Afternoon Poster Session
Location: Row A
Poster #1

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Emily Oby	Postdoctoral	Batista	SNI

Learning to generate new patterns of neural activity

Learning requires networks of neurons to generate new patterns of activity. Brain-computer interface (BCI) users can learn to modulate neural activity to control a computer cursor via a relationship specified by the experimenter and this allows us to study the changes in neural population activity that accompany learning. We used a closed-loop BCI paradigm to study learning-related changes among a population of neurons recorded in the primary motor cortex (M1) of a Rhesus monkey. Here we examine the population neural changes that accompany learning by considering first behavioral changes and then examining neural activity changes directly. 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 space of naturally-occurring neural activity patterns as the intrinsic manifold (IM). We can create new BCI mappings for the monkey to learn that require the monkey to generate patterns within the IM or outside the IM. In our previous work we found that the existing patterns of neural co-modulation shape learning: monkeys could learn perturbations of a BCI that lie within the IM and thus conform to existing patterns of neural co-modulation on the timescale of hours but usually could not learn to generate neural co-modulation patterns outside of the IM at least not within a single day (Sadtler et al. 2014). In recent experiments we have seen that monkeys can learn to control a BCI that requires patterns outside of the IM given several days of practice. Thus outside-manifold perturbations are not fundamentally unlearnable and the constraints imposed by the IM are not absolute. Instead the constraints and presumably the IM itself are plastic. The improvements in BCI behavior during multi-day learning of outside-manifold perturbations imply that the co-modulation patterns of the neural population have changed. In particular as the performance with the outside-manifold perturbation improves over days the patterns of neural activity are correspondingly further from the natural patterns of neural activity described by the IM. We interpret this to mean that the monkeys have learned to produce novel neural activity patterns i.e. patterns of activity that lie outside the intrinsic manifold.

Sadtler PT Quick KM Golub MD Chase SM Ryu SI Tyler-Kabara EC Yu BM Batista AP. Neural constraints on learning. Nature. 2014 Aug 28; 512(7515):423-6.

Afternoon Poster Session
Location: Row A
Poster #2

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Alan Degenhart	Postdoctoral	Batista	Systems Neuroscience Institute

Self-recalribrating brain computer interfaces based on population subspace alignment

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 a Rhesus macaque implanted with a Blackrock array 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 simulated recording instability 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 30 of 32 experiments we find that the self-recalibrated decoder was able to significantly improve performance in the presence of the perturbation returning control to pre-perturbation levels or better in 11 of these sessions. Furthermore we found that use of the algorithm in the absence of artificially-generated neural instabilities did not adversely alter performance. This work has the potential to increase the viability of BCI systems for clinical use.

Afternoon Poster Session
Location: Row A
Poster #3

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Sharlene Flesher	Graduate	Gaunt	Bioengineering

Intracortical microstimulation of human somatosensory cortex elicits cutaneous percepts

Dexterous object manipulation requires cutaneous sensory feedback. In its absence, simple tasks are very difficult. In prosthetic limbs controlled through brain-computer interfaces (BCIs), providing somatosensory feedback could be an important step to improving function as vision provides impoverished cues about object interactions. Intracortical microstimulation (ICMS) of primary somatosensory cortex (S1) is a potential method to restore this sensory channel, particularly in people that cannot benefit from stimulation of the peripheral nervous system. Under an Investigational Device Exemption, a 28 year old participant with a chronic spinal cord injury was implanted with 2 intracortical microelectrode arrays (MEAs) in motor cortex and 2 MEAs in area 1 of S1. Locations of the S1 MEAs were based on presurgical imaging with the goal of eliciting percepts that project to the fingers of the right hand. Electrodes were stimulated at supraliminal intensities and the participant described the locations and qualities of evoked percepts. Projected fields were located on the proximal pads of digits 2-5. Sensations were evoked on 59 of 64 electrodes, and no painful sensations or paresthesias were reported. We tested whether the subject could use this spatial information to identify which of four fingers on a robotic limb was touched by converting robot finger torque to stimulus intensity. The load-bearing finger was identified with 84.3% accuracy (54 trials). We measured detection thresholds using a two-alternative forced choice task and found the median detection threshold to be 34.9μA, with upper and lower quartiles at 60.0 and 24.8μA, respectively. Thresholds were generally stable over 11 months. Of the 32 electrodes with 3 or more measured thresholds 7 changed significantly over time, 3 of which had a negative slope, suggesting thresholds were not globally increasing. We measured the discriminability of ICMS trains differing in amplitude and found the just noticeable differences to be 15.4 ± 3.9 μA (mean ± s.d.) and independent of the magnitude of the reference stimulus. In magnitude estimation experiments, we found that perceived intensity increased linearly with stimulation amplitude (R2 = 0.98) for 5 electrodes tested. In summary, percepts were evoked at somatotopically appropriate locations with intensities that scaled linearly with amplitude over a wide range. These properties of evoked percepts can be used to convey location and intensity of object contact, key types of information for guiding interactions with objects. Providing artificial somatosensory feedback to BCI users could improve the user's control and experience with the prosthetic device

Afternoon Poster Session
Location: Row A
Poster #4

Presenting Author:	Author Type:	Mentor/Lab:	Department:
John Downey	Graduate	Collinger	Bioengineering

Encoding of intended grasp force in primary motor cortex during brain-computer interface controlled robotic arm use

Brain-computer interfaces (BCIs) for neuroprosthetic arm control are being developed as assistive devices for people with tetraplegia. Often signals from primary motor cortex (M1) are used to decode endpoint velocity but M1 is also known to encode force. For BCI-controlled grasping it is important to be able to modulate force in order to grasp objects of varying weights and fragility. We sought to determine if we could decode a BCI user's representation of grasp force during attempted grasping of virtual objects. Under an Investigational Device Exemption a 28 year-old male participant with chronic C5 motor and C6 sensory AIS B spinal cord injury was implanted with two microelectrode arrays in M1 and two microelectrode arrays in S1. Neural data was recorded while the participant watched a virtual prosthetic arm grasp a spherical object. Trials started with an auditory cue naming a graspable object (marshmallow tomato can of soup) chosen to span the range of possible grasp force representations. After a 2 s planning period he attempted to grasp with "the minimum force required to grasp and lift the cued object". He then attempted to hold the object with the appropriate amount of force for 2 s before being cued to release it. The virtual arm automatically grasped and released the object regardless of the participant's actions. To determine whether the intended grasp force was encoded in the recorded neural activity each channel's firing rate was averaged over a 1 s sliding window (0.2 s step size). Each window was used to train and test a naïve-Bayes classifier using leave-one-out cross validation to create a time series of classification accuracy. Classification accuracy of the 3 objects using firing rates in M1 peaked at 88% for the 1 s window starting 0.2 ms in to the 2 s hold time and remained above 85% for the rest of the hold time. The accuracy did not diverge from chance level until the participant began attempting to grasp the object. When the object was released the classification accuracy fell to 62% at the end of the trial. Classification accuracy using S1 firing rates followed a similar trend but increased later than M1 accuracy by approximately 0.5 s and peaked at only 67%. This study shows that graspable objects requiring a variety of forces (the participant reported relative force ratings of 1 2 and 4) can be well classified from M1 and to a lesser extent S1 in a BCI user with tetraplegia. Future work will integrate this decoded information into closed-loop BCI arm control to attempt to improve the users' ability to grasp and manipulate a variety of objects.

Afternoon Poster Session
Location: Row A
Poster #5

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Patrick Cody	Graduate	Cui	Bioengineering

Evaluation of neural cell adhesion molecule L1 coating for improved chronic recordings

Neural probes are used in brain-machine interface based prosthetics to restore movement to paralyzed individuals. Intracortical neural electrodes provide the greatest spatiotemporal resolution compared to other recording approaches to enable optimal decoding of neural activity for prosthetic control. Inflammatory brain responses including glial scarring and neural degeneration degrade and limit the longevity of recordings thereby severely hindering the clinical potential of neural probes. Our lab has demonstrated that the neural cell adhesion protein L1 may be covalently conjugated to silicon and parylene based neural probe surfaces to reduce inflammatory glial activation improve neuron survival and enhance neurite outgrowth throughout a chronic period in a rat model as verified with quantitative histological measures. Chronic electrophysiological recordings from L1 coated and uncoated parylene-C insulated Utah arrays were compared in male Rhesus monkeys and rats up to 72 and 12 months respectively. Each monkey was implanted in the motor cortex with both a coated and uncoated 96 channel Utah array while each rat was implanted in the primary monocular visual cortex with either a coated or uncoated 4x4 Utah array. Coated monkey arrays exhibit significantly greater number of units than uncoated. For rats a repeatable and established visual stimulation paradigm was used to compare evoked activity between array treatments. In addition to a battery of histological analyses laser capture micro-dissection to assay RNA expression changes in the immediate micro vicinity of the probe is developed and combined with immunohistochemical staining to better elucidate the mechanism of L1's benefits. Recording performance from rat implants is quantified with single-unit yield (percent of electrode sites recording single-units) single-unit signal-to-noise amplitude ratios and multi-unit signal-to-noise firing rate ratios. Understanding the effect and mechanism by which L1 improves neural probe performance will inform approaches to better realize the full clinical potential of neural prosthetics for treating paralysis.

Afternoon Poster Session
Location: Row A
Poster #6

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Xin 'Sally' Zheng	Graduate	Cui	Bioengineering

Functional Evaluation of a Superoxide Dismutase Mimic Coating for Chronically Implanted Neural Electrodes

Recent advancement in brain-machine interface (BMI) has shown promise in enabling functional restoration of individuals with limb loss. Often a metal electrode array is chronically implanted into the brain region of interest and neural signals can be recorded and decoded to control an external prosthesis. However due to the brain's foreign body response microglia near the electrode site become activated and secrete pro-inflammatory cytokines recruiting additional macrophages and produce cytotoxic factors such as reactive oxygen species (ROS). The presence of ROS around the implant promotes neuronal death thereby degrading neural signal quality overtime. Superoxide dismutase (SOD) can remove superoxide (a form of ROS) through dismutation by converting superoxide to molecular oxygen and hydrogen peroxide. However due to its low stability and poor bioavailability SOD has been unsuccessful in treating neurological diseases induced by oxidative stress. SOD mimics (SODm) have shown to be neuroprotective in in vitro and in vivo models of disease influenced by oxidative stress such as Alzheimer's disease and stroke. When immobilized onto the surface of neural electrodes SODm may reduce neuronal death around the implant. Here we evaluate the acute and chronic performance of electrodes coated with immobilizable SODm (iSODm) in adult rats. 16-channel linear silicon probes with or without iSODm coating were implanted in the motor cortex of adult male rats for up to 3 months. In acute evaluations animals were sacrificed 1 week after electrode implantation and immunohistochemistry was performed to compare neuronal survival around the implant. In chronic evaluations weekly impedance measurements and neurophysiological recordings of spontaneous motor activity were acquired while the animals were freely moving. At endpoint all animals were sacrificed and immunohistochemistry was performed. Significantly greater neuron density in every 50 µm zone between (0 µm — 250 µm) around the coated implants were observed after 1 week of electrode implantation. Chronically the iSODm coating showed great promise in allowing electrodes to record high quality single units throughout the 3-month period with endpoint signal to noise ratio up to 7.91 and up to 50% in single unit yield. These results indicate the iSODm coating's efficacy in promoting neuronal health around neural electrodes and have the potential to benefit chronic neural recording for BMI or basic neuroscience research.

Afternoon Poster Session
Location: Row A
Poster #7

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Santosh Chandrasekaran	Postdoctoral	Santosh	Physical Medicine and Rehabilitation

Electrical stimulation of the cervical Dorsal Spinal Cord and Roots (DSCR) for sensory restoration in upper-limb amputees

A chief drawback of current prostheses is the lack of direct sensory feedback which leads to impaired prosthetic control and is associated with exacerbating phantom limb pain. Sensory feedback greatly enhances the embodiment acceptance and also the ease of use of a prosthetic device. Electrical stimulation of the peripheral and central nervous system is the focus of extensive research as a means to provide sensory feedback. In our approach we chose the dorsal spinal cord and roots (DSCR) as the site for such electrical stimulation. These structures are ideal targets for sensory electrical stimulation as they are well-isolated from motor pathways remain intact after most amputations and are accessible via minimally invasive procedures. Here we present observations from human psychophysics experiments performed in two upper-limb amputees using FDA-approved spinal cord stimulation (SCS; Boston Scientific) leads. Study participants were temporarily implanted with three 8 or 16-contact SCS leads in the lateral epidural space spanning the C5-C8 DSCRs. Multi-polar current-steering was used to improve the focality of sensory percepts. Feedback about the modality location and intensity of perceived sensations was provided by the subject through a structured reporting setup. Preliminary testing showed that sensory percepts in the form paresthesia can be evoked via selective stimulation through different SCS lead contacts. The sensations reported by the subjects include focal percepts localized to the amputated shoulder arm hand wrist palm and fingers consistent with the established dermatome maps corresponding to the respective spinal roots. These sensations were stable for more than two weeks of testing. A subset of electrodes generated naturalistic sensations of movement of the fingers on the missing hand in one of the subjects. Continuous modulation of stimulus amplitude was perceived as intensity changes and did not affect the overall location of the percepts. Psychophysical experiments that required subjects to distinguish between amplitudes of currents in a two-alternative forced choice task revealed a consistent threshold of detection (around 550 μA) across subjects. In conclusion we have established that sensory feedback can be provided to upper-limb prosthetic users using epidural dorsal spinal cord and roots stimulation.

Afternoon Poster Session
Location: Row A
Poster #8

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Ahmed Kashkoush	Graduate	Fisher	Physical Medicine and Rehabilitation

A Prospective Study of Acute and Sub-Chronic Modulation of Phantom Limb Pain using Epidural Spinal Root Stimulation

Recent evidence suggests that phantom limb pain (PLP) is regulated by the lack of sensory feedback from the amputated limb and thus restoring non-painful phantom sensations may alleviate the condition. This study aims to use cervical spinal root stimulation to produce sensations localized to the amputated limb to modulate PLP and demonstrate a clinically significant reduction of PLP. Two subjects with transhumeral amputations were implanted with 3 spinal cord stimulator leads (Boston Scientific) in the epidural space targeting the C6-C8 spinal roots for a maximum length of 29 days. Stimulation amplitude (50-6000 μA) frequency (1-400 Hz) and pulse width (0.05-1 ms) were modulated across trials. Subjects reported the modality ('Mechanical' 'Tingle' 'Movement' 'Stimulation Pain' 'Naturalistic' 'Phantom Limb Pain') and magnitude (0-10 visual analog scale) of sensations after stimulation. Multivariate regression was used to assess the combined effects of stimulation parameters and sensation characteristics on PLP episode incidence (categorical 'yes' vs. 'no') and PLP episode intensity (continuous 0-10). Additionally the McGill Pain Questionnaire (MPQ) was administered at baseline on a weekly basis and one month following explantation to assess sub-chronic PLP modulation. A total of 1 276 trials were performed across both subjects of which 370 PLP episodes were reported (29.0%) at a mean intensity of 2.1 ± 0.2 (Table 1). Of 94 electrodes modulating stimulation was significantly associated with PLP frequency on 17 (18.1%) and PLP intensity on 6 (6.4%). Multivariate regression demonstrated stimulation amplitude to be an independent predictor of PLP intensity (p<0.01 regression coefficient [B]=0.19/mA) and pulse width of PLP frequency (p=0.03 B=0.93/ms). Both PLP frequency and intensity were positively associated with the intensity of non-PLP sensations (p<0.01) except for those of movement (p=0.162) and naturalistic (p=0.69) sensations. Both subjects experienced a clinically significant reduction (>5 points) in PLP from baseline throughout the study and at 1-month follow-up with 9 (26%) and 8-point (24%) reductions on the MPQ respectively (Figure 1). This study suggests that decreased stimulation amplitude and pulse width may reduce the intensity and likelihood of a PLP episode respectively given their positive associations with PLP. We further observed time-dependent PLP modulation such that restoring sensory feedback from the amputated limb is associated with increased PLP in the immediate post-stimulation phase but may also be coupled to a long-term reduction in PLP.

Afternoon Poster Session
Location: Row A
Poster #9

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Dylan Royston	Graduate	Collinger	Bioengineering

Native upper limb movement encoding by intracortical recordings in human sensorimotor cortex

After paralysis, attempted movement is known to activate primary motor (M1) and somatosensory (S1) cortex, although the latter is less well studied. Most previous work has been conducted with functional magnetic resonance imaging (FMRI) or magnetoencephalography (MEG). However, recent clinical brain-computer interface (BCI) trials, which have shown promise for improving function for people with paralysis, offer an opportunity to study human motor control at a single unit level. Here we investigated M1 and S1 activity using intracortical recordings while a person with tetraplegia attempted to perform movements of his arm and hand.

Afternoon Poster Session
Location: Row A
Poster #10

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Hongwei Mao	Postdoctoral	Schwartz	Systems Neuroscience Institute

Neuronal responses in the primary somatosensory cortex during reach-to-grasp movements using native and robotic arm

Primary somatosensory cortex (SI) receives afferent input from the peripheral sensory apparatus and responds with high fidelity according to characteristics of the stimulus such as location and modality. In addition to this well-recognized afferent driving of SI we are interested in the possibility of non-peripheral activation of SI cells during movement. While operating a robot arm via a brain-computer interface (BCI) movement commands from motor cortex are used to control the device and interactions between the robot hand and environment are monitored via visual feedback which might have the potential to drive SI responses. Thus this paradigm provides a unique opportunity to study SI activity during motor control but without peripherally driven somatosensory feedback. \tTwo sets of microelectrode arrays were implanted in two hemispheres of a non-human primate. Each set had one array (88 electrodes) placed in the upper arm area of the primary motor cortex (MI) and one array (32 electrodes) in the hand and finger representation of SI . The subject was first trained to perform a reach-to-grasp task using his native arm. Action potentials from arrays contralateral to the performing arm were recorded for this hand-control (HC) experiment. In the BCI experiment neural activity from the MI array was used to control the robot arm to perform the same reach-to-grasp task. Simultaneously recorded SI activity (in the same hemisphere as the MI array) and kinematics of the robotic arm were saved for offline analysis. An accelerometer attached to the arm contralateral to the recorded units was used to determine whether movement of the arm might be generating peripheral sensation during the task. Trials contaminated by movements of the native hand were excluded from analysis for the BCI experiment. \t In the HC experiment the overall activity of SI neurons was depressed during reaching began to increase before object contact and sharply peaked shortly after contact. In the BCI experiment 9 out of 29 SI neurons showed modulation around object contact. These included 7 cutaneous and 2 proprioceptive units with receptive fields in the fingers. Most of these units had a peak in activity around object contact or during grasping shortly after initial contact. One a cutaneous unit was most active when the robot hand started to close around the object at the end of reaching. Object-related activity peaks during the BCI tasks were broader than those of the same neurons in the HC tasks. These results show that SI can be modulated during motor control by both peripheral and non-peripheral input.

Afternoon Poster Session
Location: Row A
Poster #11

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Carl Beringer	Graduate	Gaunt	Bioengineering

Analysis of Intramuscular EMG Signals of the Extrinsic Hand Muscles During Single Degree of Freedom Movements

Myoelectric prosthetic hands (MPH) are motorized prosthetic devices which can use electromyography (EMG) signals as a control input to restore function and independence to upper limb amputees. Present MPH technology uses surface electrodes to collect EMG signals but are limited to muscles which are large or superficial. Intramuscular electrodes are an alternative method of capturing EMG activity directly from the muscle belly with a higher spatial resolution. Recent research has focused on development of control algorithms which use signals recorded by intramuscular electrodes placed within the extrinsic hand muscles including the compartments of the finger flexors and extensors. These algorithms often rely on a simple linear mapping which directly relates EMG activity to position or velocity. However there is a present lack in research which characterizes patterns of EMG activation in the extrinsic hand muscles. In order to address this gap in research we sought to characterize how wrist posture alters intramuscular EMG activation in the individual compartments of the extensor digitorum communis flexor digitorum superficialis and flexor digitorum profundus during single degree-of-freedom movements. We found that all assessed muscles show significant differences for peak EMG activation for different wrist postures. Our results suggest that future development of prosthetic control algorithms may require state information of the wrist in order to linearly translate EMG activity to kinematic output.

Afternoon Poster Session
Location: Row A
Poster #12

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Yoh Inoue	Graduate	Schwartz	Department of Neurobiology

Effects of speed tuning on trajectory decoding

Movement speed acts as a gain factor on the cosine tuning of motor cortical firing rate to movement direction. Failure to account for this effect can lead to decoding problems when using firing rates from a population of cells to predict movement trajectory. This may be especially problematic when the sample of recorded cells has preferred directions that are not distributed uniformly. To better characterize this problem we used a set of coefficients to fit the following equation 1: FR=b0+bxVx+byVy+bsS; where Fr is firing rate Vx and Vy are the x and y components of arm velocity and S is the speed of the arm. Empirical data from a 2D center-out task were selected from a prototype neuron and used to fit the coefficients of the equation. A set of firing rates were then calculated for a population of simulated neurons by choosing bx and by to produce different preferred directions. The average speed profile from the empirical data was used in the simulations. \tDecoding was performed using the population vector algorithm. Each unit's contribution to the population vector was calculated using the simulated firing rates from Eq. 1 in the conventional cosine tuning model: FR=br0+brxDx+bryDy where Dx and Dy are the x and y components of target direction. br0 brx and bry were found through regression. Each unit's contribution was a vector in the direction brx bry with a magnitude M= (FR-br0)/mag where mag is the magnitude of the vector [brx bry]. \tTwo simulated populations were created. The first was constructed by choosing bx and by to be uniformly distributed. The second population was non-uniform bx and by were chosen only from one half of the unit circle. Population vectors were constructed from each population to each target using the empirical speed profiles and Eq. 1 for firing rates and the conventional cosine model for each contribution. We measured the angle error time length and trajectory length and population vector magnitude for the 2 populations. The trajectories for all targets were fairly straight in uniform condition. Across targets duration trajectory length and angle error were not significantly different. The population vector length was highly correlated to speed. In contrast for the non-uniform condition the initial portions of the trajectories of all targets were skewed by the over-represented preferred directions in the sample. Compared to the uniform condition population vector magnitudes were less related to speed. \tA failure to account for speed tuning can lead to significant decoding distortion of both speed and direction when the sampled population has a non-uniform directional distribution.

Afternoon Poster Session
Location: Row A
Poster #13

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Steven Suway	Graduate	Schwartz	Neurobiology

Dynamic representation of reach speed in the motor cortex

In primate motor cortex (M1) single neurons are broadly tuned to reach direction with each cell discharging maximally for a particular direction. The speed of the reach also affects neural activity contributing both a multiplicative and additive influence on firing rates. Early studies reported a "representation" of reach speed in single units and in population analyses. However such studies commonly restricted analysis to the trial period in which the arm was moving. It was subsequently suggested that representation of speed is less robust in the firing rate fluctuations that continue after movement ceases. Recently our group identified distinct epochs in the activity of M1 neurons spanning the reaction time through the target-hold period of a reaching trial. Directional tuning of single neurons is robust and stable within an epoch but preferred direction may change from one epoch to the next. We wondered if speed encoding might also vary between epochs. We recorded spiking of M1 neurons from three monkeys during a center-out reaching task. Firing rates of each neuron were analyzed using two models: a direction-only tuning model and a velocity-speed tuning model. Both models were fitted during each epoch and the goodness-of-fit of each model was assessed. We found clear evidence of dynamic coding with the velocity-speed model fitting rates of many neurons markedly better during the early epochs. Using the population vector algorithm (PVA) we reconstructed reach trajectories using firing rates from only the speed-related epochs. We found the decoded trajectories were highly accurate and the time course of their magnitude was strikingly similar to the recorded reach speeds. Given that velocity can be extracted from the population with high fidelity by selectively utilizing segments of firing we wondered if a simpler computation using all the data could yield similar results. This would be useful for example in neural prosthetics because it would allow us to estimate arm velocity despite the ongoing changes in single unit tuning during a reach. We developed a simple regression method to find a linear combination of single unit firing rates that closely matches the measured arm velocity. The method identifies an axis in the n-dimensional population firing rate space. When the population activity is projected onto this axis we find robust and accurate velocity tuning while the hand is moving. When the arm comes to a stop and despite continued fluctuations in firing of most neurons activation along this axis drops nearly to zero. This method may be advantageous in neural prosthetics which often fail to afford subjects control of output speed.

Afternoon Poster Session
Location: Row A
Poster #14

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Rex Tien	Graduate	Schwartz	Bioengineering

Object-dependent tuning of M1 neurons during grasping

Neurons in primate primary motor cortex (M1) display patterns of activity related to arm and hand kinematics and muscle activity (movement features or MFs) during the execution of grasping movements. Previous studies have characterized the neural encoding of MFs with the concept of a "tuning function" – a linear function relating a neuron's firing rate (FR) to a combination of MFs. A central assumption of many neural prosthetic algorithms is that each neuron has a single fixed tuning function across time and behavioral contexts. Here we present evidence that neurons' tuning functions may change depending on the identity of the object being grasped. Two monkeys each grasped six different objects while we recorded neural activity wrist hand and finger joint angles and arm muscle activity. We found that assuming a single constant tuning function for each neuron (modeled using multiple linear regression) could account for about half of FR variance. The residuals from these regressions contained object-related structure as evidenced by ANOVA and classification analyses suggesting that M1 neurons also encode object identity in some way. We hypothesized that M1 neurons could encode object identity directly in their FRs or that object identity could have a more complex effect on M1 tuning functions. Using dummy variable regression we determined that for the majority of neurons the best models were those that allowed tuning parameters to change depending on the identity of the grasped object. Comparing these parameters revealed that most neurons displayed large tuning changes between object conditions; statistically significant parameter changes were just as likely when comparing between two object-specific tuning models within a single neuron as between two randomly selected neurons. The finding that tuning functions change under different behavioral contexts contributes to our understanding of the natural cortical control of goal-oriented hand movements as well as to the design of effective future upper limb neural prostheses.

Afternoon Poster Session
Location: Row B
Poster #15

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Justin Arnett	Graduate	Tyler-Kabara	Neurosurgery Physical Medicine and Rehabilitation

Clinical and Surgical Practices for Invasive Brain-Computer Interface Research

Background: Brain-Computer Interfaces (BCIs) are systems that record neural activity from the sensorimotor cortex and decode relevant activity patterns into control signals for prostheses such as computer cursors and robotic arms. While many animal studies have demonstrated successful BCI prosthesis control through microelectrode arrays (MEAs) and electrocorticographic (ECoG) arrays implanted in the sensorimotor cortex very few have demonstrated similar results in humans and to our knowledge there currently exists no literature describing in detail the clinical and surgical processes and techniques necessary for invasive human BCI research. Hypothesis: Here we describe our processes for subject selection and enrollment surgical implantation explantation and revision of electrodes postoperative management and our postoperative results and complications that had yielded successful BCI prosthetic control in all four of our subjects. Methods: From 2011 to the present day of this manuscript our group had implanted electrodes for the purposes of BCI testing in four subjects- three had received high-density ECoG arrays two had received MEAs and all five exhibited complete loss of upper extremity function prior to testing. Medical chart and study protocol review was conducted to enumerate the processes and results of subject selection screening examinations the processes and results of electrode implantation explantation or revision surgeries the postoperative findings medical complications and management thereof following surgical procedures the function and stability of implanted electrodes and briefly the success of our subjects in BCI performance. Results: Per the predefined inclusion/exclusion criteria all five subjects demonstrated significant sensorimotor cortex activation in response to attempted movement of their paralyzed upper extremity. All surgical procedures were uncomplicated with postoperative findings of only mild frontoparietal pneumocephalus in 3/5 subjects and mild mass effect in 2/5 subjects; one subject had developed symptoms related to psychiatric onset of Adjustment Disorder that persisted for 4 days following implantation and remitted with therapy. Electrode implantation was correctly targeted in all but two subjects- one in which an ECoG array shifted posteriorly to sensorimotor cortex but still resulted in stable successful BCI control; and one necessitating a revision surgery to reimplant MEAs anteriorly by one gyrus. MEA pedestal site skin retraction was observed in 2/6 total pedestal sites. Implanted arrays demonstrated stable recording performance in most electrodes throughout their implantation periods- greater than 28 days for three ECoG subjects 32 months for MEA subject 1 and greater than 12 months for MEA subject 2 (who at the time of writing this abstract is still implanted and undergoing BCI training); all subjects demonstrated successful BCI performance. Conclusions: We describe the clinical and surgical practices necessary for performing successful human invasive BCI research. We believe that this description of our methodology and findings will help standardize such practices within the BCI field as well as to serve as a basis from which future advancement in methodology can be made. References: 1) Wang W. et al. An Electrocorticographic Brain Interface in an Individual with Tetraplegia. PLoS ONE 8 (2013); 2) Collinger J. L. et al. High-performance neuroprosthetic control by an individual with tetraplegia. Lancet Lond. Engl. 381 557–564 (2013); 3) Wodlinger B. et al. Ten-

dimensional anthropomorphic arm control in a human brain-machine interface: difficulties solutions and limitations. J. Neural Eng. 12 016011 (2015);); 4) Degenhart A. D. Evaluation and Advancement of Electrocorticographic Brain-Machine Interfaces for Individuals with Upper-Limb Paralysis. (2015)

Afternoon Poster Session
Location: Row B
Poster #16

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Jordan Williams	Postdoctoral	Schwartz	Systems Neuroscience Institute

Virus opsin and immunomodulation approaches for optogenetic control of peripheral motor function

The incorporation of light sensitive opsins into peripheral motor nerves offers a promising alternative to traditional functional electrical stimulation in restoring lost motor function. Gene therapy to express such optogenetic constructs for functional optical stimulation of muscles has been successfully demonstrated in non-transgenic rodents. However the procedure for transducing opsins into peripheral motor nerves is technically difficult and only a limited catalog of proven constructs in this context exist to date. To realize a robust clinical outcome for this approach it will be necessary to demonstrate expression in primate peripheral nerves which has not yet been achieved. In light of this need our present study examines the efficacy of several viral vectors and opsins in transducing nerves sensitive to functional optical stimulation. Here we discuss ongoing experiments and results with several AAV-based vectors and non-replicating rabies virus (NRRV) vectors as well as results from constructs utilizing one of two opsins: the traditional channel rhodopsin (ChR2) as well as the more recently described Chronos. In addition we examine the efficacy of several methods and routes for virus injection including muscle nerve and spinal cord. Finally we will describe our protocol and results for immunosuppression to facilitate virus transduction into motor nerve cells. Hopefully our findings will provide valuable insight into approaches that will translate well to primate peripheral motor gene therapy.

Afternoon Poster Session
Location: Row B
Poster #17

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Takashi Kozai	Faculty	Kozai	Bioengineering

Decoding the Brain Tissue-Microelectrode Interface

Intracortical electrode arrays that can record extracellular action potentials from small targeted groups of neurons are critical for basic neuroscience research and emerging clinical applications. In general these electrode devices suffer from reliability and variability issues that impact their performance on the order of months to years. The failure mechanisms of these electrodes are understood to be a complex combination of the biological reactive tissue response and material failure of the device over time. The breaching of the blood–brain barrier (BBB) to insert devices triggers a cascade of biochemical pathways resulting in complex molecular and cellular responses to implanted devices. Molecular and cellular changes in the microenvironment surrounding an implant include the introduction of mechanical strain BBB leakage activation of glial cells loss of perfusion secondary metabolic injury and neuronal degeneration. The resulting inflammation is a key hypothesized cause of neural recording failure and at times mirror other brain injury and neurodegenerative diseases even if the scope and timescale differ. Our findings from electrophysiology impedance spectroscopy and post-mortem histology demonstrate a very poor relationship between histology and impedance to electrophysiology. For example tissue with low-levels of glial encapsulation healthy neuronal proximity and low impedance can still have poor recording performance even with neural activity is behaviorally driven. Previously we demonstrated that mechanical mismatch between iridium and silicon led to material failure in chronically implanted planar silicon electrodes. These findings were confirmed with chronic in vivo data (133–189 days) in mice V1m cortex by correlating a combination of single-unit electrophysiology evoked multi-unit recordings electrochemical impedance spectroscopy and scanning electron microscopy from traces and electrode sites with our modeling data. Several modes of mechanical failure of chronically implanted planar silicon electrodes were found that result in degradation and/or loss of recording. This can confound correlation analysis between recording performance and histological outcomes. Here we compare the results from histology and mechanical failure to recording performance and identify loss of neural recording signal despite intact electrode material and good histological outcomes. Early in vivo multiphoton data suggest dramatic axonal degradation around implanted electrodes. These results emphasize the complexity of the biological pathways that govern the reactive tissue response and longitudinal electrophysiological recordings from penetrating electrode arrays. BBB injury is not limited to chronic BBB leakage but can include vascular occlusion edema and ischemia/hypoxia which may not necessarily cause gliosis and neuronal death but can heavily modulate nearby neural activity.

Afternoon Poster Session
Location: Row B
Poster #18

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Michelle Heusser	Graduate	Gandhi	Bioengineering

Single-trial classification of saccade metrics using superior colliculus population activity

Research in brain-computer interface (BCI) technology has gained popularity in recent years due to both its clinical applications (e.g. neuroprostheses) and scientific relevance. While the majority of current research involves skeletomotor (limb movement) BCI some groups are also venturing into the realm of oculomotor (eye movement) BCI. The superior colliculus (SC) is a deep brain structure crucial for converting sensory input into a motor command for generation of a fast eye movement. We have chosen the SC as a target structure for BCI because it is a hub of sensorimotor integration and is close to the end effectors (i.e. eye muscles) in the oculomotor pathway. The first step in the development of an oculomotor BCI is accurately predicting the intended eye movement and consequently eye end position after a saccade. Therefore we aimed to assess the feasibility of using SC neural activity for the classification of saccade metrics (direction and amplitude of eye movement). In this study we classified intended saccade endpoint during the motor epoch of a delayed saccade task using SC neural population activity. One rhesus monkey (macaca mulatta) was trained to perform a delayed saccade task to peripheral visual targets that varied in either amplitude or direction on a given recording session. A multicontact laminar electrode was used to record activity of many neurons within the SC. We trained a naïve Bayes classifier on population activity from a randomly selected subset of the trials and calculated the accuracy of classified target position for the remaining individual test trials. The mean classification accuracy was highest for targets within the population's response field and was above chance level for almost all targets and time bins of classification. Trends in classifier performance were consistent across recording sessions and did not largely vary with chosen classification bin width. Overall these results demonstrate that offline decoding of intended saccade metrics is feasible on a single-trial basis. In the future we plan to implement this technique online—decoding saccade metrics in real time and incorporating saccade dynamics into the decoding algorithm.

Afternoon Poster Session
Location: Row B
Poster #19

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Ameya Nanivadekar	Graduate	Gaunt	Bioengineering

Selectivity of afferent microstimulation at the DRG using epineural and penetrating electrode arrays

Introduction: We have previously shown that microstimulation of the dorsal root ganglia (DRG) using penetrating electrodes can selectively recruit distal branches of the sciatic and femoral nerves in an acute preparation. In chronic implants however the immune response to penetrating electrodes can diminishes the long-term viability of such an approach. Epineural electrodes such as nerve cuffs which do not penetrate the nerve can achieve a stable interface with peripheral nerves albeit with lower selectivity. The goal of this study was to evaluate the recruitment properties of epineural electrodes placed on the surface of the DRG and compare their performance with that of penetrating electrodes. Here we compare the number of selectively recruited distal nerve branches and the threshold stimulus intensities between penetrating and epineural electrode arrays. Methods: To quantify the selectivity of DRG stimulation we recorded antidromic propagation of evoked action potentials along many distal branches of the femoral and sciatic nerves in 3 cats. Antidromic activity was recorded via several nerve cuff electrodes implanted around up to 9 distal branches of the femoral and sciatic nerve trunks. In each cat five-contact nerve cuff electrodes were implanted around the sciatic and femoral trunks. Distal branches were instrumented with two-contact nerve cuffs made from split silicone tubing and stainless steel wire. A custom book electrode was implanted on the tibial nerve and its branches. A laminectomy was performed to isolate the L5-S1 DRGs and epineural electrodes (silicone and platinum 750 µm diameter; Ripple LLC) were placed on the epineural surface. A binary search was carried out to identify the minimum stimulus intensity that evoked a response at any of the distal cuffs as well as whether the threshold response selectively occurred in only a single distal nerve branch. Results: Epineural stimulation was selective for 71% of all electrodes (33/46) as compared to 85% for penetrating microelectrodes across six ganglia in 3 cats. The recruitment threshold (median = 5.81 nC/phase) and dynamic range of epineural stimulation (median = 0.89 nC/phase) was significantly higher than penetrating stimulation (0.68 nC/phase and 0.36 nC/phase respectively). The patterns of nerve recruitment for each DRG were similar for stimulation through epineural and penetrating electrodes. Conclusion: Despite higher recruitment thresholds epineural stimulation provides nearly comparable selectivity and superior dynamic range to penetrating electrodes. These results suggest that it may be possible to achieve a highly selective neural interface with the DRG without penetrating the epineurium.

Afternoon Poster Session
Location: Row B
Poster #20

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Corentin Massot	Postdoctoral	Gandhi	Bioengineering

Insights into sensorimotor transformation in the superior colliculus through current-source density analysis

The superior colliculus (SC) is crucial for transforming sensory signals that register a target into motor commands that produce an orienting movement to the stimulus. The sensory response is represented as a burst of activity in visual and visuomotor neurons in the superficial and intermediate/deep (collectively deeper) layers. Saccadic eye movements are produced by yet another burst of activity in the visuomotor and motor neurons in the deeper layers. However the underlying input signals that produce this pattern of activity are not well understood. We address this gap in knowledge by recording spikes and local field potentials (LFPs) from a 16-channel laminar probe in the SC of a monkey performing randomly interleaved delayed visually-guided and memory-guided saccades. The electrode penetration was orthogonal to the SC 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 quantify LFP information with current-source density (CSD) analysis to emphasize the location and timing of incoming (source) and outgoing (sink) electrical currents across layers. Preliminary analyses reveal the following observations: The sensory burst is coincident with a robust current source signal in the intermediate layers with bleeding into the superficial layers. The magnitude of this source decreases gradually during the delay period and then increases modestly at the time of saccade onset. In contrast a current sink was observed deeper in the SC at sites of visuomotor spiking activity. This CSD switched to a weak source signal during the delay period before re-transitioning to a sink at the time of saccade onset to reveal a transient source/sink reversal between intermediate and deep layers. Intriguingly the CSD trace in the deep layers revealed a potent source signal immediately following the saccade. This cannot be a visual signature since it was also observed for memory-guided saccades. Across all layers modulations in both LFP and CSD signals during the delay and presaccadic periods were weak compared to the fluctuations observed during sensory and post-saccadic epochs. Taken together these results show key differences between the target and the motoric burst and reveal that each SC layer is involved in different local and global network activity during sensorimotor transformation.

Afternoon Poster Session
Location: Row B
Poster #21

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Gurpreet Gandhoke	Graduate	Jankowitz	Neurological Surgery

Uniform pricing of coils used to treat intracranial aneurysms - A pilot Cost-Minimization Study

Introduction: The literature has ample evidence on endovascular coiling being more expensive than surgical clipping of intracranial aneurysms. Clinical effectiveness of endovascular coiling has been universally accepted however studies with long-term follow up have failed to demonstrate cost-benefit with endovascular treatment in comparison to open clipping. We hypothesize that this is due to the ever-increasing price of the coils required to accomplish the task. We believe that a very important contributor to coil cost escalation is that physicians are not affected by device pricing since their reimbursements have not been directly related to hospital costs. We decided to test our hypothesis by switching to a capped price for coils. The question was 'If all other parameters remain the same will paying the same lump sum amount irrespective of the number of coils used to treat a particular aneurysm make any difference to the overall cost' Methods: The endovascular surgeons at our institution negotiated an agreement with company 'X' to use a capped amount of $4000 for coil cost irrespective of the number of coils used to embolize an intra-cranial aneurysm. We retrospectively reviewed the coil and cost data on 12 patients who underwent coil embolization using coils from company 'X' during the period of September 2015- June 2016. The characteristics (length diameters) and number of coils used in every patient were analyzed. For the same patients we calculated the costs to use the same number of company 'Y' coils with similar dimensions and characteristics. Company 'Y' is the highest priced company within our system. We have withheld the names of companies 'X' and 'Y' on their request. Results: Total number of coils used for the twelve patients was 67 with a mean 5.6 coils per patient. The total cost of coils for twelve patients under the new-capped policy using coils from company 'X' was $48 000. The mean cost for each coil using company 'Y' was $1727 with a range of $951 to $2420. The total cost to use similar dimensions and same number of company 'Y' coils for the 12 patients was $106 905 resulting in a potential cost saving of $58 905. Thirty-eight different types of coils with varying diameters and lengths were used for the treatment of the 12 patients. The mean cost saving (using the capped policy) per patient was $4909 (p=0.01) with a range from -$395 to $14 860. Conclusion: This preliminary analysis is an impetus to explore coil cost capitation as a potential cost minimization strategy in endovascular surgery for coiling intracranial aneurysms. We are now exploring our own database to compare 1-year pre and post coil cost capitation differences in coiling aneurysms.

Afternoon Poster Session
Location: Row B
Poster #22

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Joseph E. R. Pichamuthu	Postdoctoral	Vorp	BIOENGINEERING

WALL STRESS OF CEREBRAL ANEURYSMS DEPENDS ON RESIDUAL VOLUME AFTER COILLING NOT COIL PACKING DENSITIES

INTRODUCTION Endovascular coil embolization is commonly used for treating cerebral aneurysms (CAs) by placing metallic coils in the aneurysmal dome to induce a coil thrombus mass (CTM)[1]. Successful endosaccular packing mainly depends on the morphological features and size of the aneurysm and the relationship of the aneurysm to the cerebral arteries. However a significant number of CAs are incompletely coiled and recurrences are expected in the range of 11-36% after coil embolization depending on the degree of filling achieved [2]. The coil packing density (CPD) after coiling is therefore a major concern. Computational models of CA coiling have determined alterations on wall shear stress in the presence of the CTM [3] but the effect on wall stress has not yet been reported except in a recent study by our group on a single CA model [4]. Wall stress assessment may help clinicians determine the level of coil embolization that is necessary to prevent recanalization and help guide the need for subsequent re-intervention. Therefore the purpose of this work was to estimate wall stress in patient-specific CAs prior to coiling as well as after coiling with different degrees of CPD or different residual volume (RV) after coiling. METHODS Virtual 3D geometries of CAs were constructed from Digital Subtraction Angiography scans of patients (n=7) under observation using an approved IRB (#PRO13080334). First scans were imported into Mimics (Materialise Plymouth MI) where lumen boundaries of CAs and their parent vessels were profiled using a pixel thresholding algorithm. After isolation the boundaries were rendered into coarse 3D volumes modeling the CAs. The models were further smoothed corrected for rendering flaws and patched in Geomagic (3D Systems Rock Hill SC). Surface geometries of CA walls were then exported and a CTM was created for each CAs in SolidWorks (Dassault Systéms Waltham MA). CTMs were modeled as solids filling the dome region of the aneurysms. CA surface models and CTM solid models were then meshed into quadrilateral shell elements and tetrahedral solid elements respectively in the commercial finite element analysis software Abaqus (Dassault Systéms Waltham MA). Each CA wall was treated as a homogenous nonlinear isotropic hyper-elastic and incompressible material with a uniform thickness of 0.36mm and modeled as reported in the literature with the strain energy function Wwall [5]: W_wall=C_1 (I_1-3)+C_2 (I_2-3)+C_3 (I_1-3)(I_2-3) \t(1) where C_1 C_2 and C_3 are material parameters [59.8 16.8 5710] characteristic of CA wall properties in (kPa). I_1 and I_2 and are strain invariants. CTMs were modeled into distinct homogeneous nonlinear isotropic hyper-elastic and compressible materials. Five different mechanical properties of CTM were used in this analysis: four derived from in-vitro uniaxial compression test data of clotted blood with 0 10 20 or 30% CPD and one from literature measurement of the intraluminal thrombus from abdominal aortic aneurysm [6]. The strain energy function used for in-vitro data was derived using equation fitting built into Abaqus. A reduced fourth order polynomial strain energy function WCTM was created: W_CTM=∑_(i=1)^4▒〖C_i (I_1-3)〗^i (2) where C_i (defined in Table 1) is a set of parameters characteristic of CTM material properties. I_1 is a strain invariant. Table 1: Filling Material Parameters Filling\tCoefficient (kPa) \tC1\tC2 (x103)\tC3 (x104) ¬\tC4 (x106) Blood Clot\t92.14\t23.88 \t-80.41 \t11.03 CPD10\t405.97\t12.32 \t-35.26 \t4.41 CPD20\t336.03\t83.85 \t-281.30 \t38.53

CPD30\t702.10\t100.50\t-320.40 \t42.74 For RV simulation the distance between the parallel planes separating the sac base and dome was measured as aneurysm length and the solid sac was segmented into 25% 50% and 75% of this length which were used to quantify the RV after coiling. RESULTS Peak wall stress (PWS) was defined as the maximum wall stress noticed in the model and mean wall stress (MWS) was defined as the average von Mises stress acting on the aneu-rysm wall. Prior to coiling PWS (red color) was noticed at either dome or neck of aneurysm as seen in Fig. 1. Fig. 1: von Mises wall stress (Ncm-2) in representative side-wall (left) and branched (right) aneurysms using the mechanical properties of the AAA thrombus. PWS was maximum prior to coiling (top). When completely filled coiling effectively reduces PWS in the side-wall aneurysm but no beneficial effect on PWS was seen in branched aneurysm as there remained a stress concentration at the neck. Complete CTM filling eliminates PWS from dome and neck regions for all five CPD materials in simple aneurysms but not in branched aneurysms. There is no significant difference in the spatial distribution and magnitude of stress when the mechanical properties of clot versus intraluminal thrombus are used. In completely filled CAs the MWS was significantly lower than that of unfilled models (p < 0.05) for all CPDs and also between different CPDs (p < 0.05) as shown in Fig. 2. Fig. 2: Plot of dome mean wall stresses in log-scale for unfilled and different CPDs with no residual volume using the mechanical properties of clotted blood. MWS reductions in simple CAAs were significantly higher than that of branched models (p < 0.05). However within each model the MWS estimated for the aneurysmal dome region for each degree of RV (0 25 50 75 & 100) and for the parent vessels (P) were compared using the mechanical properties of the AAA thrombus for filling. Fig. 3 reflects the trend across our patient pool with wall stress averaged across all seven cases. Fig. 3: Comparison of AWS estimated for the aneurysmal dome region for different degrees of RV and for the parent vessel (P) in each patient model using the mechanical properties of AAA thrombus. Notice that the AWS of the unfilled aneurysmal dome region was twice that of the parent vessel in most of the models. The AWS of dome decreased to the level of the parent vessel in all cases for RV≤25% suggesting threshold filling. N=7 for each case. DISCUSSION Prior to coil embolization in both types of aneurysm the PWS was located in the aneurysmal region either at the neck or at the dome and the MWS of the dome region was at least twice that of the parent vessel. This is consistent with the greater propensity for rupture at the dome region seen clinically [7]. The CTM reduced the PWS in the dome region but the magnitude of PWS reduction depended on the type of CPD degree of RV and the aneurysm morphology. Our data suggests that for any useful outcome of coil embolization the CTM must cover the area of the wall where PWS occurs pre-treatment. Although statistically significant the reduction in resultant wall stress with increasing CPD is negligible in comparison to the difference observed after initial filling of CAs. The MWS of the dome was substantially reduced either to the level of MWS of parent vessel or less for RVs ≤ 25% suggesting the existence of a threshold level of RV for any beneficial wall stress shielding effect. These results support Sadato et al. which suggests that residual volume after embolization of CAs is the foremost consideration for preventing recanalization [8]. CTM filling did not show as much of a beneficial effect in branched aneurysm models as the PWS either remained nearly same at the neck or even elevated for different degrees of CTM filling. This may explain why certain patients are prone to recurrences and recanalization at the neck of the aneurysm after coil embolization. REFERENCES 1.\tRyttlefors M et al. Stroke 2008. 39(10): p. 2720-6. 2.\tPark JH. et al. Am J Neuroradiol 32 pp. 1756-1761. 3.\tKakalis NM. et al. IEEE tran med imag 2008. 27(6): p. 814-24. 4.\tPichamuthu J. et al. SBC 2012-80782 pp. 107-108 5.\tCostalat et al. J Biomech 44.15 2685-2691 2011 6.\tWang DH. et al. J Biomech Eng 123 pp. 536-539 7.\tCrompton M.R. Br Med J 1966. 1(5496): p. 1138-42 8.\tSadato et al. PLos One 11.5 2016.

Afternoon Poster Session
Location: Row B
Poster #23

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Patricia Stan	Graduate	Luna	Neurobiology

Differential Response Preference of Mouse V1 Excitatory Neurons to Cartesian and Non-Cartesian Stimuli

Patricia Stan Janne Kauttonen Brian Jeon Tai Sing Lee Sandra Kuhlman How neurons code different aspects of an image is central to our understanding of shape representation. Many studies have shown that neurons in the primary visual cortex (V1) have differential preference for elementary stimulus dimensions such as orientation and spatial frequency. However the majority of studies use conventional sinusoidal (Cartesian) gratings to probe the properties of these neurons and it is therefore unknown whether these neurons may have preferential responses to more complex stimuli. To further investigate this we developed a stimulus set composed of Cartesian gratings as well as polar and hyperbolic (non-Cartesian) gratings. We used in vivo two-photon Calcium imaging in awake mice to record responses of V1 excitatory neurons to Cartesian and non-Cartesian stimuli. We found that individual neurons in V1 showed variable preference to Cartesian and Non-Cartesian stimuli. Some neurons responded only to Cartesian gratings others were selective for non-Cartesian gratings and others responded to both Cartesian and non-Cartesian. Our results suggest that a subset of V1 excitatory neurons do not function as solely elementary stimulus dimension detectors but may be involved in the computation of complex shape representation. It is known that responses to Cartesian stimuli develop innately largely independent of experience. Future studies will include raising mice in the dark to determine if visual experience is required for the development of response selectivity to non-Cartesian stimuli.

Afternoon Poster Session
Location: Row B
Poster #24

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Yolandi van der Merwe	Graduate	Chan	Bioengineering

Citicoline preserves optic nerve integrity and visuomotor function following chronic intraocular pressure elevation

Purpose: Although lowering of intraocular pressure (IOP) is the only clinically proven glaucoma intervention in afflicted individuals glaucomatous neurodegeneration and visual impairment may continue to progress in some patients following this treatment. Recent studies suggest the potential of citicoline an intermediate in the generation of phosphatidylcholine from choline to improve visual outcome in glaucoma patients but its neuroprotective roles remain unclear. Here we examined the effects of oral citicoline treatment on white matter integrity and visuomotor response in a chronic IOP elevation animal model. Methods: Twenty-five Long Evans rats were intracamerally injected in the right eye with an optically clear cross-linking hydrogel consisting of 6% vinysulfonated hyaluronic acid (HA) and 6% thiolated HA that obstructed aqueous outflow. Eleven of the rats received daily citicoline treatment (500mg/kg) via oral gavaging for 7 days prior to and every 48 hours for 14 days after hydrogel injection. IOP and visual acuity (VA) were measured with a TonoLab tonometer and OptoMotry virtual reality system respectively before and for 5 weeks after hydrogel injection. Diffusion tensor imaging was performed using a 9.4 Tesla MRI scanner to measure white matter integrity indicated by fractional anisotropy (FA) in the prechiasmatic optic nerve (ON) at 5 weeks following hydrogel injection. Results: Hydrogel injection significantly elevated IOP in the right eye for 5 weeks with no pressure difference between citicoline treated and untreated animals (Fig. 1a). VA of left eye remained unchanged over time whereas VA of right eye deteriorated starting at day 7 and was significantly worse in untreated animals compared to citicoline treated animals. The decrease in FA in the ON was significantly smaller for citicoline treated animals compared to untreated animals (Fig. 1a & 1b). In addition FA in right ON was positively correlated with VA in right eye for all animals (Fig. 1c). Conclusions: Chronic IOP elevation for up to 5 weeks caused significant changes in visuomotor behavior and white matter integrity in the prechiasmatic optic nerve whereas citicoline treatment ameliorated the effects. Our results appeared consistent with recent literature that suggests citicoline can act upon impaired white matter and improve functional outcomes in neurodegenerative diseases.

Afternoon Poster Session
Location: Row B
Poster #25

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Asiyeh Golabchi	Postdoctoral	Cui	Bioengineering department University of Pittsburgh

Long term performance of PEDOT/MWCNT/Dexamethasone coated electrodes implanted in visual cortex of rats

In chronic neural recording studies the temporal degradation in signal quality such as single-unit yield and signal-to-noise ratio due to electrode material failure and development of glial scar and neuronal death has been reported. These limitations can be addressed by using organic electrode coatings which provide a combination of recording and stimulation advantages including lowered impedance and increased charge transfer and ability to incorporate and release anti-inflammatory and neuroprotective drugs. Multi-walled carbon nanotubes (MWCNTs) loaded with dexamethasone can be incorporated into poly (3 4-ethylendioxythiophene) (PEDOT) as electrode coatings. Previously we have reported that dexamethasone-loaded PEDOT/MWCNT-coated microelectrodes showed lowered impedance and reduced inflammation after 14 days of implantation and stimulation in rat dorsal root ganglion compared to uncoated electrodes. Here we further evaluate the electrode/tissue interface and recording performance during prolonged implantation period (>12 months). The coated electrodes performed very well in recording visually evoked neural response from rat visual cortex even at the chronic time points showing great promise in advancing the quality and stability of chronic neural recording.

Afternoon Poster Session
Location: Row B
Poster #26

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Kevin Mohsenian	Graduate	Gandhi	Bioengineering

Interceptive saccades revisited: a comparison of saccades to stationary and moving targets

Natural environments are dynamic and filled with sensory information that could be used by an organism to guide behaviors necessary for survival. Animals are able to extract relevant information from their environment by aligning their specialized sensory apparatus (e.g. the retinal fovea) with stationary and moving objects. Rapid eye movements have been used to study sensory motor and cognitive processes in primates but most of this research has emphasized the use of stationary targets. Under these circumstances the metrics and kinematics of saccades have been well characterized (Leigh & Zee 2015); however there have been relatively few in-depth descriptions of horizontal vertical and oblique interceptive saccades using a large range of target speeds and directions. The current abstract reports data collected from two rhesus monkeys and five human subjects who performed a delayed saccade task in which the delay duration starting target location and target speed (range: 10¬60 deg/s) and direction (inward outward upward downward) were varied randomly to elicit saccades with different vectors (amplitude and directions). Delay trials using stationary targets placed along moving target paths were randomly interleaved with delay trials using moving targets. Eye position was recorded using magnetic search coils and an eye¬tracker system for non¬human primates and humans respectively. Preliminary data are similar for both species. Analyses indicate that saccade metrics between stationary and moving targets may be more similar than previously proposed (Guan et al. 2005 Keller et al. 1996). We observed no differences in the duration peak velocity average velocity latency and saccadic error between amplitude matched saccades used to foveate stationary and moving targets across directions and speeds. The discrepancies between our observations and those previously reported could be a function of task differences. For instance we used a delay saccade task and most previously reported data were collected using a step saccade task. We also interleaved many more target trajectories than previous studies. These results suggest that the interceptive saccade vector encoded in the programming pathway is transformed in a similar temporal pattern in the brain stem as traditional saccades.

Afternoon Poster Session
Location: Row B
Poster #27

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Sanjeev Khanna	Graduate	Smith	Bioengineering

Spiking correlations in the frontal eye fields during eye movement planning

Pairs of nearby cortical neurons exhibit correlated spiking activity. There is a strong link between the correlation among neurons and the amount of information that can be represented in a neuronal population. That link is particularly important at the decoding stage when sensory signals are used to guide motor output such as eye movements. Very little is known however about the correlated activity in areas that bridge the sensory and motor divide. The frontal eye fields (FEF) are considered to be the primary locus of cortical signals controlling eye movements. Because of this and the presence of neurons with both visual and motor responses they are an ideal candidate for studying the role of correlated activity in planning and executing movements. Of particular interest is the connection between the populations of visual and motor neurons which might be important for eye movement planning. We used a linear electrode array to record from groups of FEF neurons in alert rhesus macaque monkeys performing a conventional memory guided saccade task. We measured neuronal correlation of spiking activity on both short and long time scales (spike count correlation and synchrony). We found that correlated spiking activity in FEF was similar in a number of ways such as dependence on distance and tuning similarity to previous measurements in early visual cortex. When we focused specifically on connections between visual and motor neurons we found a distinct pattern of results. The overall level of correlation between these groups was lower than visual-visual or motor-motor pairs but it showed the strongest dependence on the direction of the planned eye movement. These findings suggest that visual and motor populations of neurons in the FEF play a unique role in transforming visual information to motor output.

Afternoon Poster Session
Location: Row B
Poster #28

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Angelica Herrera	Graduate	Collinger	Bioengineering

Neural tuning properties of the primary motor and somatosensory cortices during cursor and hand tasks

Research has shown that brain-computer interfaces (BCIs) can restore lost limb function by allowing control of a prosthetic arm via signals from motor cortex (M1). However we recently reported that in addition to M1 neurons in somatosensory cortex (S1) were also tuned to cursor and hand movements. M1 showed stronger tuning than S1 in general but S1 was more strongly tuned to hand rather than cursor movements. Here we examined the temporal aspects in tuning hypothesizing that M1 would lead kinematics while S1 would lag kinematics. Two 88-channel and two 32-channel intracortical microelectrode arrays were implanted in a human subject with tetraplegia in M1 and S1 respectively. Neural data was collected during 5 test sessions while the subject performed a 2D cursor control and a 2D robotic hand-shaping task. Data was collected under 2 conditions: (1) Observation: the subject attempted to perform the tasks while the kinematics were controlled by the computer; (2) Constrained BCI: the subject's decoded neural activity (from either M1 or S1) controlled the computer cursor or robotic hand while the computer attenuated command signals orthogonal to the target direction. Neural decoding was performed using indirect optimal linear estimation based on an assumed linear encoding model where firing rates were considered to be a linear combination of the 2D endpoint velocities for each task. We examined the fit to the encoding model for each unit under multiple lag conditions. Examining the distribution of the encoding model fits for different lags neurons in M1 and S1 qualitatively appeared to be most strongly tuned to kinematics when no lag shift was implemented. However in the observed data for both the cursor and hand tasks no significant difference was found among the arrays for different shifts. For the constrained BCI dataset in the cursor and hand tasks both recording arrays were found to have fits for 0 and 50ms lag that were significantly different than the others tested and for both sensory arrays a zero lag yielded the best fit rejecting the null hypothesis. The sensory arrays were seen to have a slightly better fit than the recording arrays in the hand task; however the differences in their fits were not statistically significant. In an intact system M1 activity occurs prior to the executed movements while sensory activity lags behind resulting from inputs from peripheral afferents. Here we saw that M1 and S1 activity was predicted by movement; however this relationship was strongest with zero lag between neural activity and kinematics. Perhaps unexpected this result may be because the participant was attempting movement rather than overtly moving.

Afternoon Poster Session
Location: Row C
Poster #29

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Uday Jagadisan	Postdoctoral	Gandhi	Bioengineering

Analysis of spiking activity and local field potentials reveals patterned information flow within the superior colliculus

The superior colliculus (SC) is a major hub of sensorimotor integration in the gaze control network and plays a pivotal role in the generation of saccadic eye movements. The sensory-to-motor transformation is enabled by the intermediate and deep (collectively deeper) layers of the SC. However it is unknown whether neurons in these layers constitute a homogeneous network performing similar computations or if there exists finer spatiotemporal patterning therein. To study this in greater detail we combined linear microelectrode array recordings with multi-channel signal analyses. Linear arrays are especially amenable to recording from a column of neurons to access computations evolving in parallel within the column. We recorded from the SC in two monkeys (Macaca mulatta) performing a delayed saccade task. The electrode contacts (n=16) spanned the dorso-ventral extent of the SC allowing for the simultaneous recording of spiking activity and local field potentials (LFPs) within the deeper layers. We performed coherence and Granger causality analyses to assess the flow of information within SC. We found the following: (1) Following target onset spike-spike coherence increased between most channel pairs but only the dorsally located channels exerted a Granger causal influence on the spiking of other channels suggesting a unidirectional flow of information during sensory processing. In contrast during the saccade the middle channels exerted a causal influence on channels located both dorsally and ventrally indicating bidirectional information flow during peri-saccadic processing. (2) Spike-LFP coherence revealed stronger coherence between spiking activity recorded from dorsal contacts and LFPs recorded more ventrally both following stimulus onset and following the saccade. Intriguingly there was no significant increase in coherence in the lead up to the saccade. (3) For both epochs the spike-LFP coherence profile was biphasic with an early narrow transient and a late broader peak. Granger analyses suggested that both early coherence peaks could be the result of causal dorsal-to-ventral influence of spikes on LFP whereas the late peaks could be the result of the causal influence of LFP on spikes. (4) In all cases coherence and causality decreased as a function of distance between the pair of contacts. Moreover the strongest influences in all cases were in the sub-beta band (<30 Hz) with a slightly weaker effect in the low-gamma range (30-50 Hz) between dorsal channels. These results point to distinct communication channels for spikes and LFPs in the SC and provide evidence for multi-phase processing during sensorimotor integration.

Afternoon Poster Session
Location: Row C
Poster #30

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Maria Rubio	Faculty	Rubio	Otolaryngology

The number and distribution of AMPA receptor channels containing fast kinetic GluA3 and GluA4 subunits are target-cell-dependent at auditory nerve synapses

Neurotransmitter receptor subtype and the number the density and their distribution relative to the location of transmitter release are likely to be the key determining factors of the properties of signal transmission. AMPA glutamate receptors containing fast kinetic GluA3 and GluA4 subunits are prominently present in subsets of neurons that are capable of firing action potentials at high frequencies such as the auditory relay neurons on bushy cells and fusiform cells of the cochlear nucleus. We examined the number density and organization of GluA3 and GluA4 at the synapse of the auditory nerve on bushy and fusiform cells. Using freeze-fracture immunolabeling (FRIL) we show a positive correlation between numbers of gold particles and the size of synapses for all pan AMPA GluA3 and GluA4 subunits in the auditory nerve synapses both on bushy and on fusiform cells. These synapse types have the same number of AMPA receptors but at auditory nerve synapses on bushy cells the gold density is higher than that on fusiform cells due to smaller postsynaptic densities. GluA3 gold labeling number and density are higher at auditory nerve synapses on bushy cells whereas GluA4 gold labeling number and density are higher at those on fusiform cells. The intrasynaptic distribution of gold labeling revealed that in auditory nerve synapses on bushy cells AMPA receptors -in particular GluA3 are concentrated at the center of synapse. The center concentration of AMPA receptors is absent in GluA3-knockout mice and gold particles are found evenly distributed along the auditory nerve synapse on bushy cells. GluA4 gold labeling was found homogenously distributed along both synapse types. Our findings show that GluA3 and GluA4 subunits are target-cell-dependent at auditory nerve synapses.

Afternoon Poster Session
Location: Row C
Poster #31

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Sofia Garcia-Hernandez	Postdoctoral	Rubio	Otolaryngology

Impaired auditory processing and altered synaptic structure in mice lacking the GluA3 subunit of AMPA receptors

AMPA glutamate receptor complexes with fast kinetics subunits -GluA3 and GluA4- are essential for temporal precision in the auditory system. We evaluated the role of the GluA3 subunit in auditory processing using auditory brainstem responses (ABR) to assess auditory function and electron microscopy to evaluate the ultrastructure of the auditory nerve synapse on bushy cells (AN-BC synapse) in wild type mice (WT) and mice lacking GluA3 (GluA3-KO). Since GluA3 subunit localization increases on auditory nerve synapses within the cochlear nucleus in response to transient sound reduction we investigated the role of GluA3 in experience-dependent changes in auditory processing; we induced transient sound reduction by ear plugging one ear and evaluated ABR threshold recovery for 60 days after ear plug removal in WT and GluA3-KO mice. We found that the deletion of GluA3 leads to impaired auditory signaling that is reflected in decreased ABR peak amplitudes increased latency of peak 2 premature hearing loss and ultrastuctural changes in the AN-BC synapse. Additionally the lack of GluA3 hampers ABR threshold recovery after transient ear plugging. We conclude that GluA3 is required for normal auditory signaling normal adaptive plastic changes after transient sound reduction and normal ultrastructure of AN-BC synapses in the cochlear nucleus.

Afternoon Poster Session
Location: Row C
Poster #32

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Emily Parker	Graduate	Fisher	Department of Psychiatry

Pyramidal Cell morphology in mouse Primary Auditory Cortex

Schizophrenia (Sz) is a debilitating disease that besets approximately 1% of the global population. Dendritic spine deficits in primary auditory cortex (A1) likely contribute to auditory impairment in Sz GWAS and rare variant studies have identified risk genes associated with Sz including CACNB4, which encodes the beta4 subunit of voltage-gated calcium channels. Previously, we demonstrated that CACNB4 levels are inversely correlated with density of small dendritic spines in A1 in a postmortem study of Sz patients. Similarly, overexpression of CACNB4 in primary neuronal culture resulted in reduced density of small spines. Now we are interested in whether overexpression of CACNB4 in vivo confers morphological alterations of pyramidal cells (PCs) in A1. We performed a proof of concept study using an Adeno-associated vector expressing GFP (AAV2-CaMKIIα-EGFP) to visualize and characterize PC morphology in A1 in adult wild type mice. Determining normative morphology in A1 will enable us, and others, to better identify and characterize PC abnormalities in mouse models of auditory impairment and disease.

Afternoon Poster Session
Location: Row C
Poster #33

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Flora M Antunes	Postdoctoral	Rubio	Otolaryngology

Lack of GluA3 AMPA receptor subunit alters synaptic transmission in the auditory nerve endbulb of Held synapse

Glutamate receptors of the AMPA type (AMPARs) which are tetrameric complexes assembled from combinations of four subunits (GluA1-A4) are primarily responsible for the fast excitatory transmission at central synapses. The subunit composition of AMPARs determines gating kinetics and thus shape the postsynaptic response (Cull-Candy et al. 2006; Yang et al. 2011). Fast gating GluA3- and GluA4-containing AMPARs mediate synaptic transmission at the endbulb of Held synapse on bushy cells (BCs; Gardner et al. 1999; Trussell 1999; Wang et al. 1998) one of the fastest synapses in the brain. Our preliminary data indicate prominent GluA3 expression at the endbulb-BC synapse when compared to synapses that receive auditory nerve input but exhibit slower kinetics. Thus we hypothesized that GluA3 plays a crucial role in fast synaptic transmission at the endbulb-BC synapse. We examined the kinetic properties of evoked and spontaneous EPSCs at the endbulb-BC synapse in slices prepared from GluR3-KO and wild type mice aged P17-P22. Our results show that the absence of GluA3 altered the kinetic properties of endbulb-elicited EPSCs and their short-term depression in BCs. In GluA3-lacking neurons endbulb-elicited EPSCs exhibited slower kinetics and stronger short-term depression. Our pharmacological studies indicate an increase in the expression of flip splice variants with slower desensitization kinetics in GluR3-KO mice which can explain the slower EPSC decay time. This finding suggests that GluA3 is needed for the normal insertion of flop splice variants in the endbulb synapse an important contributor to fast AMPAR kinetics in the mature endbulb synapse (Lawrence and Trussel 2000; Gardner et al. 2001; Schmid et al. 2001). We conclude that GluA3 plays a role in maintaining normal synaptic function at the endbulb-BC synapse.

Afternoon Poster Session
Location: Row C
Poster #34

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Marc Coutanche	Faculty	Coutanche	Psychology

The influence of recent semantic learning on human visual cortex

Humans are frequently exposed to information about the many objects, animals and people we that encounter in our environments. In addition to a suite of perceptual processes that can extract information from observed items, humans have the unique ability to discover the properties of objects through abstract communication. We have investigated how the introduction of visually relevant information –the real-world size of recently introduced animals– impacts the patterns of neural activity observed in a person's visual cortex. We scanned human participants with functional Magnetic Resonance Imaging (fMRI) while we introduced them to novel and known animals and tools. At the start of the experiment, participants were exposed to images of these items through a simple 1-back task. Participants were next presented with, and tested on, new factual information about each new concept. Finally, a post-learning 1-back task was administered. We used multivariate pattern analysis (MVPA) to decode the neural patterns underlying the processing of the new and known animals and tools, in order to compare activity patterns before and after learning. We find that after introducing people to new information about items' real-world size, visual activity patterns for the newly introduced animals more closely resemble the activity patterns observed for similarly sized known animals. In contrast, learning semantic information about the intended motor manipulation of a new tool did not affect future visually generated activity patterns. Our findings suggest that learning information about a new visual concept might rapidly influence visual cortex neural activity.

Afternoon Poster Session
Location: Row C
Poster #35

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Shi Tong Liu	Graduate	Sadagopan	Bioengineering

OPTIMAL FEATURES FOR ACOUSTIC CLASSIFICATION

The recognition and categorization of complex sounds is a central goal of auditory processing. In vocal animals conspecific vocalizations or 'calls' are an ethologically central set of complex sounds that these animals are able to perceptually recognize and categorize. Typically the vocal repertoire of a given species might consist of several categories with overlapping spectral profiles making them impossible to classify using low-level cues such as the long-term spectrum. In addition because different vocalization tokens within a class exhibit high variability both within and between animals any classifier should be able to generalize across this variability. Here we propose that combinations of acoustic features of intermediate complexity can be used to categorize vocalizations. We start by extracting a large number random acoustic features from one class of marmoset calls. We use an information maximization approach to score each feature on its ability to correctly classify this call type from all other types. We then use a greedy search algorithm to select a set of features that maximize classification accuracy while minimizing redundancy. We show that high classification accuracy can be achieved using a small set of such features. If cortical neurons were indeed encoding such features we demonstrate that they would exhibit highly nonlinear and selective tuning properties. Such neurons have been observed in single-unit recordings from marmoset auditory cortex supporting the feature-based classification model. Similar feature-based approaches might be used to implement more complex tasks such as speech recognition.

Afternoon Poster Session
Location: Row C
Poster #36

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Yuanning Li	Graduate		Neurological Surgery

Distributed Information Processing across OFA and FFA Represents Individual Face Identities

In contrast to traditional hierarchical models, most current models of visual perception suggest that distributed networks of regions across the visual processing stream underlie visual recognition. For example, multiple face patches, including the occipital face area (OFA) and the fusiform face area (FFA) likely work in concert to encode individual faces. However, direct evidence for distributed computation of individual faces does not exist because to date no methods exist to examine the information represented in neural interactions. Here we develop a novel pattern recognition method, called Multi-Connection Pattern Analysis (MCPA), to extract the discriminant information about cognitive conditions solely from the shared activity between two neural populations. In MCPA, functional connectivity models are built based on shared multivariate neural activity using canonical correlation analysis for each condition. Then using these models the activity in one area is predicted solely based on the activity in the other area for each condition. Classification is achieved by comparing the predicted activity with the true activity, revealing the representational structure of the shared neural activity (e.g. the information represented in the functional interaction). MCPA was applied to analyze intracranial EEG (iEEG) data recorded simultaneously from OFA and FFA in a human subject. Our results support the hypothesis that individual-level face information is not only encoded by the population activity within certain brain populations, but also represented through recurrent interactions between multiple distributed populations at the network level. In addition, the critical time window for face individuation based on MCPA was approximately 200 – 500 ms after stimulus onset, which is consistent with our previous study based on iEEG recording from FFA only. This suggests the involvement of FFA in the face individuation process is a result of temporally synchronized, recurrent interactions between FFA and other nodes in the face-processing network, including the OFA.

Afternoon Poster Session
Location: Row C
Poster #37

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Michael Chiang	Graduate	Ross	Neurobiology

Optogenetic dissection of central pain pathways

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 ventral 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 the ventromedial 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 distinct subpopulations of LPBN neurons differentially project to subsets of recipient brain regions suggesting that certain LPBN subsets mediate 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 mediating clinically relevant aspects of pain such as those neural pathways conveying the unpleasantness of pain.

Afternoon Poster Session
Location: Row C
Poster #38

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Lindsay Snyder	Graduate	Ross	Neurobiology

Modulation of multiple modalities of somatosensory information by peripheral kappa opioid receptors

Peripherally selective kappa opioids are emerging as a novel treatment for pain and itch that have shown efficacy in several recent clinical trials. Yet, the subtypes of somatosensory neurons that express KOR remain unclear. Using a newly developed KOR-cre knockin allele, viral tracing, and single-cell PCR we reveal that that KOR is expressed in a specific subset of peptidergic afferents that are tuned for inflammatory pain and itch, but not heat or mechanical force. Consistent with this, peripherally restricted KOR agonists inhibit behavioral responses to chemical pain and itch, but not acute heat responses nor punctuate mechanical sensitivity. Unexpectedly, we also find that KOR is expressed in subsets of primary afferents that form lanceolate or circumferential endings around hair follicles, suggesting an unappreciated role for KOR signaling in the modulation of low-threshold mechanosensation. At a functional level, optogenetic experiments reveal that dynorphin inhibits glutamate release from the central terminals of KOR-expressing afferents, and genetically-labeled afferents show inhibited calcium influx in response to kappa agonists. These experiments provide key insight for the rationale use of peripherally selective KOR agonists for the modulation of inflammatory pain, itch, and potentially mechanical allodynia.

Afternoon Poster Session
Location: Row C
Poster #39

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Junichi Hachisuka	Postdoctoral		Neurobiology

Neural circuit for inhibition of itch by scratching

Counter stimuli such as scratching and cooling are known to reduce itch. However, the neural circuit mechanisms underlying this phenomenon remain unclear. To address this question, we developed a novel semi-intact preparation that allows us, for the first time, to record from lamina I spinal output neurons while controlling somatosensory input though natural stimulation of the skin and manipulating the activity of spinal interneurons though optogenetic approaches. We identify spinal projection neurons that are tuned for itch, and show that scratching the receptive field of these cells reduces itch-related responses. Moreover, we reveal that nNOS inhibitory interneurons provide strong feed forward inhibition onto these spinal projection neurons. Thus, nNOS inhibitory interneurons provide a feed forward mechanism through which counter stimuli inhibit itch.

Afternoon Poster Session
Location: Row C
Poster #40

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Douglas Ruff	Postdoctoral	Cohen	Neuroscience

Correlative and causal evidence that attention improves communication between cortical areas

Several recent studies have shown that in addition to affecting the firing rates of sensory neurons attention decreases the extent to which fluctuations in response to repeated presentations of the same stimulus are shared between pairs of neurons in the same cortical area that have similar tuning. This decrease in so-called spike count correlations combined with attention-related improvements in the sensitivity of single neurons provides support for the hypothesis that attention improves perception by affecting the fidelity with which visual stimuli are encoded within a cortical area. However attention has also been hypothesized to improve the communication of visual information between cortical areas. We tested the hypothesis that attention increases communication between areas on the timescale of behavioral trials using two independent and complementary approaches. First we recorded simultaneously from populations of neurons in primary visual cortex (V1) and the middle temporal area (MT) using similar tasks and data analysis methods as those used to measure the effects of attention within an area. We found that in contrast to its effects on correlations within an area attention increases correlations between pairs of neurons in different areas. Second we made a causal manipulation to test the hypothesis that attention improves communication between areas by electrically stimulating V1 neurons during the attention task. We found that attention increases the extent to which manipulating V1 activity affects the activity of downstream neurons in MT. Together our results provide evidence that attention acts on visual cortex in at least two ways: by affecting both the way visual stimuli are encoded within a cortical area and the extent to which visual information is communicated to downstream areas.

Afternoon Poster Session
Location: Row C
Poster #41

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Griffin Koch	Graduate	Coutanche	Psychology

The neural basis for trait memory differences

We draw on a variety of neural systems in the course of learning and then remembering the wide range of information that we encounter every day. Although all healthy humans have access to the same brain systems people differ in the extent to which they draw on one type of memory versus another. Some people tend to emphasize the factual components of a past event (semantic) while others are biased to forming memories that are rich in spatiotemporal and contextual features (episodic). The current study investigates the neural basis for trait differences in the use of semantic episodic and spatial memory systems across individuals. We scanned the brains of 20 individuals using magnetic resonance imaging (MRI) and related the volumes of key brain regions to scores in the Survey of Autobiographical Memory (SAM) which quantifies a person's self-reported episodic semantic and spatial memory traits in addition to future prospection. We find that the brain regions associated with memory systems differ in relative volume across the population in a way that systematically tracks trait memory differences. Our findings include the result that individuals with stronger semantic memory characteristics have a larger percentage of brain volume occupied by the right and left temporal poles. These anatomical findings contribute additional evidence towards identifying the anterior temporal lobes as a type of "semantic hub". More generally this study provides evidence that anatomical data can reflect an individual's memory characteristics.

Afternoon Poster Session
Location: Row C
Poster #42

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Haley Dresang Chia-Ming Lei	Graduate	Dickey	Communication Science and Disorders

Neural bases of semantic-memory deficits for events

This study investigated the neural bases of event-related semantic-memory deficits among people with aphasia due to left-hemisphere (LH) stroke. A novel task using naturalistic photographic stimuli and patient-friendly procedures was used to test event-related semantic knowledge. In the task participants decided whether depicted events were normal (represented in semantic memory) or were abnormal (not represented in semantic memory). Performance on this Event task was correlated with deficits in action- and object-concept processing and on standardized language measures especially action- and verb-processing deficits. Logistic regression analyses examined lesion correlates of patient performance on the Event task. Surprisingly increasing LH lesion size in action ROIs was associated with improved performance on the event-knowledge task. These findings suggest that action processing may play a special role in event-related semantic memory representations. Furthermore they are consistent with recent claims that the right hemisphere may be especially important for activation of event-related knowledge.

Afternoon Poster Session
Location: Row D
Poster #43

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Rebecca Gerth	Graduate	Colby	Bioengineering

Coherence between PFC and PPC local field potentials in monkeys during the memory guided saccade task

The dorsolateral prefrontal cortex (PFC) and the posterior parietal cortex (PPC) of the macaque monkey are linked to each other by dense reciprocal axonal projections. Both areas contain neurons that exhibit spatially selective cue-period delay-period and saccade-period activity during performance of a memory guided saccade task. How interconnections between the two areas contribute to their function is not yet well understood. To explore this issue we have analyzed the coherence of local field potential (LFP) signals monitored simultaneously in PFC and PPC during performance of a memory guided saccade task. During each experimental session we recorded with an eight-channel linear electrode array in each area. This approach permitted comparing signals recorded from multiple pairs of sites within a single session. However it prevented systematic placement of the saccade target relative to the response field because neurons at different sites had different patterns of spatial selectivity. We presented targets at two widely separated contralateral sites during each session and characterized spatial selectivity at each site post hoc on the basis of differential neuronal responses on trials involving the two targets. We analyzed coherence of LFPs recorded at pairs of sites one in PFC and the other in PPC. We focused on oscillations in the beta and gamma ranges (15-30 and 30-80 Hz respectively). The degree of coherence depended on time during the trial and also on whether the target was at the preferred or non-preferred location. There were modulations in the degree of coherence during the visual epoch the delay epoch and the peri-saccadic epoch. Each effect was most pronounced during trials in which the target was at the preferred location.

Afternoon Poster Session
Location: Row D
Poster #44

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Peter Niesman	Undergraduate	Kline	Physical Medicine and Rehabilitation

Motor and Cognitive Function of Day-tested Groups Compared to Night-tested Groups

The majority of behavioral assessment studies are conducted during the day which is not when rats are most active. This discrepancy may preclude optimal performance. Hence the goal of this study was to determine if differences in neurobehavior exist in traumatic brain injured (TBI) rats when assessed during the day vs. night. The hypothesis was that the night group would perform better than the day group in all behavioral tasks. Isoflurane-anesthetized adult male rats received a controlled cortical impact (2.8 mm depth at 4 m/sec) or sham injury and were randomly assigned to either day (1:00 - 3:00 p.m.) or night (07:30 - 09:30 p.m.) testing. Motor function (beam-balance and beam-walk) was conducted on post-operative days 1-5 and cognitive performance (acquisition of spatial learning) was assessed on days 14-18. No significant differences were revealed between the TBI rats tested during the day vs. night for beam-balance beam-walk or water maze (p's < 0.05). These data suggest that the time rats are tested has no impact on their performance which does not support the hypothesis. The finding is important because it validates the interpretations from numerous studies conducted when rats were tested during the day vs. their natural active period.

Afternoon Poster Session
Location: Row D
Poster #45

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Yao Wang	Postdoctoral		Neuroscience and Psychiatry

Prefrontal Cortex to Accumbens Projections in Sleep Regulation of Reward

Sleep profoundly affects the emotional and motivational state. In humans and animals loss of sleep often results in enhanced motivation for reward which has direct implications for health risks as well as potential benefits. Current study aims at understanding the mechanisms underlying sleep deprivation (SD)-induced enhancement of reward seeking. Young adult mice (8 – 12 weeks old) were trained to self-administer sucrose pellet until a stable baseline was achieved. They then underwent acute SD for 6 hr during the first half of the light phase during which they had full access to food and water. When tested immediately after SD mice exhibited selective increase in sucrose self-administration but not food intake suggesting enhanced motivation for reward. In the nucleus accumbens (NAc) a key brain region regulating emotional and motivational responses we observed a decrease in the ratio of the overall excitatory over inhibitory synaptic inputs onto NAc principle neurons after SD. The shift was partly mediated by reduced glutamatergic transmission of presynaptic origin. Further analysis revealed that there was selective reduction of the glutamate release probability at the medial prefrontal cortex (mPFC)-to-NAc synapses but not those from the hippocampus thalamus or the basal lateral amygdala. To reverse this SD-induced synaptic alteration we expressed the stabilized step function opsin (SSFO) in the mPFC; optogenetic stimulation of SSFO at mPFC-to-NAc projection terminals persistently enhanced the action potential-dependent glutamate release. Finally intra-NAc optogenetic stimulation of SSFO selectively at mPFC-to-NAc terminals restored normal sucrose seeking in mice with SD without affecting food intake. Our results highlight the mPFC-to-NAc projection as a key circuit-based target for sleep to regulate reward-motivated behaviors.

Afternoon Poster Session
Location: Row D
Poster #46

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Cecile Ladouceur	Faculty	Ladouceur	Psychiatry

Interfering with Interference: Positive Reinforcement Modulates Fronto-limbic Systems and Reduces Emotional Interference in Adolescents

The ability to resist interference from distracting emotional information while sustaining attention on goal-directed behavior is critical for adaptive behavior and depends on complex cognitive-affective processes. There is mounting evidence from developmental affective neuroscience research demonstrating greater neural activity in subcortical regions such as the amygdala to emotionally salient information in adolescents particularly those at risk for affective disorders. In parallel studies show that positive reinforcement can enhance attentional control by promoting the recruitment of prefrontal cortical regions and that this effect is greater in adolescents compared to adults. The aim of this study was to examine the functioning of fronto-limbic systems subserving emotional interference in adolescents and to test whether differential reinforcement of correct responding can enhance attentional control and modulate these neural systems in ways that promote insulation from emotional distraction. Forty healthy adolescents (ages 10-13; 19 girls) completed an emotional delayed working memory task during fMRI with emotional distracters (none neutral negative) while positive reinforcement (i.e. monetary reward) was provided for correct responses under some conditions. As in adults adolescents showed a decline in performance to negative and neutral compared to no distracters and greater activation in amygdala and dorsal and ventral prefrontal cortices. Positive reinforcement yielded an overall improvement in response accuracy and reaction times and counteracted the effects of negative distracters as evidenced by significant reductions in activation in the amygdala and prefrontal cortical regions. The present findings extend results on emotional interference from adults to adolescents and highlight positive reinforcement as a potential mechanism that can boost attentional control of emotion. These findings also suggest that it may be possible to harness adolescent neural response to the effects of positive reinforcement on prefrontal cortical function to counteract negative environmental influences and facilitate coping. Future work in a larger sample is needed to investigate underlying developmental mechanisms in healthy and at-risk youth. A challenge for the future will be to build upon these findings for constructing reinforcement-based attention training programs that could be used to reduce emotional attention biases in anxious youth.

Afternoon Poster Session
Location: Row D
Poster #47

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Witold Lipski	Postdoctoral	Richardson	Neurosurgery

Speech encoding in human subthalamic nucleus neurons and sensorimotor cortex

Speech production and control is disrupted in a number of 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. These observations and other accumulating evidence indicate an important role for the basal ganglia in speech. However a major impediment to developing treatments for speech deficits in movement disorders and reducing speech-related side effects of DBS is the absence of a neurophysiological model for basal ganglia participation in speech production. We recorded STN neuron activity STN local field potentials (LFP) electrocorticography (ECoG) over articulatory sensorimotor cortex and spoken acoustics while 9 PD subjects performed a speech task during DBS surgery in order to test how general tenets of basal ganglia organization and function apply to the speech motor system. We hypothesized that the STN contributes at multiple levels to the hierarchical control of speech production by encoding articulatory orofacial muscle movements as well as voice quality measures such as such as volume pitch and fluency. Indeed we found that of 44 isolated unit recordings in the STN 23 showed either increases or decreases in firing rate during speech production. Preliminary analysis also revealed differential STN activation during speech involving early- versus late-learned phonemes suggesting that the STN is involved in processing phonological information. Furthermore we found that speech robustly modulated beta (12-40 Hz) and gamma (75-250 Hz) STN and cortical oscillatory activity in all subjects with preliminary findings also indicating changes in cortico-subthalamic spike-phase synchronization during speech. Testing how general tenets of basal ganglia organization and function apply to the speech motor system presents both unique challenges for clinical neuroscientists and significant opportunities to advance the cognitive neuroscience of speech production. Our findings support the hypothesis that both motor and linguistic speech information is encoded at multiple levels of granularity within the STN-cortical network.

Afternoon Poster Session
Location: Row D
Poster #48

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Alberto Vazquez	Faculty	Vazquez	Radiology

Inhibitory neuron activity contributions to hemodynamic responses: Optogenetic vs. sensory stimulation

Introduction The role of inhibitory neuron activity on hemodynamic responses have been difficult to determine because it is difficult to stimulate and isolate inhibitory neuron activity in vivo particularly in cortex [1]. Recent advances in optogenetics allow for the selective stimulation of cortical inhibitory neurons [2 3]. The goal of this work is to use this optogenetic model to investigate the contributions of inhibitory neuron activity including γ-aminobutyric acid (GABA) neurotransmission on vascular responses and hemodynamic signals. Forelimb sensory stimulation was used as reference. Methods Transgenic mice expressing Channelrhodopsin-2 (ChR2) under the control of the vesicular GABA transporter (VGAT) promoter were obtained from the Jackson Laboratory (Bar Harbour ME; n=17) for experimentation. Mice were induced using ketamine and xylazine and placed in a stereo-taxic frame. An acrylic well was placed over the somato-sensory cortex and a craniotomy was performed. The location of the forelimb area was mapped using optical imaging of intrinsic signals (OIS) at a wavelength of 570nm and sensitive to changes in cerebral blood volume (CBV). A fiber optic (125µm in diameter) electrode (to measure local field potential (LFP) and multi-unit activity (MUA)) and laser Doppler flowmetry (LDF) probe were placed in the forelimb area. Hemodynamic responses were measured using LDF (CBF) and OIS (CBV). Different light stimulation (or photo-stimulation) parameters were tested and delivered for 4-sec periods (every 60-sec) using a 473nm laser light source. Forelimb stimulation experiments were performed for comparison (1mA 0.5ms pulses). Experiments were performed under four pharmacological conditions: control (n=17) glutamate receptor blockade (GRB; n=8) GABA-and-glutamate receptor blockade (GGRB; n=6) and nitric oxide synthase (NOS)-and-glutamate receptor blockade (NOSGRB; n=3). The GRB condition was established by intra-cortical administration of ionotropic glutamate receptor antagonists APV (50mM) and NBQX (5mM) to block excitatory input to excitatory and inhibitory neurons while sparing GABA neurotransmission. Recent studies have found that inhibitory neuron activity can not only dampen excitatory activity but also increase excitatory activity via inhibitory-to-inhibitory connections that disinhibit excitatory neurons. The GGRB condition was established by the administration of APV+NBQX (as before) and BMI (0.5mM; a GABAA receptor antagonist) to further isolate inhibitory activity. Lastly the NOSGRB condition was established by administering APV+NBQX and the NOS blocker L-NNA (0.5mM) in a separate cohort of animals to investigate the role of nitric oxide on the inhibitory activity-driven hemodynamic response. Results and Discussion Photo-stimulation (PS) of inhibitory neurons under control conditions generated LFP and MUA responses that were effectively modulated by the photo-stimulus duration (Figure 1). More importantly the evoked hemodynamic responses were much larger than those evoked by forelimb stimulation (FL) and were also slower (longer time-to-peak; Figure 2). Inspection of the evoked LFP activity shows features similar to that of excitatory activity akin to that of forelimb stimulation. Experiments were performed under GRB conditions to isolate inhibitory activity and robust but slightly reduced LFP and hemodynamic responses were observed (Figure 3). Experiments were also performed under the GGRB condition to also block post-synaptic inhibitory neurotransmission. Electrophysiology experiments showed temporal narrowing of the LFP and significantly reduced

hemodynamic responses (Figure 3). Lastly NOSGRB experiments were performed and although the neural activity was maintained the hemodynamic response was significantly suppressed. Additional experiments under this condition are currently under way. Conclusions In summary increasing inhibitory activity has a profound impact on vascular regulation the hemodynamic response and its dynamic features.

Afternoon Poster Session
Location: Row D
Poster #49

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Adam Large	Graduate	Oswald	Neuroscience

Somatostatin interneurons mediate an activity gradient in piriform cortex

Odor information is processed and encoded by the neural circuitry of the piriform cortex. Compared to primary sensory cortices anterior piriform cortex (APC) lacks topographic representations of odor identity and appears to be a fairly homogenous structure in terms of connectivity and sensory processing. In order to observe the spatial structure of odor-evoked neuronal populations in APC we utilized Targeted Recombination of Active Populations (TRAP) to fluorescently label neurons expressing the immediate early gene c-fos during odor presentation. We find that this active population decreases in density along the rostrocaudal (RC) axis of the APC. To investigate potential underlying mechanisms for an activity gradient we optically stimulated interneurons in APC slices from vGAT-ChR2 mice while recording IPSCs in piriform pyramidal cells and demonstrate a clear caudal bias of inhibition onto pyramidal cells. Surprisingly we also find that a majority of inhibitory interneurons receive biased inhibition but with an opposing RC gradient. Since FS cells are a major source of inhibition onto pyramidal cells we believe that the activity gradient is due to modulation of inhibition onto FS cells. This suggests that the source of FS-cell inhibition needs to decrease along the RC axis. Using genetically targeted fluorescent labeling we find that somatostatin-expressing (SST) interneurons decrease in density along the RC axis. We also find that SST-cells can provide biased inhibition to inhibitory interneurons. Taken together these results suggest a disinhibitory circuit mechanism supports an increasing gradient of inhibition resulting in enhanced odor-evoked activity of rostral pyramidal neurons but a decreasedn recruitment of caudal neurons.

Afternoon Poster Session
Location: Row D
Poster #50

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Sarah Najjar	Graduate	Gold	Neurobiology

Optogenetic investigation of epithelial-neuronal communication in the colon

Functional gastrointestinal disorders such as irritable bowel syndrome (IBS) affect up to 25% of the U.S. population and their pathophysiology is largely unknown. These painful disorders are characterized by visceral hypersensitivity which originates in the primary afferent neurons innervating the colon. In addition to intrinsic changes in these afferents epithelial cells in the colon may also contribute to this hypersensitivity. It is known that these epithelial cells can release neurotransmitters such as ATP acetylcholine and serotonin but the nature of their communication with colonic afferents remains unclear. Using optogenetic techniques in which channelrhodopsin (ChR2) is targeted specifically to the colon epithelial cells we are able to activate these cells without the simultaneous activation of primary afferents that occurs with application of mechanical and chemical stimuli onto the colon. In an ex vivo preparation we isolated the distal colon and intact pelvic nerve and recorded the activity of single fibers. Our studies show that optogenetic activation of the epithelium can directly initiate robust action potential firing in colonic afferents of different functional classifications. We further showed through pharmacology that ATP is an important chemical messenger in this epithelial-nerve communication. Application of ATP receptor antagonists decreased or abolished action potential in over half of the afferents that responded to epithelial cell activation. With additional studies targeting other receptors on primary colonic afferents we seek to further elucidate the mechanisms of epithelial cell-derived activation of colonic afferents and its relation to pain. Furthermore we will investigate how this communication changes during a state of chronic inflammation as seen in inflammatory bowel disease. Thus better understanding of the epithelial-neuronal interaction will reveal potential targets for treatment of intestinal pain.

Afternoon Poster Session
Location: Row D
Poster #51

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Robert Nicholls	Faculty	Nicholls	Pediatrics

Porcine model of phenylketonuria generated by CRISPR/Cas9 genome editing will enable brain studies and discovery of novel neurotherapeutics

Phenylalanine hydroxylase (PAH) deficiency traditionally termed phenylketonuria (PKU) results in accumulation of phenylalanine (PHE) leading to neurotoxicity and severe developmental disabilities. For over 50 years dietary PHE restriction has been the standard intervention; however after adolescence therapy non-compliance is high. Indeed most adolescents and adults exceed the recommended therapeutic range for blood PHE (≤ 360 µMol/L) leading to late onset neurodevelopmental cognitive ADHD and psychiatric symptoms. Thus there is an urgent need for more effective therapeutic modalities for PKU and even a modest improvement in metabolic capacity that increases PHE tolerance would reduce reliance of dietary PHE restriction to ease the burden of therapeutic compliance which would lead to improved neurologic function. While rodent models biochemically model classical PKU they do not display the neurological manifestations of the human disease. Since pigs more closely resemble humans in brain size development and anatomy as well as physiology and genome we propose that a PAH-null pig will provide a superior animal model for characterizing PKU neuropathophysiology and exploring novel therapies. Using bioinformatics analyses of DNA sequence fragments we assembled the 13 exon pig PAH gene encoding a 452 amino acid enzyme and characterized expression of PAH in minipig tissues. The Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-Cas9 system utilizes a guide RNA (gRNA) to target the Cas9 endonuclease to a specific DNA sequence to generate a double-strand break (DSB). Repair of two DSBs often deletes the region between them. By expressing Cas9 in an in vitro cell model with pairs of CRISPR gRNAs targeting non-polymorphic sites in PAH introns 5 and 6 we identified optimal reagents that generate deletions or inversions of exon 6 that inactivate the gene. DNA sequence analysis confirmed the recombinant breakpoints and that DNA repair of the DSBs involved non-homologous end-joining. Using zygote injections of RNA encoding a pair of gRNAs and Cas9 and culture in vitro for 1 week ~ 48% of pig pre-implantation embryos had deletions of PAH-exon 6. Subsequently the procedures were repeated but with embryo transfer (ET) to surrogates with one of five ETs giving rise to a pregnancy from which two female piglets were delivered. Biochemical analyses at 5 days of age showed normal blood PHE levels in one (141 µM) with the other having hyperphenylalaninemia (2063 µM) consistent with classical PKU. Molecular analyses including deletion-PCR and DNA sequencing demonstrated that the former was heterozygous for a deleted allele and an intact allele having mutations at each gRNA target site while the PKU piglet has deletions involving each allele. Presently clinical neurological and behavioral phenotypes of the first PKU pig are under assessment. In conclusion we propose that our development of a porcine model of PKU will provide an optimal pre-clinical model for brain-related studies as well as for development of new therapeutic approaches such as new medical food formulations drugs or experimental gene and cellular (e.g. hepatocyte transplantation) therapy.

Afternoon Poster Session
Location: Row D
Poster #52

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Meryl Warshafsky	Undergraduate	Nicholls	Pediatrics

Characterization of a ferret brain cell line expressing gene markers of epithelial-mesenchymal transition (EMT)

Mouse as a mammalian model of human disease has been a pillar of the research community largely due to the genetics and longstanding ability to modify the genome. Nevertheless mouse is often a poor model of clinical phenotypes and therapeutic treatments poorly translate from rodent to patients. As a consequence mammalian models with a physiology anatomy and genome closer to humans are needed. Indeed for brain disorders species with a gyrencephalic brain ideally of a size on the same order of magnitude to the human brain would be ideal. The domestic ferret Mustela putorius furo (Mpf) is genetically more similar to humans than mice and represents a suitable laboratory model to study human disease especially of the lung and for brain development. As an entry point we have characterized a cell line derived from a six week old ferret brain Mpf cells (Trowbridge et al. 1982 In Vitro 18 952-60). An initial point of focus was our bioinformatics analysis of the ferret genome sequence to identify the orthologous cluster of ~12 paternally-expressed imprinted genes involved in Prader-Willi syndrome a neurobehavioral disorder including those encoding proteins or snoRNAs and the cis-regulatory regions for transcriptional and imprinting regulation. Additionally the Snord116 snoRNA duplicated family was characterized in detail by genomic PCR cloning and DNA sequencing of paralogous Snord116 copies. Chromosomal analysis of Mpf cells by G-banding as well as fluorescence in situ hybridization with a Snord116 genomic probe identified mosaicism with 70% of cells being pseudodiploid and 30% of cells having aneuploidy; we are now isolating clonal pseudodiploid sublines. To assess the ability of Mpf cells to undergo genome editing vectors encoding two CRISPR guide RNAs (gRNAs) and Cas9 components as well as an EGFP marker were transfected into Mpf cells. The guide RNAs direct the Cas9 endonuclease protein to complementary target sequences to catalyze a double strand break (DSB) with DNA repair of two DSBs resulting in the intervening fragment being deleted. Deletion-PCR and DNA sequencing of the breakpoint fragments confirmed a capability for efficient genome editing in Mpf cells. Cell morphology differed when Mpf cells were cultured in different media and at different cell densities including the formation of long cell extensions with branches or beading and increased expression of some neural markers. As well as candidate gene expression assessed by RT-PCR RNA-sequencing was performed to assess genome-wide gene expression. Many of the highly expressed genes including those for transcriptional regulators and others govern the process of epithelial-mesenchymal transition (EMT). This suggests a hypothesis that Mpf cells may be representative of an early stage in the process by which neuroepithelial progenitor cells commit to a neural fate and migrate a process likened to EMT. The detailed characterization of Mpf cells provides a new in vitro brain-derived cellular model and has general utility for optimization of genome editing reagents in the development of ferret models of human disease.

Afternoon Poster Session
Location: Row D
Poster #53

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Sertgei Baranov	Postdoctoral	Friedlander	Neurosurgery

Protecting mitochondria is a key to retain neuron synapses. Single-cell analysis.

Human studies reveal synaptic dysfunction decades before predicted clinical diagnosis in neurodegenerative diseases. Loss of synapses is a characteristic of Alzheimer's and Huntington's diseases. Normal synaptic activity is highly dependent on mitochondria because mitochondria is (i) the powerhouse (ii) a participant in the regulatory/signaling pathways and (iii) a critical player in the neuronal stress response cascades. Damage to synaptic mitochondria results in the impairment of the synaptic function and synaptic loss. The unique parameter characterizing mitochondrial status is mitochondrial membrane potential. Dissipation or prolonged decrease of the potential may lead to the reduction of number of mitochondria and/or triggering of apoptosis We hypothesized that Huntington's disease associated synaptic deregulation followed by neuronal cell death among other factors caused by a decreased mitochondrial membrane potential. Using single cell analysis approach we assessed mitochondrial membrane potential in the primary neurons from mouse model of Huntington's disease. We found that mitochondrial membrane potential was decreased with the distance from nucleus to the mitochondria. The decay in the membrane potential is more apparent in the neurons obtained from HD mouse model. We showed that found mitochondrial membrane potential decrease was also associated with an increased rate of the mitochondrial protein content oxidation and an increased production of reactive oxygen species by distant mitochondria. We explained our data in the framework of unique property of neurons to form very long processes (axons and dendrites) which results in delayed protein turnover in distal mitochondria and leads to the increased vulnerability of synaptic mitochondria to stress associated with the neurological disorder.

Afternoon Poster Session
Location: Row D
Poster #54

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Jongwon Lee	Graduate	Kandler	Department of Otolaryngology

Development of structural and functional connectivity of MNTB axon collaterals to the mouse superior paraolivary nucleus

The medial nucleus of trapezoid body (MNTB) is the major source of inhibition in the auditory brainstem providing inhibitory inputs to the lateral superior olivary (LSO) as well as the superior paraolivary nucleus (SPON). Projections from the MNTB to these nuclei are tonotopically organized. In the developing LSO the tonotopic precision substantially increases via synaptic silencing and axonal pruning. In this study we investigated whether the refinement of individual MNTB axon collaterals in the LSO and SPON is coordinated. Anatomical reconstructions of biocytin-filled MNTB axons show the presence of tonotopy in the MNTB-SPON pathways shortly after birth (P2-4). Over the next three weeks axons expand and add new boutons but this growth was proportional to the expansion of the SPON resulting in no change in the tonotopic precision. Ongoing studies to map functional connectivity using laser-scanning photostimulation further support the early tonotopic organization of the MNTB-SPON projection and the absence of tonotopic refinement during the first three postnatal weeks. Our results demonstrate that MNTB axon collaterals show a dramatically different degree of tonotopic refinement and axonal pruning depending on whether they innervate the LSO or MNTB indicating that axonal pruning of these inhibitory axons is determined by the postsynaptic target.

Afternoon Poster Session
Location: Row E
Poster #55

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Jeff Dunworth	Graduate	Doiron	Mathematics

Finite Size Effects and Rare Events in Balanced Networks

Cortical neuron spiking activity is broadly classified as temporally irregular and asynchronous. Networks with a balance between large recurrent excitation and inhibition capture these two key features making them a popular framework for relating circuit structure and network dynamics. Balanced networks stabilize the asynchronous state through reciprocal tracking by the inhibitory and excitatory population activity leading to a cancellation of total current correlations driving neurons within the network. Analysis of recent data from spontaneously active mouse auditory cortex slices show balanced network activity except for intermittent periods when the network experiences macroscopic synchronous events. These data suggest that while the core mechanics of balanced activity are important we require new theories capturing these brief but powerful periods when balance fails. Traditional balanced networks with linear firing rate dynamics have a single attractor and fail to exhibit macroscopic synchronous events. Mongillo et. al. (2012) showed that balanced networks with short-term synaptic plasticity can depart from strict linear dynamics through the emergence of multiple attractors. We extend this model by incorporating finite network size and introducing strong nonlinearities in the firing rate dynamics which allows finite size induced noise to elicit large scale yet infrequent synchronous events. We carry out a principled finite size expansion of an associated Markovian birth-death process and identify core requirements for system size and network plasticity to capture the transient synchronous activity observed in our experimental data set. Our model properly mediates between the asynchrony of balanced activity and the tendency for strong recurrence to promote macroscopic population dynamics.

Afternoon Poster Session
Location: Row E
Poster #56

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Michael Leone	Graduate	Doiron	Mathematics/Center for the Neural Basis of Cognition

Improved Reliability of Synaptic Transmission Reduces Neuronal Correlations in Balanced Network Models

Neuroscientists have known for decades that synapses in the central nervous system are highly unreliable often failing to release neurotransmitter following an action potential. This stochasticity can change dynamically as a result of prior activity and behavioral state. However previous theoretical studies of recurrent networks exhibiting balanced excitation and inhibition have neglected this important feature of biology. By way of mathematical theory of a balanced network with correlated feedforward input and variable synapses we have found that unreliability of recurrent synapses robustly increases spike count correlations while the opposite is true of unreliability of synapses in the feedforward pathway. We replicated these findings via simulations of a conductance-based exponential integrate-and-fire model. Previous studies of rat barrel cortex indicate that pyramidal-cell synaptic reliability increases following stimulus onset and coincides with decreased spike count correlations. Our results are consistent with these observations and furthermore implicate improved synaptic reliability as a causal factor in the observed correlation reduction. In addition we found that unreliable transmission is a major source of intrinsically generated variability in balanced networks of arbitrary population size. This result strengthens previous claims that high spike count variability consistently observed in cortical data may arise due to synaptic unreliability. Together our results highlight the importance of modeling variable synapses in theoretical studies of cortical networks.

Afternoon Poster Session
Location: Row E
Poster #57

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Chengcheng Huang	Postdoctoral	Doiron	Mathematics

Modeling within and across area neuronal variability in the visual system

Neural variability has important consequences on neural coding. Shared variability among neurons (noise correlation) has been commonly observed in multiple cortical areas (Cohen and Kohn 2011). Moreover noise correlation can be modulated by cognitive factors such as attention (Cohen and Maunsell 2009). Recently new data suggests that attention not only decreases correlations within a cortical area but also increases correlations between cortical areas V1 and MT (Ruff and Cohen 2016). The observed opposite trends of change in correlations between-areas and within-area impose further constraints on circuit mechanisms for the generation and propagation of noise correlations. We developed a spiking neuron network with spatiotemporal dynamics which exhibits macroscopic chaos in population rates. Such chaotic dynamics result in positive and low-dimensional noise correlation in the network. Attentional effects can be modeled as depolarizing the inhibitory population which reduces the internally generated variability and allows the network to better track input signal.

Afternoon Poster Session
Location: Row E
Poster #58

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Bing Liu	Faculty	Liu	Computational and Systems Biology

Computational Modeling of Amphetamine-stimulated Dopamine Dynamics

Dopamine (DA) plays key roles in the pathology of neurological disorders such as Parkinson's disease and drug abuse. DA transporter (DAT) provides a primary mechanism that maintains the DA homeostasis. Amphetamine (AMPH) exposure induces euphoria and hyperactivity by increasing extracellular DA through a variety of mechanisms: (i) competitively binding to DAT (ii) eliciting DA efflux (iii) and enhancing DAT internalization which are governed by a network of biochemical reactions. The network involves multiple feedforward and feedback mechanisms and thus analyzing its complex dynamics requires systems biology approaches. To identify potential intervention strategies for modulating extracellular DA level we construct a comprehensible model for the downstream interaction network that underlies the AMPH-induced DA efflux and DAT trafficking. Our mathematical model takes into account the activation of Rho PKA PKC CaMKII and and G-protein signaling pathways that regulate the AMPH-stimulated DA dynamics. The model was calibrated by an optimal fit of the time course of surface DAT and cAMP levels under two conditions and was further verified to reproduce the time course of Rho activation and AMPH-cAMP dose response. Sensitivity analysis and in silico knockdown experiments suggest that AMPH modulates extracellular DA level mainly through the DA efflux pathways than DAT internalization. Interestingly simultaneously inhibiting DA efflux and DAT internalization might lead to a synergistic enhancement of DA reuptake. Our results also identify a feedforward loop that governs the time window of Rho activation and fine-tunes AMPH induced DAT internalization. These systems-level insights we gained could contribute to the development of pharmacological strategies for disrupting AMPH action.

Afternoon Poster Session
Location: Row E
Poster #59

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Amelia Versace	Faculty	Versace	Psychiatry

Effect of Higher and Lower Diffusion Gradient Directions on Fiber Estimability and Diffusion Metrics in Young Adults

Purpose: The aim of the current study was to examine in comparable diffusion imaging (DI) sequences the effect of number of gradient directions on fiber estimability and DI metrics. Materials and Methods: Twenty-nine young adults (Mean age= 21.5 SD=2.1; 16 females) completed two DI sequences with higher (197 directions with b=700 s/mm2 1000 s/mm2 and 2500 s/mm2) and lower (61 directions with b=1000 s/mm2) number of gradient directions and comparable acquisition time and parameters. Importantly for comparison purpose with the DI sequences with lower number of gradient directions the DI sequences with higher number of gradient directions was analyzed using a Gaussian mode (i.e. model 1 as proposed in bedpostX). In addition as recommended for DI sequence with multiple diffusion weightings analyses modelling non-mono-exponential diffusion decay (model 2 as proposed in bedpostX) are also reported for the DI sequence with higher number of gradient directions. Results: Using a triple tensor model (Figure 1) fiber estimability measures derived from the DI sequence with higher number of gradient directions showed increased brain coverage of voxels supporting three fibers and an increased relative volume fraction (proportion of volume per voxel accounting for the diffusivity signal of each modelled direction) in voxels supporting three fibers (Figure 2 A-B). In addition tract-based spatial statistics (TBSS) using estimates of volume fractions paralleled these findings showing widespread increased volume fractions associated with the third (and second) tensor across the skeletonized brain for the DI sequence with higher number of gradient directions. Conclusion: Findings provide preliminary evidence for improved estimability of intra-voxel crossing fibers in brain regions characterized by high complexity of fibers in data acquired with higher number of gradient directions supporting its use in future studies.

Afternoon Poster Session
Location: Row E
Poster #60

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Maria Jalbrzikowski	Postdoctoral	Luna	Psychiatry

The development of white matter microstructure and intrinsic functional connectivity between the amygdala and ventromedial prefrontal cortex

Study: Connectivity between the amygdala and ventromedial prefrontal cortex (vmPFC) is compromised in multiple psychiatric disorders many of which emerge during adolescence. To identify what extent deviation of amygdala-vmPFC maturation contributes to the onset of psychiatric disorders it is essential to characterize amygdala-vmPFC connectivity changes during typical development. We examined 1) age-associated changes in structural and functional connectivity of amygdala and vmPFC sub-regions 2) how development of amygdala-vmPFC functional connectivity is related to development of white matter microstructure between the amygdala and vmPFC and 3) how amygdala-vmPFC maturation is related to anxiety and depression. Methods: An accelerated cohort longitudinal design (1-3 time points) was used to characterize developmental changes of amygdala-vmPFC connectivity using resting state fMRI and diffusion-weighted imaging (N=246 10-25 years). Anxiety/depression scores were calculated from responses on the Youth and Adult Self-Reports. Results: Functional connectivity between the centromedial amygdala and rostral anterior cingulate anterior vmPFC and subgenual cingulate significantly decreased from late childhood to early adulthood in both males and females. Importantly this finding was replicated in an independent cohort (10-22 years N=327). Similarly structural connectivity as measured by quantitative anisotropy (QA) significantly decreased in the same regions. Functional connectivity between the centromedial amygdala and rostral anterior cingulate predicted structural connectivity in these same regions during early adulthood (ages 22-25). These results suggest that amygdala functional connectivity specific to vmPFC regions involved in the cognitive control of emotions show decreases that continue into adulthood when amygdala-vmPFC functional connectivity predicts structural connectivity. Finally a novel time-varying coefficient analysis showed that increased amygdala-vmPFC FC was associated with greater anxiety and depression symptoms during early adulthood while increased structural connectivity in amygdala-vmPFC white matter connectivity was associated with greater anxiety/depression during late childhood and early adolescence suggesting that we may be able to identify developmentally-sensitive biomarkers for those at risk for developing psychiatric disorders. Conclusion: Specific developmental periods of functional and structural connectivity of amygdala and prefrontal systems may contribute to the emergence of anxiety and depression symptoms and play a critical role in the emergence of psychiatric disorders in adolescence.

Afternoon Poster Session
Location: Row E
Poster #61

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Eric Reseland	Graduate	Fernandez-Miranda	School of Medicine

HDFT segmentation and connectivity of the Human Uncinate Fasciculus

We show that even after chronic tetraplegia, both M1 and S1 units respond to attempted movements, both covert and overt. In general, units were broadly responsive to multiple movements. Further investigation is needed to examine specific movement parameters (speed, position, etc.) to determine if additional insight regarding unit behavior can be gained. Additionally, future work should examine the activation of S1 during sensory imagery as well as motor imagery.

Afternoon Poster Session
Location: Row E
Poster #62

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Felix Nguyen	Graduate	Jankowitz	School of Medicine

Evaluation of Brain Injury and Cognitive Outcome Following Treatment of Unruptured Intracranial Aneurysms

Background: Unruptured intracranial aneurysms (UIAs) are treated through endovascular embolization or open surgical clipping to prevent the catastrophic outcomes that follow aneurysmal subarachnoid hemorrhage (aSAH). However treatment of UIAs is associated with a >10% risk of neurologic morbidity with nearly 6% of patients suffering persistent cognitive impairment 1-year after treatment. The structural etiology of impaired cognition following treatment of UIAs has not been delineated. One hypothesis is that cognitive impairment results from disruption of white matter fiber tracts caused by intra-procedural tissue retraction and/or ischemic mechanisms. The primary objective of this study was to characterize and quantify damage to white matter fiber tracts following surgical or endovascular repair of UIAs utilizing a diffusion spectrum imaging (DSI) technique called High Definition Fiber Tractography (HDFT). Methods: We performed a prospective observational study of patients undergoing treatment of UIA through either surgical clip occlusion or endovascular coil embolization. White matter fiber tract imaging and neuropsychological tests were administered both prior to and following treatment of UIAs. Imaging acquisition was performed on the 3T TrioTim MRI scanner (Siemens; Erlangen Germany). White matter fiber tracts analyzed included the arcuate fasciculus (AF) corpus callosum (CC) inferior occipitofrontal fasciculus (IOF) and uncinate fasciculus (UF). All fiber tractography was performed with DSI-Studio software using quantitative anisotropy (QA)-based generalized deterministic tracking; fiber tracts were reconstructed using regions of interest drawn on patients' diffusion maps. The presence of white matter tract damage was defined as a significant decrease post-treatment in mean QA percentage and volume when compared to pre-treatment values as determined through two-tailed unpaired t-test (a priori statistical significance p < 0.05). Results: Complete data were available for 3 patients undergoing treatment of UIA; 2 patients underwent surgical clipping and 1 had endovascular coiling for UIA repair. Patient 1 (right and left internal carotid artery aneurysms coil embolization) had reduced volume in the left AF (% change = -3.09) left IOF (% change = -6.75) and right IOF (% change = -3.49). No significant changes in QA for any track was observed in Patient 1. Patient 2 (right posterior communicating artery aneurysm clip repair) had decreased QA in the right AF (% change = -3.09) but this was not statistically significant (p = 0.129). The left UF of Patient 2 had significantly decreased QA (% change = -6.67; p < 0.01) and volume (% change = -18.1%). Patient 3 (right middle cerebral artery aneurysm clip repair) experienced volume decreases in the right IOF (% change = -23.4%) and right UF (% change = -19.3%). Reduced mean QA percentage was found in the right IOF (% change = -18.9 p < 0.01). No patient demonstrated decreased QA or volume in the CC tract. Conclusions: Surgical clip occlusion and endovascular coil embolization for repair of UIAs were both found to be associated with damage in white matter fiber tracts demonstrated by statistically significant decreases in AF IOF and UF mean QA percentage and volume. Forthcoming analyses will assess whether these findings correlate with cognitive outcomes measured by neuropsychological testing.

Afternoon Poster Session
Location: Row E
Poster #63

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Pinar Celtikci	Postdoctoral	Fernandez-Miranda	Neurological Surgery

Revealing displacement and infiltration of fiber tracts in low-grade gliomas by advanced fiber tracking: novel imaging marker of fiber tract integrity

Background Low-grade gliomas (LGGs) originate from the supporting glial cells of the central nervous system (CNS) and comprise about 15% of the primary brain tumors in adults. LGGs are most common in third and fourth decades of life among patients with high quality of life and long survival expectancy 5 9 11. These are typically slow growing tumors characteristically located in the white matter that may demonstrate local growth invasion and malignant transformation6. Four patterns of white matter alteration by CNS tumors were defined in the literature: displacement infiltration edematous and disruption10. However which of the proposed patterns are characteristic to LGGs is a matter of controversy and has not been well established yet. Knowledge of how LGGs affect the white matter tracts around them is of significant importance especially for the neurosurgeon. The presence of any functional fibers in or around the tumor their position in relation to the lesion and the decision of which tracts could be sacrificed if needed in order to reach and resect the tumor are major surgical challenges3 8. High-definition fiber tractography (HDFT) is an advanced white matter imaging technique that has shown to be superior to diffusion tensor imaging2. HDFT provides an accurate evaluation of fiber tracts in vivo allowing determination of specific fiber tracts that are being compromised by a tumor mass and might be transgressed during surgical resection8. Objectives We aimed to demonstrate the patterns of white matter fiber tract alterations caused by WHO grade II LGGs using an advanced fiber tracking method. Furthermore our goal was to characterize and validate these qualitative patterns of fiber tract alteration via quantitative analysis in search for an objective imaging biomarker of fiber tract integrity. We finally investigated the correlation of these patterns with the neuropathological diagnosis. Methods Sixteen consecutive patients with preoperative HDFT and neuropathological diagnosis of LGG (WHO grade II) were enrolled. All patients were screened to rule out any contraindication to magnetic resonance imaging (MRI) and signed an informed consent as part of our IRB approved protocol. Diffusion data were acquired using a 3-Tesla Magnetom Verio® (Siemens Erlangen Germany) with a 32-channel coil. Total scan time was 34 minutes and included a 25-minute diffusion spectrum imaging (DSI) scan (repetition time = 3439 milliseconds echo time = 150 milliseconds multiband acceleration factor = 3 voxel size = 2.4 mm3 field of view = 231 × 231 mm) including 257 non-collinear gradient directions with a maximum b-value of 7000 s/mm2 followed by a 9-minute T1-weighted structural scan (repetition time = 2200 milliseconds echo time = 3.58 milliseconds voxel size = 1.0 mm3). The diffusion data were reconstructed using a generalized q-sampling imaging method to model an orientation distribution function in each brain voxel 12. Fiber tracking was performed with DSI Studio4. Peritumoral fiber tracts were determined based on their spatial relation with the tumor mass; once identified they underwent subsequent qualitative and quantitative evaluation. Their contralateral hemisphere counterparts were used for comparison. Qualitative evaluation classified peritumoral tracts as unaffected displaced infiltrated or displaced and infiltrated at the same time. Qualitatively affected tracts were further analyzed quantitatively. Quantitative anisotropy (QA) is a novel directionally-dependent measure of anisotropy that overcomes the limitations of fractional anisotropy (FA) in assessing fiber integrity12. Regarding displaced tracts QA

values were predicted to be higher or similar whereas with infiltrated tracts these values were hypothesized to be lower compared to the contralateral healthy side. For the quantitative analysis mean QA values of both whole tracts and peritumoral segments were obtained. Mean QA values of the contralateral healthy whole tract and anatomically equivalent segment of the peritumoral portion were also noted for comparison 1 7. In order to prevent disparity in comparison secondary to possible lateralization of fiber tracts perilesional segment mean QA (S) to whole tract mean QA (W) ratio (S/W) was calculated for both sides. Results Patient characteristics clinical information and qualitative evaluation are summarized in Table 1 (mean age: 38.1 years range; 17 – 63 years). There were 7 oligodendrogliomas 5 diffuse astrocytomas 2 gemistocytic astrocytomas one pleomorphic xanthoastrocytoma and one pilomyxoid astrocytoma. Qualitative analysis of 65 peritumoral tracts revealed 9 (13.8%) unaffected 24 (36.9%) displaced 13 (20%) infiltrated tracts and 19 (29.2%) tracts that demonstrated a combination of displacement and infiltration. There were no disrupted tracts. Partial infiltration of the perilesional tract was observed in 6 out of 13 tracts with pure infiltration and in 11 out of 19 tracts with the combination of displacement and infiltration. The most common pattern in oligodendrogliomas was displacement (41.9%) while in diffuse astrocytomas the combination of displacement and infiltration (53.3%) was the most frequent. When compared with the healthy side the quantitative analysis revealed that for displaced tracts there was an increase in the S/W S and W in 71.4% 61.9% 70.6% of the tracts respectively. For the infiltrated tracts there was a decrease in the S/W S and W in 63.6% 81.8% 66.6% of the tracts respectively. For tracts that were both displaced and infiltrated there was a decrease in the S/W and S in 64.7% and 58.8% of the tracts respectively (see Table 2). The increase of S/W ratio among displaced tracts and the decrease of S value in infiltrated tracts compared to the healthy side was statistically significant (p < 0.05). The p value for the decrease in S/W ratio in infiltrated tracts was not statistically significant (p=0.055). There was no statistically significant relationship between neuropathological diagnosis and qualitative alteration types or quantitative values. Conclusions WHO grade II LGGs might displace infiltrate or cause a combination of displacement and infiltration of white matter fiber tracts. Most common patterns were displacement and combination of displacement and infiltration. Infiltration (whether pure or with displacement) could be partial or include the whole diameter of the peritumoral segment of the tract. We found that the majority of S W values and S/W were increased in displaced tracts and decreased in infiltrated tracts compared to the healthy side and the increase of S/W ratio in displaced tracts and the decrease of S value in infiltrated tracts were statistically significant. Therefore we can conclude that QA changes correlate with the qualitative alterations and expected condition of the fiber integrity which may serve as an objective imaging biomarker of fiber integrity when altered by LGGs.

Afternoon Poster Session
Location: Row E
Poster #64

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Ben Allen	Postdoctoral	Jennings	Psychiatry

Diffusion Imaging of the Superior Longitudinal Fasciculus and the Uncinate Fasciculus and Associations with Dimensions of Attention Deficit-Hyperactivity Disorder in Adults Diagnosed in Childhood

Alterations in white matter microstructure may play an important role in the pathophysiology of Attention Deficit-Hyperactivity Disorder (ADHD). However little is known about the extent to which ADHD symptom severity is associated with alterations in white matter tracts known to be involved in attention and emotional control processes. This study addresses this gap by using diffusion imaging (DI) to determine how differences in the superior longitudinal fasciculus (SLF) and the uncinate fasciculus (UF) relate to clinically relevant symptom dimensions in a sample of adults with or without a childhood diagnosis of ADHD. This sample is a subset from a longitudinal study of individuals diagnosed with ADHD as children based on standardized clinical interviews and parent/teacher ratings. For this study DSM-IV symptoms (based on self and parent report in adulthood) were averaged to create dimensions of inattention hyperactivity/impulsivity (H/I) and anger-irritability (A/I). Multi-shell diffusion weighted imaging data and T1 anatomical data were acquired in 46 adults (32 ADHD 14 nonADHD; mean age [SD]: 33 [3] years 44 males) on a 3T Siemens Trio MR scanner. Probabilistic tractography was used to reconstruct white matter tracts of interest(SLF; UF). Volume length and diffusivity metrics were extracted for each participant. Preliminary findings show that Smaller volumes for the UF ($p = .05$) and SLF ($p = .06$) in the right hemisphere in the ADHD vs nonADHD group. There were no significant group differences in diffusivity metrics for these tracts. In the ADHD group H/I symptoms were negatively correlated with length in the left and right SLF ($r = -.40$ $p = 0.01$ $r = -.40$ $p = 0.03$ respectively) and A/I symptoms were positively correlated with the volume of the right UF ($r = 0.40$; $p = 0.04$). The association between greater volume of the right UF and higher levels of A/I symptoms suggests greater connectivity between medial-temporal and orbitofrontal brain regions. Greater volume of the right UF may be indicative of more bottom-up processing in adults with high anger-irritability. Moreover diminished intra-cortical connectivity as evidenced by shorter length of the SLF may be a neurobiological substrate for higher levels of H/I symptoms in adults and represent a deficit in “cool” executive functions that enable flexible control over thought and action in pursuit of goal directed behavior. Future analyses will test whether these diffusion imaging characteristics are associated with prospectively gathered symptom trajectories from childhood.

Afternoon Poster Session
Location: Row E
Poster #65

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Shahir Mowlaei	Postdoctoral	Ghuman	Neurological Surgery

Intrinsic Brain Networks are Organized by Frequency Relationships

Studies have increasingly demonstrated the importance of oscillatory dynamics in neural coding and interregional communication. While it has become clear that frequency-specific activity is a critical feature of brain activity it remains unclear whether brain networks organize by “frequency band” or whether the spectrum does not enforce functional brain network organization. Specifically here we ask if there is a functional parcellation of the frequency spectrum or not in resting-state magnetoencephalography (MEG) data based on large-scale brain network connectivity patterns. To answer this question we used network analyses and unsupervised and supervised pattern recognition algorithms in conjunction with whole brain MEG resting-state connectivity measures. Specifically we recorded 5 minutes of eyes open fixated resting-state MEG data from 34 healthy subjects. After artifact removal in each subject for each frequency from 0.5-50 Hz with 0.5 Hz steps we calculated the source-localized all-to-all connectivity matrix based on phase locking values between each pair of points on the cortex (5124x5124 connectivity matrix). Using matrix and network similarity measures we then assessed the spatial similarity of these full connectivity matrices between each pair of frequencies. Unsupervised and supervised analyses were used to assess whether there was consistent groupings of frequencies across subjects. The results of this analysis show that there are between 7 to 9 data-driven frequency bands that organize intrinsic brain networks. These bands roughly correspond to classic frequency bands. The bands also show significant consistency across subjects allowing one to classify each frequency to the correct band at the single subject level with relatively high accuracy. The results also show that there is a substantial spatial overlap between the spatial topography of the theta and low beta bands. Furthermore the results show that the low and high beta bands are substantially distinct and therefore should not be grouped together. In addition we used network analyses to determine the characteristic brain networks that correspond to each frequency band. Taken together these results suggest that frequency bands are a strong and consistent organizing force of large-scale intrinsic brain networks.

Afternoon Poster Session
Location: Row E
Poster #66

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Kristen Eckstrand	Postdoctoral	Forbes	Psychiatry

Heightened Activity in Social Reward Networks is Associated with Adolescents' Risky Sexual Behaviors

BACKGROUND: Compared with both adults and children adolescents have an enhanced propensity to engage in rewarding risky behavior. While sexual behavior in adolescence is a normative part of development risky sexual behavior is particularly important as it involves decisions to engage in potentially highly rewarding experiences that can lead to serious health consequences. The neural circuits underlying risky sexual behavior are largely unstudied; however it is believed that increased reward responsiveness – particularly social reward – contributes to risky sexual behavior. Using a social reward fMRI paradigm we hypothesized that adolescents engaging in higher risk sexual behaviors would exhibit increased activity and functional connectivity in response to social reward. METHODS: 47 typically developing adolescents (18M 29F [16.3±1.4 yrs]) underwent fMRI on a 3T scanner using a task in which they received rewarding or neutral feedback from peers. Adolescents completed the Youth Risk Behavior Survey including sexual health risk behaviors. Based on these responses individuals were classified into higher and lower sexual risk. Activation and functional connectivity analyses comparing higher and lower sexual risk adolescents were conducted in SPM12. RESULTS: Twenty individuals had engaged in sexual intercourse; male and female participants did not differ in risky sexual behaviors. Adolescents with higher risk sexual behaviors demonstrated increased activation in the right precuneus and the right temporoparietal junction (TPJ) during receipt of social reward compared with adolescents with lower risk sexual behaviors (see Figure 1). Further adolescents with higher sexual risk demonstrated greater functional connectivity between the precuneus and both the temporoparietal junction bilaterally as well as frontal regions including one cluster involving the dorsal mPFC and anterior cingulate cortex and another involving the left ventrolateral PFC and anterior insula (see Figure 2). DISCUSSION: In response to social reward adolescents engaging higher risk sexual behaviors exhibited greater activation and functional connectivity in social reward networks. Heightened activation in these reward- self- and social-processing regions could reflect a combination of tendencies toward reward seeking and enjoyment sensitivity to socially rewarding stimuli and orientation toward social rewards among youth engaging in higher risk sexual behavior. Given the limited neurodevelopmental literature on emerging adolescent sexual behavior these results provide evidence for the particular importance of social influence on neural circuits underlying sexual risk behaviors.

Afternoon Poster Session
Location: Row E
Poster #67

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Anne Van Cott	Faculty	Hetherington	Neurology

Magnetic Resonance Spectroscopic Imaging at 7T (7T MRSI) abnormalities in PTSD and mild TBI

The goal of this project was to examine the ability of magnetic resonance spectroscopic imaging at 7T (7T MRSI) to determine if the location of brain metabolite changes were capable of differentiating veterans with a chronic history of mTBI(s) and PTSD from those with PTSD alone. A distinct pattern of imaging abnormalities has emerged that has the potential to differentiate these two populations and serve as a metabolic imaging biomarker that may assist in the diagnosis prognosis and impact of targeted intervention of mTBI and PTSD.

Afternoon Poster Session
Location: Row E
Poster #68

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Alexander Poplawsky	Postdoctoral	Kim	Radiology

Vascular architecture with CLARITY suggests that contrast-enhanced high-resolution fMRI is dominated by microvessel dilation

Introduction: Functional magnetic resonance imaging (fMRI) measures the hemodynamic response to neuronal activity but more evidence is needed to understand how far the high-resolution fMRI response spreads relative to the evoked neuronal activity. The olfactory bulb is an ideal model system to study this issue because synapses localized to a single layer can be preferentially evoked by a selective stimulation. We previously showed that fMRI signal increases due to lateral olfactory tract (LOT) stimulation are highly localized to the evoked synapses in the external plexiform layer (EPL); but it is unknown whether dilation of local microvessels is the dominating source of our fMRI measurements. Methods: In α-chloralose anesthetized rats we stimulated LOT in a block design experiment (-200 μA 200 μs pulse duration 40 Hz ~1 min stimulus duration 4 min interstimulus interval); and acquired high-resolution (55 x 55 x 500 μm3) blood volume-weighted fMRI responses at 9.4 T. We then obtained line profiles from 330-μm thick slabs that orthogonally transected the bulb layers and measured the full width at half maximum (FWHM) of the evoked fMRI peaks due to LOT stimulation. In a different rat we rendered the right olfactory bulb transparent with CLARITY-based methods and stained the blood vessels with DyLight594 Tomato lectin (Vector Laboratories DL-1177) before imaging in 3D. We then compared the FWHM fMRI data to the vessel diameters lengths and volumes calculated by analysis of the CLARITY images. Results: The mean FWHM of the fMRI peaks was 347 ± 102 μm (mean ± SD n = 30 peaks from 5 rats 3 slices each rat 2 peaks each slice) where the mean anatomical thickness of EPL at these lines was 265 ± 65 μm. The fMRI spatial spread beyond the anatomical thickness of EPL was estimated by a least squares linear regression analysis. The regression intercept (± SE) which approximates this spread was 106 ± 65 μm (r2 = 0.34 p < 0.001 df = 28). With CLARITY microvessels that had diameters <12 μm accounted for the majority of the total vascular volume (65.8%) present in EPL and had an average length of 54.8 ± 41.2 μm (± SD n = 398 vessel segments). Conclusions: Our preliminary results indicate that the LOT-evoked fMRI signal spreads ~100 μm from the evoked layer EPL (~50 μm on each leg of the fMRI response peaks). This spread is consistent to the mean length of microvessels (~50 μm) the predominate vascular compartment in EPL.

Afternoon Poster Session
Location: Row F
Poster #69

Presenting Author:	Author Type:	Mentor/Lab:	Department:
Matthew Murphy	Postdoctoral	Vazquez	Radiology

Comparison of Neuronal and Hemodynamic Dynamic Connectivity Calculated Using GCaMP Mice Data

Low-frequency, spatially coherent fluctuations present in functional magnetic resonance imaging (fMRI) time series have had a tremendous impact on brain connectomics. Their dynamic character has highlighted the complexity of brain rhythms [1-6]. Since hemodynamic signals (e.g. fMRI) are of vascular origin, the degree to which hemodynamic measurements can capture neuronal dynamics remains unclear. Hence, studies that investigate the relationship between dynamic connectivity metrics measured from neuronal and hemodynamic signals are needed. Our group previously used a transgenic animal model to simultaneously acquire bi-hemispheric images sensitive to neuronal and hemodynamic signals. We showed that hemodynamic connectivity is highly correlated with neuronal connectivity in scans >5 min [7]. This work used the same animal model and imaging method to evaluate the agreement between neuronal and hemodynamic signals using sliding window (SW) and dynamic conditional correlation (DCC) metrics [8]. Methods: Transgenic mice expressing GCaMP3, a fluorescent calcium indicator that reports changes in intracellular calcium concentration that accompany spiking activity [9], were used to simultaneously image ongoing changes in neuronal activity (GCAMP) as well as hemodynamic measurements of blood oxygenation (OIS-BOLD, analogous to fMRI) from the same animals (n=6). Bi-hemispheric GCAMP and OIS-BOLD images were acquired at 10 Hz from the exposed superior surface of the mouse brain under light ketamine anesthesia (30 mg/kg/hr) for 5 to 20 min periods. Pre-processing consisted of temporal band-pass filtering (0.02-0.20Hz). Then, k-means clustering was used on the GCAMP data to obtain 6 regions-of-interest (Figure 1) [6,7]. GCAMP and OIS-BOLD ROI time series were extracted for each mouse. We first examined the SW lengths for which the GCAMP and OIS-BOLD connectivity matrices were significantly correlated ($r>0.47$ corresponds to $p<0.05$). Over non-overlapping windows, the average SW correlation and fraction of windows with significant relationships are reported. We then examined the temporal sampling resolution for which comparisons between the GCAMP DCC and OIS-BOLD DCC connectivity matrices were significantly correlated. Results: GCAMP (neuronal) and OIS-BOLD (hemodynamic) time series were used to calculate SW and DCC connectivity matrices (Figure 2). In general, DCC captured more transient inter-node dynamics compared to SW, but these properties depended on the SW window length (Figure 2B and 2C). To examine this further, for each non-overlapping SW window, the inter-node connectivity of the GCAMP data was compared to that of the OIS-BOLD data and tested for significance using a correlation analysis. The average correlation shows significant relationships for window lengths over 20 sec, while the average fraction of significantly correlated windows was >80% for windows >40 sec (Figure 3). A similar analysis of the GCAMP and OIS-BOLD DCC connectivity shows that average significant relationships were observed for data with temporal resolution >1.4 sec, and >80% of the comparisons were significant for temporal resolutions >2.2 sec. Adjusting for temporal lags between the GCAMP and OIS-BOLD time series did not alter these results. Conclusions: The hemodynamic signals measured in this study were able to capture dynamic changes in neuronal connectivity over time scales >20 sec for sliding window correlation (SW) methods. In addition to capturing more transient changes in connectivity using the DCC algorithm, we also observed significant agreement between hemodynamic and neuronal connectivity measurements using DCC for data with temporal sampling >1-

2 sec (typical of many fMRI studies). The changes in neuronal and hemodynamic connectivity are likely bounded by the dynamics of the underlying physiology.

Afternoon Poster Session
Location: Row F
Poster #70

Presenting Author:	Author Type:	Mentor/Lab:	Department:
William Ares	Postdoctoral		Department of Neurosurgery

A Comparison of CT Angiography and Digital Subtraction Angiography in the DIagnosis of Penetrating Cerebrovascular Injury

Authors: William J. Ares David M. Panczykowski Gregory M. Weiner Felix Nguyen Bradley Gross and Brian T. Jankowitz

INTRODUCTION: The current neurotrauma practice guidelines for the diagnosis and management of penetrating cerebrovascular injury (PCVI) give equal weight to CT angiography (CTA) and formal catheter based digital subtraction angiography (DSA) stating that there is no sufficient data to support one manner of imaging. It has been repeatedly shown in the literature that DSA outperforms CTA in the diagnosis of blunt cerebrovascular injury and as such we have hypothesized that catheter based angiography would also prove superior to CTA in the diagnosis of PCVI. METHODS: This population-based cohort study included all patients undergoing evaluation of penetrating cerebrovascular injury University of Pittsburgh Medical Center between October 2010 and June 2016. Clinical data was retrospectively collected and patients were excluded if information was missing or incomplete regarding imaging. All patients underwent radiographic evaluation consisting of both 16- or 64-slice multidetector row CT angiography (mCTA; 1.25mm slice thickness with coronal and sagittal reconstructions) and 4-vessel digital subtraction cerebral angiography DSA). Primary outcome was evidence of penetrating cerebrovascular injury on DSA. Injuries were defined according to Biffl et al. grading scale for BCVI since no universally accepted injury grading scale for PCVI exists. Agreement was assessed by Cohen's kappa coefficient; discriminatory power and calibration of these imaging modalities were assessed using multiple regression analyses and indicated by the area under the receiver operating characteristic curve (AUC). RESULTS: A sample of 21 patients was available for analysis. Agreement between diagnostic modalities was 76% (expected 57%) with a Kappa of 0.44 representing fair agreement (p=0.02). The sensitivity and specificity for mCTA for PCVI detection was 67% (95%CI 22-96%) and 80% (95%CI 52-96%) respectively. Multidetector CTA demonstrated adequate discriminatory ability for prediction of PCVI (AUC 0.73 95%CI 50-96%). The negative likelihood ratio of the patient suffering a PCVI despite having a negative mCTA for arterial injury was 0.42 (95%CI 0.13-1.3) while the negative predictive value of a normal mCTA was 86% (95%CI 57-98%). CONCLUSION: When compared to the gold standard of digital subtraction angiography CT angiography displays limited sensitivity and specificity for the diagnosis of PCVI. Patients who suffer penetrating neurotrauma may benefit from the definitive diagnosis offered by DSA if there is sufficient practitioner concern for PCVI.