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The cortical thickness correlates of clinical manifestations in the mid-stage sporadic Parkinson's disease

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HIGHLIGHTS

- Correlation between UPDRS–I and right Frontal-Sup-Orb, Rectus.
- Correlation between DB and right Frontal-Sup-Orb, Frontal-Inf-Orb.
- Correlation between SDS and right Frontal-Sup-Orb, Frontal-Mid-Orb.
- Correlation between SDS and right Rectus, Cingulum-Ant.
- Frontal Orb, rectus, cingulum thinning was pathology of some sPD manifestations.

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ABSTRACT

The cortical thickness has gained an extensive attention as a pathological alteration of sporadic Parkinson's disease (sPD), the alteration of pathological cortical thickness may distinctly contribute to the consistent clinical manifestations. Therefore, we investigated the cortical thickness correlates of clinical manifestations in the mid-stage sPD from the Han population of Chinese mainland (HPCM). A sample of 67 mid-stage sPD patients and 35 matched controls from HPCM were performed a corticometry of magnetic resonance imaging (MRI) and the assessment of clinical manifestations including the demographic and disease-related characteristics, and underwent the final analysis of the cortical thickness correlates with the clinical manifestations. In our result, we demonstrated that no significant differences in the demographic characteristics were found among the two groups. The tests of clinical disease-related characteristics demonstrated that the significant differences in the Hoehn and Yahr scale, the UPDRS Part I–IV, the symptom-dominant side (right/left/double), the tremor subscoree off (e), the tremor subscoref on (f), Webster, MMSE, HDS-R, DF, DB, SVFT, SDS, HAMD17, HAMD 24, CDT, CDR, LEDD and PDSI were observed between the mid-stage sPD patients and the controls. The analysis about the cortical thickness correlates with the clinical manifestations revealed that a significant correlation between UPDRS–I and Frontal-Sup-Orb-R and Rectus-R; DB and Frontal-Sup-Orb-R and Frontal-Inf-Orb-R; SDS and Frontal-Sup-Orb-R, Frontal-Mid-Orb-R, Rectus-R and Cingulum-Ant-R respectively in the mid-stage sPD patients from HPCM. Our data showed that the cortical thinning in the right frontal Orb, rectus and cingulum were the pathological base of some clinical manifestations including the cognitive impairment, hallucinations, psychosis, the depressed mood, the anxious mood, apathy, the sleep problems, the nighttime or/and daytime sleepiness, the short term memory stores and the central execution, as well as the sexual desire disorder in the mid-stage sPD patients, suggesting that the dysfunctions of brain regions of some cortical thinning are closely correlated with some clinical manifestations of the mid-stage sPD.

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1. Introduction

Sporadic Parkinson's disease (sPD) is mainly characterized by the motor symptoms, such as bradykinesia, the muscular rigidity, the resting tremor and the postural instability [1]. These cardinal motor symptoms are known to be mainly related to the dopamine depletion caused by the degeneration of dopaminergic neurons in the substantia nigra-striatum loop [2]. However, the nigrostriatal dopaminergic system only is responsible for the partial symptoms, there are also a variety of symptoms of sPD including some motor and no motor symptoms, which could not be explained by the degeneration of simple nigrostriatal dopaminergic system [3,4]. Among these symptoms, which consist of the olfactory dysfunction, the rapid-eye-movement sleep, the behavior disorder, the cognitive impairments, depression, the autonomic dyfunctions including the abnormal thermoregulation and the urinary tract dysfunction, and other clinical manifestations [1,4,5].

Functional magnetic resonance imaging (fMRI) is a more sensitive method than the conventional MRI for detecting the central neural structure lesion. It can be used for detecting the microstructural alteration in cortex and for measuring the volume, thickness, surface and density of cortex [6–8]. Several fMRI studies have been conducted to detect the microstructural changes in sPD, which found the cortex thinning in the certain regions in the sPD patients using the fMRI analysis [9–12]. The fMRI analyses also have revealed that the cortical deficits are closely related to some clinical manifestations of sPD [13–15]. Although the fMRI analysis has been widely used in investigating the correlation between the brain structure lesion and the symptoms of sPD, the relationship of the consistent brain regions lesion with the corresponding clinical manifestations of sPD has not been completely understood up to now. In order to further investigate the correlation between the brain structure lesion and the clinical manifestations of sPD, we measured the cortical thickness and analyzed the correlation between the cortical thickness alteration and the clinical manifestations of sPD.

In this study, we aimed to detect the brain cortical thickness alterations between the sPD patients and the controls from the Han population of Chinese mainland (HPCM) using fMRI. For the evaluation of the brain cortical thickness, we adopted a voxel-based analysis technique using fMRI anatomical scans known as corticometry, because this method has a high sensitivity for identifying the cortex deficits, which has recently been also extensively used in investigating the local cortical thickness by some researchers [16]. In the voxel-based analysis of cortical thickness, we conducted the cortical thickness analysis of the regions of interest (ROI) to evaluate the cortical thickness changes. Meanwhile, we comprehensively evaluated the demographic and disease-related characteristics in our studied subjects. We attempted to detect whether or not the alteration of cortical thickness in some brain regions was related to some clinical manifestations in sPD using fMRI methods, to find the more pathological evidences of sPD, and to provide some objective diagnostic criterions of MRI for sPD.

2. Materials and methods

2.1. Patient selection

One hundred patients with the mid-stage sPD (Intermediate, Progressive or Advanced sPD) consecutively were recruited from the First Hospital of Nanchang University between July 2011 and December 2014. Forty five healthy controls were selected from the spouses, relatives or neighbors of patients. Thirty three patients and five controls were excluded from further analysis due to technical artefacts/factors, the brain abnormalities, the presence of motion artifact or the imperfect of clinical information. A total of 67 patients and 35 sex- and age-matched controls were included in the final analysis. The demographic and clinical characteristics of the two groups were presented in Table 1. These age- and sex- matched control subjects had not the history of neurologic or psychiatric diseases. sPD was diagnosed by three experienced neurologists according to the United Kingdom Parkinson's Disease Society Brain Bank criteria [17]. The severity of symptoms was assessed at the time of off medication according to the Hoehn and Yahr scale [18] and the UPDRS-III [19]. The sPD who have the 2.5–3 score of Hoehn and Yahr and the 31–45 score of UPDRS-III were recruited as the mid-stage sPD. Clinical follow-up of 12 months or more after MRI imaging further confirmed the absence of symptoms of atypical sPD or Parkinsonism. Participants were excluded if they had a history of traumatic brain injury, stroke or any other neurological disorders. The experienced neuroradiologists who were blinded to the patients' diagnosis examined all brain images. The Institutional Review Board of the First Hospital of Nanchang University approved the study protocol and each subject provided a written, informed consent.

2.2. MRI acquisition

Brain MRI scans were obtained using a 3.0 T Siemens Tim Trio whole-body imaging system of MRI, Participants were scanned at the Department of Radiology, the First Affiliated Hospital of Nanchang University using a three-dimensional T1-weighted magnetization-prepared rapid gradient echo (MPRAGE) sequence. The scanning parameters were as follows: TR/TE/TI: 1900/2.26/900 ms, the flip angle: 9°, the slice thickness: 1 mm, the field of view: $256 \times 256\ mm^2$, the acquisition matrix: 256×256, the voxel size: $1 \times 1 \times 1\ mm^3$, 8-channels coil, 176 slices, The structural MRI series included the T1-weighted 3D fast image, the spoiled gradient recalled echo image and the other sequences such as the T2-weighted and FLAIR images to visualize the focal lesions of cortical or white matter that might be exclusionary.

2.3. Image processing

All image processing were performed by the State Key Laboratory of Cognitive Neuroscience and Learning and IDG/McGovern Institute for Brain Researching, Beijing Normal University, China [20]. Briefly, the CIVET pipeline was used to measure the cortical thickness as previously described [21], the native T1-weighted MRI were firstly linearly aligned into the stereotaxic space and corrected for nonuniformity artefacts using the N3 algorithm [22,23]. This algorithm does not require the prior knowledge for the brain tissue classes, and can iteratively estimate both the multiplicative bias field and the distribution of true tissue intensities for the automatic correction of intensity nonuniformity in MRI data. The resultant brain images were then automatically segmented into cortex, the white matter, CSF, and background using a partial volume (PV) classification algorithm, in which a trimmed minimum covariance determinant method was applied for estimating the parameters of the PV effect model, the parameter β controlling the relative strength of the Markov random field was set to 0.1 [24]. The cortical thickness was measured between the two surfaces at 40,962 vertices per hemisphere using the linked distance in the native space [25]. The cortical thickness was defined using the link method, which measures the Euclidean distance between the linked vertices of the inner and outer surfaces [26,27]. The thickness map was further blurred with a 30 mm surface-based diffusion smoothing kernel [28]. Using the thickness information on native surfaces was transformed to a template after diffusion smoothing with 20-mm full-width half-maximum to increase the signal-to-noise ratio and improve the detection ability of population changes [27]. These methods have been validated using both