Resting-State Network Connectivity in Newly Diagnosed Drug-Naïve Parkinson's Disease Patients With Mild Cognitive Impairment

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Research Article

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Abstract

Background: Cognitive impairment (CI) is one of the most frequent non-motor features in Parkinson's disease (PD). The frequency of mild cognitive impairment (MCI) was reported to exceed 40% in a large cohort of newly diagnosed PD patients.

Method: Resting-state functional MRI (rs-fMRI) data was collected in 47 newly diagnosed drug-naïve PD patients (including 28 PD patients with MCI (PD-MCI subgroup) and 19 PD patients with cognitively unimpaired (PD-CU subgroup)) and 28 age- and sex-matched healthy controls (HCs). Independent component analysis (ICA) can decompose rs-fMRI data into resting state networks (RSNs). Brain intra- and inter-network alterations were investigated in RSNs among PD-MCI, PD-CU, and HCs groups.

Results: Seven large-scale brain networks were extracted. The default mode network (DMN), visual network (VN) and sensorimotor network (SMN) were selectively vulnerable in the PD-MCI subgroup relative to the HC group. In PD-MCI patients, the reduced functional connectivity (FC) within the DMN was positively correlated with brief visuospatial memory test-revised (BVM-T-R) scores (memory function); the reduced FC within the VN was positively correlated with clock copying test (CCT) scores (visuospatial function). In whole PD patients, the reduced FC within the SMN was negatively correlated with the Unified PD Rating Scale (UPDRS) part III scores. Moreover, FC between the SMN and limbic network, and between the ventral attention network (VAN) and VN were more prone to be damaged in PD patients.

Conclusions: The DMN, VN and SMN were disrupted in PD-MCI patients. FC between the SMN and limbic network, and between the VAN and VN were also impaired in PD patients. The impaired intra- and inter-connectivity could provide further insights into the pathophysiological alterations of brain connectivity in newly diagnosed drug-naïve PD.

1.0 Introduction

Parkinson's disease (PD), as the second most common neurodegenerative disorder, is characterized by motor symptoms and a broad spectrum of non-motor symptoms (NMS). Cognitive impairment (CI) has been one of the most frequent non-motor features of PD. The dementia has high prevalence (up to 80%) in PD patients with long disease course [1, 2]. And the mild cognitive impairment (MCI) is also prevalent in nondemented PD patients with a mean of 26.7% (range 18.9%-38.2%) [3]. Another study reported that the frequency of MCI even exceeded 40% in a large cohort of newly diagnosed PD patients [4]. PD with MCI is at a higher risk of progression to PD with dementia (PDD) that can contribute to a poorer quality of life [5] and has attracted lots of attention in recent decades.

Several mechanisms have been reported that the formation of protein aggregates, the dysfunction of neurotransmitter systems and the genetic mutations (e.g., *MAPT*, *GBA*) are closely related to CI in PD [6]. In addition, there is a "dual syndrome hypothesis", that is, dopaminergic dysfunction in fronto-striatal regions and cholinergic dysfunction in temporal and posterior cortical regions are involved with different

cognitive functions in PD [7]. Although the underlying pathology of CI in PD has been widely studied, no effective biomarker for predicting PD-MCI or PDD has been confirmed [8].

A number of neuroimaging techniques have been employed to explore the pathological substrates of PD and other neurodegenerative disorders [6]. The resting-state functional magnetic resonance imaging (rs-fMRI), as one promising technology with reliability and reproducibility, can characterize the functional activities in cerebral resting state networks (RSNs) through the independent component analysis (ICA) [9]. These RSNs have different brain function and display specific functional alterations for a particular disease [10]. As one of the famous RSNs, the default mode network (DMN) has been widely reported to participate in cognitive processing. Other RSNs, including the fronto-parietal network (FPN), dorsal attention network (DAN), and ventral attention network (VAN), are also relevant for the cognition process [11, 12].

In this study, we planned to quantify changes in the intra and inter-network connectivity in newly diagnosed drug-naïve PD patients with and without MCI using the ICA. We supposed that PD-MCI patients would show special functional connectivity (FC) alterations in both within and between several cognitive-related networks in the newly diagnosed drug-naïve state.

2.0 Materials And Methods

2.1 Participants

Our study was approved by the local ethics committee, and we got the written informed consents from all participants. A total of 75 subjects enrolled from West China Hospital, including 47 newly diagnosed drug-naïve PD patients and 28 healthy controls (HCs). All patients met the United Kingdom PD Society Brain Bank criteria for PD, and were reconfirmed after 1 to 2 year from the first assessment. PD patients were excluded if they had a history of other neurological and psychiatric diseases, moderate or severe head tremor, and any disorder that interfered with the assessment of PD symptoms. HCs had normal neurological status and brain structure, absence of any history of neurological or psychiatric disorders.

Motor disease severity was assessed with the unified PD rating scale (UPDRS) and the Hoehn & Yahr stage (H&Y). The NMS was evaluated by the NMS scale (9 domains), the Hamilton depression rating scale (HDRS), and the Hamilton anxiety rating scale (HARS). In addition, the overall cognitive functions of all participants were assessed by the complete neuropsychological battery (5 domains), (1) attention/working memory (adaptive digit ordering test (DOT-A) and backward digit span test (DST)); (2) executive function (verbal fluency test (VFT) and clock drawing test (CDT)); (3) language (Wechsler intelligence scale for adult-Chinese revised (WAIS-RC) and Boston naming test (BNT)); (4) memory (Hopkins verbal learning test-revised (HVLT-R) and brief visuospatial memory test-revised (BVMTR)); and (5) visuospatial function (Benton line orientation (BLO) and clock copying test (CCT)) [13] (details were seen in the Supplementary material.1 (Suppl.1)). Based on the HC group's means and standard deviations (SD), we calculated actual z-scores for PD patients. Meantime, expected z-scores for PD

patients were calculated with age, sex, and education adjusted in a multiple regression analysis. Patients were classified as having MCI if the actual z-score for a test was more than 1.5 standard lower than the expected score in at least two tests in one domain or in one test per domain in at least two domains [14, 15]. In the present study, 28 PD patients diagnosed as having MCI (the PD-MCI subgroup) and 19 PD patients diagnosed as cognition unimpaired (the PD-CU subgroup).

2.2 MRI data acquisition

We used a three Tesla system (Tim Trio; Siemens Healthineers, Erlangen, Germany), equipped with an eight-channels head coil, to collect functional and conventional MRI images. The resting-state fMRI data was acquired using an echo-planar-imaging (EPI) sequence. Repetition time [TR] = 2000 ms, echo time [TE] = 30 ms, flip-angle [FA] = 90°, field-of-view [FOV] = 240 × 240 mm², matrix size = 64 × 64, voxel size = 3.75 × 3.75 × 5 mm³, axial slices = 30, number of time points = 240. The conventional MRI data including axial T1-weighted, T2-weighted and fluid-attenuated inversion recovery imaging was collected (details were seen in the Suppl.2). All subjects were instructed to lie comfortably on the scanner bed, and be awake with their eyes closed.

2.3 fMRI data preprocessing

All fMRI volumes underwent a preprocessing based on SPM12 (<http://www.fil.ion.ucl.ac.uk/spm>) and DPABI 3.0 (<http://www.rfmri.org/dpabi>), including (1) removing the first 10 time points; (2) slice-timing correction; (3) spatial realignment; (4) spatial normalization into the standard Montreal Neurological Institute (MNI) space and resampling into 3 × 3 × 3 mm³; (5) spatial smoothing with a 6 mm full-width half-maximum (FWHM) isotropic Gaussian kernel. In addition, the displacement and angular rotation of all participants in the x, y, or z plane were < 1.0 mm and < 1.0° respectively.

2.4 ICA

The group ICA (gICA) was used for all subjects, through the GIFT toolbox (v3.0a) (<http://mialab.mrn.org/software/gift/>) with several steps: (1) estimating the number of independent components (IC) by the MDL criterion [16]; (2) auto-filling data reduction values; (3) selecting a neural network algorithm (Infomax); (4) repeating 250 times in ICASSO [17]; (5) running gICA serially. GICA3 back-reconstruction was performed to estimate spatial maps and timecourses for each subject.

The spectral characteristics of component timecourses and the quality index (Iq) were used to select reliable RSNs from the physiological noise. The spectral characteristics include two parameters (“dynamic range” and “low frequency to high frequency power ratio”). And Iq shows the reliability and consistency of the decomposition with range from 0 to 1. Then the component was excluded when it has at least one of the following metrics: (1) dynamic range < 0.025 [18]; (2) ratio < 3.4; (3) Iq < 0.9.

Then, 14 remaining ICs were anatomically labeled according to the correlation sorting criteria with the spatial correlation between the spatial map of each IC and the template from a previous study containing

7 main brain functional networks (DAN, DMN, FPN, limbic network, sensorimotor network (SMN), VAN, and visual network (VN)) [19] (see in the Fig. 1).

2.5 FC analysis

The FC analysis was based on SPM12 and DPABI 3.0 with steps after the fMRI data preprocessing: (1) linear detrending; (2) nine nuisance covariates (the white matter (WM) signal, cerebrospinal fluid (CSF) signal, global signal and six head motion parameters) regression; (3) bandpass filtering (0.01–0.08 Hz). Then, these 14 ICs divided into 7 RSNs were regarded as 7 binary masks to analyze the Pearson's correlation coefficient between each pair of RSNs, and z-scores were computed via a Fisher r-to-z transformation.

2.6 Statistical analysis

Demographic and clinical data were performed by the one-way analysis of variance (ANOVA), student's t-test, or Chi-square test, as appropriate base on the SPSS 22.0. For intra-connectivity within each RSN, we used a design model of one-way ANOVA base on SPM12 to compare the z-value maps among the PD-MCI, PD-CU, and HC groups with age, sex and education as covariates, and then the post hoc two-sample t-tests were performed ($p < 0.001$ at the voxel level and $p < 0.05$ at the cluster level corrected by Gaussian Random Filed (GRF), one-tailed) (<http://restfmri.net/forum/index.php?q=rest>). In addition, voxel-wise correlation analysis with clinical and cognitive scores was assessed based on RESTplus 1.2 (<http://restfmri.net/forum/index.php?q=rest>) with age, sex and education as covariates ($p < 0.05$, uncorrected). For inter-connectivity between each RSN, we also used the ANOVA base on the SPSS 22.0 among three groups with post-hoc t tests.

3.0 Results

The demographic and clinical data of all participants are listed in Table 1. There was no significant difference in age, sex, and education between PD patients and HCs. No significant difference was found in disease duration, H&Y stage, UPDRS score, NMS scores and HDRS/HARS scores between PD-MCI and PD-CU subgroups. Notably, the education level was lower in the PD-MCI subgroup relative to the PD-CU subgroup.

Table 1
Demographic and clinical characteristics of all subjects

Parameter	PD, all	HC	PD-CU	PD-MCI	p ¹	p ²	p ³
Number, n	47	28	19	28	-	-	-
Handedness of writing (R: L)	47: 0	28: 0	19: 0	28:0	-	-	-
Age, y	55.00 ± 9.27	52.06 ± 7.00	54.88 ± 10.89	55.07 ± 8.20	0.152	0.361	0.937
Gender, M/F	23/24	8/20	8/11	15/13	0.083	0.164	0.440
Duration of disease, years	1.74 ± 1.61	-	1.87 ± 1.32	1.65 ± 1.80	-	-	0.649
H & Y stage	-	-	1.87 ± 0.37	1.82 ± 0.58	-	-	0.756
UPDRS score	-	-	-	-	-	-	-
Part I	-	-	0.79 ± 1.72	0.86 ± 1.21	-	-	0.875
Part II	-	-	6.63 ± 3.18	6.21 ± 4.09	-	-	0.710
Part III	-	-	20.79 ± 7.44	19.79 ± 8.71	-	-	0.683
Part IV	-	-	0	0	-	-	-
NMS score	-	-	21.95 ± 20.82	25.96 ± 21.73	-	-	0.530
HAMD score	-	-	5.21 ± 6.87	6.79 ± 5.32	-	-	0.381
HAMA score	-	-	3.79 ± 4.88	5.68 ± 4.30	-	-	0.169

*Indicates significant difference;

¹ Comparison between all PD patients (PD-MCI and PD-CU) and HCs.

² Comparison among PD-MCI, PD-CU patients, and HCs.

³ Comparison between PD-CU and PD-MCI patients.

Keys: PD, Parkinson's disease; HC, healthy control; PD-CU, PD patients with cognitive unimpaired; PD-MCI, PD patients with mild cognitive impaired; R, right; L, left; M, male; F, female; H & Y, Hoehn & Yahr; UPDRS, unified PD rating scale; NMS, non-motor symptoms; HAMD, Hamilton depression rating scale; HAMA, Hamilton anxiety rating scale; MoCA, Montreal cognitive assessment; EDU, education.

Parameter	PD, all	HC	PD-CU	PD-MCI	p ¹	p ²	p ³
MoCA score	-	-	27.89 ± 2.49	24.89 ± 3.28	-	-	0.002*
EDU, years	10.04 ± 4.01	10.29 ± 3.75	12.53 ± 3.03	8.36 ± 3.74	0.796	0.001*	< 0.001*
*Indicates significant difference;							
¹ Comparison between all PD patients (PD-MCI and PD-CU) and HCs.							
² Comparison among PD-MCI, PD-CU patients, and HCs.							
³ Comparison between PD-CU and PD-MCI patients.							
Keys: PD, Parkinson's disease; HC, healthy control; PD-CU, PD patients with cognitive unimpaired; PD-MCI, PD patients with mild cognitive impaired; R, right; L, left; M, male; F, female; H & Y, Hoehn & Yahr; UPDRS, unified PD rating scale; NMS, non-motor symptoms; HAMD, Hamilton depression rating scale; HAMA, Hamilton anxiety rating scale; MoCA, Montreal cognitive assessment; EDU, education.							

The DAN comprises IC 16, 23, and 25 in bilateral superior parietal lobules; the DMN comprises IC 15, 28 and 29 in bilateral post cingulate cortices and precuneus; the FPN comprises IC 20 and 26 in bilateral inferior parietal lobules; the limbic network comprises IC 5 in bilateral rectus, olfactory cortices and orbitofrontal gyri; the SMN comprises IC 14 in bilateral postcentral gyri, precentral gyri, paracentral gyri and supplementary motor areas (SMA); the VAN comprises IC 37 in bilateral middle cingulate cortices; the VN comprises IC 2, 3, and 6 in bilateral calcarine and lingual areas (see in the Fig. 1).

We found abnormal intensity of intra-network connectivity in PD-MCI patients. Compared with HCs, PD-MCI patients displayed lower intrinsic activities in the right precuneus of the DMN, left paracentral gyri and SMA of the SMN, and bilateral calcarine and lingual areas of the VN (see in the Table 2 and Fig. 2). Meantime, the BVMT-R scores (memory performance) were positively correlated with the intrinsic activity in the precuneus within the DMN in PD-MCI patients; the CCT scores (visuospatial performance) were positively correlated with the intrinsic activity in the calcarine and lingual areas within the VN in PD-MCI patients. For all PD patients, the UPDRS part III scores were negatively correlated with the intrinsic activity in areas of the SMN (see in the Table 3 and Fig. 3). On the other hand, we detected abnormal FC between RSNs. Specifically, compared with the HC group, both PD-MCI and PD-CU subgroups had lower FC between the SMN and limbic network, and between the VAN and VN.

Table 2
Clusters derived from voxel-based comparisons between PD-MCI patients and HCs.

RSNs	N	Size	Region	T	MNI		
					X	Y	Z
DMN	1	36	Precuneus_R	4.69	3	-54	21
SMN	1	65	Paracentral lobule_L	5.19	-9	-21	75
			Supplementary motor area_L	3.96	-3	-18	60
VN	1	122	Calcarine_L	4.51	-3	-96	9
			Calcarine_L	4.06	-9	-84	-3
			Lingual_L	4.03	-15	-69	-9
	2	62	Lingual_R	4.04	9	-75	3
			Lingual_R	3.88	15	-66	-3
			Lingual_R	3.66	21	-66	-9
Keys, PD, Parkinson's disease; MCI, mild cognitive impairment; HC, healthy control; DMN, default mode network; SMN, sensorimotor network; VN, visual network; R, right; L, left.							

Table 3
Clusters derived from voxel-wise correlation analyses.

RSN	N	Size	Region	T	MNI		
					X	Y	Z
DMN	1	68	Precuneus	0.71	-3	-66	21
	2	64	Inferior Frontal Gyrus	0.65	-48	27	3
VN	1	96	Lingual_L	0.67	-15	-48	-6
	2	91	Calcarine_R	0.62	27	-66	6
SMN	1	91	Temporal_Sup_L	0.48	-57	-21	12
	2	50	Paracentral Lobule	0.48	-6	-21	48
Keys, DMN, default mode network; SMN, sensorimotor network; VN, visual network; Sup, superior; R, right; L, left.							

4.0 Discussion

Using ICA, the sources of signal variation was blindly separated, and 7 large-scale brain networks were extracted. The DMN, VN and SMN were selectively vulnerable in newly diagnosed drug-naïve PD patients

with MCI. Moreover, FC between the SMN and limbic network, and between the VAN and VN were more prone to be damaged in PD patients.

The DMN was characterized by reduced activation in task-based situation compared with the resting state [20]. In PD, DMN is the most studied intrinsic connectivity network, which is consistent with previous research on other neurological and psychiatric disorders [21]. The first study to explore the relationship between the resting state FC in DMN and cognitive performance in PD was focused on cognitively unimpaired PD patients while medicated, and suggested reduced FC in the right medial temporal lobe and bilateral inferior parietal cortex within the DMN using the ICA [22]. Our previous study using the same method found lower FC in the left inferior parietal lobule within the DMN in cognitively unimpaired drug-naïve PD patients with akinetic-rigidity subtype [23]. Even though these patients did not meet the criteria for cognitive impairment, the altered FC within the DMN was significantly associated with cognitive function. Various studies investigated the resting-state networks in PD patients with cognitive impairment, and a meta-analysis including seventeen studies reported cognitive impairment in PD was prominently relevant with reduced FC in the DMN [6].

More recent studies indicated connectivity changes in several RSNs rather than a single intrinsic connectivity network. However, changes of intrinsic connectivity network and even the association between the altered network and specific cognitive performance hold a considerable heterogeneity, which is likely due to the variability in the inclusion of patients, appliance of cognitive tests, and preprocessing strategies.

A dynamic functional analysis in PD suggested two discrete connectivity states, within-network state (state I) with more frequent and sparse connectivity, and between-network state (state II) with less frequent and strong interconnectivity [24]. In the state I, sparse connections were located mainly within DMN, VN, and SMN, which might play a vital role in the pathogenesis of PD manifestations. Our study observed abnormal FC within the DMN correlated with deficits in memory function, within the VN correlated with deficits in visuospatial function, as well as within the SMN correlated with the severity of disease. Cortical visual processing regions have been involved in a number of neuroimaging studies about PD [25], reporting occipital-cortical thinning, metabolic deficits, and hypoperfusion. A longitudinal fMRI study demonstrated a progressive loss of FC mainly in posterior parts of brain strongly correlated with decreasing cognitive performance [26]. The visuospatial deficit in PD was regarded as primary posterior cortical pathology rather than dopamine deficits, which might be a sensitive predictor of progression to dementia in PD [27]. Several lines of evidence suggested disrupted sensorimotor integration in PD [28]. The cortico-striatal loops were commonly impaired in previous studies investigating SMN connectivity in PD patients. It can be noted that dopamine deficiency might be one of the potential mechanisms underlying impaired SMN in PD.

According to Braak staging [29], the pathological process of PD occurs primarily in the brain stem, pursues an ascending process, and arrives to the neocortex in the final stage. One previous study reported reduced FC in mesolimbic-striatal and cortico-striatal circuits in drug-naïve PD patients, which reflects

pathologic changes of early non-motor and motor deficits, corresponds to Braak staging, and further provides insight into the network integration in the early-state of PD [30]. The structural and functional connectivity in the SMN and limbic networks have been investigated separately in PD, less is known about the correlation between these two RSNs. A connectomic analysis revealed that the amygdala, as a key structure in the limbic system, had a close interplay with areas within the SMN, including the postcentral gyrus, the precentral gyrus and the paracentral lobule, suggesting a limbic–motor interface involved in the emotional modulation of complex functions [31]. The impaired emotion perception can contribute to the damage of smiling mimicry in PD, which is closely related to fibers connection between the amygdala and SMN. Our finding of decreased FC between the SMN and limbic network was in line with previous literature and fostered this idea of existing alterations of limbic–motor interface in newly diagnosed drug-naïve PD patients.

More than a decade ago, two attention systems (DAN and VAN) with distinct anatomy and function has been introduced, and their roles in the visuospatial attention system were mainly described [32]. The DAN can be active when attention is overtly or covertly oriented in space, and the VAN can be active when faced with unexpected stimuli associated with behavior. In advanced PD, the visual processing impairment (e.g., misperception and hallucinations) was closely related to the DMN, DAN, VAN and VN [33]. When the DAN is unable to recruit activation, the DMN and VAN can frequently functionally interactive and relatively overactive. Our finding of decreased FC between the VAN and VN might be an early change in the visuospatial attention system of PD, and subsequent changes and the significance remain to be further studied.

There are some limitations within the present study. First, the level of education differs between the PD-MCI and PD-CU subgroups, which might be an important confounder. In the analyses, the variable was regarded as covariate to reduce the influence. Another concern is the modest sample size, which limited the generalizability of our findings.

5.0 Conclusion

We reported that functional changes in the DMN, VN and SMN were more evident in our newly diagnosed drug-naïve PD-MCI group. These alterations were associated with memory and visual functions, and motor symptoms. Altered FC between the SMN and limbic network, and between the VAN and VN reflected early dysfunction in the disease process, and can offer additional insight into the pathophysiological alterations of brain connectivity in PD.

List Of Abbreviations

ANOVA, analysis of variance; BLO, Benton line orientation; BNT, Boston naming test; BVMT-R, brief visuospatial memory test-revised; CCT, clock copying test; CDT, clock drawing test; CI, cognitive impairment; CSF, cerebrospinal fluid; DAN, dorsal attention network; DMN, default mode network; DOT-A, adaptive digit ordering test; DST, backward digit span test; EPI, echo-planar-imaging; FC, functional

connectivity; FPN, fronto-parietal network; FWHM, full-width half-maximum; gICA, group ICA; GRF, Gaussian Random Filed; HARS, Hamilton anxiety rating scale; HCs, healthy controls; HDRS, Hamilton depression rating scale; HVLT-R, Hopkins verbal learning test-revised; H&Y, Hoehn & Yahr stage; IC, independent components; ICA, independent component analysis; MCI, mild cognitive impairment; MNI, Montreal Neurological Institute; NMS, non-motor symptoms; PD, Parkinson's disease; PDD, PD with dementia; rs-fMRI, resting-state functional magnetic resonance imaging; RSNs, resting state networks; SMN, sensorimotor network; UPDRS, unified PD rating scale; VAN, ventral attention network; VFT, verbal fluency test; VN, visual network; WAIS-RC, Wechsler intelligence scale for adult-Chinese revised.

Declarations

Ethics approval and consent to participate: This study was conducted in agreement with the Ethics Committee of West China Hospital of Sichuan University. All participants had provided a written informed consent. All the methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are available from the corresponding author by reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YBH:1) Research project: A. Conception, B. Organization, C. Execution; 2) Statistical Analysis: Design; 3) Manuscript: Writing of the first draft;

QQW: 1) Statistical Analysis: Review and Critique; 2) Patients enrollment;

RWO: Patients enrollment and follow up;

LYZ: Patients enrollment and follow up;

XQY: Patients enrollment;

QYG: 1) Research project: Conception; 2) Statistical Analysis: Review and Critique; 3) Manuscript: Review and Critique;

FHS: 1) Research project: Conception; 2) Statistical Analysis: Review and Critique; 3) Manuscript: Review and Critique;

All authors read and approved the final manuscript.

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Figures

Figure 1

Resting state networks (RSNs) inferred using group ICA. Fourteen independent components (ICs) were anatomically labeled into 7 RSNs. Keys, DAN, dorsal attention network; DMN, default mode network; FPN, fronto-parietal network; SMN, sensorimotor network; VAN, ventral attention network; VN, visual network. Color bar means different numbered ICs.

PD-MCI<HC

Figure 2

Differences in the connectivity patterns are shown between PD-MCI patients and HCs within the DMN, SMN and VN ($p < 0.001$, Gaussian Random Filed (GRF) corrected). Keys, PD, Parkinson's disease; MCI, mild cognitive impairment; HC, healthy control; DMN, default mode network; SMN, sensorimotor network; VN, visual network; R, right; L, left.

Figure 3

(1) In PD-MCI patients, the reduced FC within the DMN was positively correlated with BVMT-R scores; the reduced FC within the VN was positively correlated with CCT scores; (2) In PD patients, the reduced FC within the SMN was negatively correlated with UPDRS part III scores. Keys, PD, Parkinson's disease; MCI, mild cognitive impairment; FC, functional connectivity; DMN, default mode network; BVMT-R, brief

visuospatial memory test-revised; VN, visual network; CCT, clock copying test; SMN, sensorimotor network; UPDRS, the unified PD rating scale.

Figure 4

Figure 4

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