University of Victoria | Graduate Studies

Notice of the Final Oral Examination
for the Degree of Master of Science

of

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BSc (McGill University, 2015)

"Resting-State BOLD Variability in Alzheimer's Disease: A Marker of Cognitive Decline or Cerebrovascular Status?"

Department of Psychology

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9:00 A.M.
Cornett Building
Room A228

Supervisory Committee:
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Abstract

Background: Alzheimer's disease (AD) is a neurodegenerative disorder for which there is presently no cure. As a result, there is a critical need to improve upon early detection methods through the identification of ideally non-invasive biomarkers, such as functional magnetic resonance imaging (fMRI). Recently, novel approaches to the analysis of resting-state fMRI data have been developed that focus on the moment-to-moment variability in the blood oxygen level dependent (BOLD) signal. However, the findings on BOLD signal variability have thus far been equivocal, with some findings showing decreased BOLD variability with age and cognitive decline, and others suggesting that increased BOLD fluctuations may serve as a physiological signal reflecting underlying cerebrovascular challenges. Given the paucity of research in this area, the objective of the current study was to investigate BOLD variability as a novel early biomarker of AD and its associated psychophysiological correlates.

Method: Neuroimaging and cognitive data were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) 2 database from 19 participants with AD (mean age = 72.7 ± 6.5) and 19 similarly-aged controls (mean age = 74.7 ± 6.9). All analysis steps were performed using tools within the Functional MRI of the Brain Software Library (FSL). For each participant, a map of BOLD signal variability (SDBOLD) was computed as the standard deviation of the BOLD timeseries at each voxel within both grey and white matter regions. Firstly, group comparisons were performed to examine global differences in resting state SDBOLD in AD versus healthy controls. Correlations were then examined between participant SDBOLD maps and (1) ADNI-derived composite scores of memory and executive function and (2) neuroimaging markers of cerebrovascular status (total white matter hyperintensity [WMH] burden, as computed from FLAIR scans).

Results: Between-group comparisons revealed significant ($p < 0.05$) increases in SDBOLD in patients with AD relative to healthy controls in right-lateralized grey and white matter frontal regions, including the superior frontal and precentral gyri, and widespread regions of the corona radiata. Due to the novelty of the current study, secondary analyses investigating the association between SDBOLD and psychophysiological correlates were examined with a more liberal threshold ($p < 0.1$). Results revealed that lower memory scores were associated with greater SDBOLD in the medial temporal lobe and adjacent structures in the healthy control group. Conversely, higher total WMH burden was associated with greater SDBOLD in highly localized grey and white matter regions in the healthy control group. No association between SDBOLD and cognitive or cerebrovascular measures was identified in the AD group.

Conclusion: The current study provides proof of concept that a novel resting state fMRI analysis technique that is non-invasive, easily accessible, and clinically compatible, can differentiate patients with AD from healthy controls. To further explore the potential of SDBOLD as a biomarker of AD, additional studies in larger, longitudinal samples are needed to better understand the changes in SDBOLD that characterize earlier stages of disease progression and their underlying psychophysiological correlates.