Our hypothesis is that AANAT is actively transported across the mitochondrial membrane and that this transport is disrupted in neurons expressing mHTT. The consequences of defective import of AANAT would be decreased melatonin level which could make HD neurons more vulnerable to stress contributing to the pathology of HD disease. How AANAT import is effected in HD mitochondria will provide important insights for future studies to investigate dysregulation of neuronal melatonin synthesis in HD.

First Author: Yuanning Li (Graduate)	Poster Session: am
Presenting Author: Yuanning Li (Graduate)	Location: 49
Mentor/Lab: Avniel Ghuman	Category: Brain Models and Systems
Department: Neurological Surgery	

Title: Neurodynamics of expression coding in human fusiform

Summary: Using intracranial EEG data from human subjects and multivariate pattern analysis techniques we showed that facial expression information can be decoded from the neural activity in different subdivisions of human fusiform cortex at different stages of the process. This suggests that fusiform activity may contribute to the representation of the structural difference between facial expressions and the posterior and anterior fusiform are dynamically involved in distinct stages of facial information processing.

Abstract: Face processing is mediated by a network involving multiple distributed areas in the brain with the occipital face area (OFA) fusiform face area (FFA) and posterior superior temporal sulcus (pSTS) considered the core nodes of the network. Results suggest that OFA is primarily involved in early perception of facial features FFA is mainly involved in the processing of the static aspects of faces and pSTS is mainly involved in the processing of the dynamic aspects of faces. Based on these results the first models of the neural basis of face processing posited that pSTS codes for expression and FFA codes for identity. Recently several neuroimaging studies have suggested that the FFA is involved in the processing of facial expressions and recent models have posited that the FFA is involved in structural encoding of face expression. To mediate between these hypotheses we recorded intracranial electroencephalography (iEEG) data from 19 patients with electrodes in the OFA FFA and/or pSTS during face expression perception. Using pattern classification techniques our results confirmed the existence of facial expression encoding in the fusiform area. At the early stage of visual information processing (50-250 ms after stimulus onset) neural activity from posterior fusiform area contains facial expression information; and at the late stage of visual processing (250-450 ms after stimulus onset) neural activity from anterior fusiform area contains facial expression information. In addition facial expression information is seen in OFA and pSTS at the early stage of the process. Notably the effect size of fusiform encoding of facial expressions is much smaller than the encoding for facial identity. Taken together these results suggest that fusiform activity may contribute to the representation of the structural difference between facial expressions and the posterior and anterior fusiform are dynamically involved in distinct stages of facial information processing.

First Author: Witold Lipski (Faculty)	Poster Session: am
Presenting Author: Witold Lipski (Faculty)	Location: 18
Mentor/Lab: Richardson	Category: Brain-Machine Interfaces
Department: Department of Neurosurgery	

Title: Speech encoding in the human subthalamic nucleus

Summary: The neurophysiological mechanisms underlaying speech production is understood largely in terms of neocortical structures located on the brain surface because they can be studied non-invasively in humans. However the contributions of deep brain structures such as the subthalamic nucleus are not well understood. Here we present evidence of speech encoding in the subthalamic nucleus and suggest ways in which these data can influence our models of speech production as well as how these findings can improve treatment of patients with movement disorders.

Abstract: Speech production and control is disrupted in many neurological diseases that involve the basal ganglia. Notably hypophonia and hypokinetic dysarthria (characterized by decreased motor gain) are prevalent in patients with Parkinson's disease (PD). Deep brain stimulation (DBS) of the subthalamic nucleus (STN) produces predictable improvements in other motor symptoms of PD but does not result in consistent improvement in speech and can negatively impact language function. However neurophysiological models of speech production typically do not account for the involvement of basal ganglia nuclei. To examine the role of the STN in speech production we recorded STN neuron activity STN local field potentials (LFP) and spoken acoustics while 14 PD subjects performed a speech task during awake microelectrode recording (MER)-guided DBS surgery. On each trial subjects were asked to read aloud a consonant-vowel-consonant syllable presented on a computer screen. Spike waveforms were sorted into single- and multi-unit recordings. LFP signals were bandpass filtered into canonical bands (delta 2-4Hz theta 4-8Hz alpha 8-12 Hz beta 13-30Hz and gamma 50-90Hz). Power changes were calculated as a z-score relative to baseline after applying a Hilbert transform to estimate signal amplitude and phase. First we found evidence for the participation of STN neurons in speech production. Nearly half of single unit recordings (22 of 45 in 13 subjects) showed either increases or decreases in firing rate when aligned to speech onset. STN LFP recordings also showed evidence for modulation related to speech production. Consistent with tracking the motor aspects of speech we found an increase in gamma power in 13/14 subjects locked to the onset of speech but not locked to cue presentation. In contrast theta power increases were locked to cue presentation rather than speech onset (11/14 subjects) and this modulation was associated with an increase in inter-trial phase consistency (ITPC) (7/14 subjects) suggesting a role for theta-encoding in cognitive processing prior to speech onset. Likewise we observed alpha and beta power decreases locked to cue presentation but not to speech onset. Importantly in a subset of these recordings we observed differences in both alpha and beta ITPC that were specific to whether the presented stimulus was a real word or a non-word. Lastly we observed delta power and ITPC increases in relation to both cue presentation and speech onset (11/14 subjects) further suggesting that several types of speech-related information transfer occur within the STN.

First Author: Shi Tong Liu (Graduate)	Poster Session: am
Presenting Author: Shi Tong Liu (Graduate)	Location: 37
Mentor/Lab: Srivatsun Sadagopan	Category: Sensory
Department: Bioengineering	

Title: Optimal features for auditory recognition

Summary: Using a theoretical information approach we extracted a set of auditory features that can be used to identify vocalizations types from any given marmoset vocalizations. These features also closely correspond to previously found nonlinear neural responses in marmoset A1 suggesting that the tuning properties of neurons in higher auditory cortical stages are likely the result of goal-directed optimization.

Abstract: A central challenge in auditory neuroscience is to understand how observed patterns of neural activity in the auditory system relate to behavior. For example neurons in primary (A1) as well as higher auditory cortical areas exhibit highly nonlinear and surprisingly specific tuning properties but our understanding of these responses is only at a descriptive level and the critical question of how these responses might support behavior remains unresolved. Here we show that nonlinear A1 responses encode essential features for the classification of ethologically-relevant sounds such as conspecific vocalizations (calls). In vocal animals increasing neural resources are committed for the processing of calls as one ascends the auditory processing hierarchy. Therefore the categorization of call types is a reasonable computational goal for the auditory cortex in these animals. We asked using a theoretical information maximization approach how this goal can be best accomplished. We used marmoset vocalizations as our experimental model. First we transformed the vocalizations into spectrotemporal patterns of auditory nerve activity (cochleagrams) using a highly realistic model of the auditory nerve. Based on an earlier model for visual classification we then randomly generated a large number of features or spectrotemporal snippets from these cochleagrams. We used a greedy-search algorithm to choose the most informative and least redundant feature set for call categorization. We found that call categorization could be accomplished with high accuracy using just a small number of features. Highly informative features tended to be of intermediate size and complexity. Most interestingly the responses of model feature-selective neurons predicted nonlinear neural responses in marmoset A1 in astonishing detail. These results demonstrate that the auditory cortex uses a mid-level feature based strategy for the recognition of complex sounds. These results further suggest that the tuning properties of neurons in higher auditory cortical stages are likely the result of goal-directed optimization.

First Author: Emanuel Loeza (Postdoctoral)	Poster Session: am
Presenting Author: Emanuel Loeza (Postdoctoral)	Location: 43
Mentor/Lab: Michael Gold	Category: Sensory
Department: Neurobiology	

Title: Peripheral GABAA receptors regulate colonic afferent excitability

Summary: Peripheral GABAA receptors can modulate the colonic afferent activity

Abstract: The role of GABAA receptors located at central terminals of primary afferents fibers in the regulation of afferent input to the superficial dorsal horn has been well established. However there is evidence that GABAA receptors are trafficked to peripheral terminals as well with at least some evidence suggesting that in the presence of tissue injury these receptors are functional. Because there are several sources of GABA in the colon in the absence of tissue injury we hypothesized that the excitability of colonic afferents is established at least in part via GABA acting at GABAA receptors on the peripheral terminals of these afferents. To test this hypothesis we utilized an in vitro mouse colorectum-pelvic nerve preparation in which GABAA receptor agonists and antagonists could be applied to the receptive field of functionally identified afferent fibers as a means of assessing changes in stimulus response properties. Using single-fiber recordings of the pelvic nerve we found that the application either GABA or muscimol results in both an increase in the amount of colon stretch required to evoke an action potential a decrease in the number of stretch-evoked action potentials. Both agonists also increased the electrical-threshold and decreased the apparent conduction velocity of the evoked action potential. Conversely the GABAA-antagonist bicuculline or blocker picrotoxin decreased the stretch threshold and increased the number of stretch-evoked action potentials. Picrotoxin also increased the apparent conduction velocity of the electrical stimulation evoked action potential evoked by electrical stimulation. These results suggest that peripheral GABAA receptors are not only present and functional in the peripheral terminals of colonic afferents but that activation of these receptors via endogenous GABA release contributes to the establishment of colonic afferent stimulus-response properties. These results raise the intriguing possibility that approaches to selectively increase peripheral GABAA receptor signaling could be used to treat visceral pain in the absence of central nervous system side effects. Work supported by NIH grant R01 DK107966.

First Author: Jacob Mann (Graduate)	Poster Session: pm
Presenting Author: Jacob Mann (Graduate)	Location: 32
Mentor/Lab: Donnelly	Category: Neurology & Neurodegenerative Diseases
Department: Neurobiology	

Title: Optogenetic Induction of TDP-43 Proteinopathy

Summary: Aggregation of various disease-linked proteins is a common pathological process experienced in neurodegenerative diseases such as Alzheimer's Disease Amyotrophic Lateral Sclerosis and Parkinson's Disease among others. However experimentally controlling this process of protein aggregation has been historically problematic. Here we show a new model of protein aggregation by using light-responsive proteins isolated from plants that allows for a previously unachievable level of spatial and temporal control.

Abstract: Over the last twenty years mutations in over 35 different genes have been linked to the development of familial forms of ALS (fALS); however fALS only accounts for roughly 10% of all ALS cases. The remaining 90% of patients suffer from sporadic ALS (sALS) with no family history of disease and unknown causes of pathogenesis. Regardless of all this genetic and pathogenic complexity remarkably nearly every single ALS patient (~97%) shares a common neuropathology in the form of cytoplasmic aggregates of a protein called TAR DNA-binding protein of 43 kDa (TDP-43) found in degenerating regions of the nervous system. Current cellular models of this neurodegenerative proteinopathy often rely on the overexpression of disease-linked mutant proteins to induce pathological protein aggregation. However mutations in the TARDBP gene only account for ~1% of sporadic (sALS) and 4% of familial ALS (fALS) cases. The vast majority of patients do not harbor mutations in this gene yet still experience TDP-43 aggregation. Similarly rodent models of ALS produced from the overexpression of these mutant proteins have been historically unreliable and often fail to generate TDP-43-positive inclusions. Here we present a novel optogenetic-based technique to induce pathological aggregation of TDP-43 with a previously unachievable level of spatial and temporal control. Using this approach we show the tunable oligomerization and aggregation of TDP-43 and disease-related truncations of the protein in response to varying light stimulation paradigms. These induced TDP-43 aggregates share similar pathological characteristics with TDP-43 inclusions observed in ALS patient tissue and also appear to result in endogenous TDP-43 loss-of-function mechanisms that have been previously implicated in disease progression. Utilizing this technique we have uncovered perturbed oligomerization dynamics due to fALS-linked mutations in TDP-43 that may underlie the enhanced aggregation properties and neurotoxicity of these mutated proteins. We have also begun to identify novel pathway modulators of TDP-43 aggregation that may play a role in the development of both fALS and sALS. This technique can be applied to a number of different disorders will allow for more precise temporal and spatial control over protein aggregation than has been previously possible. Additionally the ability to reliably induce protein aggregation with light alone will allow for in-depth investigations into the effects of these pathological aggregates on various cellular pathways and downstream pathological processes.

First Author: Elizabeth Manning (Postdoctoral)	Poster Session: pm
Presenting Author: Elizabeth Manning (Postdoctoral)	Location: 49
Mentor/Lab: Ahmari	Category: Psychiatry
Department: Psychiatry	

Title: Impairments in cognitive flexibility relevant to OCD and accompanying alterations in cortico-striatal activity in SAPAP3 knockout mice

Summary: Patients with obsessive compulsive disorder (OCD) have trouble flexibly adapting their behavior. A leading genetic OCD mouse model was examined in a flexible decision making task. This revealed that approximately half of the OCD mice failed the flexible decision making task and the half that were successful showed activation of specific brain circuits that aren't activated in normal mice during flexible decision making.

Abstract: Background: Functional imaging studies have strongly implicated cortico-striatal circuit dysfunction in the pathophysiology of obsessive compulsive disorder (OCD). However the mechanisms by which this dysfunction gives rise to OCD symptoms are unclear with hyperactivity typically observed at baseline and during symptom provocation and hypoactivity typically observed during cognitive testing. Studies in preclinical rodent models provide a unique opportunity to investigate this discrepancy. To date transgenic mouse models have provided substantial insight about striatal dysfunction underlying OCD-relevant compulsive grooming. In contrast there have been no studies examining the neural mechanisms underlying cognitive impairment in OCD-relevant mouse models. Methods: SAPAP3 knockout mice (KOs)–a leading transgenic OCD model– and wild-type (WT) littermate controls were tested in an operant reversal learning paradigm to assess cognitive flexibility. Cortical and striatal activation associated with training on day 1 of reversal learning was assessed in a separate cohort of mice via quantitative cFos expression in 10 regions of interest (ROIs). Interactions between regional cFos expression genotype and reversal performance (correct vs incorrect lever presses) were assessed using linear regression analysis. Results: SAPAP3 KOs were significantly impaired in reversal learning (p<0.001) with ~40% of mutant mice (n=13/29) failing to acquire a reversed contingency (criteria: <20 active lever presses per day across 5 days of reversal training). Reversal learning impairment was unrelated to the severity of compulsive grooming observed in SAPAP3 KOs. Impaired reversal learning was also observed in female SAPAP3 KOs (n=9 WT 8 KO; 4 KOs failed reversal and 4 KOs acquired the task; training day x active lever press interaction p=0.008). Analysis of reversal learning-related cFos expression revealed genotype differences in the association between activity in the prelimbic prefrontal cortex (PrPFC) and nucleus accumbens shell (NAcS) and reversal performance (response ~ Genotype x ROI cFos x lever press type p<0.005). Both regions appeared to show compensatory neural activity in SAPAP3 KOs which was associated with improved acquisition of correct lever pressing following reversal. No such relationship was observed in WT mice. Conclusions: Our studies are among the first to describe neurocognitive impairments in a transgenic OCD mouse model. These findings implicate compensatory neural activity in the PrPFC-NAcS circuitry in successful reversal learning in SAPAP3 KO mice in line with recent studies demonstrating that stronger functional connectivity in cortico-striatal circuits is associated with intact cognition in OCD patients (Vaghi et al. 2017). Ongoing studies using in vivo microscopy to measure neural activity in SAPAP3 KOs during reversal learning are directly testing this hypothesis. Our results also highlight the utility of using OCD-relevant cognitive paradigms in preclinical mouse models to gain mechanistic insight regarding the role of cortico-striatal circuit dysfunction in OCD.

First Author: Misagh Mansouri Boroujeni (Postdoctoral)	Poster Session: am
Presenting Author: Misagh Mansouri Boroujeni (Postdoctoral)	Location: 11
Mentor/Lab: Robert Gaunt	Category: Brain-Machine Interfaces
Department: Physical Medicine and Rehabilitation	

Title: Differences in Intramuscular EMG Activity in Able-bodied Subjects and Transradial Amputees during Structured Hand Movements

Summary: By combing neural data directly from the residual muscle of an amputee with accurate biomimetic models of an intact hand we can inform the design of bio-inspired controllers that generate prosthesis control signals from the biomechanical function of the muscles and the resulting movement dynamics.

Abstract: Commercial myoelectric prostheses have limited capabilities to simultaneously control multiple degrees of freedom. These prostheses typically rely on signals recorded from surface EMGs placed on the residual limb which are not the full set of extrinsic hand muscles required to actuate individual fingers. In addition standard control approaches usually use pattern recognition or map muscle activity to specific prosthesis movements while largely ignoring underlying biomechanics. Understanding the coordinated activity of extrinsic hand muscles and how their activity results in individual joint movements across a wide range of hand configurations is an essential step towards improving the dexterity of prosthesis control. Here we use dimensionality reduction and clustering techniques to investigate these relationships in able-bodied subjects and an amputee.

First Author: Corentin Massot (Postdoctoral)	Poster Session: am
Presenting Author: Corentin Massot (Postdoctoral)	Location: 51
Mentor/Lab: Neeraj J. Gandhi	Category: Brain Models and Systems
Department: bioengineering	

Title: Laminar Organization of the Spiking Activity in the Superior Colliculus

Summary: The superior colliculus plays a major role in oculomotor sensorimotor transformation. Here we show that SC has a laminar organization of its spiking activity. This organization may reflect a network architecture suited for realizing the sensorimotor transformation.

Abstract: The superior colliculus (SC) plays a major role in transforming sensory signals that register a target into motor commands that produce an eye movement to the stimulus. However the underlying network activity that produces the sensorimotor transformation is not well understood. The sensory and movement responses are represented by two bursts of activity across the different layers of SC. Previous studies have shown that neurons in SC can be grouped according to their spiking activity during delayed saccade tasks. However is there also a laminar organization of the spiking activity in SC? Here we addressed this question by recording populations of neurons using a 16-channel laminar probe in SC of two rhesus monkeys performing randomly interleaved delayed visually-guided and memory-guided saccades. The electrode penetration spanned all layers of SC and was orthogonal to its surface; hence the optimal target locations and/or saccade vectors were comparable across all recording contacts. The target was positioned either close to the center of the response field or at the diametrically opposite location. Here we looked at the spiking activity at different epochs during each trial and classified the neuron's response into visual burst movement burst and build-up neuron. Preliminary analyses reveal a 4-fold division of the SC: 1)\tNeurons presenting visual burst activity without pre-saccadic build-up activity nor movement burst activity were mostly found at the most dorsal positions. 2)\tNeurons presenting visual and movement burst activity without pre-saccadic build-up were mostly found deeper than the neurons described in 1). 3)\tNeurons presenting visual and movement burst activity with a pre-saccadic build-up of activity were mostly found deeper than the neurons described in 2). 4)\tNeurons presenting movement burst activity without pre-saccadic build-up activity were mostly found deeper than the neurons described in 3) and at the most ventral positions. Taken together these results may suggest the existence of a laminar organization of the spiking activity in SC. What makes this functional organization a suited neural network architecture for realizing the sensorimotor transformation will be the object of future research.

First Author: Kevin Mohsenian (Graduate)	Poster Session: am
Presenting Author: Kevin Mohsenian (Graduate)	Location: 32
Mentor/Lab: Dr. Neeraj Gandhi	Category: Sensory
Department: Bioengineering	

Title: Population activity in the superior colliculus for saccades to moving targets

Summary: The population activity in the superior colliculus for saccades to moving targets is unknown. We plan to combine neural recordings to be able to estimate the ensemble response for saccades made the amplitude matched locations and compare the activity for different speeds and directions. We will test different saccade vector encoding mechanism that the superior colliculus may employ.

Abstract: The ability to intercept moving targets is crucial for both survival and success. The superior colliculus (SC) a central hub for sensory-motor integration issues the movement command to produce saccadic eye movements. For saccades to stationary targets the SC population activity is characterized as a Gaussian distribution. The SC contributes to the generation of saccades to moving targets also but its exact role in not clear. In particular delays in neural transduction cause the sensory representation of a moving target's position to lag its actual position by 50-100 msec. Target motion during this delay must be accounted for in order to direct action to its future location. Previous work recording single units in the SC reported that some neurons issue the saccade command to a target's location 50-100ms prior to saccade onset. Incidentally other SC neurons seem to account for the neural transduction delay reflecting activity for the executed saccade vector. Our objective here is to determine the population activity of the SC for saccades to moving targets. To address this knowledge gap we recorded neural activity from a rhesus monkey which performed a delayed saccade task. The delay period initial target location target speed (range: 15-45 deg/s) and target direction (inward outward) were varied randomly to elicit saccades with different vectors (amplitude and angle). Trials using stationary targets and moving targets were randomly interleaved. SC population activities of the two trial types were compared through matching the saccade vector performed by the subject. Preliminary results lend support to an alternative view – namely that the SC population activity when the target is moving is not Gaussian. We will assess whether the non-Gaussian population can be used to differentiate between prominent algorithms (weighted vector summation vs. weighted vector averaging) for decoding SC activity for saccade generation.

First Author: Pilar Montes Lourido (Postdoctoral)	Poster Session: am
Presenting Author: Pilar Montes Lourido (Postdoctoral)	Location: 39
Mentor/Lab: Srivatsun Sadagopan	Category: Sensory
Department: Neurobiology	

Title: Emergence of selectivity and invariance in primary auditory cortex

Summary: In real world conditions the sounds that we hear are degraded by environmental factors such as noise echoes or other speakers. Our auditory system is able to maintain sound perception despite all these disturbances. This study is aimed at understanding how the brain accomplished this feat.

Abstract: Humans and vocal animals use vocalizations to communicate and interact with members of their species. Real-world environments add noises echoes and other sounds to the intended message degrading its acoustic content. However we can maintain stable sound perception independent of listening conditions. We aim to determine the neural mechanisms by which stable sound perception can be achieved. To address this question in the context of natural behaviors we use Guinea pig (GP) vocalizations as an experimental model. Previous studies in GPs have shown that at the level of the inferior colliculus and thalamus few neurons show selective responses for individual vocalization categories. In primary and secondary cortical areas more neurons become selective for particular vocalization categories. It is not known however at which stage of the auditory hierarchy this selectivity arises and how it is preserved or changed in the presence of real-world distortions. Here we first tested if GPs can perceive vocalizations presented in a wide range of noisy environments using pupillometry as a behavioral readout. This allowed us to determine the GP's threshold for detecting a vocalization in noise. We then recorded single-unit activity in the medial geniculate body (MGB) and auditory cortex (A1) of awake GPs passively listening to vocalizations in different listening conditions. We discovered that neurons in MGB and thalamorecipient A1 layers (A1 L4) have low selectivity for vocalization categories and are more susceptible to acoustic distortions. In contrast superficial layers of A1 (A1 L2/3) were highly selective for vocalizations and more invariant to distortion. These data demonstrate that both vocalization selectivity and invariance to listening conditions co-emerge in A1 L2/3. These results suggest that a dense representation of complex sounds in A1 L4 is transformed into an invariant and sparse representation in A1 L2/3.

First Author: David Montez (Postdoctoral)	Poster Session: am
Presenting Author: David Montez (Postdoctoral)	Location: 60
Mentor/Lab: Beatriz Luna	Category: Learning
Department: Psychiatry	

Title: Developmental stabilization of neural gain signals improves mean behavioral performance and behavioral variability

Summary: We develop a computational model of working memory processes that accounts for developmental changes in behavioral performance observed during adolescence.

Abstract: Behavioral variability is an important barometer of cognitive functioning. During adolescent development behavioral responses both improve on average as well as stabilize. Mechanistically accounting for the stabilization of behavior is critical to our understanding of adolescent neural development. Here we report results from a longitudinal working memory study performed over 10 years in a cohort of 126 subjects between the ages of 8 and 33 years. We develop a computational model of memory-guided saccade (MGS) performance and demonstrate that improvements in mean behavioral performance and behavioral variability can be accounted for solely in terms of stabilizing neural variability. We find that behavioral performance in the memory-guided saccade task improves and stabilizes during adolescence. By incorporating multiple sources of independent gain variability in a high-dimensional drift diffusion race model that we can account for the improvements in mean behavior and behavioral variability that are observed during adolescent development. Analysis of the trial-to-trial relationship between memory-guided saccade reaction times and accuracies reveals a peculiar U-shaped speed-accuracy relationship. Further analysis shows that this relationship can be accounted for by a balance of independent variability affecting working memory and response threshold gain signals. Our results indicate that independent trial-to-trial variability in gain signals that affect working memory maintenance and response thresholds can account for peculiar speed-accuracy relationships observed in our data. Moreover developmental improvements in both mean behavioral performance and behavioral variability can both be accounted for by the parallel stabilization of two independent sources of neural gain variability.

First Author: Sarah Najjar (Graduate)	Poster Session: am
Presenting Author: Sarah Najjar (Graduate)	Location: 42
Mentor/Lab: Dr. Kathryn Albers	Category: Sensory
Department: Neurobiology	

Title: Sensory Innervation of the Enteric Nervous System: A Two-Way Street?

Summary: This study investigates the pathways connecting the gut's own nervous system (called the enteric nervous system) to the central nervous system. Understanding these connections will help us to understand the origin of and treatments for gastrointestinal disorders.

Abstract: The enteric nervous system (ENS) consists of a mesh-like network of neurons intrinsic to the gastrointestinal (GI) tract which controls GI function. Extrinsic sensory neurons innervating the gut also have a key role in GI processes as they initiate autonomic reflexes and convey sensory information (e.g. pain and bloating). Thus far it has been difficult to parse out the function of these sensory neurons due to the dense autonomic innervation of the gut (in addition to sensory innervation). Our lab has overcome this limitation by employing calcium imaging techniques to explore the connectivity between the ENS and its extrinsic sensory inputs. Using mice that express GCaMP6 in all cells we developed an ex vivo preparation in which the activity of ENS neurons and sensory neurons in L6 dorsal root ganglia (DRG) can be recorded. We recorded L6 sensory neuron activity in response to stimulation of the colon. We then applied electrical stimulation to the L6 DRG and imaged activity in the myenteric ganglia of the ENS. Surprisingly we found that 20 Hz stimulation of the DRG resulted in calcium signals in 17.1±2.8% of cells per myenteric ganglion and the average calcium influx (ΔF/F) was 24.8±5.5 (n=54 cells). This DRG stimulation also resulted in smooth muscle contraction in the colon 1.19±0.16 seconds after application of stimulus (and usually after activation of the myenteric ganglia cells). Finally we found that electrical stimulation of the DRG impacted the activity of the gut's non-neuronal pacemaker cells in the sub-mucosal plexus (interstitial cells of Cajal; ICCs). The 20 Hz stimulus decreased the frequency of ICC oscillations to 90±1.8% of baseline (or by 1.3±0.3 cycles per minute). Taken together these data indicate extrinsic sensory neurons have a significant efferent role in the ENS. Our imaging methods will enable further exploration of ENS-sensory neuron connectivity and how these interactions may become disordered in pathological states (e.g. visceral pain associated with irritable bowel syndrome and inflammatory bowel disease).

First Author: Ameya Nanivadekar (Graduate)	Poster Session: am
Presenting Author: Ameya Nanivadekar (Graduate)	Location: 47
Mentor/Lab: Rehab Neural Engineering Labs/Lee Fisher	Category: Sensory
Department: Bioengineering	

Title: Modulation of phantom limb pain using epidural stimulation of the cervical dorsal spinal cord

Summary: Electrical stimulation of the cervical dorsal spinal cord can result in acute and sub-chronic changes in the intensity and incidence of phantom limb pain in upper limb amputees.

Abstract: Introduction: Pain is a common comorbidity of conditions such as peripheral nerve injury substance-induced neuropathy and trauma. Nearly 1.5 billion people worldwide suffer from chronic pain with the estimated cost of health care nearly $275 billion. The mechanisms of neuropathic pain are poorly understood and its evaluation in humans is complex because most stimuli required to induce neuropathic pain produce irreversible damage. Recent evidence suggests that the incidence of chronic phantom limb pain can be regulated by delivering sensory feedback that is relevant to the amputated limb. This study aims to determine whether cervical spinal root stimulation to elicit sensations localized to the amputated arm can also result in concomitant changes in PLP Methods: All procedures were approved by the University of Pittsburgh Institutional Review Board and the US Army Human Research Protection Office. Two study participants were implanted with three 8 or 16 contact spinal cord stimulation leads (Boston Scientific) in the lateral epidural space of the cervical spinal cord. Stimulation electrode amplitude frequency and pulse width were varied across trials. The location intensity and modality of the evoked percepts was recorded. The intensity of PLP was recorded on a visual analog scale (VAS) after every stimulation trial. Additionally the McGill Pain Questionnaire (MPQ) was administered on a weekly basis and again one month following explantation. The leads were explanted after 2-4 weeks. Results: A total of 1493 trials evoked localized sensations of which 580 PLP episodes were reported (38.9%) at a mean intensity of 2.5 ± 1.9 on the VAS. For the 115 electrodes that evoked a sensation stimulation amplitude and pulse width were related to the intensity and incidence of PLP respectively. Furthermore a clinically significant (>5 points) reduction in PLP was observed on the MPQ in subject 1 (9 points) and subject 2 (8 points) at 1-month follow-up. Additionally a strong correlation between the modality of stimulation evoked non-PLP sensation and the intensity of PLP reported was observed. Conclusion: This study suggests that stimulation amplitude and pulse width may modulate the intensity and frequency of a PLP episode. We further observed time-dependent PLP modulation such that the immediate post-stimulation phase was associated with increased PLP that may be coupled to a long-term reduction in PLP.

First Author: Amy Ni (Postdoctoral)	Poster Session: am
Presenting Author: Amy Ni (Postdoctoral)	Location: 58
Mentor/Lab: Marlene Cohen	Category: Learning
Department: Neuroscience	

Title: Neuronal population changes underlying visual perceptual learning and attention

Summary: Attention and perceptual learning can both improve perception on the same visual task. However they operate on very different timescales. We found a single robust relationship between changes in neuronal activity and changes in behavioral performance whether those changes occurred quickly with attention or slowly with perceptual learning.

Abstract: Understanding the way that different processes that improve perception affect populations of neurons might help identify the aspects of the neural code responsible for perception and cognition and test the hypothesis that a single neuronal computation underlies all processes that improve perception. We compared the neuronal correlates of attention which improves perception of important parts of a crowded scene to those of perceptual learning which slowly improves observers' ability to discriminate well-practiced stimuli. While these two processes both improve perception they operate on very different timescales: attention can fluctuate on the scale of hundreds of milliseconds while perceptual learning improves performance over weeks to months of repeated practice. We recorded from populations of neurons in V4 using multi-electrode arrays while two rhesus monkeys learned to perform a visually guided task that required that they switch attention between two visual stimuli. This approach allowed us to simultaneously measure the effects of attention and perceptual learning on perception and on populations of visual neurons. Both attention and perceptual learning improved perceptual performance and both affected the extent to which trial-to-trial variability in response to repeated presentations of the same stimulus was correlated between pairs of neurons. Further we found a single robust relationship between correlated variability and behavioral performance whether correlated variability changed quickly with attention or slowly with perceptual learning. Finally we found that correlated variability was oriented along the dimensions in population space used by the animal on a trial-by-trial basis to make decisions. These findings support the hypothesis that all processes that improve perception use similar neuronal computations.

First Author: Emily Oby (Postdoctoral)	Poster Session: am
Presenting Author: Emily Oby (Postdoctoral)	Location: 16
Mentor/Lab: Aaron Batista	Category: Brain-Machine Interfaces
Department: SNI	

Title: Learning to generate new patterns of neural population activity

Summary: If we can understand the neural mechanisms of learning then we can harness those mechanisms to improve clinical applications of brain machine interfaces. In the lab we train animals to learn very challenging BMIs and can observe the neural strategies whereby they learn.

Abstract: Learning requires networks of neurons to generate new patterns of activity. We can study the changes in neural population activity that accompany learning by using a brain-computer interface (BCI) in which users modulate neural activity to control a computer cursor. A BCI paradigm has advantages for studying the neural population mechanisms of learning because in a BCI we record from all the neurons that directly influence the behavior the causal relationship between neural activity and behavior is known exactly and that relationship can be altered by the experimenter to induce learning. Here we examine the changes in population activity in primary motor cortex (M1) of Rhesus monkeys that accompany the learning of a new BCI mapping for which optimal performance would require the generation of new population patterns of activity. We use dimensionality-reduction techniques to observe neural changes. The activity of a neural population can be represented as a point in a high-dimensional neural space wherein each dimension corresponds to the activity of one neuron. Characteristic patterns of co-modulation among the neurons comprise a low dimensional subspace within the neural space. We refer to this subspace of naturally-occurring neural activity patterns as the intrinsic manifold. We confront animals with new BCI mappings for which successful control would require neural activity patterns that are outside the intrinsic manifold. We find that when given many days of practice animals can learn to use these new BCI mappings. This raises the question of how neural activity patterns develop to support this new behavioral capacity. Here we present three neural strategies for learning. A suboptimal strategy is to take advantage of the existing population activity patterns by reassociating them with different movements. While this strategy could lead to behavioral improvements control is not expected to be optimally efficient. Optimal strategies require activity patterns to realign with the BCI mapping in a manner that maximizes behavioral performance. This realignment could happen in a way that adheres to the existing co-modulation relationships i.e. the population activity patterns are within the intrinsic manifold. Alternatively realignment could disregard the existing co-modulation relationships i.e. the population activity patterns are outside of the intrinsic manifold. This outside manifold realignment would yield the best control but is also the strategy we expect to be hardest for a network of neurons to achieve. We see evidence of a combination of these strategies within a given experiment. We conclude that under sufficient learning pressure animals can indeed exhibit new neural population activity patterns. However this learning takes time and even then it seems to occur only when necessary.

First Author: Sandip Panesar (Postdoctoral)	Poster Session: am
Presenting Author: Sandip Panesar (Faculty)	Location: 3
Mentor/Lab: Juan Fernandez-Miranda	Category: Imaging Techniques
Department: Neurological Surgery	

Title: High-Definition Fiber Tractography of Ventral External-Capsule White Matter

Summary: High definition fiber tractography is able to visualize white-matter pathways in living subjects. There is significant controversy pertaining to the structure and connectivity of two critical white-matter pathways (inferior fronto-occipital fasciculus and uncinate fasciculus). We have been able to consistently reproduce the aforementioned tracts in MRI scans of 30 single-subjects and have a template consisting of MRI data from 842 subjects averaged into one which we have used to validate our findings.

Abstract: High-definition fiber tractography (HDFT) is an in vivo imaging modality derived from diffusion-weighted magnetic resonance imaging (dwMRI) data. HDFT addresses a major limitation of diffusion tensor imaging (DTI) based tractography namely its inability to visualize areas of crossing white-matter fibers. Two important association fascicles traverse the ventral external capsule: Inferior fronto-occipital fasciculus (IFOF) and uncinate fasciculus (UF). These pathways are thought to play critical roles in language functions amongst other functions. Significant controversy exists in the literature regarding origins subdivisions and cortical terminations of both tracts. We conducted HDFT in 30 single subjects from the human connectome project and used a novel atlas consisting of averaged diffusion data from 842 individual subjects to verify our findings. We found distinct tripartite division of the IFOF with conserved bihemispheric volumetry. UF consisted of two components on the left however bipartite structure was inconsistently found on the right. As such left-hemispheric UF's demonstrated significantly greater volumetry compared to the right. Our findings were verified by the atlas. Our findings indicate that the IFOF may indeed play a role in language particularly semantic tasks and UF may play a role in both language and emotion.

First Author: Andrew Papale (Postdoctoral)	Poster Session: am
Presenting Author: Andrew Papale (Postdoctoral)	Location: 50
Mentor/Lab: Bryan M. Hooks	Category: Brain Models and Systems
Department: Neurobiology	

Title: Corticostriatal projections map the organization of inter-area corticocortical connectivity

Summary: The motor system relies on convergence of sensory and motor inputs from cortex to subcortical structures such as the motor system's basal ganglia in order to develop motor skills. In this work we study the connections from cortex to basal ganglia for different types of cortical neurons.

Abstract: A leading circuit model of corticostriatal connectivity is that cortical motor regions form parallel functional loops through the basal ganglia. This model explains the pattern of projections from cortical areas to different regions of striatum and provides a basis for classifying subdivisions of striatum based on divergence of cortical inputs. We tested the generality of this model by examining striatal projections from layer-specific subtypes of pyramidal neurons. Mice expressing Cre in either intratelencephalic layer 5A or pyramidal tract layer 5B were injected with three different Cre-dependent fluorescent viral vectors in primary somatosensory primary motor secondary sensory and frontal cortical areas. Following sectioning and imaging images were aligned to a reference atlas using BrainMaker software (MBF Bioscience). Axonal projections in the striatum were then assessed and compared with corticocortical projections. Voxel fluorescence was correlated in striatum across injection sites to look for patterns of projections across cortical input structures. Clustering of fluorescence in striatum showed distinct clusters that were well-matched with cortical input. For example primary motor and primary sensory areas clustered together. Examining correlations across the dorsoventral rostrocaudal and mediolateral dimensions of striatum suggested a distinct anterior/medial region of the striatum where all areas of the sensorimotor system converged. Differences in the precision of projections to striatum emerged when looking at intratelencephalic layer 5A versus pyramidal tract layer 5B neurons. 3D K-means clustering of striatal voxel fluorescence suggested clear subdivisions of the striatum consistent with pre-existing classifications. These findings are discussed in light of the parallel functional loop theory of basal ganglia.

First Author: Emily Parker (Graduate)	Poster Session: pm
Presenting Author: Emily Parker (Graduate)	Location: 54
Mentor/Lab: Sweet	Category: Psychiatry
Department: Psychiatry	

Title: Synaptic remodeling of small dendritic spines over adolescent auditory cortex development

Summary: Recently our group discovered that in schizophrenia in the primary auditory cortex (A1) the loss of dendritic spines important synaptic structures on excitatory neurons is driven by the selective reduction of the smallest spines and that the protein CaVβ4 could play a role in this loss. We hypothesized that like in schizophrenia spine loss in A1 is selective for the smallest dendritic spines during synaptic remodeling of excitatory circuits in normal mouse adolescent development and that CaVβ4 plays a role in this process. We found that the smallest spines are indeed selectively lost over mouse A1 adolescent development but could not confirm if CaVβ4 drives this loss as our data indicate that CaVβ4 levels modestly decrease and that levels of CaVβ4 were not significantly associated with reduced number of small spines over mouse A1 adolescent development.

Abstract: *This poster abstract was submitted to accepted and will be presented at SfN 2017 Dendritic spines are motile postsynaptic structures at excitatory synapses. Following synaptic remodeling of excitatory circuits during adolescence in normal development dendritic spine density is reduced in cortical areas including primary auditory cortex (A1) in adulthood. Excess synaptic remodeling during adolescence is thought to occur in schizophrenia (Sz) resulting in excessive loss of dendritic spines. Reduced dendritic spine density has been observed in multiple brain regions in Sz in adulthood including in A1. We recently reported that the dendritic spine density reduction in Sz in A1 is limited to dendritic spines of smaller volumes which are presumed to be predominantly transient. Further we found that increased levels of a peptide shared among CaVβ isoforms was associated with reduced density of small but not large dendritic spines in A1. Overexpressing CACNB4 which encodes CaVβ4 led to reduced density of small dendritic spines in primary neuronal culture. For the current study we hypothesized that previous observations of reduced A1 dendritic spine density during adolescent development is driven by and selective for small dendritic spine loss. We measured dendritic spine density over A1 adolescent development using stereological and quantitative confocal fluorescence microscopy techniques and found that mean density of small dendritic spines was significantly reduced in adult (P84) as compared to early adolescent (P28) mouse A1 (p<.001). The density of large dendritic spines was not altered. These findings suggest that the smallest and likely transient dendritic spines are targeted during synaptic remodeling in A1 during adolescent development. We will report findings from experiments that characterize CaVβ levels over normal A1 mouse development to determine if elevated CaVβ4 levels are associated with dendritic spine density reduction during adolescent development in mouse A1.

First Author: Fen Pei (Graduate)	Poster Session: pm
Presenting Author: Fen Pei (Graduate)	Location: 34
Mentor/Lab: Lansing Taylor	Category: Neurology & Neurodegenerative Diseases
Department: Computational biology department	

Title: Connecting Neuronal Cell Protective Pathways and Drug Combinations in a Huntington's Disease Model through the Application of Quantitative Systems Pharmacology

Summary: Through the application of a chemogenomics platform we investigated the protective effects of small molecule probes and probe combinations for HD disease model Computational analysis of these probes revealed a convergence of pathways indicating activation of PKA.

Abstract: Quantitative Systems Pharmacology (QSP) is a drug discovery approach that integrates computational and experimental methods in an iterative way to gain a comprehensive unbiased understanding of disease processes to inform effective therapeutic strategies. We report the implementation of QSP to Huntington's Disease with the application of a chemogenomics platform to identify strategies to protect neuronal cells from mutant Huntingtin induced death. Using the STHdhQ111 cell model we investigated the protective effects of small molecule probes having diverse canonical modes-of-action to infer pathways of neuronal cell protection connected to drug mechanism. Thirty-two mechanistically diverse protective probes were identified most of which showed less than 50% efficacy. Specific combinations of these probes were synergistic in enhancing efficacy. Computational analysis of these probes revealed a convergence of pathways indicating activation of PKA. Analysis of phospho-PKA levels showed lower levels in the cytoplasm of STHdhQ111 cells compared to the wild type STHdhQ7 cells and these levels were increased by several of the protective compounds. In addition the PKA inhibitor H89 at pharmacodynamically active non-toxic concentrations inhibited the effects of several protective compounds thereby supporting the hypothesis that these protective compounds may be working in part through activation of the PKA network. The systems-level studies described here can be broadly applied to any discovery strategy involving small molecule modulation of disease phenotype.

First Author: Matthew Phillips (Graduate)	Poster Session: pm
Presenting Author: Matthew Phillips (Graduate)	Location: 5
Mentor/Lab: Jon Johnson	Category: Neurology & Neurodegenerative Diseases
Department: Neuroscience	

Title: Characteristics of NMDA receptor channel block by the novel polycyclic amines RL-202 and RL-208

Summary: New drugs (the compounds RL-202 and RL-208) show similar biophysical properties to the Alzheimer's disease drug memantine sharing a conserved basic mechanism of action and overlapping binding sites in the NMDA receptor a brain protein necessary for learning and memory. Interestingly these drugs perform some forms of inhibition more strongly than memantine. Studying how RL-202 and RL-208 affect the NMDA receptor can help us further understand how channel blocking compounds function and will aid in future design of better drugs.

Abstract: NMDA receptors (NMDARs) are a class of ionotropic glutamate receptors (iGluRs) expressed at nearly all vertebrate synapses. NMDARs display a variety of properties unique amongst iGluRs including dependence upon co-agonists voltage-dependent Mg2+ block slow kinetics and permeability to Ca2+. NMDAR activity is critical for many types of synaptic plasticity and is a key player in memory formation and learning. Conversely aberrant NMDAR activation is implicated in a variety of nervous system disorders such as Alzheimer's disease and stroke. Pharmacological targeting of NMDARs with channel blockers has shown therapeutic promise for protection from excitotoxicity as well as the treatment of Alzheimer’s disease and major depressive disorder. Despite sharing similarities in binding site and mechanism of inhibition the clinical utility of NMDAR channel blockers with differing structure can vary dramatically. Further investigation into how channel blockers differentially affect receptor function may provide insight into their varying clinical efficacy and aid in future drug design. Here we provide pharmacological characterization and comparison of two novel NMDAR channel blockers the polycyclic amines RL-202 and RL-208 with the Alzheimer’s disease drug memantine (Mem). RL-202 and RL-208 were found to be voltage-dependent trapping channel blockers that possess similar IC50 values to Mem. Interestingly both RL-202 and RL-208 display stronger second site inhibition (SSI) a form of antagonism that involves drug binding to a site outside the NMDAR channel in the absence of agonist than Mem despite their similar structures and traditional potencies. Our findings suggest that these compounds could be useful tools for elucidating and differentiating mechanisms of NMDAR inhibition by channel blockers.

First Author: Sean Piantadosi (Graduate)	Poster Session: pm
Presenting Author: Sean Piantadosi (Graduate)	Location: 48
Mentor/Lab: Ahmari	Category: Psychiatry
Department: Psychiatry	

Title: Using in vivo microscopy to assess the role of striatal medium spiny neurons in compulsive behavior and response to pharmacological treatment

Summary: The therapeutic mechanisms of the leading drug treatment for obsessive compulsive disorder are poorly understood. In this study brain activity was measured in a region called the striatum in a leading genetic mouse model of OCD using miniature microscopes that can visualize individual brain cells. This revealed that brain cells were overactive in the OCD model at baseline and that treatment with an effective OCD drug therapy normalized this activity.

Abstract: Study: Perseverative thoughts and actions are hallmark symptoms of Obsessive Compulsive Disorder (OCD) and are often present in other severe neuropsychiatric illnesses including autism and schizophrenia. Aberrant activity in cortico-striatal circuitry has been linked to compulsive behavior in both correlative studies in humans and causal studies in rodents. Using head-mounted mini-microscopes for in vivo calcium imaging (Inscopix) we sought to determine the role of medium spiny neurons (the principal striatal cell type) in mediating compulsive behavior in mice with a highly penetrant compulsive grooming phenotype (Sapap3-KO mice). We have also investigated how the first-line OCD pharmacotherapy the selective serotonin reuptake inhibitor fluoxetine alters striatal activity patterns. Methods: Sapap3 knockout (KO) mice which have both a hyperactive striatum and compulsive OCD-like grooming phenotype were injected with AAV-GCaMP6m and implanted with a GRIN lens in the centromedial striatum (CMS) to visualize striatal calcium activity during spontaneous grooming behavior. All mice received 7 days of treatment with the SRI fluoxetine (5 mg/kg) and underwent imaging and grooming assessments on days 3 5 and 7 of treatment. Results: At baseline Sapap3-KO mice displayed elevated grooming behavior and increased calcium activity during grooming relative to WT mice. This increase in calcium activity may stem from a strong increase in striatal activity at the onset of grooming events a phenomenon that was not observed in WT mice. Further activity of D1-MSNs is elevated at a trend level in Sapap3-KO mice suggesting an increase in direct pathway drive. Treatment with the SRI fluoxetine reduced observed calcium activity in all striatal cells with a rapid (3 day) time-course. Ex vivo data suggest that fluoxetine may be modulating the activity of striatal fast spiking interneurons (FSIs) in order to normalize striatal activity. Ongoing work is further dissecting striatal patterns that may contribute to compulsive behavior and its treatment. Conclusion: Hyperactivity of the striatum and compulsive grooming behavior can be reversed with successful SRI treatment in a valid mouse model of OCD-like behaviors. Significance: Understanding cell-type specific effects of successful and unsuccessful SRI treatment may help us develop treatments for patients with improved efficacy and fewer side effects.

First Author: JORGE PINEDA (Postdoctoral)	Poster Session: am
Presenting Author: JORGE PINEDA (Postdoctoral)	Location: 44
Mentor/Lab: MICHAEL GOLD	Category: Sensory
Department: DEPARTMENT OF NEUROBIOLOGY	

Title: Characterization of chemotherapeutic-induced visceral neuropathy

Summary: Cancer survivors have reported the presence of pain in different areas of the body after a chemotherapeutic treatment. We study the possible relation between cancer treatment and the development of visceral pain.

Abstract: Chemotherapeutic-induced peripheral neuropathy (CIPN) characterized by numbness tingling and ultimately pain in the hands and feet remains the primary dose-limiting side effect of some of the most effective anti-cancer drugs. But while the primary focus of CIPN research has been on the somatic nervous system clinical data suggest a variety of persistent visceral symptoms may have the most deleterious impact on the quality of life in cancer survivors. Both because of the nature of the persistent symptoms and our recent data suggesting that unique features of a subpopulation of somatic afferents make them particularly vulnerable to chemotherapeutics we hypothesized that the persistent visceral symptoms reflect a chemotherapeutic-induced “visceral” neuropathy (CIVN). To test this hypothesis we assessed changes in visceral sensory neurons (the vagus and nodose ganglia) and the enteric nervous system in rats a week after the last of six IV infusions of the combination of paclitaxel (2 mg/kg) and carboplatin (30 mg/kg) administered over three weeks. Changes in somatic afferents were used for comparison. Combination- but not vehicle-treated rats developed mechanical and cold sensitivity within the first week of drug administration that did not resolve. Combination-treatment was also associated with a significant (~50%) reduction in the conduction velocity of A- and C-fibers in both sciatic and vagal nerves. The chemokine MCP-1 was increase in a subpopulation of neurons in both L4/L5 dorsal root ganglia (DRG) and nodose ganglia. There was also an increase in the mitochondria protein TOM-20 in a subpopulation of DRG and nodose neurons. Our results are consistent with our initial hypothesis. Whether the same mechanism(s) are responsible for the damage to visceral and somatic afferents remains to be determined. Identification of the mechanisms responsible for the damage to visceral neurons however may suggest novel treatments for patients suffering from these persistent symptoms. Work was supported by Grant R01 DK107966

First Author: Kristin Quick (Postdoctoral)	Poster Session: am
Presenting Author: Kristin Quick (Postdoctoral)	Location: 19
Mentor/Lab: Jen Collinger and Rob Gaunt	Category: Brain-Machine Interfaces
Department: Physical Medicine and Rehabilitation	

Title: Velocity-Tuning of Sensory Cortex during Cursor and Hand Shaping Tasks

Summary: A participant with chronic spinal cord injury was able to use sensory cortex instead of motor cortex to control a brain computer interface.

Abstract: Introduction: Neurons in motor cortex (M1) are known to relate their activity levels to movement kinematics such as velocity. This velocity-relationship can be used by a person with paralysis to control an external device such as a computer cursor or the grasping of a robotic hand. When the person attempts to control the device the brain computer interface (BCI) translates their M1 activity into a velocity command which moves the device to the desired position. In addition to M1 studies have also found that sensory cortex (S1) increases its neural activity during movements (di Prampero et al. 1996) and that neurons are tuned to the direction of movement (Prud'homme and Kalaska 1994). However it is unknown whether S1 is also tuned to the velocity of movement. If tuned to movement velocity it might be possible to instead use S1 activity to control an external device. In this set of experiments a participant performed two types of tasks. In the first task a cursor moved on a computer screen. In the second task a robotic hand moved between different hand shapes. We hypothesized that 1) S1 would show velocity-tuning during these tasks. Additionally since the S1 arrays were placed in the hand area we expect that 2) S1 velocity-tuning would be stronger for the hand shaping than cursor movements and 3) the performance of the S1 decoder for hand shaping would be higher than the performance of the S1 decoder for cursor movements. Methods: A participant with chronic C5 motor and C6 sensory AIS B spinal cord injury was implanted with two 88-channel intracortical microelectrode arrays in M1 targeting the arm and hand representation and two 32-channel microelectrode arrays targeting the hand region of area 1 in S1. To provide a fair comparison 64 M1 channels with the same spatial layout as the S1 channels were used in this work. We recorded neural activity while the subject attempted to mimic 2D cursor or hand shaping movements that were under computer control. A linear velocity-based encoding model was fit to the neural activity recorded on each channel. We then compared the S1 and M1 model fits for the cursor task and the hand shape task. After comparing model fits we created S1-only and M1-only decoders (optimal linear estimator OLE) for both the cursor and hand shape tasks (total of 4 decoders). To allow for a more complete comparison online BCI performance was tested with computer assistance that cancelled any decoded velocities orthogonal to the path from the current position to the target. Results: We found significant velocity-tuning in S1 to both cursor movements and hand shape movements. However S1 velocity-tuning was significantly reduced compared to M1 for both the cursor and hand shape tasks. When looking in more detail at S1 we found that velocity-tuning for hand shaping was significantly stronger than for cursor movements. Next the four decoders were tested. For cursor movements the S1 decoder achieved 47% success and the M1 decoder achieved 100% success. For hand shaping the S1 decoder achieved 60% success and the M1 decoder achieved 90% success. We found that the participant could utilize the S1 decoder for hand shaping (S1 performance was 67% of M1 performance) better than the S1 decoder for cursor movements (S1 performance was 47% of M1 performance). Conclusion: As expected velocity-tuning was present in S1 for both cursor movements and hand shaping movements albeit at a reduced strength compared to M1 tuning. Additionally the strength of S1 velocity-tuning was stronger for hand shaping than cursor movements. This finding carried over into the participant's performance during online control. The S1 hand shape decoder outperformed the S1 cursor decoder perhaps because the S1 hand shape decoder was more congruent with the cortical hand representation in which the arrays were placed. Velocity-tuning has been shown to

model M1 activity well. However it is possible that S1 activity may better fit tuning models that encode a different movement parameter(s) or incorporate a lag between the kinematics and neural activity. An optimized S1 encoding model would likely further improve S1 BCI control.

First Author: Anne Robertson (Faculty)	Poster Session: pm
Presenting Author: Anne Robertson (Faculty)	Location: 13
Mentor/Lab: Robertson	Category: Neurology & Neurodegenerative Diseases
Department: Mechanical Engineering and Materials Science	

Title: ROLE OF CALCIFICATION IN ANEURYSM FAILURE- A CASE STUDY

Summary: The rupture of a brain aneurysm has high mortality and disability rates. To date the cause of rupture is poorly understood limiting possibilities for screening patients for aneurysms at risk for rupture. The objective of this work is to use use mutiple imaging and mechnical testing modalities to assess the role of calcification in aneurysm rupture.

Abstract: Intracranial aneurysms are believed to exist in approximately 5% of the adult population. While rupture is relatively rare intracranial hemorrhage due to rupture has devastating effects with high mortality and disability rates. Since risks associated with aneurysm treatment can exceed the natural risk of rupture there is an urgent need for a reliable method to identify fragile aneurysms at risk of rupture from those that can be safely monitored. In order to better understand rupture risk it is valuable to consider the wall prior to rupture since substantial biological geometric and structural changes can occur after rupture and possibly even days or even weeks prior to rupture. In our earlier work we introduced a classification system for dividing unruptured cerebral aneurysm tissue into robust and vulnerable groups. Here we build on this work and introduce an approach for exploring wall vulnerability using micro-CT imaging mechanical testing and computational studies. We consider a case study of an unruptured cerebral aneurysm and explore the source of wall vulnerability.

First Author: Tristen Inagaki (Faculty)	Poster Session: am
Presenting Author: Lauren Ross (Graduate)	Location: 6
Mentor/Lab: Social Health Affective Neuroscience Lab	Category: Imaging Techniques
Department: Psychology	

Title: The Benefits of Giving Social Support: Giving Targeted and Untargeted Support

Summary: These studies examine the potential benefit of giving support to others. In study 1 giving targeted support (to an identifiable individual) resulted in increased septal area (SA) activity and was associated with decreased amygdala activity. In study 2 self-reports of giving targeted support were associated with less amygdala activity during an amygdala reactivity task.

Abstract: Giving support significantly contributes to the link between social ties and health. However the neural mechanisms linking the provision of support to health are not known. It has been suggested that giving support leads to benefits via neural regions implicated in parental care in animals. The current studies therefore assess the contribution of parental caregiving-related neural regions to giving support in humans and as a further theoretical test examine whether the benefits of giving targeted support to a single identifiable individual in need extends to giving untargeted support to larger societal causes. Study 1 (N = 45) demonstrates that giving targeted (vs. untargeted) support results in greater feelings of social connection and feelings that the support was effective. Further greater septal area (SA) activity one of the key regions involved in parental care in animals to giving targeted support is associated with less amygdala activity to social threat. However SA activity to giving untargeted support is not related to amygdala activity. Using a large independent neuroimaging sample Study 2 (n = 384) replicates and extends this second finding to show that self-reports of giving targeted support are associated with less amygdala activity to a different socially threatening task. Once again giving untargeted support is not related to amygdala activity. Results highlight the unique benefits of giving targeted support and elucidate neural pathways by which giving support may lead to health benefits.

First Author: Dylan Royston (Graduate)	Poster Session: am
Presenting Author: Dylan Royston (Graduate)	Location: 7
Mentor/Lab: Collinger	Category: Brain-Machine Interfaces
Department: Bioengineering	

Title: Investigating the effects of goal-directed sensory information on intracortical hand representations in human sensorimotor cortex

Summary: When we use our hands to interact with objects several brain areas are recruited to transform goal-related sensory information into effective movement plans. We are studying how the activity of neurons in human motor and somatosensory cortex change to encode simple vs goal-directed movements. Understanding how this activity reflects different kinds of object-related sensory information can help improve rehabilitation practices and further our understanding of complex brain functions.

Abstract: Intracortical brain-computer interfaces (BCI) can allow people with spinal cord injury (SCI) to control robotic limbs by translating neural activity recorded from microelectrode arrays in motor cortex (M1) into intended movements. This technology is based on research relating specific patterns of neural modulation to movement kinematics; however the M1 activity encoding hand grasping appears to change when different objects are presented even when the grasp kinematics remain the same. These results suggest that visuomotor transformations influence the activity in M1 but it remains unclear which visuomotor or contextual properties influence M1 activity independent of kinematics. Here we seek to investigate how visual auditory and somatosensory cues during attempted movements influence neural population activity by measuring intracortical neural activity from a person with tetraplegia. We are collecting intracortical recordings from two microelectrode arrays implanted in the primary motor (M1) cortex and two arrays implanted in the primary somatosensory (S1) cortex of a human participant with a C5-motor/C6-sensory incomplete SCI. Data are recorded while the participant views and attempts to perform rhythmic sensorimotor tasks with their right hand such as hand grasping and having their fingertips touched. Each task is presented with 4 levels of multimodal sensory information: simple (video of basic movement/sensation) goal (object-directed) audio (object-directed + auditory timing cue) and stim (object-directed + auditory cue + vibrotactile timing cue). For example a hand grasp task is presented as simple (a hand opening/closing) goal (a hand squeezing a ball) audio (a hand squeezing a ball + a chime at full closure) and stim (a hand squeezing a ball + a chime + vibration at full closure). To determine how sensorimotor encoding is affected by task context we will analyze changes in both single-unit encoding and population-level representations. Single-unit encoding will be quantified by performing Fourier transforms on each unit's time-series activity and determining the amplitude of the peak spectral power at frequencies matching the kinematic pacing of the tasks. Population-level representations will be quantified by using principal component analysis (PCA) to determine the similarity between the population-wide patterns of activity representing each movement. By comparing the activity encoding each movement across different levels of sensory enrichment as well as the effects of this enrichment on neural activity recorded from different areas of cortex we can determine how a task's context alters how it is encoded in cortical hand representations. These analyses will help determine how goal-directed sensory information shapes the neural representation of intended hand movements in sensorimotor cortex informing our understanding of sensorimotor integration and providing a potential avenue for improving the utility of intracortical BCI systems.

First Author: Caroline Runyan (Faculty)	Poster Session: am
Presenting Author: Caroline Runyan (Faculty)	Location: 54
Mentor/Lab: Caroline Runyan	Category: Brain Models and Systems
Department: Neuroscience	

Title: Communication between cortical networks: context inhibition and neuromodulation in cells and circuits

Summary: The meaning of a sensory stimulus can change depending on the current situation and the ability to flexibly and appropriately adjust behavioral responses in changing contexts is critical for survival. The goal of my research is to understand the circuit mechanisms that control the flow of information between brain regions.

Abstract: The brain is often bombarded by information from multiple sources simultaneously and rapidly changing contexts can shift the behavioral relevance or meaning of a sensory stimulus requiring an animal to respond to the same stimulus differently depending on the current situation. The ability to flexibly and appropriately adjust behavioral responses in changing contexts is critical for survival and disruptions in this flexibility characterize many complex brain disorders such as addiction autism and schizophrenia. The goal of my research is to dissect the circuit-level mechanisms underpinning cognitive and behavioral flexibility to enable new systems-level approaches to understanding these disorders in the near future. To understand the neural underpinnings of perception attention and behavioral flexibility it is critical to study the interaction between brain areas as even regions of primary sensory cortex do not operate on feedforward inputs in isolation. Each local patch of cortex in sensory and association regions receives feedforward lateral and feedback inputs. We will use optogenetics and two-photon imaging of calcium responses in genetically defined cell classes to dissect the local circuit mechanisms controlling the efficacy of signal transmission between cortical regions with different hierarchical relationships in changing behavioral contexts.

First Author: Alessandro Salatiello (Graduate)	Poster Session: am
Presenting Author: Alessandro Salatiello (Graduate)	Location: 26
Mentor/Lab: Dr. Gelsy Torres-Oviedo	Category: Motor
Department: Bioengineering	

Title: Interference in Locomotor Adaptation

Summary: In this work we aimed to study the interaction of the instantiation of competing memories of adapted walking patterns. We found that this competition manifests itself as a reduction in the rate of memory expression.

Abstract: Split-belt treadmill walking in which legs move at different speeds can be used to improve patients' mobility by correcting their gait asymmetry (e.g. Reisman et al 2013). For this strategy to be effective it is necessary to maximize the retention of motor memories acquired during the training. In order to do so it is important to know how motor memories learned within the same environment influence each other. In this study we specifically tested whether learning two locomotor patterns counteracting equal and opposite perturbations is possible or instead the memories interfere with one another. To this end we studied unimpaired subjects' ability to counteract the same perturbation twice after either experiencing an opposite perturbation in-between (interference group n=8) or walking without any perturbation (savings group n=8). Critically unlike prior work (Malone et al 2011) we removed the opposing perturbation gradually to reduce the experienced errors known to reinforce the motor memory initially learned (Herzfeld et al. 2014). As a measure of error we used step length asymmetry. We compared across groups 1) the change in initial error that subjects experienced when the perturbation was introduced 2) the change in steady state value reached and 3) the percent change in adaptation rate. We found that while both groups had similar initial change in errors (and thus where similarly perturbed p=0.69) and similar change in steady state values (indicating a comparable ability in facing the perturbation at steady state p=0.11) the dynamics of adaptation were significantly different. In fact the interference group readapted 38.27% slower (p=0.035 95% bootstrap CI [3.52% 80.99%]) whereas the savings group readapted as fast as during the first exposure. In sum our results indicate that the memory of adapted walking patterns is subject to interference and that this memory can be reinforced by the errors experienced during de-adaptation. These findings can inform the design of more effective rehabilitation techniques to counteract step length asymmetry in stroke survivors.

First Author: Natalie Sandel (Postdoctoral)	Poster Session: pm
Presenting Author: Natalie Sandel (Postdoctoral)	Location: 38
Mentor/Lab: Anthony Kontos PhD	Category: TBI-Concussion
Department: Orthopaedic Surgery	

Title: Comparing near point of convergence distance in concussed adolescents and healthy controls

Summary: Adolescent athletes evaluated within 10 days of their concussion demonstrate a convergence insufficiency a reduced ability for the eyes to team together upon near vision relative to healthy controls. Convergence appears to return back to normal when concussed athletes are cleared to return back to sports.

Abstract: Near vision oculomotor dysfunction such as an accommodation or convergence insufficiency is common after brain injury. Nearly 40% of athletes with a sports-related concussion exhibit a convergence insufficiency in which there is a reduced ability for the eyes to team together upon near vision (Pearce et al. 2015). A convergence insufficiency can cause several symptoms including blurred or double vision headache and difficulty with reading or computer work. Despite evidence of oculomotor deficits after brain injury limited research has explored whether these posttraumatic vision changes remit after a concussion. The goal of the current study was to compare near-point convergence (NPC) distance within concussed individuals at the time of initial visit compared to their NPC distance at the time of clearance back to sports based on international criteria (McCrory et al. 2012) relative to a group of healthy controls. Participants were aged 12 to 20 years old (M=15.13 SD=2.05). A total of 39 concussed participants (53.8% male) were matched closely to healthy controls (N=28 64.3% male). Concussed participants were diagnosed with a concussion by a neuropsychologist at their initial visit within 10 days of their injury (M=6.51 SD=2.55) and serially assessed across subsequent follow-up visits. NPC was measured in healthy controls at only one time point. Among concussed individuals 59.8% were formally cleared by their fourth visit (Mdn=22 days post injury Range=10-193 days). All participants underwent Vestibular/Ocular Motor Scoring (VOMS) screening including NPC measurement. An average NPC measurement greater than 5cm was considered abnormal (Mucha et al. 2014; Scheiman et al. 2003). Independent t-tests were conducted to determine if concussed athletes differed from controls at initial visit and time of clearance. A paired samples t-test compared NPC measurements of concussed athletes at initial visit and time of clearance. Results of an independent t-test comparing NPC at initial visit in concussed (M=6.88cm SD= 10.05cm) versus controls (M=1.61cm SD= 2.54cm) was significant $t(43.25)=3.10$ $p=.003$ with concussed participants demonstrating poorer NPC as a group. In the control group 14.3% demonstrated an abnormal NPC while in the concussed group 36.8% demonstrated an abnormal NPC. A paired-samples t-test for comparison of the concussed participants' NPC at initial visit (M=6.34 SD=10.36) versus at time of clearance (M=1.77 SD=2.82) yielded a significant difference $t(21)=2.23$ $p=.04$ with greater NPC at the initial visit. Lastly an independent t-test for NPC between concussed participants at their clearance visit (M=1.81cm SD= 2.76cm) versus controls (M=1.61 SD=2.54cm) was non-significant $t(49)=0.27$ $p=.79$ indicating no difference in NPC between individuals cleared from their concussion and healthy controls. Individuals with a concussion demonstrate a significantly worse near point of convergence initially after injury relative to healthy controls. Abnormal near point of convergence after concussion appears to return to normal over time and/or with treatment. This study was limited by the attrition of participants who did not return for follow-up evaluation and a lack of repeated measurement for the control group.

First Author: Chao Sang (Graduate)	Poster Session: pm
Presenting Author: Chao Sang (Graduate)	Location: 12
Mentor/Lab: Anne Robertson	Category: Neurology & Neurodegenerative Diseases
Department: Mechanical Engineering and Materials Science	

Title: MECHANICAL RESPONSE AND FIBER REMODELING IN ELASTASE-INDUCED RABBIT ANEURYSMS

Summary: As in an evolving human cerebral aneurysm the rabbit aneurysm wall experiences changing tensile loads after creation and must adapt its extracellular matrix. The average wall strength increased over time suggesting effective fiber remodeling in adaptation to the increased axial load. The medial layer demonstrated a transition from largely circumferential loading to multiple fiber directions better suited to manage the biaxial loading found in the aneurysm wall.

Abstract: An intracranial aneurysm (IA) is most commonly a saccular enlargement in the wall of a cerebral artery. Aneurysm rupture is associated with high morbidity and mortality and hence there is a pressing need to better understand disease progression and to identify clinically useful metrics for assessment of rupture risk. It is commonly accepted that stress factors such as abnormal hemodynamics can lead to wall degradation that sometimes present in the clinic as changes to the aneurysm shape and size. However in most cases such longitudinal information is not available and aneurysm size is used for risk assessment. Human intracranial aneurysm samples can be obtained following treatment by surgical clipping and have provided valuable information about the heterogeneity in the aneurysm wall among patients. Recent studies have addressed the relationship between hemodynamics and changes to the aneurysm wall. A challenge is that harvested aneurysm tissue from patients only represents one time point in the pathology. Animal models for IAs provide a means of studying the evolving aneurysm wall. In this work we used an elastase induce aneurysm model in rabbits to study progressive changes in wall structure and mechanical properties. As in an evolving human cerebral aneurysm the rabbit aneurysm wall experiences changing tensile loads after creation and must adapt its extracellular matrix. We used multi-photon microscopy to measure collagen fiber remodeling and uniaxial testing to evaluate the corresponding changes to mechanical properties. The average wall strength increased over time suggesting effective fiber remodeling in adaptation to the increased axial load. This remodeling occurred in a non-homogeneous manner across the wall thickness. The medial layer demonstrated a transition from largely circumferential loading to multiple fiber directions better suited to manage the biaxial loading found in the aneurysm wall. In the future the rabbit model can be used to evaluate cellular activities responsible for these changes and to test pharmacological treatments that augment these changes.

First Author: C. Elizabeth Shaaban (Graduate)	Poster Session: pm
Presenting Author: C. Elizabeth Shaaban (Graduate)	Location: 15
Mentor/Lab: Dr. Caterina Rosano	Category: Neurology & Neurodegenerative Diseases
Department: Epidemiology	

Title: Response of venous-side microvasculature in older adults to physical activity intervention: A study at 7T

Summary: We found that a structured walking routine and increases in brain-derived neurotrophic factor a growth factor can beneficially impact the brain's small veins even among very old adults. These may be promising ways to prevent or treat Alzheimer's disease or small vessel disease in the brain but future studies will be needed to confirm this.

Abstract: BACKROUND: We have recently shown that tortuosity of brain small veins are cross-sectionally associated with having at least one APOE4 allele and with lower levels of vascular endothelial growth factor (VEGF) (Shaaban et al. 2017). Prior work has shown that PA can lower severity of brain small vessel disease (SVD) and risk of Alzheimer's disease (AD). Here we test the hypothesis that physical activity reduces tortuosity of brain small veins. We also explore the effects of VEGF and brain-derived neurotrophic factor (BDNF) because of their beneficial effects on the vasculature. METHODS: Participants of the LIFE study (N=14 7 in each arm) mean age 77 (range 70-86) 85.7% female 42.9% non-white) were randomly assigned to a 24-month program of center-based walking 2x/week (PA) or a health education (HE) program. Moderate levels of PA were objectively measured by accelerometry as cumulative minutes/day spent at baseline and at 6 12 and 24 months. APOE4 genotype was determined via TaqMan and Pyrosequencing. Vein length and serum levels of vascular endothelial growth factor (VEGF) and brain-derived neurotrophic factor (BDNF) were measured at baseline and after 24 months. Lengths of tortuous and straight veins within a periventricular region of interest were measured and tortuosity ratio of total tortuous length to total straight length was considered a marker of SVD. Percent change from baseline to 24 months was computed for all measures of interest. Spearman correlations assessed relationships of percent change in venular markers with PA and molecular markers with alpha of 0.10. RESULTS: Intervention groups did not differ significantly at baseline ($p>0.05$). Greater cumulative PA by accelerometry predicted decrease in tortuosity ratio independent of arm assignment (rho= -0.533 $p=0.06$). Increase in BDNF also predicted decrease in tortuosity ratio independent of arm assignment (rho= -0.614 $p=0.03$). Neither change in VEGF nor APOE4 allele were related to change over time in tortuosity ratio ($p>0.10$). CONCLUSIONS: Greater cumulative PA and increased BDNF levels were associated with reduced tortuosity ratio. A structured walking intervention and greater BDNF levels may beneficially impact the venous-side microvasculature even among very old adults. Future studies should clarify the long-term effects of PA and BDNF on SVD and progression to AD.

First Author: Diane Carlisle (Faculty)	Poster Session: pm
Presenting Author: Tanisha Singh (Postdoctoral)	Location: 3
Mentor/Lab: Diane Carlisle	Category: Neurology & Neurodegenerative Diseases
Department: Neurological Surgery	
Title: Characterizing Mitochondrial Dysfunction in Sporadic ALS Patient Motor Neurons	
Summary: In this project we investigate characterize dysfunction in human motor neurons from sporadic ALS patients.	
Abstract: Approximately 5-10% of ALS cases are familial (fALS). In fALS autosomal mostly dominant mutations have been reported in several genes such as C9orf72 (40%) SOD1 (20%) TAR DNA-binding protein-43 (TDP-43) (3%) FUS/TLS (5%) and TAF-15 (1%). Among the multiple proposed mechanisms based mainly on experimental in vivo and in vitro models a key role is attributed to the activation of mitochondrially mediated neuronal death signaling pathways. However the majority (90-95%) of ALS cases are sporadic (sALS). The pathobiology of sALS is largely unknown despite suspected genetic and environmental factors at play. In sALS patients no specific molecular biology characterization or timing of mitochondrial changes during neuronal maturation have been reported. Using established protocols we generated induced pluripotent stem cells (iPSCs) from sALS patients and differentiated iPSCs into neural progenitor and mature motor neurons (MNs). We examined mitochondrial parameters in sALS cells from all three developmental stages and compared them with controls. Our studies demonstrate that developmental stage plays a crucial role in the ALS phenotype in vitro and that these cells can be used to investigate mitochondrial dysfunction in sALS.	

First Author: Aaron Sinnott (Graduate)	Poster Session: pm
Presenting Author: Aaron Sinnott (Graduate)	Location: 40
Mentor/Lab: Neuromuscular Research Lab/Christopher Connaboy Anthony Kontos	Category: TBI-Concussion
Department: Sports Medicine and Nutrition	

Title: Do Changes in Symptom Burden Affect Clinical Outcomes following Concussion?

Summary: Post-concussion symptoms are hallmark signs of injury and injury prognosis. The current study investigated clinical measures with symptom complaints after injury.

Abstract: Objective: Initial symptom burden is an important factor to consider when evaluating concussed patients as it is prognostic of poor clinical outcomes. However researchers have yet to examine the role of changes in symptom burden in relation to clinical outcomes following concussion. The aim of the current study was to compare neurocognitive performance across recovery in adolescents and adults who did not improve in symptoms to those who did improve. Design: The study employed a prospective repeated measures design and involved clinical data collected from a concussion testing program between 2009 and 2017. A total of 243 (96F/147M) adolescents and adults aged 14-29 years within 7 days of clinically diagnosed concussions were enrolled in the study. Participants were categorized as either: 1) improved (upper tertile) or 2) not-improved (lower tertile) based on changes in reported symptoms from within 7 days post-injury to within 10 days post-injury. All participants completed the Immediate Post-Concussion Assessment and Testing (ImPACT) and Post-concussion Symptom Scale (PCSS) at baseline 3 and 10 days post-injury. A series of 2 (group) x 3 (time) ANOVAs with Bonferroni correction were conducted for verbal and visual memory visual motor processing speed and reaction time. Results: 162/243 (30.8%) eligible participants were included in the sample. 81 participants (45.7% 37F) were categorized as improved and 81 (25.9% 21F) were categorized as not-improved. Results supported group X time interactions for verbal memory F (2 159) =11.80 p<.001 η2=.13 visual motor speed F (2 159) = 8.710 p<.001 η2=.10; and reaction time F (2159) =12.80 p<.001 η2=.14. Participants in the improved group performed worse than the not improved group at 3 days post-injury on visual and verbal memory and reaction time (p=.001-.003); but not 10 days after injury. As expected there were significant within subjects changes from pre to post-injury across all outcomes (p=.001-.02). There were no differences in outcomes from baseline to 10 days post-injury. Conclusions: Adolescents and adults with large symptom fluctuations perform worse initially but neurocognitive deficits recover compared to those who experience little symptom change after injury. Findings confirm that neurocognitive performance will resolve 10 days after injury despite variations in initial symptom burden.

First Author: Nathaniel Sisterson (Graduate)	Poster Session: am
Presenting Author: Nathaniel Sisterson (Graduate)	Location: 20
Mentor/Lab: Brain Modulation Lab/Mark Richardson MD PhD	Category: Brain-Machine Interfaces
Department: Department of Neurological Surgery	

Title: Theta-gamma wave ratio differentiates spiking and low voltage seizure onset

Summary: The NeuroPace Responsive Neurostimulator is an implantable device recently approved for people with severe epilepsy that reduces the number of seizures using electrodes and programmable detectors to identify abnormal brain activity and deliver stimulation therapy. We analyzed brainwave activity recorded from the implantable electrodes in one patient and demonstrated that the ratio of theta to gamma brain waves was different during the 20 seconds preceding two common seizure-onset patterns. This difference in theta to gamma ratios may further improve seizure outcomes by allowing detection and stimulation settings specific to the type of seizure.

Abstract: Hypothesis Closed-loop or responsive neural stimulation systems represent a new and promising therapy for managing the debilitating and degenerative seizures in the 75% of drug-resistant epilepsy patients who are either not surgical candidates or do not respond adequately to surgery. However the mean time to 50% seizure reduction of 2 years is too long delaying quality of life benefits while incurring serious healthcare costs. The identification of biomarkers in intracranial electroencephalography (iEEG) recordings may better differentiate seizure types and accelerate optimal detection and stimulation settings. We hypothesize that electrographic seizures characterized by spiking versus low voltage fast seizure onset patterns have a 3:2 or greater ratio of pre-seizure electrographic theta-gamma power ratios. Methods iEEG recordings were captured by the closed-loop NeuroPace RNS device for one patient with mesial temporal lobe epilepsy. The recordings were manually reviewed by an expert to differentiate electrographic seizures from inter-seizure bursts and to categorize seizures as either low-voltage fast or spiking onset. Recordings with <20s of pre-seizure data available were removed from the set. Spectral analysis of the 20s preceding seizure onset was performed for the theta (4-7 Hz) and gamma (30-70 Hz) bands for each channel of each recording using Fast Fourier Transform. An unpaired T-test was used to compare mean theta-gamma power ratios for low-voltage fast versus spiking seizure types. Results A total of 1532 four-channel iEEG recordings representing a 26 month period were screened resulting in 113 (47 spiking and 66 low-voltage fast) 20s pre-seizure iEEG segments with four channels each (452 total segments). The mean theta-gamma ratio for spiking onset seizures was 0.200 (median=0.119) and 0.137 (median=0.114) for low-voltage fast onset seizures. The ratio of theta-gamma ratios was 2.9:2 (0.063 absolute difference; SD=0.324; p<0.05) for seizures characterized by spiking versus low-voltage fast onset. Conclusions Theta-gamma power ratio in the 20s preceding seizure onset is greater in spiking versus low voltage fast onset in one patient with mesial temporal lobe epilepsy which may be a useful biomarker for spiking versus low-voltage fast seizures.

First Author: Kristen Smith-Edwards (Postdoctoral)	Poster Session: am
Presenting Author: Kristen Smith-Edwards (Postdoctoral)	Location: 41
Mentor/Lab: Davis	Category: Sensory
Department: Neurobiology	

Title: Mapping Functional Connections in the Gut's Brain

Summary: Using genetic techniques that make cells light up when they are active we can watch neural activity within the colon to understand how these cells communicate with each other and coordinate the movement of fecal matter through the digestive system.

Abstract: Kristen M. Smith-Edwards Sarah A. Najjar Kathryn A. Albers Brian M. Davis The gut is equipped with its own local nervous system the enteric nervous system ('the gut's brain') and similar to the central nervous system there are neuronal subpopulations responsible for detecting sensory information integrating and processing this information and providing signals for motor execution. In the colon these neuronal populations communicate with each other and to other non-neuronal cells (e.g. interstitial cells of Cajal ICC and smooth muscle cells) to coordinate movement of fecal matter however up to 70% of people will experience gastrointestinal motility dysfunction at some point in their lives. Mapping the functional connections among enteric subpopulations of cells would provide the means to regulate gastrointestinal functioning. Toward this end we used mice that express GCaMP in all cells to image spontaneous and evoked calcium signals in real-time using an ex vivo colon preparation. Different patterns of spontaneous activity were observed in enteric neurons and ICC. Twenty-one percent of neurons in a given myenteric ganglion (21.0 ±1.6% N=3 mice n=56 ganglia) displayed irregular spontaneous calcium transients that did not appear to be synchronized whereas ICC located in deeper layers of the colon exhibited rhythmic synchronized calcium oscillations that occurred 11.7±1.1 cycles per minute (N=3 mice n=19 fields of view). Interestingly activation of enteric neurons by electrical stimulation of the colon slowed ICC oscillations to 74.0±6.0% of baseline indicating neuronal modulation of ICC pacemaker activity. Lastly stimulation of the colon either rostral or caudal to the myenteric ganglion in the imaging field activated different subsets of neurons with minimal overlap (24.6±3.3% N=2 mice n=7 ganglia) suggesting discrete ascending versus descending interganglionic communication in the colon. Future studies will probe into the molecular identity of the various functional subpopulations of enteric neurons described here using immunohistochemistry pharmacology and optogenetic techniques.

First Author: Seungmoon Song (Postdoctoral)	Poster Session: am
Presenting Author: Seungmoon Song (Postdoctoral)	Location: 28
Mentor/Lab: Motor Adaptation and Rehabilitation Group / Gelsy Torres-Oviedo	Category: Motor
Department: Department of Bioengineering	

Title: Can split-belt treadmill walking be explained with a reflex-based model?

Summary: Human gait adaptation for example on split-belt treadmills is often explained by the modulation of central pattern generators which is assumed to govern the spinal locomotor circuits. Here we show with a neuromechanical simulation model that such a human gait adaptation on split-belt treadmills can be explained without central pattern generators but by modulations of spinal reflexes. Moreover with this spinal-reflex based model we investigate the physiological criteria that drive gait adaptation such as metabolic energy and muscle fatigue.

Abstract: Gait adaptation on split-belt treadmills provides insights on the underlying control structure for walking. For example observations on infants and adults walking on split-belt treadmills with various speed configurations have led to a consensus that the locomotion controller consists of separate functional networks for each leg and for different locomotion modes (e.g. forward vs. backward walking). However most of the interpretations of these experiments are based on an assumption that the spinal motor circuits are governed by central pattern generators (CPGs). Here we investigate the possibility that humans adapt their gait without CPGs. In other words we evaluated the extent to which human gait adaptation on split-belt treadmills moving the legs at different speeds can be reproduced in simulation by a spinal-reflex-based neuromechanical model which consists of a network of spinal reflexes mediated by supraspinal control without CPGs. Our results show that the reflex-based neuromechanical model can successfully generate stable split-belt walking with one leg moving at 1.5 m/s and the other one at 0.5 m/s. Moreover our preliminary results show that when the reflex control parameters are optimized for minimum metabolic consumption the model reproduces most of the stepping features observed in human split-belt treadmill walking. Specifically we performed a one-sample t-test to find significant differences between the gait features of nine healthy subjects and those produced by our model and found that both the subjects and the model converged to the same step-position ($p=0.25$) step-time ($p=0.010$) and step-velocity ($p=0.056$). Interestingly we found differences in the step length asymmetry reached by the simulation and the experimental results ($p<0.001$) suggesting that metabolic consumption may not be the only factor optimized in humans. We are currently investigating the effect of optimizing for different costs including metabolic energy muscle fatigue and gait asymmetry to explore the physiological basis of human gait adaptations upon sustained changes in the walking environment imposed by the split-belt treadmill. Once we identify the cost function driving locomotor learning we will further investigate the contributions of individual reflex pathways in the gait adaptation of the model. The findings will allow us to augment gait rehabilitation with devices such as the split-belt treadmill.

First Author: Judy Cameron (Faculty)	Poster Session: am
Presenting Author: Samantha Sostorecz (Graduate)	Location: 59
Mentor/Lab: Working for Kids: Building Skills	Category: Learning
Department: Neuroscience and Psychiatry	

Title: Evaluation of the Effectiveness of a New Neuroscience Education Program to Inform Communities about How to Improve Children's Brain Development

Summary: Working for Kids: Building Skills (WFK) a neuroscience outreach program is designed to teach the general public about healthy childhood brain development in a fun and interactive way. In six hour periods WFK trained professionals who work with children and pre-professional college students on the importance of strengthening children's brain pathways. We found that there is no significant difference between how well the material is learned between the two groups suggesting WFK is very effective in teaching nonscientists the basics of developmental neuroscience and that the material is equally accessible to pre-professional students.

Abstract: Children who have faced significant early life stresses are at a much higher risk of not reaching their maximal potential in terms of education physical health mental health and economic success in the workplace. Increasing the availability of supportive and enriching experiences can improve children's outcomes but in stressed communities there is often little knowledge of how to help children strengthen the many brain pathways they need for successful life skills. The Working for Kids: Building Skills™ (WFK) educational platform was designed based on principles of developmental neuroscience to educate the general public about how to strengthen children's brain pathways for a diversity of cognitive skills and social-emotional skills. The educational tools are fun easy to use and designed to be useful for those with a variety of educational and cultural backgrounds. Topics covered explain how experiences shape brain development the importance of supportive environments and the value of community supports in counteracting the effects of early life stresses. This study was designed to assess the effectiveness of WFK in teaching professionals (social workers home visitors public health professionals) how experiences can strengthen children's brain pathways. 175 professionals received the WFK six hour educational program. Three questionnaires each comprised of 5 true/false questions were given over the course of training to evaluate how well the participants learned basic neuroscience principles. Professionals correctly answered questions 88.98 ± 3.79% 91.34 ± 5.63% and 91.1 ± 5.12% after sessions 1 2 and 3 respectively. Seventy pre-professional college students also received WFK training. Pre-professionals who only completed session 3 correctly answered questions 94.9 ± 3.88% not significantly different from the professionals who were trained. WFK also collected qualitative data asking participants what was most interesting about the program and what they would change. 51.2% enjoyed learning about brain development and 31.3% enjoyed the Brain Architecture Game an active learning game showing the impact of life experiences on brain development.17.5% enjoyed other parts of the educational program such as how the program was presented. 64.79% said they would change nothing about the educational program while others suggested covering more topics. Overall we conclude that the WFK educational program is very effective in teaching nonscientists the basics of developmental neuroscience and that the material is equally accessible to pre-professional students. It is our hope that this program will be effective and engaging enough to have widespread adoption in stressed communities. Ongoing studies are evaluating the effectiveness of the WFK train-the-trainer program in teaching non-professional adults living in these communities about how to facilitate sturdy brain development in children.

First Author: Patricia Stan (Graduate)	Poster Session: am
Presenting Author: Patricia Stan (Graduate)	Location: 34
Mentor/Lab: Sandra Kuhlman	Category: Sensory
Department: Neurobiology	

Title: Function of tuning diversity in visual coding

Summary: Neurons in primary visual cortex (V1) are diverse in their orientation selectivity (their response to a select number of orientations of a bar) with some neurons responding to few orientations (sharply tuned) while others respond to many orientations (broadly tuned); our goal is to discover what the role of this diversity is in visual coding and how experience may affect this diversity. Sharply tuned neurons are shown to be important for detecting edges but the role of broadly tuned neurons is unclear. Our studies indicate that broadly tuned neurons are important for processing stimuli containing complex features.

Abstract: Neurons in primary visual cortex (V1) are diverse in their orientation selectivity – their response to a select number of orientations of a bar. Computational modeling studies indicate that this diversity is important for the discriminability of natural scenes with neurons of different orientation selectivity playing different roles. While the more commonly studied two-thirds of V1 neurons which are sharply tuned for orientation (respond to few orientations; orientation selectivity index OSI is > 0.44) are thought to play a role in edge detection the role of neurons broadly tuned for orientation (respond to many orientations; OSI < 0.3) remains unclear. We hypothesize that neurons broadly tuned for orientation are important for processing stimuli containing complex features. To examine this we used large field of view calcium imaging in awake mice to compare the responses of excitatory neurons (upwards of 400 neurons per imaging session 9 imaging sessions from 7 mice) to classic sinusoidal gratings versus complex stimuli (hyperbolic and spiral stimuli created from hyperbolic and polar coordinate systems) at a range of orientations and spatial frequencies (SF). Using greedy decoding algorithms we designed tasks to identify ensembles of neurons best at performing edge detection (decoding grating orientation) or orientation-invariant attribute detection of complex stimuli (decoding hyperbolic or spiral SF). We found that the properties of neurons comprising the ensembles best at decoding hyperbolic and spiral SF are distinct from those associated with edge detection (OSI for grating = 0.57 hyperbolic = 0.24 and for spiral = 0.22) with some ensemble neurons having no response to gratings (13-17% of the neurons within the high-accuracy complex SF ensembles). To identify the response properties that give rise to high accuracy we used linear regression analysis and determined properties that were significantly correlated with accuracy (Wilcoxon rank sum test of median fit coefficients) for each task. As expected decoding accuracy of grating orientation was positively correlated with sharpness of orientation tuning (p<0.01) and negatively correlated with sharpness of SF tuning (p<0.01). In contrast decoding of hyperbolic SF was negatively correlated with sharpness of orientation tuning (p<0.05) and positively correlated with sharpness of SF tuning (p<0.01). Similarly to decoding of hyperbolic SF decoding of spiral SF was positively correlated with sharpness of SF tuning (p<0.05) yet these ensembles were largely non-overlapping (spiral-hyperbolic ensemble overlap=14.4%). In summary we identified ensembles of neurons useful for encoding orientation-invariant features of complex stimuli at the earliest stages of visual cortical processing and found that these neurons tend to be broadly tuned for orientation. Furthermore there appears to be specialization in V1 for hyperbolic versus polar coordinate systems. Future studies will examine how altered visual experience affects the distribution of orientation selectivity and other response properties.

First Author: Kevin Sullivan (Postdoctoral)	Poster Session: pm
Presenting Author: Kevin Sullivan (Postdoctoral)	Location: 9
Mentor/Lab: Mary Ganguli	Category: Neurology & Neurodegenerative Diseases
Department: Epidemiology	

Title: Dementia Incidence in Four Population-Based Cohorts: The MYHAT and MoVIES Studies

Summary: Several epidemiological studies worldwide have reported decreasing dementia incidence rates (new cases) for more recent birth cohorts (born after 1920) compared to earlier both cohorts (born before 1920). We aimed to examine dementia incidence rates in four birth cohorts (1902-1911 1912-1921 1922-1931 1932-1941) across two Western PA population-based epidemiological studies to see if we observed the same downwards trend.

Abstract: Several large epidemiological studies have reported a decrease in incident dementia rates for more recent birth cohorts particularly in developed nations. Examining dementia incidence trends have many implications for preventive interventions. Pooling data from two large prospective population-based epidemiological dementia studies in Western Pennsylvania between 1987-Present we were able to identify four birth cohorts: 1902-1911 (n=421) 1912-1921 (n=1399) 1922-1931 (n=1075) 1932-1941 (n=670). With a total starting sample of 3565 we examined the incident dementia rates (dementia defined as Clinical Dementia Rating ≥ 1) using a proportional hazards model based on birth cohort with adjustment for baseline age sex education and study. Cohort effects in dementia incidence rates were observed with the most recent cohort reference group (1932-1941) having significantly lower incidence dementia rates compared to all three of the earlier birth cohorts (p<.01). Additionally dementia incidence trended downwards from the earliest birth cohort (1902-1912) with each successive birth cohort. This trend was unexplained by adjustment for baseline age education sex or study. Data from our pooled population-based studies supports other reports of declining dementia incidence rates in more recent birth cohorts and that this decline is not due to differences in education sex baseline age or which of the two pooled studies the participant was in. Further investigations into risk factors that may account for this trend are necessary.

First Author: Yalikun Suofu (Postdoctoral)	Poster Session: pm
Presenting Author: Yalikun Suofu (Postdoctoral)	Location: 19
Mentor/Lab: Friedlander	Category: Neurology & Neurodegenerative Diseases
Department: Neurological Surgery	

Title: Dual role of mitochondria in producing melatonin and driving GPCR signaling to block cytochrome c release

Summary: Melatonin is exclusively produced in mitochondria. Mitochondria membrane melatonin receptor type 1 respond to melatonin by activating heterotrimeric G proteins located in the mitochondria intermembrane space and inhibit stress-mediated cytochrome c release. Therefore the signaling pathway contributes to neuroprotection from ischemia-induced brain injury.

Abstract: G protein-coupled receptors (GPCRs) are classically characterized as cell-surface receptors transmitting extracellular signals into cells. Here we show that central components of a GPCR signaling system comprised of the melatonin type 1 receptor (MT1) its associated G protein and β-arrestins are on and within neuronal mitochondria. We discovered that the ligand melatonin is exclusively synthesized in the mitochondrial matrix and released by the organelle activating the mitochondrial MT1 signal-transduction pathway inhibiting stress-mediated cytochrome c release and caspase activation. These findings coupled with our observation that mitochondrial MT1 overexpression reduces ischemic brain injury in mice delineate a mitochondrial GPCR mechanism contributing to the neuroprotective action of melatonin. We propose a new term "automitocrine" analogous to "autocrine" when a similar phenomenon occurs at the cellular level to describe this unexpected intracellular organelle ligand-receptor pathway that opens a new research avenue investigating mitochondrial GPCR biology.

First Author: Steven Suway (Graduate)	Poster Session: am
Presenting Author: Steven Suway (Graduate)	Location: 25
Mentor/Lab: Andy Schwartz	Category: Motor
Department: Neurobiology	

Title: Temporally segmented coordinate systems in the motor cortex

Summary: We previously found evidence that the motor cortex changes functional state rapidly during behavior. However the behavioral factors driving these state changes are not clear. Here we provide preliminary evidence that visual information can be an important driver of these state changes which is surprising given that the motor cortex is often assumed to participate in lower-level muscle activation.

Abstract: We recently showed that directional tuning in motor cortical (M1) neurons is temporally segmented during center-out reaching (Suway et al. 2017). We found that preferred directions (PDs) change over time in discrete steps between segments but are stable for the duration of each segment. This raised the possibility that M1 changes functional state rapidly during behavior. Our lab has previously shown that some neurons in M1 express directional tuning in vision-centered coordinates rather than arm-centered coordinates. Here we explored the relationship between step-changes in PD and the coordinate systems of those PDs. We used a visuomotor perturbation to dissociate vision from action during reaching. Preliminary data show that the tuning of single neurons can change between segments to/from “arm coordinates” or “vision-sensitive” coordinates. This result extends our recent finding that directional tuning of single neurons occurs in discrete segments and lends support to the notion of discrete changes in functional state in M1 during behavior.

First Author: Chenxiao Tang
(Graduate)

Poster Session: pm

Presenting Author: Chenxiao Tang
(Graduate)

Location: 17

Mentor/Lab: Samuel Poloyac

Category: Neurology & Neurodegenerative Diseases

Department: Pharmaceutical Sciences

Title: Screening 20-HETE Formation Inhibitors in Microsomal Incubates Using UPLC-MS/MS

Summary: 20-HETE formation inhibitors were screened in in vitro system. Lead compounds with better solubility metabolic stability and potency could be used in preclinical animal model to evaluate its PK/PD.

Abstract: Introduction: 20-hydroxyeicosatetraenoic acid (20-HETE) is a metabolite of arachidonic acid (AA) by CYP4A11 and CYP4F2 in human with potent microvascular constriction activity. Inhibition of 20-HETE formation has neuroprotective effect in subarachnoid hemorrhage (SAH) cardiac arrest and thromboembolic stroke preclinical models. Clinical evidence shows that high level of 20-HETE is associated with three-fold increased mortality and unfavorable outcomes in SAH patients. These findings suggest that inhibition of 20-HETE formation is a potential therapeutic strategy for neuroprotection after brain injury. HET0016 a commonly used 20-HETE inhibitor is not suitable for clinical use due to its poor solubility and short half-life. At this point a clinically relevant 20-HETE inhibitor is not available to be evaluated as a therapeutic intervention. Hypothesis: Drug-like compounds that inhibit 20-HETE formation can produce neuroprotective effect in secondary brain injury by improving CBF and attenuating ischemic brain damage. Methods: Test compounds were obtained either via virtual screening against a CYP4F2 homology model or from scaffold hopping from structures of known inhibitors. Four different types of microsomal systems including human liver microsome (HLM) recombinant CYP4F2 (rCYP4F2) rat liver microsome (RLM) and rat kidney microsome (RKM) were used for microsomal incubations. AA was incubated in microsomes with/without compound for 20 min. 20-HETE formation rate was quantified using a validated UPLC-MS/MS assay and normalized by vehicle control group. Other eicosanoids including 15- 12-HETEs epoxyeicosatrienoic acids (EETs) and dihydroxyeicosatrienoic acids (DiHETs) were monitored simultaneously. Selected compounds metabolic stability was tested in HLM throughout 60-min incubation time the remaining compound was measured by UPLC-MS/MS and normalized to corresponding 0-min values. Results: We identified UPMP 10 as the hit compound. The IC50 of UPMP10 in HLM is 443.4nM. UPMP19 showed improved 20-HETE inhibitory effect with an IC50 of 187.1nM. Both UPMP10 and UPMP19 did not inhibit EETs or DiHETs formation up to 50000 and 10000 nM respectively. UPMP10 and 19 were more stable with 91.4±11.0% and 100.4±1.7% remaining compound at 30min in HLM compared to 35.1±5.7% of TS_24. After structure modification UPMP22 is the most potent compound with a IC50 of 49.56 nM. None of the six compounds inhibit epoxygenase pathway of AA. All the compounds were slowly metabolized in HLM throughout 60 min incubation time. UPMP22 has 85.4±1.51% remaining compound at 30 min time point. Conclusion: These results suggested that UPMP22 is a potent selective metabolically stable 20-HETE formation inhibitor. It can serve as preclinical lead for further structure modifications that may lead to novel 20-HETE formation inhibitors.

First Author: Tobias Teichert (Faculty)	Poster Session: am
Presenting Author: Tobias Teichert (Faculty)	Location: 40
Mentor/Lab: Teichert	Category: Sensory
Department: Psychiatry and Bioengineering	

Title: Tracking the gradual formation and decay of auditory sensory memory using behavior and concurrent EEG recordings in macaque monkeys

Summary: For several seconds past sounds are stored as a gradually decaying memory trace. This trace plays a fundamental role for many auditory functions such as speech perception yet remains unclear how it is implemented in the brain. This work tests the hypothesis that each sound reduces the signaling capacity of neurons that respond to it and thus leave a negative trace of past sounds that persists until the signaling capacity has been replenished over the course of several seconds.

Abstract: Background. For several seconds auditory information is passively stored in auditory sensory memory. Despite the importance of auditory sensory memory for many aspects of auditory function its neural mechanisms are still a matter of debate. However it has been noted that the amplitude of the auditory evoked N1 which is reduced immediately after a tone has been processed recovers back to baseline at the same rate at which information decays from auditory sensory memory. Here we tested the hypothesis that amplitudes of auditory evoked potentials (AEPs) elicited by a specific tone are smaller if that tone is encoded more strongly in auditory sensory memory. Methods. To that aim we recorded AEPs from 32 cranial EEG electrodes while macaque monkeys performed a novel delayed pitch-discrimination task designed to track the dynamic formation and decay of auditory sensory memory. In the task animals listened to sequences of standard tones and released a lever when they identified a pitch-deviant target tone. The stimulus-onset asynchrony (SOA) of consecutive tones varied randomly between 0.250 and 12 sec. The target could occur between sequence positions 2 and 13. The frequency-difference between standard and target (ΔF) varied between 0 and 1.2 octaves. On catch trials (ΔF=0) animals were rewarded for not releasing the lever. Results. Target detection rate increased with ΔF. The slope of the corresponding psychometric function was used to quantify discrimination performance as a function of SOA and the number of preceding standards. Preliminary data showed that discrimination performance gradually increased with repetition number and decreased with SOA. Comparison to behavior in homolog signal detection tasks without sensory memory component suggests that changes of performance in the discrimination task reflect the gradual strengthening of sensory memory with repetition and its gradual decay during periods of silence. The hypothesis that small AEPs are a marker of strong memory encoding thus predicted that AEP amplitude would be small for short SOAs and after many repetitions. Indeed several AEPs such as the P31 and the N85 –the presumed monkey homolog of the N1– were smallest for the shortest SOAs. However contrary to the prediction AEP amplitudes generally increased with stimulus repetition. Both effects shared similar timing and topography with one key exception: between 40 and 60 ms after tone-onset fronto-central electrodes (human Fz homolog) encoded SOA while the effect of repetition number was either completely absent or substantially weaker. Interestingly ERPs at the same latency and topography were reduced by stimulus-specific adaptation in a passive listening task. Conclusion. Taken together these findings suggest a specific role for this fronto-central EEG component in stimulus-specific adaptation and sensory memory. However additional quantitative analyses are needed to link this component more closely to performance in the delayed tone-discrimination task and single-cell responses in auditory cortex.

First Author: Brenden Tervo-Clemmens (Graduate)	Poster Session: pm
Presenting Author: Brenden Tervo-Clemmens (Graduate)	Location: 42
Mentor/Lab: Laboratory of Neurocognitive Development	Category: Psychiatry
Department: Psychology & Psychiatry	
Title: Brain-based Structure of Psychiatric Comorbidity	
Summary: People with one psychiatric disorder frequently meet diagnostic criteria for another disorder. However little is known about the brain-basis for the co-occurrence of psychiatric disorders. In this project we demonstrate core brain systems associated with cognition and emotion are associated with multiple psychiatric disorders.	
Abstract: Across the lifespan latent variable modeling reveals dimensional higher-order psychopathology factors that account for patterns of comorbidity amongst common psychiatric disorders. However little is known about the structure of psychiatric comorbidity in the brain. To identify neural systems associated with psychiatric comorbidity we utilized resting-state functional magnetic resonance imaging (rsfMRI) data and psychopathology symptom endorsement from 748 subjects of the Philadelphia Neurodevelopment Cohort. Symptom-severity connectivity matrices were created for nine psychiatric disorders and patterns were examined using exploratory factor analysis. Four factors emerged representing general psychopathology (p) fear approach-avoidance and externalizing behavior. Regional expression of these higher-order factors implicated brain-regions associated with transdiagnostic cognitive (DLPFC general psychopathology; ACC externalizing behavior) and affective (amygdala fear; OFC & basal ganglia approach-avoidance) behaviors. Our results suggest common neural systems may contribute to multiple psychiatric disorders highlighting the importance of investigating core psychopathology features in clinical neuroimaging.	

First Author: Nicholas Todd (Graduate)	Poster Session: pm
Presenting Author: Nicholas Todd (Graduate)	Location: 6
Mentor/Lab: Thathiah	Category: Neurology & Neurodegenerative Diseases
Department: Neurobiology	

Title: G protein-coupled receptor kinases as a therapeutic target for Alzheimer's Disease

Summary: Of the top ten leading causes of death worldwide Alzheimer's disease (AD) is the only one that we cannot prevent cure or slow down. We identified the orphan G protein-coupled receptor (GPCR) GPR3 as a primary modulator of AD pathology. Here we investigate the pathophysiological role that GPCR kinases (GRKs) play in modulation of GPR3 function and disease progression. Results from these studies will not only address a major challenge in understanding disease mechanisms in AD they will also provide new avenues for the development of potential therapeutic targets to mitigate and/or halt the neurodegenerative changes observed in this devastating neurodegenerative disorder.

Abstract: Alzheimer's disease (AD) is characterized by the accumulation of aggregates of the amyloid-β (Aβ) peptide formed by sequential cleavage of the β-amyloid precursor protein (APP) by the β- and γ-secretases. Changes in APP and/or Aβ homeostasis lead to Aβ aggregation that critically contributes to the pathological abnormalities associated with AD. As such pharmacologically targeting of Aβ is one of the primary approaches investigated to treat AD. G protein-coupled receptors (GPCRs) are the most common target for therapeutic drug discovery. Several GPCRs have also been associated with multiple stages of APP proteolysis. Our lab identified the orphan GPCR GPR3 as a modulator of Aβ pathology. Furthermore we determined that the GPR3-mediated effect on Aβ generation requires the GPCR adaptor protein β-arrestin 2 (βarr2). GPCR kinases (GRKs) bind GPCRs upon ligand activation and phosphorylate GPCRs triggering βarr2 recruitment and subsequent downstream signaling. Significantly evidence suggests that levels of GRK2 and GRK5 are altered in the human AD brain. Despite these findings the putative involvement of GRKs in AD pathology has not been investigated in any context. Indeed identification of the GRKs involved in the modulation of GPR3 and βarr2 function could provide fundamental novel insight into the contribution of this important class of kinases under physiological and pathophysiological conditions. In preliminary studies genetic deletion of each of the four ubiquitously expressed GRKs namely GRKs 2 3 5 and 6 using a CRISPR/Cas9 genome-editing strategy indicates that GRKs 2 3 and 5 differentially regulate Aβ generation. We are currently testing the hypothesis that specific GRKs also regulate βarr2 recruitment to GPR3 and/or the phosphorylation status of GPR3 and the γ-secretase. Collectively these studies will determine the pathophysiological involvement of GRKs in the regulation of γ-secretase function establish which GRKs are involved in GPR3 phosphorylation and βarr2 recruitment and provide a potentially innovative therapeutic approach to treat AD.

First Author: Chelsea Vadnie (Postdoctoral)	Poster Session: pm
Presenting Author: Chelsea Vadnie (Postdoctoral)	Location: 43
Mentor/Lab: Colleen McClung	Category: Psychiatry
Department: Psychiatry	

Title: Using optogenetics to determine the role of the suprachiasmatic nucleus in mood-like behaviors

Summary: Disruptions in circadian rhythms rhythms that repeat approximately every 24 hours commonly occur in people with mood disorders. The suprachiasmatic nucleus (SCN) in the brain drives and synchronizes circadian rhythms but it is unclear whether perturbing SCN neural activity affects mood. Here we have developed a procedure to study the mood-like effects of delaying or advancing SCN activity in mice.

Abstract: Circadian rhythm disruptions commonly occur in mood disorders. Recent clinical findings suggest that phase delayed rhythms more commonly occur during depressive episodes whereas phase advanced rhythms more frequently occur during manic episodes. The suprachiasmatic nucleus (SCN) synchronizes bodily rhythms with the environment and may underlie the misaligned rhythms observed in mood disorders. Recently disrupting molecular rhythms in the SCN was shown to cause mood-like disturbances in mice suggesting that disrupting SCN neural activity rhythms may affect mood. Thus our goal was to develop a model system to determine if phase-delaying and phase-advancing manipulations of SCN neural activity have differential effects on mood-like behaviors. Channelrhodopsin-2 (ChR2) was genetically introduced into the SCN by crossing mice expressing Cre recombinase in GABAergic neurons with mice expressing Cre-dependent ChR2. Optic fibers were implanted above the SCN and mice were housed in cages equipped with piezoelectric floor sensors to monitor circadian rhythms and sleep. Mice were then placed in constant darkness (DD) to observe their SCN-driven rhythms. Mice subsequently received stimulations (1 h 10 ms pulse width 8 Hz) every three days at times early or late into their active phase to induce phase delays or phase advances respectively. After six stimulation sessions mood-like behaviors were assessed. Stimulating the SCN early in the active phase induced phase delays increasing the period of activity rhythms (24.40 ± 0.06 hr) relative to control mice (24.13 ± 0.06 hr). Stimulating the SCN late in the active phase induced phase advances decreasing the period of activity rhythms (23.55 ± 0.07 hr) relative to controls (23.95 ± 0.02 hr). Thus optogenetic stimulation of GABAergic neurons in the SCN induced phase shifts in circadian activity rhythms that resembled the known effects of light pulses applied in DD. We are currently assessing the effects of the stimulation paradigms on mood-like behaviors. Importantly we have developed a model system to determine the role of SCN-mediated phase shifts of circadian rhythms in mood regulation.

First Author: Amber Van Laar (Faculty)	Poster Session: pm
Presenting Author: Amber Van Laar (Faculty)	Location: 23
Mentor/Lab: Greenamyre Lab	Category: Neurology & Neurodegenerative Diseases
Department: Neurology	

Title: Progressive parkinsonism in rats following brief rotenone exposure: a novel model of Parkinson's disease

Summary: A more predictive and accurate model of Parkinson's disease is needed to facilitate the development of disease-modifying therapies. In this study we have developed and characterized a novel progressive animal model of Parkinson's disease. A key distinction of this model is the ability to test new possible therapies once the disease process is underway or even after symptom onset which is directly relevant to the Parkinson's disease patients in the clinic.

Abstract: A major barrier in treatment advancement for Parkinson's disease (PD) has been the lack of preclinical models that recapitulate the complexities of human PD with fidelity. The need for parkinsonian models with greater clinical predictive value has never been greater. Rotenone – a pesticide linked to increased PD risk and a potent inhibitor of mitochondrial respiration – has been a useful tool in PD research. Rotenone exposure has previously been demonstrated to produce a parkinsonian behavioral phenotype in rats associated with nigrostriatal degeneration when administered chronically. We have now found that just a brief exposure to rotenone triggers a downstream cascade of neurodegenerative events with progressive development of behavioral and neuropathological features analogous to human PD. Wildtype aged Lewis rats (6-9mo) were administered rotenone (i.p.) for only 5 days. The rats developed a parkinsonian phenotype during rotenone treatment but within 2 weeks after discontinuation of rotenone all rats recovered to their behavioral baseline where they remained until about 10 weeks. After this period of neurologic normalcy all rats spontaneously developed mild parkinsonian behavioral features that slowly progressed over the next 3-4 months. Immunohistochemical analyses revealed that during the behaviorally quiescent period while animals are at baseline nigral dopaminergic neurons began to accumulate alpha-synuclein which gradually begins to consolidate into Lewy body-like inclusions by 3 months when the parkinsonian phenotype returns. Microglial activation accompanies the accumulation of alpha-synuclein and loss of nigral dopamine neurons which indolently progresses over several months. Alpha-synuclein accumulation was also found outside of the nigrostriatal system including cortex and hippocampus in rats aged out to 9 months after the start of rotenone. We propose that this delayed rotenone model with a progressive endogenous alpha-synucleinopathy provides a more clinically predictive parkinsonian model to rigorously investigate PD-relevant disease mechanisms and potential therapeutics. A key advantage to this model is the delay of parkinsonian symptom onset after the brief rotenone exposure providing an opportunity to evaluate neuropathogenic mechanisms and therapeutic strategies both before and after symptom onset. The spontaneous development of symptoms that progresses over months - akin to human PD - allows testing of therapeutic interventions at multiple clinically-relevant time points. The prolonged survival after symptom development also allows for evaluation of therapeutic response over a period of months. The delayed parkinsonian rotenone model stands to serve as a preclinical and neurobiological surrogate for human PD. This new PD model provides for more accurate and efficient assessment of potential therapeutics thereby promoting the translation of impactful treatments more readily into clinical practice.

First Author: Victor Van Laar (Faculty)	Poster Session: pm
Presenting Author: Victor Van Laar (Faculty)	Location: 20
Mentor/Lab: Berman Lab	Category: Neurology & Neurodegenerative Diseases
Department: Neurology	

Title: Mitochondrial Mitofilin as a Novel Therapeutic Target for Parkinson's Disease

Summary: Currently there are no therapies for Parkinson's disease patients that alter or halt disease progression. Mitofilin a protein crucial for regulating mitochondrial function is an intriguing target for researching neuroprotective therapies and we have evidence that mitofilin overexpression is protective against Parkinson's-related neurotoxins in vitro. In this study we provide the first characterization of mitofilin in Parkinson's brain and begin evaluating mitofilin as a potential target for researching neuroprotective therapeutic treatments for Parkinson's disease.

Abstract: Parkinson's disease (PD) is the most common neurodegenerative movement disorder affecting 1% of people over the age of 65. At present there is no cure for PD and available treatments only address disease symptoms. Research is needed to identify novel targets for the development of neuroprotective therapies that will hinder or halt the progressive neuron loss in PD. Mitochondria are a major focus for PD research as mitochondrial dysfunction is a known contributor to PD pathophysiology. We have identified mitochondrial mitofilin a protein which functions as a unique nexus for regulating mitochondrial function and cellular stress response as a promising target for study. Mitofilin also known as mic60 is a scaffolding protein of the inner mitochondrial membrane and is critical for maintaining mitochondrial membrane structure and function. Mitofilin/mic60 also interacts with and regulates PINK1 a mitochondrial protein integral in signaling damaged mitochondria for degradation and associated with a heritable form of PD. Loss of mitofilin/mic60 has severely detrimental effects on mitochondrial morphology and respiration. Mitofilin/mic60 is also highly susceptible to oxidative stress. We and others have shown that mitofilin/mic60 protein levels are decreased in dopaminergic cells in models of PD. We have also previously shown that mitofilin/mic60 is a target for modification by oxidized dopamine the neurotransmitter used by the substantia nigral neurons that are uniquely vulnerable to PD. Further we found that a specific loss of mitofilin/mic60 in dopaminergic cells in vitro exacerbated cellular vulnerability and impaired respiratory capacity in response to rotenone a pesticide and mitochondrial Complex I inhibitor associated with increased PD risk. Conversely overexpression of mitofilin/mic60 promoted cellular survival and mitochondrial respiration. These results suggest that altering levels of mitofilin/mic60 in dopaminergic neuronal cells significantly affects both mitochondrial homeostasis and cellular vulnerability to PD-relevant stressors. We are now investigating mitofilin/mic60 for its role in PD pathogenesis and its neuroprotective potential. We have carried out an initial analysis of mitofilin/mic60 expression in PD patient brain. Post-mortem tissue from PD patient and age-matched control brains were immunohistochemically analyzed for mitofilin/mic60 expression level and cellular localization using confocal microscopy. To our knowledge this is the first such characterization of mitofilin/mic60 in human PD brain. We have also developed an adeno-associated viral vector for overexpression of mitofilin/mic60 in dopamine neurons in vivo which we will use to begin examining the neuroprotective properties of mitofilin/mic60. Our ultimate goal is to assess the neuroprotective capabilities of mitofilin/mic60 in vivo in preclinical models of PD.

First Author: Nathan Vogler (Graduate)	Poster Session: am
Presenting Author: Nathan Vogler (Graduate)	Location: 36
Mentor/Lab: Thanos Tzounopoulos	Category: Sensory
Department: Otolaryngology	

Title: Activity-dependent Plasticity of Synaptic Zinc Signaling in the Dorsal Cochlear Nucleus - a Novel Synaptic Plasticity Mechanism

Summary: Many synapses in the brain contain zinc which functions as a neurotransmitter. Synaptic zinc is modulated by sensory experience but the mechanism of how this occurs has been unknown. This research demonstrates that zinc signaling is modulated by synaptic activity and identifies crucial components of the mechanism underlying this process.

Abstract: In many excitatory synapses mobile zinc is found within glutamatergic vesicles and is co-released with glutamate. Ex vivo studies established that synaptically released (synaptic) zinc inhibits excitatory neurotransmission at lower frequencies of synaptic activity but enhances steady state synaptic responses during higher frequencies of activity (Mcallister & Dyck 2017; Kalappa et al. 2017). Recent in vivo studies established that synaptic zinc modulates cortical auditory processing by enhancing the gain of sound-evoked responses in auditory cortical principal neurons and reducing the gain of cortical interneurons (Anderson et al. eLife in press). Zinc-mediated modulation of neurotransmission and presynaptic zinc levels are modulated by activity in many brain areas such as somatosensory and visual cortex the retina and the dorsal cochlear nucleus (DCN) an auditory brainstem nucleus (Nakashima & Dyck 2009; Li et al. 2017; Kalappa et al. 2015). However the signaling mechanisms underlying this plasticity remain unknown. To study these mechanisms we employed in vitro electrophysiological recordings in DCN brain slices. Application of the extracellular zinc chelator ZX1 (100μM) potentiates AMPAR and NMDAR EPSCs evoked by stimulation of parallel fibers demonstrating AMPAR/NMDAR inhibition by synaptic zinc. High frequency stimulation (HFS 3 x 100 Hz) of parallel fibers eliminates potentiation by ZX1 indicating activity-dependent plasticity of zinc-mediated inhibition (zinc plasticity). Zinc plasticity is blocked by the intracellular calcium buffer BAPTA (10mM) as well as the metabotropic glutamate receptor (mGluR) antagonist MCPG (500μM) and the Type 1-specific mGluR antagonists MPEP (4μM) and LY367385 (100μM). Furthermore application of CPA (20μM) an inhibitor of SERCA ATPase which depletes calcium from intracellular stores is sufficient to induce zinc plasticity. Application of the Type 1 mGluR agonist DHPG at a low concentration (5μM) also eliminates zinc-mediated inhibition; however DHPG at a higher concentration (50μM) increases zinc-mediated inhibition. Our results demonstrate the activity-dependent plasticity of zinc-mediated inhibition at DCN parallel fiber synapses. Zinc plasticity involves activation of Type 1 mGluRs and release of calcium from intracellular stores. Furthermore our results suggest a role for mGluR signaling in the bidirectional modulation of zinc plasticity. Together these results reveal a novel synaptic plasticity mechanism that modulates zinc-mediated inhibition of glutamatergic neurotransmission.

First Author: Maxwell Wang (Graduate)	Poster Session: pm
Presenting Author: Maxwell Wang (Graduate)	Location: 44
Mentor/Lab: Howard Aizenstein MD PhD	Category: Psychiatry
Department: Psychiatry	

Title: Predicting Remission in a Late-Life Depression Treatment Trial

Summary: Identifying an effective depression treatment regimen requires a lengthy trial and error cycle where each drug must be taken for several weeks before a clinician can determine whether the drug was effective. As this cycle continues the patient often spirals further into depression leading to worsening outcomes. Here we present the usage of functional MRI and machine learning towards shortening these several weeks of trial and error down to a 24 hour experiment.

Abstract: Treatment of major depressive disorder typically involves a lengthy trial and error process (around 6-8 weeks in the late-life depression subtype) to identify an effective regimen. This lengthy period delays overall improvement causes patients to drop from care and increases risk of suicide. These patterns are even worse in late-life. However recent work demonstrates that during a venlafaxine (serotonin-norepinephrine reuptake inhibitor) trial significant perturbations in neural functional connectivity occurred rapidly (within 24 hours) following the first dose. In this project we propose an analysis framework to translate these perturbations in functional networks into accurate predictors of clinical remission. Utilizing ten-fold cross-validation and ROC-based metrics we find that our approaches yield significant increases in predictive accuracy over baseline clinical measures such as the Montgomery-Asberg depression rating scale (MADRS). We hope that our model also provides additional insight into the mechanism of venlafaxine within the context of the brain's latent network architecture to motivate possible ways to refine and improve treatment options.

First Author: Jillian Weeks (Graduate)	Poster Session: pm
Presenting Author: Jillian Weeks (Graduate)	Location: 55
Mentor/Lab: Sved	Category: Psychiatry
Department: Neuroscience	

Title: Nicotine reinforcement is not increased in the MAM rodent model of schizophrenia

Summary: Individuals with schizophrenia smoke at a rate 4 to 5 times higher than the general population and with greater frequency and intensity but the mechanism behind this is unknown. This experiment used an animal model of schizophrenia to determine if increased reward from nicotine the primary psychoactive component of tobacco drives this increase in smoking.

Abstract: Despite progress in reducing smoking over the past several decades up to 80% of individuals with schizophrenia (SCZ) continue to smoke. SCZ patients also smoke more intensely and with greater frequency contributing to a disproportionately negative impact on health. However no clear mechanistic connection between SCZ and smoking has been established. One hypothesis underlying the behavior is that SCZ brain pathophysiology confers an increased propensity to take nicotine (NIC) the primary psychoactive component of cigarette smoke. We sought to characterize NIC reinforcement as measured through a self-administration paradigm in a neurodevelopmental rat model of SCZ. Pregnant dams were treated with either methylazoxymethanol acetate (MAM; 1 mg/kg i.p.) or saline (CTL) on gestational day 17. Adult male and female offspring were allowed to self-administer NIC across a range of doses (0 - 60 micrograms/kg/infusion 7 days/dose) paired with neutral cue (CS) or reinforcing visual stimulus (VS) in daily 1 hr sessions. MAM and control rats did not differ in infusions + CS earned at any NIC dose (e.g. 15 microgram/kg/infusion dose females; MAM n = 22 mean = 9.8 ± 1.2 infusions; CTL n = 18 mean = 9.9 ± 0.9 infusions). MAM rats earned fewer infusions of NIC paired with VS at all doses tested (e.g. 30 microgram/kg/infusion dose males; MAM n = 9 mean = 17.2 ± 1.4 infusions; CTL n = 10 mean = 21.9 ± 1.3 infusions) but also responded less for VS alone. This suggests that VS may be less reinforcing to MAM animals which may in turn reduce the relative magnitude of NIC enhancement of VS reinforcement. To capture patterns of responding across an extended period rats in a separate experiment were allowed to self-administer NIC + CS for 23-hr sessions. No differences in NIC-taking between MAM and CTL rats were observed in 23-hr sessions. Overall GD17 MAM did not produce an increase in NIC self-administration in male or female rats which suggests that SCZ pathophysiology as modeled in these animals does not elevate NIC intake due to increased NIC reinforcement.

First Author: Jeffrey Weiss (Graduate)	Poster Session: am
Presenting Author: Jeffrey Weiss (Graduate)	Location: 12
Mentor/Lab: RNEL/Collinger	Category: Brain-Machine Interfaces
Department: Bioengineering	

Title: Artifact-free recording during human intracortical microstimulation

Summary: We developed a method to record electrical signals produced by the brain while simultaneously applying electrical stimulation to an adjacent brain area. We used this method in a closed-loop brain-computer interface enabling a paralyzed person to both control and feel a robotic arm.

Abstract: We have previously demonstrated brain-computer interface (BCI) control of a robotic arm using signals recorded from motor cortex (M1) and that intracortical microstimulation (ICMS) of human primary somatosensory cortex (S1) can evoke tactile percepts. We wish to combine these results in a closed-loop BCI system which must be capable of continuously recording and stimulating adjacent regions of cortex. This problem is non-trivial due to the presence of large amplitude electrical stimulus artifacts which mask smaller-amplitude extracellular potentials generated by active neurons. Additionally filtering of the recorded signals an essential step for spike detection can compound the problem by distorting artifacts in time such that the signal is corrupted for a duration longer than the stimulus pulse width. We developed a simple artifact elimination (AE) scheme to record in M1 during ICMS of S1 without complex real-time processing. Under an Investigational Device Exemption (NCT01894802) a man with a C5/C6 spinal cord injury was implanted with two recording microelectrode arrays in M1 and two stimulation microelectrode arrays in S1. During each 700 μs biphasic stimulus pulse a sample-and-hold digital filter was applied to the raw recorded signal to eliminate stimulus artifacts prior to additional filtering. A 750 Hz first-order high-pass Butterworth filter was then applied to the signal prior to thresholding for spike detection. These parameters were chosen to meet the specifications of a fast return to baseline after perturbations elimination of filter ringing in the step response and an overall increase in signal-to-noise. This AE scheme allowed for reliable spike detection as soon as 800 □s after the offset of each stimulus pulse corresponding to a 15% loss of neural data when stimulating at 100 Hz. We demonstrated the effectiveness of the AE scheme in a closed-loop BCI task. A 5 DOF velocity decoder was trained to control a robotic arm. The subject was instructed to use the robotic arm to transfer an object across a 20 cm region as many times as possible during a two-minute period. During ICMS trials 8 electrodes were simultaneously stimulated between 18-46 μA at 100 Hz when the fingers generated torque against the object. A one-way ANOVA found significant differences in performance between baseline (no ICMS) ICMS and ICMS+AE conditions ($p < .01$). Post-hoc tests revealed a significant decrease in performance with ICMS without AE compared to baseline ($p < .01$) but no significant difference between baseline and ICMS+AE conditions ($p = .621$). The proposed system is relatively simple to implement and requires minimal parameter tuning to produce reliable recordings during ICMS for closed-loop BCI control.

First Author: Steven Wellman (Graduate)	Poster Session: pm
Presenting Author: Steven Wellman (Graduate)	Location: 30
Mentor/Lab: Takashi Kozai	Category: Neurology & Neurodegenerative Diseases
Department: Bioengineering	

Title: Two-photon imaging reveals processes extension and cell body migration of reactive NG2 glia during acute brain injury

Summary: Recent studies suggest there are other immune cells besides just microglia and astrocytes involved in the development of a glial scar after injury. A critical function of NG2 glia which is to maintain neuronal health and physiology through the formation of synapses with neurons may be compromised after an insult to the brain. Using real time imaging techniques we observed NG2 glia respond to brain implant injury by changes in cell morphology extension of cellular processes and migration of cell bodies toward the lesion site similar to microglia yet at a slower rate indicating novel features of scar development after injury.

Abstract: Activation of microglia and astrocytes and their contribution to neuronal loss are historically the focus of investigations into scar tissue formation after brain injury. However recent studies have implicated other effectors in the progression of reactive gliosis. NG2 glia which arise from the oligodendrocyte lineage during development are widely distributed across the adult brain and exist as a separate glial entity with distinctive characteristics. Known also as oligodendrocyte precursor cells they are responsible for differentiating into myelinating oligodendrocytes in normal CNS physiology and after incidences of demyelination. Unique to glial cells NG2 glia form functional synapses on neurons with the ability to influence neuronal viability through secretion of neurotrophic factors and modulation of neuronal networks. Therefore NG2 glia may display alternative behavior under pathological conditions that could potentially be detrimental to brain tissue health. After injury NG2 expression is known to increase following migration and proliferation of NG2-expressing cells around lesion sites. Due to their intrinsic potential to differentiate into astrocytes and express axon-growth inhibitory molecules NG2 glia have been implicated in the formation of the glial scar. Here we use in vivo two-photon microscopy to characterize the initial NG2 glia scar formation around brain implant injuries in the cortex through changes in cell shape transforming from an inactive ramified state to a transitional morphology. Similar to microglia NG2 glia are seen extending cellular protrusions and migrating towards the surface of the electrode. However unlike microglia cells who respond immediately on the order of minutes to electrode insertion NG2 glia do not extend processes or migrate cell bodies until hours post-insertion. This delay in cell response between microglia and NG2 cells may imply unique possibly chemotactic cell-cell interactions between glia in the reactive tissue response after injury. Fully comprehending the role of NG2 glia in the disease state and their divergence from normal physiological function can offer previously unknown insights into the inflammatory tissue reaction after brain injury and potentially foster novel strategies towards attenuating those responses.

First Author: Jordan Williams (Postdoctoral)	Poster Session: am
Presenting Author: Jordan Williams (Postdoctoral)	Location: 13
Mentor/Lab: Andrew Schwartz Motorlab	Category: Brain-Machine Interfaces
Department: Systems Neuroscience Institute	

Title: Peripheral optogenetic stimulation of motor function in non-human primates toward restoration of volitional motor control in a brain-machine interface

Summary: This work examines the use of viral gene therapy techniques in monkeys in order to stimulate muscle activity using light as an alternative to traditional electrical stimulation. The results presented here present a first step toward translating this technology to restore voluntary movements and independence to patients such as those with spinal cord injury

Abstract: Artificial muscle activation can be used to reanimate muscles that have been rendered inactive by disease or injury. Most approaches to muscle reanimation have used functional electrical stimulation (FES) which has several considerable drawbacks. Recently peripheral motor nerves expressing channelrhodopsin (ChR2) have been optically stimulated to elicit functional muscle activity in transgenic mouse lines as well as through viral mediation in rodents. Functional optical stimulation (FOS) of muscle activity in this manner offers several advantages over FES in terms of its potential use in chronic BMI applications. Prior to realizing its potential as a human gene therapy however viral transduction of light-sensitive opsins such as ChR2 in peripheral motor nerves must be demonstrated and optimized in non-human primates – a task which has proven difficult for viral optogenetic techniques in the brain and has yet to be demonstrated in the periphery. Here we present successful transduction of ChR2 and a newer variant Chronos in peripheral motor nerves of adult macaques following injection of AAV6 based vectors into target muscles. EMG activity elicited acutely through fiber optic stimulation demonstrated selective recruitment of muscle fascicles within a targeted muscle. In addition we examined patterns of sensitivity to optical stimulation histology multi-photon and whole sample optical imaging techniques to evaluate the expression patterns of opsins in the spinal cord and periphery with implications for chronic LED cuff placement. Together these results can help direct avenues of investigation that need to be addressed before this therapy may be translated to clinical use.

First Author: Jesse Wood (Postdoctoral)	Poster Session: am
Presenting Author: Jesse Wood (Postdoctoral)	Location: 53
Mentor/Lab: Ahmari	Category: Brain Models and Systems
Department: Psychiatry	

Title: Stimulation of medial orbitofrontal cortex terminals in ventromedial striatum causes neuroplastic changes in cortex

Summary: Stimulating cortical neuron terminals in striatum causes plasticity in cortical networks

Abstract: Optogenetic stimulation of specific neuronal projections is a powerful tool for dissecting neural circuit function but the network effects of axon terminal stimulation have not been thoroughly explored. To study these effects we optogenetically stimulated medial orbitofrontal cortex (mOFC) projections in ventromedial striatum (VMS) while recording electrophysiological activity in mOFC networks during 10 days of repeated ChR2 stimulation. We observed that stimulation of terminals in VMS caused highly entrained population spikes in mOFC; single unit spikes rarely occurred during the inter stimulus interval (i.e. between light pulses). To facilitate identification of population spikes we developed a novel optogenetic stimulation paradigm To investigate the chronic effects of this synchronous entrainment we measured pairwise cross correlations between mOFC neurons in 15-minute periods preceding and following stimulation. Prior to stimulation in session 1 there was no mOFC synchrony in ChR2 animals (0/66 pairs of simultaneously recorded mOFC neurons). Immediately following stimulation in the first session synchrony between mOFC neuron pairs had begun emerging. Synchrony grew more prominent in sessions 5 and 10 in mOFC networks in association with repeated optogenetic stimulation. In contrast significant pairwise synchrony was extremely rare in control mice. These data demonstrate that terminal stimulation of corticostriatal projections causes antidromic activation and entrainment of mOFC and that this activation induces neuroplastic changes in mOFC networks. These findings have broad implications for the effects of terminal stimulation on corticostriatal networks. The dissolution of distributed single unit spiking suggests that entrainment of recorded neurons was highly uniform and potentially spread to non-VMS projecting neurons. Furthermore because increased cortical synchrony is reflective of increased shared connections between neurons these data raise the possibility that antidromic activation of corticostriatal projections induces a long-lasting change in connectivity within the cortex. Taken together these findings provide evidence for a novel mechanism through which optogenetic stimulation of specific projections can alter circuit activity and plasticity in a broader manner than previously suspected.

First Author: Man Wu (Graduate)	Poster Session: am
Presenting Author: Man Wu (Graduate)	Location: 56
Mentor/Lab: Stephen D. Meriney	Category: Brain Models and Systems
Department: department of neuroscience	

Title: GV-58 a novel calcium channel gating modifier reverses aging-induced weakness in transmitter release from mouse neuromuscular synapses.

Summary: GV-58 could be developed as a symptomatic treatment for neuromuscular weakness associated with aging.

Abstract: We have studied the changes in neuromuscular junction (NMJ) structure and function as these synapses mature and undergo age-related changes. Our goal was to test the hypothesis that our newly developed calcium channel agonist gating modifier (GV-58) could provide symptomatic relief for normal aging-related NMJ weakness. First we documented changes in NMJ organization and function with aging. Neuromuscular synapses matured to their adult form and function over the first few months after birth and then remained relatively stable at a quantal content of about 80 for about 14-16 months. The first aging-related changes appeared to be postsynaptic as receptor staining broke apart (documented by small patches of α-bungarotoxin staining) and acetylcholine sensitivity appeared to be reduced (as evidenced by reductions in miniature endplate potential amplitude). These postsynaptic changes began at about 17-18 months of age and progressed gradually until death (between 24-32 months of age). The hypothesized reduction in postsynaptic acetylcholine receptor sensitivity was supported by what appeared to be a presynaptic homeostatic increase in transmitter release between 18-24 months of age (quantal content averaged 131.6 + 10.4 at 20 months of age). This transient increase in quantal content reversed and transmitter release was reduced such that by 25-30 months of age quantal content was significantly lower than normal adult values. This age-related biphasic time-course of changes in presynaptic quantal content gradually led to NMJs with reduced immunohistochemical staining for presynaptic markers of active zone organization (bassoon and Cav2.1 calcium channels). Interestingly after NMJs became weaker than normal adults (quantal content averaged 23.0 ± 3.6) and before they degenerated to the point that transmitter release was nearly eliminated (endplate potentials less than 2 mV) our novel calcium channel agonist gating modifier (that prolongs mean open time) could reverse synaptic weakness (increasing quantal content to an average of 45.7 ± 6.5; or a paired analysis increase of 2.35 ± 0.3 fold). These data provide evidence that GV-58 could be developed as a symptomatic treatment for neuromuscular weakness associated with aging.

First Author: Wenting Xie (Graduate)	Poster Session: pm
Presenting Author: Wenting Xie (Graduate)	Location: 21
Mentor/Lab: Edward A. Burton	Category: Neurology & Neurodegenerative Diseases
Department: PIND	

Title: Mitochondrial-Telomere ROS Cross-Talk in Parkinson's Disease

Summary: We hypothesize that ROS cross-talk induced a self-perpetuating cycles of damage between telomeres and mitochondria that underlies neurodegeneration in PD.To test this we generated transgenic zebrafish models in which we can uncouple telomeric and mitochondrial damage in the relevant disease-susceptible dopaminergic neurons in vivo using a novel chemoptogenetic ablation method.

Abstract: Mitochondrial reactive oxygen species (ROS) are regarded central to Parkinson's disease (PD) pathogenesis; however the role of mitochondrial oxidative damage to telomeres is unknown. Recent evidence suggests that telomeric dysfunction can result in mitochondrial defects. We hypothesize that ROS cross-talk induced a self-perpetuating cycles of damage between telomeres and mitochondria that underlies neurodegeneration in PD. To test this we generated transgenic zebrafish models in which we can uncouple telomeric and mitochondrial damage in the relevant disease-susceptible dopaminergic neurons in vivo using a novel chemoptogenetic ablation method. The method allows regulated generation of singlet oxygen in specific cellular locations. Since the effective range of the short-lived singlet oxygen is extremely small this results in oxidative damage to surrounding cellular components with a remarkable organelle-level degree of spatial resolution and with graded severity dictated by light dose. This new technology will enable us to test our hypothesis by inducing selective damage at mitochondria or telomeres while measuring ROS flux and dysfunction at both sites. Our initial data provide proof of concept that we can induce both functional and morphological changes both acutely and chronically in mitochondria targeted by our novel chemoptogenetic approach in zebrafish neurons in vivo resulting in neurological phenotypes.

First Author: Svitlana Yablonska (Postdoctoral)	Poster Session: pm
Presenting Author: Svitlana Yablonska (Postdoctoral)	Location: 27
Mentor/Lab: Robert M. Friedlander	Category: Neurology & Neurodegenerative Diseases
Department: Neurological Surgery	
Title: Disruption of mitochondrial proteostasis in Huntington disease	
Summary: Mutant huntingtin cause protein disbalance in brain mitochondria of HD patients.	

Abstract: Growing evidence indicates that mitochondria play an important role in the pathogenesis of neurodegenerative diseases including Huntington's disease (HD). The majority of mitochondrial proteins are encoded in the nucleus and imported into mitochondria through pore complexes of translocases of mitochondrial membranes (TOM40 TIM23 TIM22). Mutant huntingtin (mHTT) the causative gene in Huntington's Disease associates with the translocase of mitochondrial inner membrane (TIM23) complex interfering with its normal function [Yano 2014]. To determine the biological consequences of this association we quantified the levels of specific mitochondrial proteins in postmortem frozen human cortex tissue of HD grade 4 patients. We found decreased amounts of the matrix and inner membrane bound proteins that should have been imported through TIM23 complex. Multi-span proteins of inner membrane that are imported using the TIM22 pathway do not change nor do multi-span proteins in the outer mitochondrial membrane. Therefore the association of mHTT with the TIM23 import pathways disturbs mitochondrial proteostasis of specific proteins and may lead to neuronal death in HD pathogenesis.

First Author: Yanjun Zhao (Postdoctoral)	Poster Session: pm
Presenting Author: Yanjun Zhao (Postdoctoral)	Location: 8
Mentor/Lab: Zak Wills	Category: Neurology & Neurodegenerative Diseases
Department: Neurobiology	
Title: Amyloid Beta Peptides Block New Synapse Assembly by Nogo Receptor Mediated Inhibition of T-Type Calcium Channels	
Summary: Imaging and electrophysiological studies of Nogo receptor - Amyloid beta signaling in hippocampus	
Abstract: Compelling evidence links amyloid beta (Abeta) peptide accumulation in the brains of Alzheimer's disease (AD) patients with the emergence of learning and memory deficits; yet a clear understanding of the events that drive this synaptic pathology are lacking. We present evidence that neurons exposed to Abeta are unable to form new synapses resulting in learning deficits in vivo. We demonstrate the Nogo receptor family (NgR1-3) act as Abetareceptors mediating an inhibition of synapse assembly plasticity and learning. Live imaging studies reveal Abeta activates NgRs on the dendritic shaft of neurons triggering an inhibition of calcium signaling. We define T-type calcium channels as the target of Abata-NgR signaling mediating Abeta's inhibitory effects on calcium synapse assembly plasticity and learning. These studies highlight deficits in new synapse assembly as a potential initiator of cognitive pathology in AD and pinpoint calcium dysregulation mediated by NgRs and T-type channels as key components.	

First Author: Xin 'Sally' Zheng (Graduate)	Poster Session: am
Presenting Author: Xin 'Sally' Zheng (Graduate)	Location: 21
Mentor/Lab: Tracy Cui	Category: Brain-Machine Interfaces
Department: Bioengineering	

Title: Soft and elastomeric electrodes for muscle and nerve interfaces

Summary: We have developed an implantable electrode that is soft and elastic. These electrodes are capable of interfacing with both the nerves and the muscle. Chronically these electrodes elicit minimal foreign body response.

Abstract: Functional electrical stimulation of the peripheral nervous system (PNS) has the potential to restore functions of amputees and to treat neuromuscular atrophy. Electrodes that are chronically implanted in the PNS use conventional conductive materials such as stainless steel (e.g.Cooner wire) and platinum wires which are significantly stiffer than neural tissue and cause inflammatory tissue response and performance failure. Many efforts have been made to develop flexible electrodes for PNS interfaces such as the polyimide based thin film longitudinal intrafacicular electrode (Navarro et al 2007) and the polydimethylsiloxane based flat interface cuff electrode (Tyler et al 2002). We have developed a soft and elastomeric electrode capable of electrophysiological recording and stimulation for the brain (Kolarcik et al 2015; Du et al 2017). The soft electrode consists of a blend of a PEG-modified PEDOT conducting polymer and polydimethylsiloxane elastomer and utilizes an electrically-insulating fluorosilicone coating. This composition had a Young's modulus of 974kPa and showed excellent chronic tissue integration with healthy neurons at the interface and reduced BBB leakage and gliosis. To translate this technology to the more dynamic and mechanically demanding peripheral environment carbon nanotubes have been incorporated into the conducting elastomer core to enhance electrical properties of the composition while maintaining favorable mechanical properties. In acute in vivo evaluations electrical stimulation is achieved through implanting a stimulating soft wire electrode (90 um) in the rat's sciatic nerve and two recording soft wire electrodes (180 um) in the rat's gastrocnemius muscle. The 90 um soft wires successfully elicited muscle twitch at 2 uA (biphasic pulse 500 uS pulse width 50uS interphase delay) and resulted in a graded increase in compound muscle action potential of the rat gastrocnemius measured by the 180 um soft wires. For recording a 90 um soft wire was implanted in the tibial nerve and manual brushing of the posterior hind limb elicited multiunit activity and sortable single units. Chronically the soft wires implanted in the muscle remained intact and demonstrated efficacy in eliciting muscle twitch one month after implantation. Post mortem histology showed decreased fibrotic scarring around the soft wire implant compared to the stiff wire control implants. Our soft wires have the potential to improve the interface with the peripheral nervous system and to improve the control of prosthetic limbs for research and clinical applications.