Disrupted fronto-temporal function in panic disorder: a resting-state connectome study

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Accepted: 21 September 2021 / Published online: 19 October 2021 © The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2021

Abstract
Recent neuroimaging studies have identified alterations in activity and connectivity among many brain regions as potential biomarkers for panic disorder. However, the functional connectome of panic disorder is not well understood. Therefore, a graph-theoretical approach was applied in this study to construct functional networks of patients and healthy controls in order to discover topological changes in panic disorder. 31 patients and 33 age and sex matched healthy controls underwent resting-state functional magnetic resonance imaging. Brain networks for each participant were structured using nodes from the Anatomical Automatic Labeling template and edges from connectivity matrices. Then, topological organizations of networks were calculated. Network-based statistical analysis was conducted, and global and nodal properties were compared between patients and controls. Unlike controls, patients with panic disorder displayed a small-world network. Patients also revealed decreased nodal efficiency in right superior frontal gyrus (SFG), middle frontal gyrus (MFG), right superior temporal gyrus (STG), and left middle temporal gyrus (MTG). Decreased functional connectivity was found in panic disorder between right MTG and extensive temporal regions. Among these disrupted regions, the decreased nodal efficiency of SFG showed a positive correlation with clinical symptoms while nodal betweenness centrality in angular gyrus showed a negative correlation. Our results indicated decreased function of global and regional information transmission in panic disorder and emphasized the role of temporal regions in its pathology.

Keywords Magnetic resonance imaging · Graph theory · Network-based statistic · Temporal lobe

Introduction
Patients with panic disorder (PD) suffer from the core symptom of recurring panic attacks which often manifest as palpitations, dizziness, accelerated heart rate, trembling, sweating, and fear of going crazy or even dying (Sobanski & Wagner, 2017). Besides panic attacks, PD patients also experience related cognitive and behavioral changes resulting in anticipatory anxiety and avoidance behaviors. An epidemiological study showed the lifetime prevalence of PD is 4.7% (Kessler et al., 2006).
Over the past few decades, a large number of imaging studies have tried to reveal the neural mechanism of PD, but the pathogenesis remains unclear. The fear network...
hypothesis was the first modal raised theory by Gorman (Gorman & M., 2000) about the neuropathology of PD, which pointed to overactivation of amygdala and disrupted inhibitive function of prefrontal cortex (PFC) as the main cause of panic attacks. This theory has been supported by many studies reporting abnormal top-down processing (Kent et al., 2005; Lueken et al., 2014; Nash et al., 2008). Lai proposed an advanced fear network modal, adding temporal, parietal, and occipital regions (C. H. Lai, 2019), which emphasized disrupted sensory information transmission from sensory regions to frontal regions. Excluding PFC and limbic regions, sensory regions including temporal and occipital regions have been reported to be altered in PD (C. H. Lai & Wu, 2013b; Wade-Bohleber et al., 2020). In line with Lai’s hypothesis, our previous meta-analysis of voxel-based morphometry (VBM) studies also identified decreased gray matter volume (GMV) in temporal regions including middle temporal gyrus (MTG) and superior temporal gyrus (STG) in PD (Wu et al., 2018). Though many researchers have reported alterations of brain regions involved in the fear network hypothesis, the inconsistencies of these findings remind us that the neural mechanism of PD remains unclear.

Another obstacle in studying the neural mechanism of PD is that the traditional analysis approach that is widely used in most resting-state research is seed-based rather than network-based, which can only provide limited contributions to the understanding of disrupted network attributes in PD. The developed tool, network-based statistic (NBS) analysis, may solve this problem by identifying network components that differ between groups (Zalesky et al., 2010). Using the NBS approach, Lai’s study reported a decreased network component in PD that included left parahippocampal gyrus and bilateral precentral gyrus, emphasizing the importance of limbic regions and the connection between sensory and motor regions (C. H. Lai & Wu, 2016).

Recently, another emerging method called connectome analysis based on graph theory brought us a new perspective of information transmission for the interpretation of network changes. Connectome analysis has already been applied in many psychiatric studies, such as schizophrenia (Liu et al., 2008), major depressive disorder (MDD) (Zhang et al., 2011), and anxiety disorders like social anxiety disorder (SAD) (Zhu et al., 2017). In graph theory, networks could be evaluated according to two aspects: the speed and the fault tolerance of information transmission. For example, it has been widely proven that the human brain is characterized by small-worldness under multiple task conditions (Eguiluz et al., 2005), as well as in resting-state conditions (van den Heuvel et al., 2008), which implies both high global efficiency of information transmission across the whole brain and high local efficiency within each local functional network. Patients with psychiatric disorders have been found to have decreased small-worldness (Liu et al., 2008; L. Wang et al., 2009). However, how the network attributes could change in PD patients is still unknown.

The present study aimed at deepening our understanding of the pathological mechanism of PD from the perspective of information transmission and sought to explore topological biomarkers of PD during the resting state. According to the fear network hypothesis and the consistently reported brain regions altered in PD, we hypothesized that PD patients would exhibit disrupted functional connectivity (FC) and topological properties in PFC, amygdala, STG and MTG. To test this hypothesis, we evaluated FC changes and altered network attributes of PD using data-driven approaches including NBS analysis and connectome analysis and explored the relationship between neural changes and clinical symptoms.

Materials and methods

Participants

PD patients were recruited from Brain Hospital of Nanjing Medical University, and healthy participants were recruited from the community from September 2014 to January 2019. The inclusion criteria for PD patients included: (1) PD diagnosis according to DSM-5 criteria and the Chinese version of the Mini-International Neuropsychiatric Interview criteria; (2) Age between 18 and 55 years old; (3) Right-handed. General exclusion criteria included: (1) Neurological or other psychiatric illnesses; (2) Severe somatic diseases; (3) Contraindicated factors for MRI, such as claustrophobia, discomforts while undergoing MR examination, a pacemaker in the body, pregnancy, or nursing.

This project was approved by the Ethics Committee of the Nanjing Brain Hospital, affiliate of Nanjing Medical University. After complete explanation of the procedures to participants, written informed consent was obtained.

Clinical assessments

Clinical symptoms were measured with 3 scales: Panic Disorder Severity Scale (PDSS) was used by several trained psychiatrists to assess the severity of panic symptoms, Hamilton Anxiety Scale (HAMA) was used to assess the anxiety level of patients, and the Chinese revision of the Anxiety Sensitivity Index (ASI-R) was used to evaluate the anxiety sensitivity of patients.
Resting-state fMRI acquisition

All imaging data were obtained with a 3.0 T Siemens version scanner in the afternoon between 14:00–16:00 as soon as the participants were inducted into the study. Whole-brain functional magnetic resonance imaging (fMRI) was acquired using an 8-min echo-planar imaging sequence in 36 slices at 240 time points (repetition-time/echo-time = 2000 / 30 ms, flip angle = 90°). The slice thickness was 4 mm and the matrix size was 64×64, resulting in voxels of 3.75×3.75×4.0 mm³. Participants were instructed to close their eyes and rest, but to stay awake and not to sleep.

High-resolution T1-weighted structural MRI was obtained for subsequent processing of BOLD data co-registration using three-dimensional spoiled gradient-echo sequence (176 slices, repetition-time/echo-time/inversion time = 1900 / 2.48 ms / 900 ms, voxels 1×1×1 mm³, matrix = 256×256, flip angle = 9°). The slice thickness was 1 mm with a gap of 0.5 mm.

Data preprocessing

Functional data were preprocessed using the Data Processing Assistant for Resting-State fMRI (DPARSF_V4.0) in DPABI (http://rfmri.org/dpabi) (Yan et al., 2016). This toolbox is based on Statistical Parametric Mapping (SPM8, http://www.fil.ion.ucl.ac.uk/spm) and the Matlab platform (http://www.brain-connectivity-toolbox.net). DPARSF is developed for more convenient preprocessing steps and is widely used in resting-state fMRI studies (Chao-Gan & Yu-Feng, 2010). To attain magnetization equilibrium, the first 10 time points were discarded. For each participant, images were slice-timing corrected using sinc interpolation and then realigned. After head motion correction, linear regression was performed to remove Friston’s twenty-four head motion parameters and confounding signals of white matter, cerebrospinal fluid, and global signals. All images were normalized by using each participant’s T1 image unified segmentation and spatially smoothed with a 6-mm full-width half maximum Gaussian kernel. Finally, temporal band-pass filtering was performed using a cut-off frequency of 0.01–0.1 Hz. Participants whose head motion exceeded 2.5 mm or 2.5 degrees were excluded.

Network construction

According to graph theory, a network is composed of nodes and edges between nodes. The atlas of Automated Anatomical Labeling (AAL) was used to represent 90 nodes of the network since it has been widely used in many neuroimaging studies (Tzourio-Mazoyer et al., 2002). The network edges were defined using resting-state FC, which was calculated using pairwise Pearson correlations between any two regions’ mean time series. Then, FC values were normalized to z-scores by Fisher’s transformation. From this, a 90×90 correlation matrix, or a binarized (based on a range of sparsity), undirected graph was derived for each subject.

Network-based statistical analysis

A non-parametric approach called network-based statistic (NBS) (Zalesky et al., 2010) was used to evaluate connectivity disruption by computing multiple test statistics while controlling the family-wise error rate. NBS analysis was conducted using GRETRA toolkit (J. Wang et al., 2015) to find differences between PD and HC groups with age, gender, and education information as covariates.

The NBS approach included the following steps. First, a set of supra-threshold links were identified using the t-statistic with an uncorrected threshold of p < 0.001. Then, a breadth first search (Ahuja, Magnanti, & Orlin, 1994) was used to determine connected components in which any two voxels were connected to each other through a path comprising supra-threshold links. The number of links in each connected component (component size N) was also stored at this step. Permutation testing was conducted with a p-value controlled for Family Wise Error (FWE) ascribed to each connected component on the number of links it comprised. A total of 10,000 random permutations were generated independently, during which the group a participant belonged to (PD or HC) was randomly exchanged. The permutation process yielded a null distribution for the size of the largest connected component so that a corrected p-value could be determined by calculating the proportion of permutations for which the largest connected component size was larger than N. The result of altered components in PD was visualized by BrainNet Viewer (corrected p < 0.05) (Xia et al., 2013).

Graph-theory network analysis

Graph-theory metrics were calculated using GRETRA. Both global measures and local measures were used to describe the network’s topological characteristics.

Global measures included: characteristic path length (Lp), clustering coefficient (Cp), global efficiency (Eg), and small-worldness (σ). Lp is defined as the average of the shortest path lengths (the minimum number of edges from a particular node to another) between any pair of nodes in the network. Cp describes the extent of local connectivity of a network and is defined as the average clustering coefficient (see below) of all nodes in the network. Eg measures a network’s ability to transmit information, which is defined by the average inverse path length of the shortest paths connecting all nodes in a network (Gong et al., 2009).

High global efficiency implies fast information transmission and close topological relationship of nodes throughout the network.
Small-worldliness is a parameter integrating the efficiency of both local and global information transfer. A small-world network is defined by high Cp and low Lp (Watts & Strogatz, 1998). Small-worldliness was calculated as the ratio of the Cp of the actual brain network to that of a random network (γ) divided by the ratio of the Lp of the real brain network to that of a random network (λ) (Bassett et al., 2011; Humphries & Gurney, 2008).

Local measures included: nodal degree centrality, nodal betweenness centrality, nodal global efficiency, and nodal clustering coefficient (Eloc). Nodal degree centrality is defined by the total number of edges of a particular node. Higher nodal degree centrality indicates greater importance of this particular node in the network. Betweenness centrality is calculated as ratio of the number of shortest paths between any two nodes traversing a particular node to the number of all the shortest paths between any two nodes. This parameter is often used to define hubs which may be crucial in the network and closely connected to other nodes. Nodal global efficiency reflects the efficiency of information transmission from one particular node to other nodes. Clustering coefficient is defined as the number of connections between neighbor nodes of a particular node divided by maximum possible number of such nodes. A high clustering coefficient implies a more specialized and integrated topological organization and a network’s ability to defend against attack.

All the graph-theory metrics were calculated at a sparsity range from 5 to 40% of the strongest connections within the connectivity matrix (Achard & Bullmore, 2007; Y. He et al., 2008). For each metric, area-under-the-curve (AUC) was calculated across all values of sparsity in 1% intervals. These AUC values were used for statistical comparisons (Y. He et al., 2008).

Statistical analyses

A general linear model was performed with each global / regional network metric as independent variables and age, gender, and education information as covariates. For multiple comparison correction, an alpha level of 1/90 (p < 0.01) was used to declare significance for regional properties (Lynall et al., 2010). All the comparison processes were conducted using GRETNA toolkit.

The relationship between topological metrics with significant group differences and clinical symptoms of PD was calculated using Spearman’s correlation coefficient.

Results

Demographic data and clinical symptoms

A total of 31 patients with PD (17 males and 14 females) and 33 HCs (14 males and 19 females) were recruited in the study. At the time of MR scanning, 24 out of 31 patients received no medications or psychological treatments, three patients were taking escitalopram, two patients were taking lorazepam and escitalopram, and one patient was taking fluvoxamine. After preprocessing, MRI data of 1 PD and 4 HCs were discarded due to excessive head motion. Therefore, the neuroimaging data of 30 PD and 29 HC were used in the final analyses.

No significant differences in age, gender, or years of education were found between two groups (Table 1).

Altered functional connectivity in PD

NBS analysis identified a single network showing significant decreased FC in PD patients (p = 0.048, FWE corrected). A total of 5 nodes and 4 edges were involved (Fig. 1A, Table 2). Nodes with altered FC were localized mainly in the temporal lobe in the right hemisphere. Right MTG was involved in all 4 altered edges, indicating the significance of MTG in PD. The correlation analysis found that FC between right MTG and right transverse temporal gyrus showed significant positive correlation with HAMA score (Fig. 1B).

Disrupted global properties in PD

Global properties under different connection sparsity are depicted in Table 3. PD and HC groups all had small-world properties (σ > 1). Compared with HC group, the AUC value of σ was significantly lower in PD group (Fig. 2). The comparison of the AUC of γ and λ yielded no significant difference between PD and HC. No significant correlations were found between the AUC value of σ in PD group and the PDSS score (r = −0.303, p = 0.104), between the AUC of σ and the ASI score (r = −0.001,
Disrupted regional properties in PD

The comparison of regional properties between PD and HC showed PD patients had increased nodal degree centrality in right posterior cingulate gyrus (PCC) and left superior occipital gyrus and decreased nodal degree centrality in right superior frontal gyrus (SFG) and left MTG. Increased nodal betweenness centrality was found in right rectus and left angular gyrus and decreased nodal global efficiency was found in extensive frontal and temporal regions of PD patients (Table 4). The comparison of nodal clustering coefficient yielded no significant group difference.

$p = 0.995$ or between the AUC of $\sigma$ and the HAMA score ($r = -0.048$, $p = 0.800$).

**Fig. 1** A altered network in PD patients. PoCG.L, left postcentral gyrus; HES.L, left transverse temporal gyrus; HES.R, right transverse temporal gyrus; MTG.R, right middle temporal gyrus; TPOsup.R, right temporal pole: superior temporal gyrus. B, correlation between FC values in the right MTG and right transverse temporal gyrus connection and HAMA scores.
The brain-symptom correlation analysis showed that the AUC of nodal global efficiency of right SFG had a significant negative correlation with ASI-R score ($r = -0.444$, $p = 0.018$) (Fig. 3A); the AUC of nodal betweenness centrality of left angular gyrus had significant positive correlation with HAMA score ($r = 0.448$, $p = 0.013$) (Fig. 3B).

**Discussion**

This study characterized resting-state network alterations in PD from two perspectives: both connectivity and topological property changes. To our knowledge, this is the first study to investigate FC changes and topological network alterations in PD using NBS analysis and topological measures.

From the perspective of global attributes, PD patients showed lower small-worldness than HC. The “small-world” network is characterized by high $C_p$ and short $L_p$ (Watts & Strogatz, 1998). High $C_p$ means high local information transmission speed and low $L_p$ ensures good global information transmission capability (Sporns & Zwi, 2004). Decreased small-worldness in PD indicates the disruption of local efficiency and fault tolerance as well as the information-carrying capacity of the brain in PD. These abnormalities may correlate with loss of long-range communication among parts of the brain in PD (Latora & Marchiori, 2001). This result is consistent with a previous research that reported decreased small-worldness in SAD (Zhu et al.,...
### Table 4  Regional property changes in PD patients

| Regions                              | $M_{AUC} \pm SD_{AUC}$ | $t$     | $p$   |
|--------------------------------------|-------------------------|---------|-------|
| PD                                   | HC                      |         |       |
| Right superior frontal gyrus         | 5.961 ± 1.067           | 6.842 ± 0.943 | −3.116 | 0.003 |
| Right posterior cingulate gyrus      | 7.307 ± 1.615           | 6.338 ± 1.498 | 2.937  | 0.005 |
| Left superior occipital gyrus        | 6.582 ± 1.260           | 5.767 ± 0.828 | 3.276  | 0.002 |
| Left middle temporal gyrus           | 6.232 ± 1.374           | 7.228 ± 1.369 | −2.717 | 0.009 |

**Regions showing significant difference between PD and HC in nodal degree centrality**

| Regions                              | $M_{AUC} \pm SD_{AUC}$ | $t$     | $p$   |
|--------------------------------------|-------------------------|---------|-------|
| Right rectus                         | 21.306 ± 10.977         | 13.677 ± 5.648 | 3.003  | 0.004 |
| Left angular gyrus                   | 31.322 ± 14.578         | 20.266 ± 6.481 | 3.314  | 0.002 |

**Regions showing significant difference between PD and HC in nodal betweenness centrality**

| Regions                              | $M_{AUC} \pm SD_{AUC}$ | $t$     | $p$   |
|--------------------------------------|-------------------------|---------|-------|
| Right superior frontal gyrus         | 0.181 ± 0.011           | 0.188 ± 0.008 | −3.241 | 0.002 |
| Right middle frontal gyrus           | 0.181 ± 0.009           | 0.188 ± 0.010 | −2.695 | 0.009 |
| Right superior temporal gyrus        | 0.194 ± 0.015           | 0.202 ± 0.009 | −2.961 | 0.005 |
| Right temporal pole: superior temporal gyrus | 0.195 ± 0.010     | 0.202 ± 0.013 | −2.764 | 0.008 |
| Left middle temporal gyrus           | 0.184 ± 0.013           | 0.192 ± 0.012 | −2.725 | 0.009 |

**Fig. 3**  

A, correlation between the AUC of nodal global efficiency of right superior frontal gyrus and ASI-R scores;  
B, correlation between the AUC of nodal betweenness centrality of left angular gyrus and HAMA scores

$t$ value > 0 means PD > HC; $t$ value < 0 means PD < HC
fractional anisotropy (FA) (Han et al., 2008) were found matter deficits (C.-H. Lai, Hsu, & Wu, 2010) and higher structural and functional MRI studies. For instance, gray network, PCC changes have been reported repeatedly in gyrus in PD. Although PCC is not a typical part of the fear pathogenesis of PD.

The frontal lobe is an essential component in the neuropathology of PD since the fear network hypothesis was raised in 2000 (Gorman & M., 2000). The disruption of SFG has been widely reported in many studies (Feldker et al., 2016; Killgore et al., 2014; Wedekind et al., 2011). SFG and STG were found to be involved in the extinction phase in fear conditioning (Lueken et al., 2014; Sehlmeyer et al., 2009). In extinction circuitry, PFC inhibits the amygdala’s ability to regulate fear extinction (Quirk et al., 2006; Sotres-Bayon et al., 2006). Our previous meta-analysis of VBM studies also found gray matter deficits in extensive frontal regions and STG and co-atrophy between bilateral dorso-medial PFC, orbital frontal cortex (OFC), and STG (Wu et al., 2018). Decreased nodal global efficiency in frontal and temporal regions provides evidence for the important role of the frontal and temporal lobe in the fear network from the perspective of network information transmission, and the negative correlation found between the AUC of nodal global efficiency of SFG and STG and co-atrophy between bilateral dorso-medial PFC, orbital frontal cortex (OFC), and STG (Wu et al., 2018). Decreased nodal global efficiency in frontal and temporal regions provides evidence for the important role of the frontal and temporal lobe in the fear network from the perspective of network information transmission, and the negative correlation found between the AUC of nodal global efficiency of SFG and STG and co-atrophy between bilateral dorso-medial PFC, orbital frontal cortex (OFC), and STG (Wu et al., 2018).

Nodal degree centrality and nodal betweenness centrality are two indicators that reflect the importance of a particular node in the network. Consistent with the decreased nodal global efficiency in right SFG and right MTG, decreased nodal degree centrality of these two regions were also found in PD patients, which revealed extensive disrupted connectivity of SFG and MTG across the whole brain and again emphasized the important role of SFG and MTG in the pathogenesis of PD.

Nodal degree centrality comparisons also found increased degree centrality in right PCC and left superior occipital gyrus in PD. Although PCC is not a typical part of the fear network, PCC changes have been reported repeatedly in structural and functional MRI studies. For instance, gray matter deficits (C.-H. Lai, Hsu, & Wu, 2010) and higher fractional anisotropy (FA) (Han et al., 2008) were found in PCC in PD patients. Greater activation in PCC was also found in PD while facing threat-related stimuli (Maddock et al., 2003). Moreover, a recent fMRI study found increased activation in PCC in PD in a breath-holding task and a positive relationship between activation of PCC and self-reported fear (McIntosh et al., 2020). As a partial region involved in default mode network (DMN), PCC is correlated with self-referential and internally generated thoughts (Buckner et al., 2008). Thus, increased degree centrality in PCC may indicate overactivation of DMN posterior sub-network, which might cause excessive attention to internal and external threat-related stimuli in PD (Coutinho et al., 2016; C.-H. Lai & Wu, 2014). Increased degree centrality in left superior occipital gyrus in PD proved the “extent fear network” hypothesis (C. H. Lai, 2019). In Lai’s advanced fear network model, the occipital lobe might also be involved in fear identification and adaptation along with the thalamus, amygdala, frontal regions, and other sensory regions (C. H. Lai, 2019; Leitman et al., 2008). The occipital lobe is associated with face recognition (Japee et al., 2009), visual spatial attention (Macaluso et al., 2000) and fearful stimuli processing (Bayle & Taylor, 2010). Increased degree centrality in occipital gyrus indicated the abnormality of sensory information, especially fear signals processing and transmission to the fear network (van de Riet et al., 2009), which might be related to the sensitivity of fearful stimuli and excessive anxiety in PD (Tauscher et al., 2001).

Increased nodal betweenness centrality in left angular gyrus, which is involved in fear conditioning (Spoormaker et al., 2011), indicated excessive FC of angular gyrus with other regions in PD. On the other hand, decreased regional homogeneity was reported in angular gyrus in remitted PD patients after antidepressant treatment (C. H. Lai & Wu, 2013a). Our study also found a positive relationship between betweenness centrality of angular gyrus and HAMA scores, which corresponded with previous studies showing angular gyrus abnormalities in patients with anxiety disorders (Eren et al., 2003; Liao et al., 2010; Qiu et al., 2011).

NBS analysis identified lower FC between MTG and 4 other regions located mainly in bilateral temporal lobe and left postcentral lobe. This result was inconsistent with Lai’s, which may be due to different patient samples and a stricter statistical indicator (voxel $p < 0.001$) in our study (C. H. Lai & Wu, 2016). Decreased FC in extensive temporal regions supported the “extended fear network” hypothesis raised by Lai (C. H. Lai, 2019), which emphasized the role of temporal lobe in the fear network. Corresponding with our previous meta-analysis of VBM studies of PD (Wu et al., 2018), MTG played a crucial role in the neuropathology of PD. Decreased GMV of MTG in PD has been reported in several structural MRI studies of PD (Massana et al., 2003; Sobanski et al., 2010) although functional fMRI studies of PD have shown inconsistent results. As a crucial part of the
temporal lobe, MTG is involved in many functions: semantic processing (Carin et al., 2010; Mcdermott et al., 2003), auditory stimuli processing (Mirz et al., 1999), facial expression processing (Sato et al., 2012), and reasoning (Goel et al., 1998). For example, a recent study reported higher activation in MTG in PD patients during negative picture viewing (Reinecke et al., 2015). FC abnormalities of MTG might indicate greater cognitive dysfunctions in PD (except for emotion regulation) (Galderisi et al., 2008). Decreased FC between right MTG and right transverse temporal gyrus revealed disrupted information transfer in perceptive and cognitive function in PD. However, a positive relationship between the FC of these two regions and anxiety symptoms may indicate different connectivity patterns between PD and HC.

There are several limitations in our study. First, the sample size is small and the conclusions of this study need to be verified repeatedly. Second, some patients were taking medicines at the time of MRI scanning. Future studies could recruit drug-naive patients to reduce bias caused by sample heterogeneity; Third, the present study used the AAL template, which divided the brain on an anatomical basis. The parcellation of the brain into meaningful regions remains an open issue (Yong He & Evans, 2010; Wang & Jinhui, 2010; Wig et al., 2011). Random parcellation might also be needed. Finally, the present study is cross-sectional; longitudinal studies are still needed to follow up with patients.

Conclusion

Our results suggested that PD patients had decreased global and regional information transmission. Decreased nodal network efficiency of SFG, STG and MTG suggests disrupted inhibitory function of fear response in PD. Lower FC between MTG and other temporal regions might indicate the important role of temporal regions in the pathology of PD.

Acknowledgements We would like to thank all the research assistants who supported the recruitment and scanning for this study.

Authors’ contributions Author contributed included conception and study design (CW), acquisition of data (MP, HX, HD), statistical analysis (YZ, GZ, YL), interpretation of results (NZ), drafting the manuscript work (YZ) or revising it critically for important intellectual content (all authors) and approval of final version to be published and agreement to be accountable for the integrity and accuracy of all aspects of the work (all authors).

Funding This study was supported by National Natural Science Foundation of China [Grant Numbers 81971289, 81871344, 81671667, 81471644]; Jiangsu Provincial key research and development program [Grant Number BE2019609]; Natural Science Foundation of Jiangsu Province [Grant Number BK20191369]; the Natural Science Foundation of the Higher Education Institutions of Jiangsu Province, China [Grant Number 18KJB190003]; Qing Lan project of higher education institutions of Jiangsu Province.

Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Code availability Not applicable.

Declarations

Conflict of interest All authors report no biomedical financial interests or potential conflicts of interest. This study has not been published previously and has not been reproduced from prior publications.

Ethical approval This study was reviewed and approved by the Ethics Committee of the Nanjing Brain Hospital, affiliate of Nanjing Medical University.

Consent to participate After complete explanation of the procedures to participants, written informed consent was obtained.

Consent for publication All the authors agreed to publish this study in this journal.

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