Altered functional network in different stage of patients with Parkinson's disease: evidence from resting-state fMRI

Qin Chen[1], Pinglei Pan[1], Wei Song[1], Hehan Tang[2], Dong Zhou[1], Qiyong Gong[2], and Huifang Shang[1]

[1]Department of Neurology, West China Hospital of Sichuan University, Chengdu, Sichuan, China, People's Republic of, [2]Department of Radiology, West China Hospital of Sichuan University, Chengdu, Sichuan, China, People's Republic of

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, SPECT [1]. Recent studies have applied functional MRI to investigate the altered brain function on PD patients[2,3], but it still remains unclear about how the neural network changes in different stages of PD. The present study aims to examine alterations pattern of regional and neural network function in PD patients in different stages by using resting state fMRI.

Method

Thirty-six right handed PD patients (23 males and 13 females, age: 56.3±10.8 years) and 27 healthy controls were recruited in this study. Patients were enrolled based on their clinical inclusion requirements. The PD patients were divided into two subgroups: early stage PD (ePD, H&Y stage I or II) and late stage PD (lPD, H&Y stage III to V). 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) and Mini-Mental State scores (MMSE) (Table 1). 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 each patient group were performed with ANOVA using the SPM8 ($P < 0.05$, FWE corrected). The corresponding ALFF from altered brain regions were subsequently extracted 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).

Results

Compared with control group, ePD patients had significantly increased ALFF in bilateral post cingulate cortex (PCC), right insula, right inferior frontal lobe, right inferior parietal gyrus and right supramarginal gyrus, while decreased ALFF was observed in bilateral cuneus and occipital lobe. Meanwhile, lPD patients had significantly increased ALFF in bilateral post cingulate cortex, right fusiform gyrus and cerebellum, while decreased ALFF was also observed bilateral occipital lobe. Between the two patient groups, ePD patient had increased ALFF in right middle frontal gyrus, with decreased ALFF in left postcentral gyrus and right temporal gyrus. (Figure 1)

ALFF values in right fusiform, cerebellum, inferior temporal gyrus had significantly positive correlation with UPDRS-III, while ALFF values in right middle frontal gyrus had significantly negative correlation with UPDRS-III. The correlations between UPDRS-III scores and ALFF values in other regions were not significant.

Discussion

Current study demonstrated for the first time that the different brain function alteration patterns in PD patients with different stages, including a complex neural network with hyperactivity and decreased neural function. Particularly, it dynamically indicate that a complementary hyperactivity neural network in the early stage, but shifted to a normal level or even decreased function in the late stage in patients with PD.

Table 1 Demographic information for Parkinson patients and Healthy controls

	ePD	lPD	Controls
No.	14	22	27
Sex (F/M)	7/7	6/16	12/15
Age(years)	50.2±9.6	52.4±12.7	53+9.9
UPDRS-III	27±12.8	43.6±14.3	--
Disease Duration (years)	3.6±2.2	5.5±5.1	--
MMSE	28.1+2.9	26.3±3.6	--

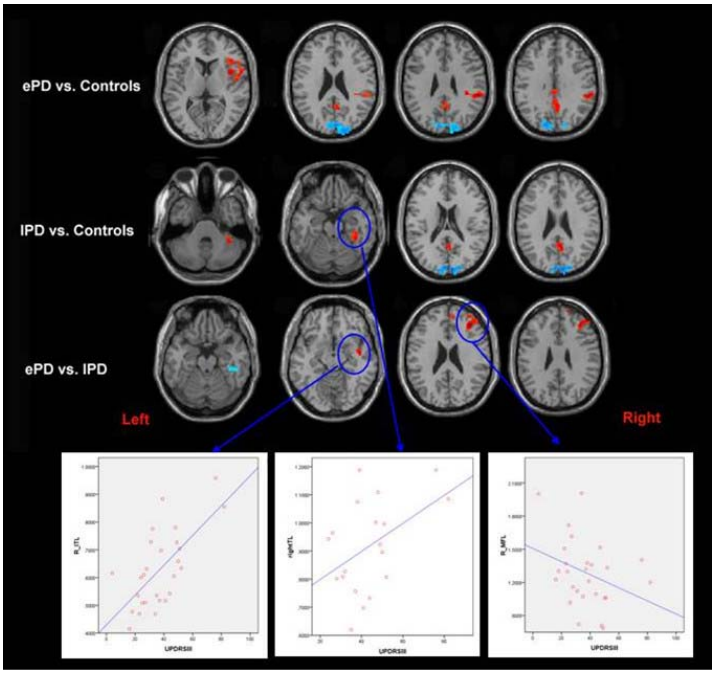

Figure 1 Regions showing increased ALFF (red areas) and decreased ALFF (blue areas) compared between each patient group and controls ($p<0.05$ corrected). Scatter plot figures show significant positive and negative correlations between regional ALFF (the structure in blue circle) and the Unified Parkinson's Disease Rating Scale (UPDRS-III) scores in the patient group ($p<0.05$). ePD: early stage PD; lPD: late stage PD.

Reference

1.Dodel R., et al., Mov Disord, 2010. **25**(1): p.97-107.
2. Skidmore FM., et al.,Neuroimage. 2011.
3. MacDonald PA., et al, Brain, 2011. **134**(Pt 5):1447-63