Online Proceedings

POSTER SESSION 2

Commons East, Easel 84

1:00 PM to 2:30 PM

Development and Identification of *Tbr2*+ Neurons in the Mouse Midbrain

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CoMotion Mary Gates Innovation Scholar, Mary Gates Scholar, UW Honors Program
Mentor: Robert Hevner, Neurological Surgery

The midbrain is a critical region of the brainstem that houses the cranial nuclei necessary for coordinating eye movements. It has been observed that neurons in the midbrain express T-box Brain 2 (*Eomes*/*Tbr2*), a transcription factor generally associated with development of glutamatergic neurons. Because it has such a diverse role throughout the development of multiple neural structures (i.e. cerebral cortex, olfactory bulb, retina, and cerebellum), *Tbr2* is thought to be implicated in the development of certain forms of autism. The purpose of our experiments was thus two-fold: first, we investigated the neurotransmitter phenotype of *Tbr2*+ neurons in the midbrain. Second, we wanted to identify the function of *Tbr2*+ neurons in the brain by studying these populations in relation to known, molecular markers of specific, anatomical features. In order to accomplish these aims, we collected tissues at various ages from transgenic mice. We utilized endogenous reporters such as VGlut2-Cre^{Ai14} and Tbr2mTnG alongside immunohistochemical staining with the following antibodies: urocortin-1 (UCN-1; which marks the centrally-projecting Edinger-Westphal nucleus, EWcp, in the postnatal brain); cocaine- and amphetamine-regulated transcript (CART, which marks EWcp in the embryonic and postnatal brain); and 2H3 (which marks neurofilaments). We then used a confocal microscope to visualize fluorescence and collect images. We found that *Tbr2*+ neurons in the midbrain were glutamatergic but not cholinergic. We also found that *Tbr2* neurons were not Edinger-Westphal cells, leaving their ultimate anatomical identity unknown. Understanding the identity of Tbr2 cells is a prerequisite for beginning to understand the constellation of features that make up autistic spectral disorder, thereby guiding future clinical and scientific research.

POSTER SESSION 2

Commons East, Easel 53

1:00 PM to 2:30 PM

A Graph Theoretical Analysis of Pediatric Sports Concussion using Diffusion Tensor Imaging

Samantha H Sun, Senior, Bioengineering
CoMotion Mary Gates Innovation Scholar
Mentor: Christine Mac Donald, Neurological Surgery

Every year there are at least one million new cases of sport-related concussion in children younger than 18 in the United States. Current diagnostic screening tools, such as CT and MRI, are insensitive to the subtle microstructural changes that occur following concussion, and in pediatric concussion, there is additional complexity of the still-developing brain and how concussion affects its long-term development. While these patients' radiographic images often appear normal, they report an array of post-injury symptoms, which questions the true extent of brain injury after concussion. The aim of this research project is to utilize advanced neuroimaging and analysis tools, diffusion tensor imaging (DTI) and graph theory, to explore short-term and longitudinal changes in the brain following pediatric sports concussion and to obtain a more reliable and sensitive method to diagnose pediatric concussion. Children aged 10 – 14 with unresolved symptoms from a sports-related concussion and age-matched controls were included in this study. Each participant underwent MRI scans and clinical assessments 4-6 weeks post-injury and 6 months after the initial visit . We used DTI, which has been shown to be sensitive to microstructural changes related to concussion in adults. In addition, we analyzed the DTI data using graph theory, which is a mathematical tool that models information as a network. We investigated differences in network properties between concussed and non-concussed children and used random generated networks as a control. We confirmed that the network properties of children were distinct from random networks. We also observed a 9% reduction in global clustering and 16% increase in local connectivity in the concussed patients, suggesting overall network disconnect and stronger, but more segmented, local network groups. These preliminary results encourage further exploration of the methods employed and display clinical relevance in distinguishing between concussed and non-concussed youth.

POSTER SESSION 2

Commons East, Easel 83

1:00 PM to 2:30 PM

Deciphering the Role of Tbr2 Protein in the Production of Unipolar Brush Cells in Cerebellar Tissue

Katie Kaur Mand, Senior, Neurobiology
Mary Gates Scholar
Mentor: Robert Hevner, Neurological Surgery

Previous research has revealed that as new neural progenitor cells divide and migrate from the ventricular zone to the cortical plate in cerebellar mice tissue, they express a distinct sequence of transcription factors, including Tbr2, during phases of their migration. These proteins are presumed to be linked to vital events that occur during neurogenesis, and therefore can be used as markers to map both the birth, and trajectory of new neurons in mice. Tbr2 in particular, has been found to be a marker for Unipolar Brush Cells (UBCs) - a unique type of glutamatergic interneuron that is prominent in the cerebellar area of the brain. Work done previously in the Hevner lab has since shown that an ablation of Tbr2 in mice correlates with a marked decrease in UBC production. Therefore, we have hypothesized that first, Tbr2 is expressed in both mice and human cerebella, and may play similar roles in development. Second, Tbr2 is necessary for UBC development in mice cerebella. To test the first claim, slices of human cerebellar tissue ranging from 18 weeks of age (gestational), to 2 months of age (postnatal) were examined using immunohistochemical techniques. High magnification images were then collected using AxioVision software. From the collected data, we have concluded that humans also express Tbr2 in the cerebellum during neurogenesis. In order to test our second claim, we are using the Cre-Lox recombination system to develop a Tbr2 conditional knock-out mouse. We anticipate that this mouse tissue will demonstrate the dependence of UBC production and development on Tbr2 protein. Continuing to decipher the characteristics of these cells and the various developmental patterns that occur in the cerebellum, are the fundamental first steps in developing practical applications of neurological research.

POSTER SESSION 3

MGH 241, Easel 131

2:30 PM to 4:00 PM

Low Doses of Ketamine Improve Cardiac and Respiratory Rhythms in Rett Syndrome: A Clinical Pilot Study

Vy Yen Huynh, Junior, Biochemistry, Neurobiology
Mentor: Franck Kalume, Neurological Surgery and Pharmacology, UW/ Seattle Children's

Rett Syndrome (RTT) is a neurodevelopmental disorder that is first recognized in infancy and almost exclusively affects females. The syndrome is characterized by normal development in the first 6 to 18 months of life, followed by a regression of developmental milestones, particularly the loss of mobility skills and purposeful use of the hands. Additional features of RTT include severe disturbances in cardiac and respiratory functions. These are characterized by prolonged QT intervals as well as increased respiratory rate and occurrence of abnormal respiratory events such as breath holds. RTT results from mutations in the gene encoding the protein MECP2, which helps to regulate gene activity. The location and type of the MECP2 gene mutation influence the course and severity of the syndrome. Previous animal studies and clinical case reports have suggested that ketamine administered at a low dosage can reduce deficits in brain activity and improve neurological function in RTT. In this pilot study, we sought to determine the efficacy of ketamine in reducing the respiratory and cardiac phenotype observed in RTT. Electrocardiography (ECG) and respiration patterns were recorded before and after treatments of four RTT patients with low doses of ketamine. Examination of these recordings showed that ketamine decreases heart rate variability, respiratory rate, and the number of abnormal respiratory events within the 20 hours post drug administration. These results suggest that low-dose ketamine treatment may potentially serve as an effective future treatment for the cardiac and respiratory symptoms of RTT.

POSTER SESSION 3

MGH 241, Easel 150

2:30 PM to 4:00 PM

Towards Deep Brain Monitoring with Superficial EEG Sensors Plus Neuromodulatory Focused Ultrasound

Lucas Chen, Junior, Pre-Sciences
Edward Lou, Senior, Electrical Engineering
Madison Lee Selby, Sophomore, Pre Engineering
Mentor: Pierre Mourad, Neurological Surgery

Electroencephalograms (EEG's) are a common form of measuring electrical activity in the brain. Electrical activity from the brain directly correlates to neuronal activity, providing information that can be used for disease diagnosis or research on brain mechanisms. EEG recordings are limited in practicality and efficiency in some circumstances due to poor spatial resolution, vulnerability to noise, and consistency. Subdermal electrodes are unable to capture deep brain activity, which can only be obtained through surgically implanted intracranial electrodes. As a result, for patients in a condition where surgery is not optimal, the subdermal EEG offers little to no information in terms of deep brain activity. Through previous work, we have shown that applying 1050 Hz pulsed focused ultrasound (pFU) resulted in EEG readings above

normal physiological frequencies. Natural brain activity frequencies can be derived from the amplitude demodulation of the 1050 Hz signal. The ultrasound is amplifying the electrical activity in the region it is focused upon, allowing the EEG to record these signals. In this study, we attempted to increase the capabilities and specificity of EEG noninvasively through coupling it with pFU. We continued our previous work by applying pFU transcranially to the left visual cortex of a C57BL/6J mouse brain while stimulating the right eye with light. The observed frequencies collected by EEG were analyzed for neuronal stimulation in addition to sensory stimulation elicited from the ultrasound. A technological breakthrough in this field may someday lead to the ability to measure brain activity non-invasively from anywhere in the brain.