UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 17, 2019 Mary Gates Hall

Online Proceedings

SESSION 1T

BRAIN FUNCTION, DYSFUNCTION AND REPAIR

Session Moderator: Kathleen Millen, Pediatrics
JHN 175
12:30 PM to 2:15 PM

* Note: Titles in order of presentation.

Using Resting-State Functional Connectivity to Detect Uncomplicated Mild Traumatic Brain Injury
Josh Wolfe, Senior, Psychology
UW Honors Program
Mentor: Tara Madhyastha, Radiology
Mentor: Christine Mac Donald, Neurological Surgery

Detection of uncomplicated mild traumatic brain injury (mTBI) is difficult because there are no visible brain lesions that are often associated with more severe forms of TBI. New biomarkers would allow doctors to more sensitively screen for mTBI using neuroimaging methods. One promising biomarker technology is resting-state functional connectivity, which is brain activity measured at rest using functional magnetic resonance imaging. One particularly salient resting-state network is the Default Mode Network (DMN). Our research focused on identifying differences in resting-state functional connectivity between individuals diagnosed with mTBI and healthy controls. We examined mTBI in 254 U.S. military personnel deployed to a combat theatre in the Middle East from 2010-2013. Each subject underwent initial magnetic resonance imaging and screening for TBI following medical evacuation to Landstuhl Regional Medical Center (LRMC), the primary triage center for all evacuated combat casualties, up to 30 days post-injury. We used four distinct groups for our analysis; Blast/Non-Blast (n=79, 44) TBI, and Blast/Non-Blast Control (n=35, 96) while covarying for age and gender. We hypothesized that resting-state networks will be disrupted in TBI and blast populations when compared to controls. We used two different methodologies; the first was a seed-based analysis examining group differences in the correlations from the Posterior Cingulate Cortex (PCC, a key hub within the DMN) to the whole brain. The second analysis used the Yeo Seven Network parcellation to compute correlations between all seven networks to the DMN. We were unable to distinguish any group from controls, suggesting that early differences in functional connectivity are not a robust biomarker of injury.

POSTER SESSION 2

MGH 241, Easel 124
1:00 PM to 2:30 PM

Characterizing Microstructural Changes in Perineuronal Nets in the Presence of Neuroinflammation and Oxidative Stress
Hugo F. (Hugo) Pontes, Senior, Chemical Engineering
CoMotion Mary Gates Innovation Scholar, UW Honors Program, Washington Research Foundation Fellow
Mentor: Elizabeth Nance, Chemical Engineering
Mentor: Mike McKenna, Chemical Engineering
Mentor: Chad Curtis

As the global burden of neurological diseases continues to grow each year, there exists a need for drug delivery vehicles that can overcome barriers specific to the brain. The heterogeneous brain extracellular matrix (ECM) is an understudied barrier to effective therapeutic delivery, particularly in the presence of disease states. We utilize a novel multiple particle tracking (MPT) approach to characterize microstructural changes in perineuronal nets (PNNs), a key structural mediator of plasticity, in the developing brain. Our overarching goal is to develop a combined approach of MPT, statistical analysis using Python-based software packages, immunohistochemistry (IHC), and mRNA expression profiles to monitor changes in PNN structure and function through development and in the presence of neuroinflammation and oxidative stress processes. For this, we cultured 300 μm-thick organotypic whole hemisphere (OWH) brain slices prepared from postnatal day 35 (P35) rats. We treated slices with 100 ng/mL lipopolysaccharide (LPS, induced-inflammation model) or 100mM glutamate (MSG, induced-excitotoxicity model) for 3 h, removed the toxin and fixed slices at 1 h, 6 h, and 24 h after toxin removal. Fixed slices were stained using Wisteria floribunda agglutinin (WFA) and PNN counts were quantified using the ImageJ software package. In LPS and MSG-treated slices, 100-nm particles were added to live slices stained with WFA and MPT was performed in WFA+ regions, followed by statistical analysis of individual nanoparticle trajectories. From the IHC imaging and PNN count quantification, we observed differences in the number and morphology of PNNs present in the MSG and LPS models when com-

pared to healthy controls. Characterizing structural changes in PNNs in living tissue furthers our understanding of the impact of neuroinflammation and oxidative stress on neuronal plasticity, and the subsequent impact on progression of neuropsychiatric diseases.

POSTER SESSION 2

MGH 241, Easel 150

1:00 PM to 2:30 PM

Effect of SS-31 on SOD1KO Model of Sarcopenia

Kevin Andrew Nguyen, Senior, Biology (Physiology)
UW Honors Program
Mentor: David Marcinek, Radiology
Mentor: Matthew Campbell, Radiology

Sarcopenia, or age-related of loss of muscle mass and function, is associated with a decline in quality of life for elderly populations and few effective treatment options. Sarcopenia is linked to mitochondrial dysfunction and elevated mitochondrial oxidant production. We are investigating the role of mitochondrial oxidative stress in sarcopenia using a mitochondrial targeted therapeutic and a mouse model of accelerated sarcopenia. SS-31 is a mitochondrial targeted peptide that associates with cardiolipin, decreases oxidant production, and increases ATP production. Superoxide dismutase 1 knockout (SOD1KO) mice lack superoxide dismutase 1 (an enzyme that converts the oxidant superoxide into hydrogen peroxide and molecular oxygen) resulting in an accelerated sarcopenia phenotype. We are testing whether treatment with SS-31 preserves muscle function in the SOD1KO mice. We hypothesize that improving mitochondrial function with SS-31 treatment will delay the decline in muscle function in the SOD1KO mice. To test this, we are administering SS-31 to SOD1KO mice through surgically-inserted osmotic pumps for 8 weeks between 3 and 5 months of age (the published timeframe for the onset of skeletal muscle decline in SOD1KO mice) and performing in vivo muscle function measurements of the gastrocnemius before pump insertion and monthly after pump insertion for 3 months. We compare muscle functional measurements with histological and biochemical analyses of mouse tissue samples upon euthanasia and determine skeletal muscle fiber type, metabolite and protein concentrations, and muscle fiber respiration and oxidant production. We expect SOD1KO mice with SS-31 to have a lower rate of decline in muscle force production and increased fatigue resistance over time, higher max ATP production, and decreased oxidative stress. The effect of SS-31 on muscle function, mitochondrial quality, and redox homeostasis has exciting potential as a translational therapeutic treatment for human sarcopenia.

POSTER SESSION 2

MGH 241, Easel 123

1:00 PM to 2:30 PM

Characterizing an LPS-Induced Rat Model of Pre-Adolescent Depression

Dorsa Toghani, Senior, Bioengineering
Mary Gates Scholar, UW Honors Program
Mentor: Elizabeth Nance, Chemical Engineering

Depression is a neuropsychiatric disorder with a high rate of recurrence and increased mortality. One in six people experience depression at some point in their life, and the disease burden was over $200 billion in 2013. While little is known about the underlying neurobiological processes, the presence of inflammation in the central nervous system has been observed in those suffering from depression. This inflammation, mediated by microglial activation, astrocytosis, and pro-inflammatory cytokine production is involved in the progression of this disease. Past research has focused on the response of microglia in adults, but there are limited studies on the developmental features. Therefore, using a Sprague-Dawley rat model of lipopolysaccharide (LPS)-induced inflammation, this study aimed to understand the progression of the inflammatory response in the development of depressive-like behavior. We determined a suitable dosing scheme to induce inflammation while minimizing mortality to be an intraperitoneal injection (i.p.) of 0.05 mg/kg LPS on postnatal day (P) 7 and 0.1 mg/kg LPS on P9, P11, and P13. Control animals were injected with saline. The presence of inflammatory response was evaluated at P14, P21, and P35. This study showed that rats exposed perinatally to LPS had an increased number of microglia in the hippocampus as well as a hyper-ramified microglial phenotype in comparison to control animals. Similarly, rats treated with LPS showed decreased expression of anti-inflammatory TGF-β and increased expression of pro-inflammatory cytokines TNF-α and IL-6. LPS treated rats also tended to display more anxiety-related behavior including avoiding the open arms of an elevated-plus maze. These results support that LPS exposure in rats can be used as a model to study the effects of inflammation in the developing brain of rats displaying depressive behavior.

POSTER SESSION 2

MGH 241, Easel 126

1:00 PM to 2:30 PM

Deep Learning-Based Image Analysis to Extract Brain Region Features

Emily Rachel (Emily) Rhodes, Senior, Chemical Engineering
Mentor: Elizabeth Nance, Chemical Engineering
Mentor: Sarah Stansfield, Anthropology, Epidemiology
Mentor: Mike McKenna, Chemical Engineering

Computer vision models are used to help analyze biomedical images for diagnosis and treatment through looking for differences between images by a comparison to a template image. For instance, optical coherence tomography (OCT) is used to diagnose and treat retinal issues. When looking at the brain, injury, cellular uptake and characteristic features vary across regions, therefore images are often segmented into established brain regions to determine how the brain is impacted in a particular study. Current models fail to work in segmenting brain regions because each brain has variation in local microstructure, making it difficult to compare one brain to another. Furthermore, when brains are sliced, the exact location within the brain can be difficult to pinpoint, particularly in regard to depth, because the regions vary slice to slice. Therefore, my research addresses the increasing need for a method of analysis to align and compare images from brain regions across slices from a single brain, and from brain to brain. Using scikit-image analysis tools, I extracted information from cell images and videos of nanoparticles obtained in brain slices and determined trends within various regions. My program extracted cell density, shape, and death, then analyzed the uptake of nanoparticles to determine where a small segment of an image is most likely located within the brain. Iterating over the entire image generated a rough map of the regions within the brain which is refined using mapping descriptions detailed in literature. This research resulted in a systematic program that uses image analysis tools to extract features of defined brain regions. This program allows for quick, accurate and consistent analysis of regional differences of cellular features, nanoparticle distribution, toxicity, and other important measures.

SESSION 2H

MEDICAL IMAGING AND DEVICES

Session Moderator: Eric Seibel, Mechanical Engineering

MGH 251

3:30 PM to 5:15 PM

* Note: Titles in order of presentation.

Optimizing Diffusion Weighted MRI for Non-Contrast Enhanced Breast Cancer Detection

Michaela Del Priore, Senior, Bioengineering
Mentor: Savannah Partridge, Radiology
Mentor: Debosmita Biswas, Radiology

Dynamic-contrast enhanced (DCE) MRI has a very high sensitivity for breast cancer detection. However, the high costs, long scan-times and safety issues associated with injecting gadolinium-based contrast agents prompt the need to explore non-invasive, non-contrast-based diffusion-weighted imaging (DWI) as a possible alternative. DWI reflects the microscopic cellular environment and at high sensitizations (b-values), DWI can highlight malignant breast tissues without the aid of gadolinium. Acquiring images at high b-values increases image distortions and lengthens scan times. By simulating these high b-value images, lesion conspicuity can be increased while minimizing scan time and maintaining image quality. The purpose of this study was to compare lesion conspicuity across b-values and between acquired (aDWI) and computed (cDWI) DWI. Twenty women with invasive breast cancer were enrolled to undergo a research DWI scan. aDWI was acquired at multiple b-values of b=0/100/800/1500/2500 s/mm^2. Apparent diffusion coefficient (ADC) maps were generated and cDWI images were then computed for b-values ranging from b=200-2500s/mm^2 using: S_b = $S_1 00$ e$^{-}\Delta$b*ADC.$Lesioncontrast - to - noiseratio(CNR)wascalculatedforbothaDWIandcDWIateachb - value.CNRmeasuresacrossb - valuesfromcDWIandaDWIwerecon$ $ranktest.Lesionconspicuity, asmeasuredbyCNR, increasedwithinc$ $value, withnosignificantdifferencebetweenaDWIandcDWI.Ourf$ $1100 - 1500s/mm^2$, which is higher than typical diagnostic breast DWI protocols. However, lesion conspicuity likely varies with breast density and other patient and tumor characteristics. Potential advantages of cDWI include shorter scan times and flexibility to retrospectively generate images at any b-value for optimal interpretation, warranting further exploration of the value of this technique for breast imaging.