

Amplitude of low frequency fluctuation of BOLD signal and resting-state functional connectivity analysis of brains of Parkinson's disease

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Introduction

Parkinson's disease (PD) is a slowly progressive disorder, characterized by progressive degeneration of dopaminergic neurons in the substantia nigra. Previous studies revealed that PD is associated with abnormal activity in spatially distributed neural systems mediating the motor and cognitive manifestations of this disorder by PET or SPECT [1]. The present study aims to apply resting state fMRI to examine both regional cerebral function and functional integration in patients with PD.

Method

Eleven right handed PD patients (6 males and 5 females, age: 51.5 ± 11.9 years) and ten healthy controls were recruited in this study. Patients were enrolled based on their clinical inclusion requirements. The motor score of patients was determined in the "off" state (after 12h without any symptomatic antiparkinsonian medication) to avoid confounding effects on the clinical examination. Clinical examination included the motor score of the Unified Parkinson's Disease Rating Scale (UPDRS-III) which was 31.0 ± 9.5 (mean \pm SD). All subjects were scanned using a gradient-echo echo-planar imaging (EPI) sequence on a 3T MR imaging system (EXCITE, General Electric, Milwaukee, USA). Amplitude of low-frequency (0.01–0.8 Hz) fluctuations (ALFF) of the blood oxygenation level-dependent (BOLD) signal, which is thought to reflect spontaneous neural activity [2], was used to characterize regional functional alteration. The amplitude of LFF (ALFF) was calculated using REST software. Voxel based analysis of the ALFF maps between control and patient groups was performed with two sample t-test using the SPM2. The corresponding ALFF were subsequently extracted from all patients and input into SPSS13.0 along with UPDRS-III scores. The Pearson correlation coefficient was used in exploratory analyses to estimate the relationships between the averaged ALFF values in these regions of interest and UPDRS-III scores with a statistical threshold of $P < 0.05$ (two tailed).

Subsequently, using the ROI areas of bilateral caudate nucleus and putamen, a method based on the seed-voxel correlation approach was used to examine the relationship of the symptoms and the functional connectivity. This approach included following steps: (1) Obtaining seed reference by averaging the fMRI time series of all voxels within the areas with ALFF alteration; (2) Temporally bandpass filtering (0.01–0.08 Hz) for each time series; (3) Correlation analysis of the seed reference with the rest of the brain in a voxel-wise manner using the realigned images, and subsequently individual relativity value (r-value) map was produced, and (4) the correlation coefficients were transformed to z-values using the Fisher r-to-z transformation to improve normality prior to averaging data across subjects. Individual z-values in each voxel were compared across groups using a two-sample t-test in SPM2 with statistical inferences being made at $p < 0.05$ (after correction for multiple comparisons).

Results

Compared to controls, the PD group showed significantly decreased ALFF in left inferior temporal gyrus ($p < 0.05$ after correction for multiple comparisons) and increases in ALFF in bilateral putamen, insula and left caudate nucleus were increased ($P < 0.001$, uncorrected) (Figure 1). Significant positive correlations were observed between ALFF values in the left inferior temporal gyrus and UPDRS-III scores ($p < 0.05$). Meanwhile, the seed-voxel correlation revealed that the functional connectivity between. However, comparison of the two groups of functional connectivity revealed that patients had decreased functional connectivity within a distributed network that included the bilateral putamen, caudate, left substantia nigra, right insula, frontal lobe cortex ($p < 0.05$ after correction for multiple comparisons) (figure 2).

Discussion

Current study demonstrates the altered brain activity and functional connectivity in patients with PD. These findings suggest that the involved network may have utility as an objective biomarker of functional alteration in PD patients. In addition, resting state fMRI could provide unique insights into the mechanism underlying abnormal clinical manifestation in PD. Further work of longitudinal study in PD patients may provide further insight into how alterations in brain function evolve over time.

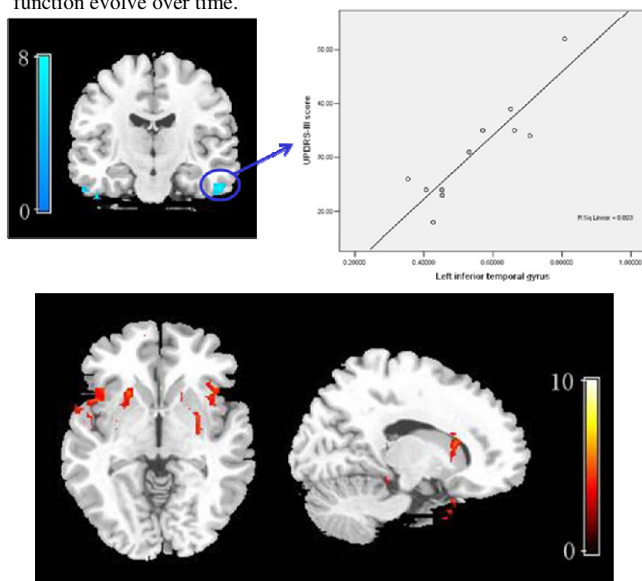


Figure 1. Regions showing increased ALFF in PD patients (red areas) compared to controls ($p < 0.05$ corrected). Scatter plot figures show significant positive correlations between regional ALFF (the structure in blue circle) and the UPDRS-III scores in patient group ($p < 0.05$).

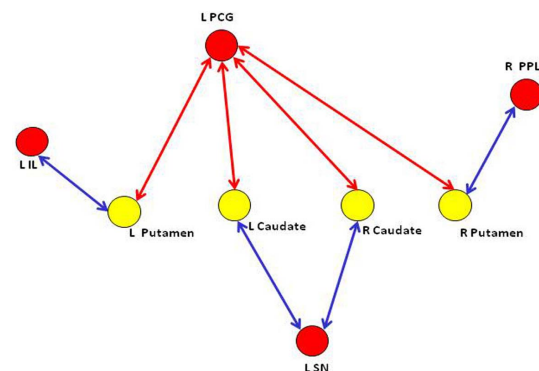


Figure 2. Sketch map shows decreased (blue arrows) and increased (red arrows) functional connectivity involving areas with basal ganglia (yellow circles) and other cortical/sub-cortical areas (red circles) in PD patients compared to control group ($p < 0.05$, corrected for multiple comparisons). R: right, L: left, PCG: precentral gyrus, IL: insula lobe, PPL: pre-frontal lobe, SN: substantia nigra

Reference

1. Huang C., et al., *Changes in network activity with the progression of Parkinson's disease*. Brain, 2007. **130**: p. 1834-1846.
2. Cordes D., et al., *Frequencies contributing to functional connectivity in the cerebral cortex in "resting-state" data*. Am J Neuroradiol. 2001. **22**(7): p. 1326-33.