Undergraduate Research Symposium May 19, 2017 Mary Gates Hall

Online Proceedings

POSTER SESSION 1

MGH 241, Easel 150

11:00 AM to 1:00 PM

Comparison of MRI-CT Registration Algorithms for Evaluating Electrode Placement in Deep Brain Stimulation Experiments

Victor Florian (Victor) Sanchez, Sophomore, Pre-Sciences
Mentor: Swati Rane, Radiology, UW Medical Center
Mentor: Kurt Weaver, Radiology
Mentor: Andrew Ko, Neurological Surgery

Deep brain stimulation or DBS is a medical treatment procedure for Parkinsons patients who have exhausted all medication-related therapy or who have debilitating motor issues. DBS involves placement of electrodes into the brain to stimulate target regions with electrical impulses. Surgeons typically use both CT and MRI scans to help them plan the placement of electrodes. While MRI provides excellent tissue contrast, it cannot be used to assess electrode placement due to the metal in the electrode. CT scans show only bone and metal but no details of the brain tissue. A combination of MRI and CT images is therefore necessary to ascertain that the electrodes are indeed in the predetermined location. There are challenges due to the use of two imaging modalities. The MRI and CT images differ in resolution and do not align with each other. The goal of our project is to apply and compare multiple inter-modal image registration methods to determine the best approach to combine the MRI and CT images. We registered the CT image (which shows the electrodes) to the MRI (which shows the brain tissue) in FSL using mutual information, correlation ratio, or normalized correlation ratio. We also use similar registration algorithms from Advanced Normalization Tools (ANTs) for this purpose. We found the method that works best for patients on a case-by- case basis, and also one that gives the best results in a wide variety of cases. Our preliminary work suggested that the mutual information based registration approach using FSL provides the best registration between images.

POSTER SESSION 1

MGH 241, Easel 151

11:00 AM to 1:00 PM

Cerebrovascular Reserve as a Biomarker for Early Alzheimer's Disease in Elderly Patients

Leonard Daniel Chen, Senior, Bioengineering
Mentor: Swati Rane, Radiology, UW Medical Center
Mentor: Swati Rane, Radiology

Cerebrovascular reserve (CVR) is the dilatory response of blood vessels to match the perfusion needs of the brain. CVR is necessary for regulating oxygen and nutrient transport to maintain normal brain function. Individuals with Alzheimer's disease (AD) often exhibit vascular pathology due to reduced perfusion. We believe that in patients with early AD, CVR can serve as a biomarker for early vascular pathology. Using breath-hold BOLD fMRI, CVR can be measured quantitatively and spatially. Older adult subjects (n = 48, age >65 years) were asked to perform normal paced breathing for 20s followed by a 15s breath-hold. This process was repeated 6 times. MRI data was processed using Python and FSL. Python was used to extract breath-hold signals from the MRI scanner. With FSL, BOLD fMRI data was corrected for motion and baseline drift. The breathing time course was used as a stimulus regressor in FSL FEAT to obtain voxel-wise maps of CVR. The CVR maps were registered to the anatomical T1 image and subsequently to the standard MNI template to obtain region-specific values of CVR. As data processing is ongoing, we have not obtained conclusive results. However, we expect to see in patients with onset of AD, CVR ability is lowered throughout regions of the brain, most notably in the frontal and parietal brain regions. Our preliminary studies in 30 older adults indicate that overall gray matter CVR in healthy older adults was $0.42 \pm 0.13\%$, but was $0.38 \pm 0.16\%$ in individuals with cognitive impairment and at risk for AD. The results of this study will demonstrate the usefulness of cerebrovascular imaging to understand vascular pathology in patients with AD at an early stage, thereby allowing for treatment to begin sooner, and slowing down disease progression.

SESSION 1O

CANCER BIOLOGY

Session Moderator: Hannele Ruohola-Baker, Biochemistry

MGH 389

12:30 PM to 2:15 PM

* Note: Titles in order of presentation.

An Observational Study on Breast Size Metrics for a Seattle Cancer Screening Population

Payton Mark (Payton) Christiano, Senior, Bioengineering
Siying (Lysia) Li, Senior, Informatics: Data Science
Mentor: Larry Pierce, Radiology, UW Medical Center
Mentor: Paul Kinahan, Radiology, UW Medical Center

Current trends in the healthcare industry are focused on providing precision medicine for more individualized patient care. Many researchers are actively designing specialized devices specific to the imaging and care of breasts. However, we are unaware of any comprehensive large-scale studies that analyze population breast sizes that provide design guidelines for such precision medicine machines. In order to fill this knowledge gap, we collected nearly 15,000 mammograms from the Seattle Cancer Care Alliance and built a database of the images and DICOM (Digital Imaging and Communications in Medicine standard) header information. Images which were selected to be analyzed were run through a MATLAB algorithm to extract length and width measurements of each individual breast in the General Electric mammography unit. Around 2,400 images with Cranio-Caudal view, without magnification, and without foreign objects, were run through the MATLAB algorithm. With the measurement results from this algorithm, we studied the statistical distribution of the breast size and shape from this population. The extent of the breasts from the chest wall into the scanner had a mean of 96.19 +/- 29.04 mm , while the width of the breast had a mean of 184.69 +/- 29.00 mm. With the database in place, the next phase of our research was dedicated to analyzing breast density among the population. Women with dense breasts are at higher risk of false negatives in cancer screening and many states require that clinicians notify a woman if she has dense breasts. Nevertheless, there exists the problem of intra- and interobserver variability for judgement of breast density. To address this, some researchers have proposed automated algorithms to quantify breast density. We used our existing database to analyze the variability within these automated algorithms.

POSTER SESSION 2

Balcony, Easel 114

1:00 PM to 2:30 PM

An Organotypic Brain Slice Model of Glutamate Excitotoxicity

Belinda Garana, Senior, Chemical Engineering
Mary Gates Scholar
Mentor: Elizabeth Nance, Chemical Engineering

Less than 3% of therapeutics can cross the blood-brain barrier, and the lack of penetration of therapeutics into the brain is the most cited failure for neurological clinical trials. In order to assess the efficacy of developing therapeutics which have the potential to address these issues, we are working towards establishing a high-throughput organotypic ex vivo brain slice model. We are specifically interested in developing a model that allows us to study and characterize the brain in the presence of glutamate excitotoxicity. Glutamate excitotoxicity is cell death due to an excess of the excitatory neurotransmitter glutamate, and is a common disease hallmark in neurological injury. The slice model we developed consists of cultured newborn rat brain slices to simulate an *in vivo* brain environment. However, in slice form, we have the ability to systematically study key pathophysiological variables, such as exposure to various excitotoxins that induce glutamate excitotoxicity. We use quantitative assessments of cytotoxicity (cell death) through cellular staining and imaging, as well as assays for lactate dehydrogenase (LDH), an enzyme released from the cytoplasm during cell death. We have established percent cytotoxicity profiles for both healthy untreated and maximum death control brain slices, and developed a protocol for testing excitotoxins to simulate glutamate excitotoxicity. With this slice platform, we will be able to compare the efficacy of potential therapeutics based on the decreases in rates of cell death they produce in brain slices with induced glutamate excitotoxicity. This research represents a promising platform to assay behavior, mechanism, and efficacy of therapeutics in development for the treatment of neurological disorders associated with glutamate excitotoxicity.

POSTER SESSION 2

MGH 241, Easel 161

1:00 PM to 2:30 PM

Using the Generalized Additive Model Regression Algorithm to Predict Depression Levels in Individuals with Alzheimer's and Mild Cognitive Impairment

Johnathan Wayne (Johnathan) Hill, Senior, Psychology
Mary Gates Scholar
Mentor: Tara Madhyastha, Radiology

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by decline predominantly in episodic memory. Previous research has demonstrated that individuals with AD suffer from depression at higher rates than healthy individuals. Predicting depression levels in individuals with AD may be important for mental health care preparation as the disease progresses. To predict depression levels, I trained a generalized additive model (GAM) regression algorithm to predict scores on the Geriatric Depression Scale (GDS) using diffusion tensor imaging (DTI) data of fraction anisotropy (FA) means in 15 different regions of interest (ROIs). The GAM regression algorithm is a non-parametric expansion of the linear regression model. Data were gathered from the Alzheimer's Disease Neuroimaging Initiative (ADNI). This data set includes 150 subjects with DTI and GDS scores at the 6-month visit for individuals with AD, early mild cognitive

impairment (EMCI), late mild cognitive impairment (LMCI) and healthy controls. A k-fold cross-validation method was used to split data into testing and training data. After training and testing the data on a GAM regression algorithm, we attempted to predict depression scores from contemporaneous FA data. The accuracy of this algorithm was assessed by calculating the mean-squared error (MSE) of the testing data. The MSE measured how well the GAM regression model formed from the training data fits the testing data. We evaluated sensitivity, specificity and area under the receiver operator curve for depression prediction as a binary outcome. The purpose of this project was largely to gain experience with machine learning. Fitting a predictive model could inform our understanding of how white matter microstructure might relate to depression in AD.

POSTER SESSION 2

MGH 241, Easel 163

1:00 PM to 2:30 PM

Evaluation of a Novel Method for Diffusion Tensor Imaging and Analysis

Sabreena Shanthoshi (Sabreena Rajan) Rajan, Senior, Biochemistry
Jonathan Mark Wolf, Junior, Computer Science
Mentor: Tara Madhyastha, Radiology

The axons in the nervous system are collectively referred to as white matter. White matter forms intricate fiber connections among the brain's grey matter (neurons). These connections change with development, learning, and disease, and therefore are of interest to several medical researchers. Tract-Based Spatial Statistics (TBSS) is an analysis technique which is used to analyze white matter integrity. Currently, this is the best existing method to align and analyze white matter. However, we are creating and evaluating an improved method to more accurately measure changes to integrity. Diffusion Tensor Imaging (DTI) Voxel Based Morphometry (DTIVBM) is a technique that we are developing which allows us to compare white matter statistics by using nonlinear registration to align the DTI image to a structural image and then a standard template. We are comparing several variations of DTIVBM with the established method of TBSS. We are using four different datasets, three of which contain adult brains ranging from ages 18-35, and one containing preteen/teen brains ranging from ages 11-15. One of the datasets also contains a mixture of normal brains and brains affected by neurodegenerative disease. Each subject has two separate brain images taken within a month's gap. By running both the DTIVBM scripts and TBSS scripts on these brain images, we will be able to determine which method is more reliable, as measured using an Intra-Class Correlation (ICC) statistic. We are currently in the process of gathering the results, but we expect to see that DTIVBM will have higher reliability on most datasets than TBSS over a wider range of white matter. If this is true, we would have demonstrated a potentially better method to analyze white matter changes through aging and development, which will require fewer people and allow us to see changes in more of the brain.

POSTER SESSION 2

MGH 241, Easel 162

1:00 PM to 2:30 PM

Analysis of Hippocampal-Dependent Cognition in Alzheimer's Disease

Briana Eugene Lee, Senior, Biochemistry
Mentor: Tara Madhyastha, Radiology

Alzheimer's disease (AD) is the most prominent cause of dementia worldwide, affecting up to 5.3 million elderly Americans. AD pathology includes decreased neuronal count and synaptic connections, intracellular pathology and increased affinity for neurofibrillary tangles resulting in cognitive deterioration. The hippocampus is known to be particularly vulnerable and is an early structural biomarker of AD. Our aim is to investigate the longitudinal relationships between hippocampal volume and memory performance using neuroimaging data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. The ADNI database contains biomarker, neuroimaging, cognitive, and behavioral data from hundreds of elderly individuals, divided into groups including normal/normal aging (CN), Alzheimer's Disease (AD), Early Mild Cognitive Impairment (EMCI), and Late Mild Cognitive Impairment (LMCI). Cerebrospinal fluid biomarkers are a "gold standard" for detecting the presence of amyloid and tau pathology. Neuroimaging methods include amyloid PET tracers (i.e. F-18 florbetapir), which detects amyloid beta plaques and FDG-PET imaging which measures metabolic activity within the brain. Both techniques reflect neurodegeneration and synaptic dysfunction. Structural MRI imaging is used to assess neuroanatomy as a measure of brain atrophy and changes in neuronal density. Cognitive assessment data quantifies the extent of memory loss and general cognitive decline. Using the R programming language, we will conduct longitudinal analyses of neuroimaging analyses to examine the relationship between cognitive, structural and metabolic neuroimaging variables across different diagnostic groups over time. This initial investigation is preparation for learning longitudinal methods that will later be applied to physiological measures within the entire brain. Our hypothesis is that a decrease in hippocampal volume will be less correlated to decline in memory in CN than in other groups. If our hypothesis is correct, it suggests that compensatory mechanisms preserve cognition in early stages of AD, which we can explore using subsequent extended analyses of functional connectivity.

POSTER SESSION 3

Balcony, Easel 115

2:30 PM to 4:00 PM

The Relationship between Social Dysfunction and Internalizing Behavior in Children with Autism Spectrum Disorder

Madelyn Lehualani (Maddy) Mc Keague, Senior, Biology (Molecular, Cellular & Developmental), Biochemistry
Mentor: Francisco Velasquez, Radiology, University of Washington Medical Center

Autism spectrum disorder (ASD) is characterized by deficits in social communication, repetitive patterns of behavior, and sensory sensitivities. Notably, studies have found that greater ASD severity is associated with lower levels of anxiety and depression. This finding raises the question as to which of these defining ASD characteristics influences internalizing behaviors. We explored the influence of social communication and interaction (SCI) on internalizing behavior symptoms between children with ASD and two comparison groups: typically developing (TD) children and children with sensory processing challenges (SPC). It was hypothesized that children with ASD would show greater levels of internalizing behavior symptoms than both the TD and SPC groups, and that social dysfunction would have a greater influence on internalizing behavior in children with ASD than in our comparison groups. Analyses of variance (ANOVA) were conducted to test for group differences in the relationship between internalizing behavior scores and social subscales from the Vineland and Social Responsiveness Scale surveys. An overall group difference in internalizing behavior symptoms $F(2, 42)=21.46$, $p < 0.001$ was found. However, a follow-up t-test did not yield differences between symptoms in children with ASD and SPC $t(25)=1.03$, $p=0.793$. We then ran a multiple regression to test for group differences in the effect of SCI on internalizing behaviors. We found a significant group difference in the relationship between SCI on internalizing behaviors, significantly explained by the slope of the ASD group, $R2 =.495$, $t(39)=2.988$ $p =.005$. These results suggest that while children with ASD and SPC show similar rates of social deficits and internalizing behaviors, social dysfunction contributes to internalizing behaviors significantly more in children with ASD than children with SPC. This finding indicates that in children with ASD, social dysfunction may be a contributing factor to internalizing behaviors and consequently an important target for intervention.

POSTER SESSION 4

Balcony, Easel 107

4:00 PM to 6:00 PM

Relationship between Regional Brain Chemistry and IQ in Autism Spectrum Disorder

Nicholas (Nick) Wapstra, Senior, Biochemistry
UW Honors Program
Mentor: Neva Corrigan, Radiology
Mentor: Natalia Kleinhans, Radiology

Numerous imaging studies have reported brain chemical alterations in children with autism spectrum disorder (ASD). Neurochemical concentrations have been linked to specific cognitive abilities and behaviors in both typical and atypical populations. This preliminary study investigates the relationship between neurochemical profiles in high-functioning children between 8 and 12 years of age with ASD (n = 17) and typically developing (TD) children (n = 21) in relation to IQ as measured by the Wechsler Abbreviated Scale of Intelligence (WASI). All data were collected as part of an ongoing study. Cognitive, behavioral, and diagnostic evaluations were performed by clinical psychologists at the UW Autism Center. Concentrations of N-acetylaspartate, choline, creatine, and glutamate in the left cerebellum and left amygdala were measured using single-voxel proton magnetic resonance spectroscopy (1H-MRS) on a 3T MR system. Significant positive correlations between choline concentration and Performance ($p<0.01$), Verbal ($p<0.05$), and Full Scale ($p<0.01$) IQ were found in the ASD sample in the amygdala, and between choline concentration and Performance IQ ($p<0.01$) in the cerebellum. No significant correlations were found between brain metabolites and IQ scores in the TD sample, or between other metabolites and WASI IQ scores in the ASD sample. Additionally, there were no significant group differences in metabolite concentrations between the ASD and TD groups. Choline is a precursor to the neurotransmitter acetylcholine, which plays an important role in memory, attention, and cognitive flexibility. These preliminary findings suggest that small differences in brain choline concentrations may have a larger impact on cognition in children with ASD than in TD children.