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 Levendovszky, 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 Levendovszky, 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.

POSTER SESSION 3

MGH 241, Easel 155

2:30 PM to 4:00 PM

Heterogeneity of Risk across Non-Vascular Risk Factors for Specific Cognitively-Defined Alzheimer's Disease Subgroups

Julia Bauman, Senior, Neurobiology
Mary Gates Scholar
Mentor: Paul Crane, Medicine

Preliminary work has revealed genetic heterogeneity among Alzheimer's disease (AD) subtypes defined by cognitive domain-specific impairments. There are currently no reports of risk factor associations for these AD subgroups. We used cognitive data from 825 Adult Changes in Thought (ACT) participants at the time they were identified with probable or possible AD to generate scores for memory, executive functioning/attention, language, and visuospatial ability. We determined individual mean scores across all domains, and identified specific impairments as >0.75 SD below each individual's mean domain score. Depressive symptom severity was measured with the CES-D, and study staff collected self-reported data on traumatic brain injury (TBI) exposure. We used multinomial logistic regression with the "no prominent domain group" designated as the reference category. We determined risk ratios for depression and TBI for each subgroup vs. the no prominent domain subgroup, and tested significance of any heterogeneity with an omnibus test. We controlled for age, sex, APOE genotype, and years of education. Education's role as a risk factor varied across the five cognitively-defined AD subgroups (omnibus p=0.04). Education predicted development of memory prominent AD rather than AD with no prominent domain (risk ratio [RR] = 1.08 per year of education, 95% confidence interval (CI) 1.00, 1.16, p=0.05; omnibus p=0.04). Depression also varied across AD subgroups (omnibus p = 0.04). Higher CESD scores were associated with lower risk of developing memory prominent AD compared to no prominent domain AD (RR = 0.93 per point on the CESD, 95% CI 0.88, 0.98, p=0.01). We did not find differences in risk associated with TBI. Cognitively-defined AD subtypes show heterogeneity in their associations with depressive symptoms and education. It is possible that these risk factors are associated with biological differences across subgroups.

POSTER SESSION 3

MGH 241, Easel 156

2:30 PM to 4:00 PM

Differential Vascular Risk Factors for Cognitively-Defined Alzheimer's Disease Subgroups

Mack Paller Moore, Senior, Biology (Molecular, Cellular & Developmental)
Mentor: Paul Crane, Medicine

Alzheimer's Disease (AD) is a debilitating neurodegenerative disease that currently affects over 5 million Americans. We have previously demonstrated genetic and neuropathology-based variation across cognitively-defined AD subgroups. Here we sought to determine whether patterns of vascular risk factors differed across cognitively defined subgroups. We used data from the Seattle-based Adult Changes in Thought (ACT) prospective cohort study of individuals age 65+ and dementia-free at enrollment. ACT follows people at 2-year intervals to identify incident dementia and AD. We used cognitive data at the time of AD diagnosis to determine scores for memory, visuospatial abilities, language, and executive functioning. We used these scores to determine each individual's average cognition and then domain-specific deficits below that individual average. We used these data to define six groups: no prominent domain, memory-, visuospatial-, language-, or executive functioning-prominent. We evaluated risk factors for these six groups from self-reported medical conditions including diabetes, stroke, and hypertension, and diagnosed atrial fibrillation or coronary artery disease. We used multinomial logistic regression models with the no prominent domain group as the reference. To account for multiple comparisons, we present tests of the null that each risk factor is unrelated to each subgroup, and an omnibus test of the association between each risk factor and any subgroup. Of 825 cases, nearly half had no prominent domain, a few had multiple prominent domains, and a single domain was prominent for the remainder. Memory-prominent domain was more common in people with diabetes and executive functioning-prominent was less common, although the omnibus test did not reach statistical significance (p=0.08). Despite low statistical power due to small group sizes, our results suggest possible differences in risk associated with diabetes. Subsequent work will refine these investigations using medications and evaluating glucose levels over time. These results support additional efforts to further understand cognitively-defined AD subgroups

POSTER SESSION 4

MGH 206, Easel 177

4:00 PM to 6:00 PM

Microfluidic Yeast Replicative Lifespan

Toby Nathan Ven, Junior, Bioengineering
Mentor: Kenneth Chen, Genome Sciences
Mentor: Matthew Crane, Pathology

MSN2 is an environmental stress response transcription factor that is activated in yeast by multiple different stresses—e.g. glucose deprivation, heat, oxidative stress, misfolded proteins among many others—and in turn activates a collection of downstream transcriptional programs. Interestingly, while MSN2 becomes increasingly activated with age, deletion of MSN2 increases the replicative lifespan of the budding yeast. We show that in a glucose-rich environment, MSN2 misreads the environment and drives a pathological glucose starvation response that limits lifespan. Our experiments are

facilitated by a novel budget microfluidic/microscopy method rather than the golden standard of microdissection. This innovative system analyzes data through time-lapse images to develop replicative lifespan curves rather than picking off daughter cells with a needle. Microfluidics drastically increases the throughput of experiments and allows for whole-lifespan monitoring of aging yeast cells. The system allows us to efficiently further the research of MSN2 and other transcription factors so that we can potentially translate this to other complex organisms that have similar types of transcription.