Doctoral Thesis Candidate

Project title: Cognitive phenotypes in Parkinson's disease based on multimodal neuroimaging pattern identification (CogPaT)

Summary of the project:
Parkinson's disease (PD), the second most frequent neurodegenerative disease, is associated with motor and non-motor features. Among its non-motor manifestations, cognitive impairment is a major cause of disability. However, there is ample heterogeneity in the profiles, severity, and progression rates of cognitive deficits in PD, suggesting the existence of disease subtypes. Identification of subtypes is critical for defining targets for treatments that potentially improve the prognosis of PD. This can be especially relevant in the case of newly-diagnosed PD patients. To determine the existence of subtypes without a priori hypotheses, methodological approaches such as cluster analysis can be used. Cluster analysis, a type of unsupervised learning algorithm, can be used to divide patients based on potentially relevant parameters.

Using a range of motor and non-motor clinical features, previous studies have revealed the existence of PD subtypes with different prognoses. Evidence regarding the potential of neuroimaging for classifying PD patients into subtypes, however, is scarce. In a recent study performed by our group, we used structural magnetic resonance imaging (MRI) and cluster analysis to find subtypes of patients based on the pattern of cortical degeneration (Uribe et al., Movement Disorders, 2016). We identified three patterns: one with fronto-temporo-parietal cortical thinning, associated with worse cognitive performance; a pattern with prefrontal and occipital cortical thinning associated with younger age at PD onset; and a pattern with no detectable cortical atrophy. These findings provide evidence that PD patients can be classified into clinically-relevant subtypes based on patterns identified through structural MRI. To our knowledge, however, the potential of other neuroimaging modalities has not been addressed.

The objective of this proposal is to use data-driven cluster analysis techniques to provide a thorough characterization of PD subtypes based on unbiased, objective, and replicable multimodal MRI measures. MRI modalities will include high-resolution structural brain images; diffusion-weighted images to assess the microstructural properties of the cerebral white matter and measures of structural connectivity; and resting-state functional images to characterize whole-brain functional connectivity.