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

of

LISA OHLHAUSER

BSc (University of British Columbia, 2014)

“Microstructural Changes in White Matter in Prodromal and Clinical Parkinson’s Disease”

Department of Psychology

Friday, July 27, 2018
9:00 a.m.
Cornett Building
Room A228

Supervisory Committee:
Dr. Jodie Gawryluk, Department of Psychology, University of Victoria (Supervisor)
Dr. Colette Smart, Department of Psychology, UVic (Member)

External Examiner:
Dr. Sandra Hundza, School of Exercise Science, Physical & Health Education, UVic

Chair of Oral Examination:
Dr. Andre Smith, Department of Sociology, UVic

Dr. Stephen V. Evans, Acting Dean, Faculty of Graduate Studies
Abstract

Background: Parkinson’s disease (PD) is a neurodegenerative disorder that causes distinct motor impairments (i.e., resting tremor, bradykinesia, rigidity, postural instability) and affects approximately one percent of the global population over the age of 60 years. Currently, there is no cure and diagnosis remain challenging due to the lack of well validated biomarkers. Prodromal PD is a phase that predates the onset of motor symptoms but includes brain changes and nonmotor symptoms, such as rapid eye movement sleep behaviour disorder (RBD) and hyposmia. Diffusion tensor imaging (DTI) provides non-invasively acquired metrics of microstructural changes in white matter and subcortical tissue and has potential as a biomarker for PD. To date, most DTI studies have focused on the clinical phase of PD. Investigating potential biomarkers in the prodromal phase of the disease is key for early diagnosis and treatment. This study had two primary objectives: (1) to investigate how white matter microstructure changes in different phases of PD progression, and (2) to investigate how sleep and motor symptoms relate to white matter microstructure in different phases of PD.

Methods: All study data was downloaded from the Parkinson’s Progression Markers Initiative database. Subjects included 21 healthy controls (mean age=68.17±4.69; 6 female), 20 individuals with prodromal PD (14 with RBD and 6 with hyposmia) (mean age=67.95±5.90; 6 female), and 17 individuals with clinical PD (mean age=67.69±5.97; 6 female) (at baseline and one-year later). Tract based spatial statistics were used to determine between group differences in fractional anisotropy (FA) and mean diffusivity (MD) at the whole brain level and in a region of interest (ROI), the substantia nigra. The relationship between sleep or motor symptoms and DTI metrics were investigated within each group.

Results: There were no differences between the groups in age, education level, or cognitive scores. Clinical PD had significantly higher motor symptoms than healthy controls or prodromal PD, and this significantly increased from baseline to one-year later. Between group comparisons showed increased MD (reflecting increased neurodegeneration) in prodromal PD relative to clinical PD (both at baseline and one year later), while there were no group differences between either prodromal or clinical PD and healthy controls at the whole brain level or within the ROI. Increased motor symptoms were associated with neurodegeneration (i.e., decreased FA and increased MD) for healthy controls, while increased sleep symptoms were associated with decreased MD for clinical PD.

Conclusion: This was the first to study of white matter microstructure differences in a mixed prodromal PD group relative to clinical PD. The detected early brain changes may support an RBD subtype of PD with overall different pattern of neurodegeneration. However, these results are preliminary and future studies must be conducted to clarify and expand upon the microstructural differences between prodromal and clinical PD, ideally with longitudinal follow-up.

Keywords: Parkinson’s disease, diffusion tensor imaging, prodromal, biomarker, rapid eye movement sleep behaviour disorder