Altered Topological Properties of Functional Connectome in Early-Stage PD Revealed by Graph Theoretical Analysis

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Purpose: Parkinson's disease (PD) is a progressive neurodegenerative disease manifesting principally as resting tremor, rigidity, kinesis and postural instability. Previous resting-state fMRI studies of PD have primarily focused on region of interest methods which are very investigator-independent. And the stage of the PD patients was vague. Recently there have been emerging studies employing graph theoretical approaches to investigate the brain connectome. Therefore, our study aims to explore the topological properties of whole-brain functional connectome of early-stage PD.

Methods: The resting state data were obtained from 53 early-stage PD patients and 66 age- and sex-matched healthy controls. Their brain images were segmented into 90 regions using AAL atlas. Functional connectivity between these regions was established using partial correlation coefficient. Whole-brain functional connectome was constructed by thresholding the resultant partial correlation matrix (90*90). Graph theory analysis was then employed to examine group specific topological characteristics of the functional connectomes. Nonparametric permutation test was used for multiple comparison correction. In addition, we investigated the relationships between topological properties and Unified PD Rating Scale part III (UPDRS-3) which was used to assess the motor disability.

Results: Both the PD and control group exhibit small-world topology in the functional connectomes (Figure 1). However, the PD group showed significant decrease in clustering coefficient (C_p), normalized characteristic path length (λ), local efficiency (E_{loc}) and global efficiency (E_{glob}), and increase in the characteristic path length (L_p) (Figure 2). Besides, these connectomes exhibited decreased nodal centralities in the right precentral gyrus, supplementary motor area, inferior frontal gurus and posterior cingulate gyrus, left middle frontal gyrus, heschl gyrus and precuneus, bilateral postcentral gyrus, rolandic operculum, gyrus rectus, fusiform gyrus, superior temporal gyrus, supramarginal gyrus and angular gyrus (Figure 3A). Furthermore, the nodal efficiency of left postcentral gyrus was found negatively correlated with the UPDRS-3 in PD patients (Figure 3B).

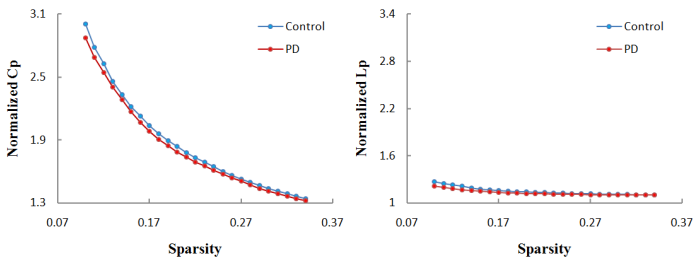

Figure 1. The key small-world parameters of functional connectome as a function of sparsity threshold. Both PD and controls showed normalized Cp larger than 1 and normalized Lp approximately equal to 1, indicating both groups exhibited a small world topology (P<0.05, uncorrected).

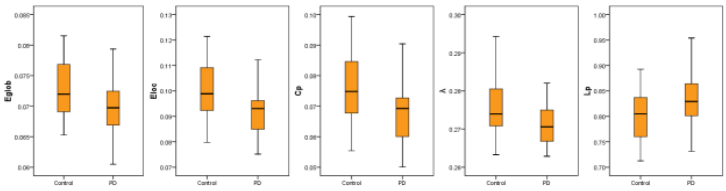

Figure 2. Differences in global topological properties of brain functional connectome between PD patients and controls (P<0.05, uncorrected).

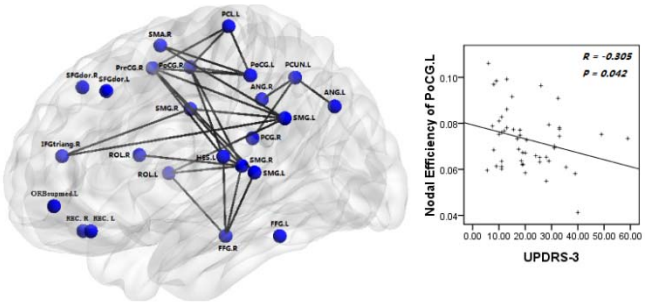

Figure 3. (A) Significantly decreased nodal centralities of brain functional connectome in PD patients relative to controls (P<0.05, FDR corrected). These connections formed a single connected network with 18 nodes and 27 connections, which was significantly (P<0.05, FDR corrected) decreased in the patients. (B) A scatter plot of nodal efficiency of the left postcentral gyrus against UPDRS-3 scores in PD patients.

Discussion: This study examined the topological architecture of the functional connectome in early-stage PD patients. The results revealed that individuals with PD had a decreased E_{loc} and E_{glob}, implying a disturbance in the normal local specialization and global integration of the whole-brain functional connectomes. Our findings (decreased C_p and increased L_p) of loss of small-world characteristics suggested PD may have less optimized network organizations, providing insights into the brain dysfunction associated with this disease. In addition, the most brain regions with decreased nodal centralities in PD were the components of the sensor-motor related, prefrontal and parietal cortex. And only decreased functional connectomes within these areas were found in this cohort. The observed functional connectomes in the prefrontal and parietal cortex might be related to non-motor symptoms typical for PD patients such as executive dysfunction, and attention problems. Furthermore, the nodal efficiency of the left postcentral gyrus was negatively correlated with the UPDRS-3 in PD patients, demonstrating that the postcentral gyrus may be associated with underlying pathology of some motor manifestation in PD.

Conclusion: Our findings offers topological insight into the early functional integration of neural networks in PD, and may be used as a potential biomarker to detect brain abnormalities in early-stage PD.