Comparison of Resting-State Spontaneous Brain Activity between Treatment-Naive Patients with Schizophrenia and Obsessive-Compulsive Disorder

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Research Article

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1 **Comparison of Resting-State Spontaneous Brain**
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3 **Schizophrenia and Obsessive-Compulsive Disorder**

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Background: Schizophrenia (SZ) and Obsessive-compulsive disorder (OCD) share many demographic and clinical symptoms, genetic risk factors, pathophysiological underpinnings, and brain structure and function. However, the differences in the spontaneous brain activity patterns between the two diseases remain unclear. Here this study aimed to compare the features of intrinsic brain activity in treatment-naïve patients with schizophrenia (SZ) and obsessive-compulsive disorder (OCD) and to explore the relationship between spontaneous brain activity and the severity of symptoms.

Methods: Twenty-two treatment-naïve patients with SZ, twenty-seven treatment-naïve patients with OCD, and sixty healthy controls underwent resting-state functional magnetic resonance imaging (fMRI). The amplitude of low-frequency fluctuation (ALFF), regional homogeneity (ReHo) and degree of centrality (DC) of SZ group, OCD group and healthy control (HC) group were compared.

Results: Compared with SZ group and HC group, patients with OCD had significantly higher ALFF in the right angular gyrus and the left middle frontal gyrus/precentral gyrus, and significantly lower ALFF in the left superior temporal gyrus/insula/rolandic operculum and the left postcentral gyrus. Compared with HC group, lower ALFF values in the right supramarginal gyrus/inferior parietal lobule and DC values of the right

lingual gyrus/calcarine fissure and surrounding cortex of the two patient groups, higher ReHo values in OCD group and lower ReHo values in SZ group in the right angular gyrus/middle occipital gyrus brain region, and higher DC values in the right inferior parietal lobule/angular gyrus in SZ group were documented in the present study. In addition, the ALFF values of the left postcentral gyrus were positively correlated with positive subscale score and general psychopathology subscale score respectively on the Positive and Negative Syndrome Scale (PANSS) in SZ group. The ALFF values in the left superior temporal gyrus/insula/rolandic operculum of patients with OCD were positively correlated with compulsion subscale score and total score respectively on the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS).

Conclusion: Our data showed various patterns of spontaneous brain activity damage in resting-state between treatment-naïve patients with SZ and OCD, which might imply different underlying neurobiological mechanisms in SZ and OCD.

Keywords: schizophrenia, obsessive-compulsive disorder, resting-state fMRI, amplitude of low-frequency fluctuation, degree centrality, regional homogeneity

52 **Background**

53 Although Schizophrenia (SZ) and obsessive-compulsive disorder (OCD) are separate
54 diagnostic entities, they both share high comorbidity, and the family history of OCD is
55 a risk factor for SZ, suggesting that they may have some common neurobiological bases
56 [1]. SZ and OCD equally belong to neurodevelopmental disorders and are characterized
57 by similar traits, e.g., reportedly numerous overlaps between the two disorders in some
58 domains, like demographic and clinical characteristics, genetic risk factors,
59 pathophysiological underpinnings, and brain structure and function [2, 3].
60 There is increasing evidence that SZ and OCD share neurobiological abnormalities [4,
61 5], but some studies have failed to find overlap between them. For example, some
62 studies have found that compared with OCD, SZ represents more serious biological
63 disorders and greater neurological abnormalities [6-8]. It was found that there were
64 abnormalities in brain structure and brain function activity in patients with SZ and OCD
65 compared to those in healthy controls [9-12]. However, the unique and shared
66 neuroanatomical characteristics of the two diseases have not been fully identified [2, 5,
67 8]. To address the issue, there have been increasing research proposals to directly
68 compare the brain imaging characteristics between SZ and OCD under the same

research methodology and framework, which is conducive to a better understanding of the relationship between the two disorders [5, 8, 13, 14].

Resting-state functional magnetic resonance imaging (rs-fMRI) is a promising tool for examining the blood oxygen level-dependent (BOLD) signal of the spontaneous fluctuation of the whole brain, which does not require subjects to participate in cognitive activities and is more convenient in clinical practice [15, 16]. Several methods such as the amplitude of low-frequency fluctuation (ALFF), regional homogeneity (ReHo), and degree centrality (DC) have been proposed to explore spontaneous brain activity in local and distant brain regions. These three values complement each other and define brain functional characteristics from different perspectives [17-23]. ALFF is an indicator that is used to detect the regional intensity of spontaneous fluctuation in the BOLD signal, which pinpoints the spontaneous neural activity of a specific region and physiological state of the brain in a resting state [17, 19]. The ReHo method, testing the local correlations in BOLD time series by using Kendall's coefficient of concordance (KCC), is often used to investigate regional synchronizations of temporal changes in the brain. A higher ReHo value for a given brain region indicates greater regional coherence [20, 21]. Based on the voxel level, DC is a measure of the connectome graph indexing the number of direct connections for a given node and

reflects its functional connectivity (FC) within the whole brain network without requiring a priori selection [22, 23]. A node with high DC indicates that it has many direct connections to other nodes in the brain networks. In recent years, these three values have been widely used to investigate functional modulations in numerous neuropsychiatric disorders [23-28].

Previous studies have found that patients with OCD showed a variety of impairments, such as executive function, visuospatial and verbal memory, and emotional processing [9, 10]. Neurobiologically, these functional defects are considered to be related to functional abnormalities within not only the cortico-striato-thalamo-cortical (CSTC) circuits, but also more extensive local brain outside the CSTC circuits, e.g., the prefrontal cortex, parietal cortex, occipital cortex, and other brain regions [9, 10, 23, 29, 30]. Patients with SZ can be involved in visual, auditory, and other sensory impairments and cognitive impairments [31, 32]. It is believed that schizophrenia has a complex etiopathogenesis and is related to a wide range of neural circuits [33]. A meta-analysis reported that patients with SZ had abnormal brain function in a wide range of brain regions such as frontal, temporal, parietal, occipital, and orbitofrontal cortices [34]. As for fMRI studies, decreased FC in distinct occipital subdivisions were reported by a recent resting-state study in patients with OCD [10]

and increased activation in the bilateral dorsolateral prefrontal cortex (dlPFC), as well as a decreased activation in the left inferior occipital gyrus (IOG), were demonstrated in executive function and emotional processing fMRI studies by a recent meta-analysis [9]. In addition, previous fMRI studies have shown that the ALFF is lower in people with either SZ [27, 35, 36] or OCD [37-39], and the ReHo is impaired in people with either SZ [40] or OCD [41]. Also, the DC declines in people with SZ [42, 43] or OCD[44, 45]. Moreover, SZ and OCD may putatively share common neural networks in several crucial regions, including the anterior cingulate gyrus, orbitofrontal cortex (OFC) and thalamus, based on the review of several previous researches [46]. Particularly, under the same research conditions, our previous diffusion MRI study showed that SZ and OCD had different patterns of anatomical and topological organizations, which both present more severe and extensive disruptions in SZ [8]. Taken together, associations of brain networks between patients with SZ and OCD have been proposed and furthermore many previous fMRI studies have demonstrated abnormalities of ALFF, ReHo, and DC in multiple brain regions of patients with either SZ or OCD, whereas no consistent conclusion has been reached.

However, as far as we know, there have been very few studies combining multiple values to directly compare intrinsic brain abnormalities between SZ and OCD.

Therefore, in the present study, we aimed to compare the characteristics of resting-state spontaneous brain activity between treatment-naive patients with SZ and OCD by adopting ALFF, ReHo and DC, and further to explore the relationships between brain spontaneous activities and clinical symptoms. We hypothesized that both SZ and OCD have abnormal spontaneous neural activity, whereas they share distinct neural activity. This study was to compare the SZ mechanism with the OCD mechanism in ALFF, ReHo and DC.

Methods

Participants

This study was approved by the Research Ethics Review Board of Wuxi Mental Health Center. All methods were performed in accordance with the relevant guidelines and regulations, and all participants provided written informed consent. We collected imaging data of 29 patients with SZ, 29 patients with OCD and 65 healthy controls (HC). All patients met the DSM-IV-TR criteria and none of them had received any pharmacologic treatment or psychotherapies before the MRI scanning of this study. MRI scans and evaluations of clinical symptoms of the patients were completed on the same day. Positive and Negative Syndrome Scale (PANSS) was conducted in patients

with SZ by experienced psychiatrists. As for patients with OCD, the severity of obsessive-compulsive symptoms, anxious and depressive symptoms were respectively assessed by Yale-Brown Obsessive Compulsive Scale (Y-BOCS) [47], Hamilton Anxiety Rating Scale (HARS) [48] and 24-item Hamilton Rating Scale for Depression (24-HDRS) [49], respectively. Individuals having a lack of current or historic diagnoses of any psychiatric disorder were chosen as healthy controls. Besides, individuals with family histories of any psychiatric disorders or neurological illnesses were excluded from healthy controls. All recruited participants were right-handed when assessed with Edinburgh Handedness Inventory [50]. Besides, exclusion criteria for all participants include brain injury, intracranial pathology, substance abuse, neurological illness, pregnancy, contraindications of MRI, and head movements during scanning more than 3 mm or 3.0° in any direction. Four patients with SZ and 1 healthy control were excluded because of incomplete collection function. Three patients with SZ, 2 patients with OCD, and 4 healthy controls were excluded due to excessive head motion cumulatively more than 3 mm or 3° in any direction. Finally, 22 patients with SZ, 27 patients with OCD, and 60 healthy controls were included in the statistical analysis. Table 1 provides detailed demographic and clinical characteristics.

Data acquisition

MRI was performed at the Department of Medical Imaging, Wuxi People's Hospital, Nanjing Medical University by using a 3.0-Tesla Magnetom Trio Tim (Siemens Medical System, Erlangen, Germany) and a 12-channel phased-array head coil. All participants, whose heads were fixed with foam pads to reduce scanner noise and head motion, were required to close their eyes, to relax their minds but not to fall asleep, and to move as little as possible during imaging acquisition. Three-dimensional T₁-weighted images were acquired using the 3D magnetization-prepared rapid acquisition gradient-echo sequence with the following parameters: time repetition (TR) = 2530 ms, time echo (TE) = 3.44 ms, flip angle = 7°, field of view (FOV) = 256 × 256 mm², matrix size = 256 × 256, slice thickness = 1 mm, 192 sagittal slices, acquisition voxel size = 1 × 1 × 1 mm³, total acquisition time = 649 s. Resting-state fMRI was conducted by using a gradient-echo planar imaging sequence. T₂-weighted images were taken (single shot, TR = 2000 ms, TE = 30 ms, flip angle = 90°, FOV = 220 × 220 mm², matrix size = 64 × 64, slice thickness = 4 mm, 33 axial slices, acquisition voxel size = 3.4 × 3.4 × 4 mm³, resulting in 240 volumes).

Data preprocessing

Analysis of the RS-fMRI data was performed by using Data Processing and Analysis of Brain Imaging [51] (DPABI; http://rfmri.org/DPABI_V4.3) in MATLAB 2013b (The

Math Works, Natick, MA, USA) based on Statistical Parametric Mapping (SPM12;
<http://www.fil.ion.ucl.ac.uk/spm/software/spm12>). The first 10 time points were
discarded for initial signal stabilization. The remaining 230 volumes were corrected for
the intra-volume acquisition time delay using slice timing correction and were realigned
for head movement correction. If the head movement was more than 3 mm or 3°, the
data were excluded from the analysis. To further eliminate the residual effect of motion
on resting-state fMRI measurement, Jenkinson's mean framewise displacement (mean
FD) was calculated based on their realignment parameters to quantify head motion,
which was used as a covariable of all voxel-wise group functional analyses [17, 52].
Each T₁-weighted image was registered with the average functional image, and the
image was divided into white matter, gray matter, and cerebrospinal fluid tissue maps.
Then the image space was normalized to the standard Montreal Neurological Institute
(MNI) space, and the resampling was $3 \times 3 \times 3\text{mm}^3$. Subsequently, the generalized
linear model was used to regress the signals from white matter and cerebrospinal fluid
and the covariates of Friston-24 parameters, and linear trends of the time courses were
removed from the fMRI data [53, 54]. Before ALFF analysis, a Gaussian filter (6-mm
full-width half-maximum, FWHM) was used for spatial smoothing, but smoothing was
performed after ReHo and DC calculations. Smoothing before the calculation of ReHo

and DC will cause the regional correlation of adjacent voxels and affect the calculation of the above two values, so smoothing was usually carried out after calculation to reduce spatial noise and reduce the incompleteness of the registration effect of the subjects [22, 55]. Finally, DPABI_V4.3 was used to calculate the values of the ALFF, ReHo and DC.

ALFF analysis

After data preprocessing, the time series for each voxel was transformed to the frequency domain using fast Fourier transforms, and the square root of this spectrum was calculated for each frequency and then averaged across 0.01–0.08 Hz [19]. This averaged square root was used as an ALFF index. For standardization, the ALFF of each voxel was divided by the global mean ALFF, to get the mALFF map [56, 57].

ReHo and DC analyses

ReHo and DC values were measured based on unsmoothed data. After preprocessing, a temporal filter (0.01–0.08 Hz) was applied to reduce the influences of high-frequency physiological noises and low-frequency drifts.

The ReHo value was obtained on a voxel-by-voxel basis by calculating Kendall's coefficient of concordance of a given voxel with those of its 26 nearest neighbors [20].

211 Then the ReHo value of each voxel was divided by the global mean ReHo of each
212 individual, to get the mReHo map [56, 57]. Next, mReHo maps were smoothed with a
213 6-mm FWHM Gaussian kernel.

214 After data preprocessing, fMRI data were used to calculate the voxel-wise DC,
215 and then Pearson's correlation method was utilized to correlate the time series of each
216 voxel with the time series of every other voxel, after which a matrix of Pearson's
217 correlation coefficients matrix was obtained. Next, the correlation coefficient of $r = 0.25$
218 was used as the lowest threshold to eliminate the low time correlation caused by signal
219 noise [22, 58]. Subsequently, the binary degree centrality values of the whole-brain
220 network were calculated [57, 59]. As a result, each participant obtained a map of the
221 DC value of each gray matter voxel. Before group-level statistical analysis, we divided
222 DC of each voxel by the global mean DC, to get the mDC map, and then used Gaussian
223 smoothing kernels (full width half maximum, half-width = 6 mm) to spatially smooth
224 all individual mDC maps [56, 57].

225 **Statistical analyses**

226 The demographic and clinical data of the subjects were analyzed by SPSS 25.0 software
227 (SPSS, Chicago, IL, United States). The normal distribution data were described as the

average $\pm$ standard deviation, while the non-normal distribution data were presented by the median (the first quartile-the third quartile). The age and education level of the three groups showed normal distribution, and then a one-way analysis of variance (ANOVA) was used to test differences among the three groups. The course of disease of the two patient groups was not subject to the normal distribution, and a Mann-Whitney U test was used to assess between-group differences. The mean framewise displacement (FD) was also not subject to the normal distribution, and a Kruskal-Wallis test was used to detect whether there were significant differences among the three groups. A P value of < 0.05 was considered to be statistically significant.

The statistical analysis of fMRI data was conducted using SPM12 software. The voxel-wise ANCOVA was used to test the differences in ALFF, ReHo and DC among the three groups. The confounding factors of age, sex, the level of education, and Jenkinson's mean FD were controlled as covariates. The multiple comparisons correction of statistical F-maps was performed with family-wise error (FWE) cluster-corrected ($P < 0.05$) when using a primary voxel determining the threshold of $P < 0.001$ to protect against false-positive findings. For the clusters showing significant differences among the three groups, the mean ALFF, ReHo and DC values were extracted from the cluster for each participant. Then the post-hoc analyses were

conducted using SPSS25.0, and the analyses were corrected for multiple comparisons using Bonferroni correction at a statistical significance level of $P < 0.05$. Moreover, partial correlation analysis was performed to evaluate the relationship between the ALFF, ReHo and DC values extracted from the above-mentioned significant difference clusters respectively and the severity of symptoms (Y-BOCS and PANSS scores). Age, sex, the level of education, Jenkinson's mean FD, and course of disease were taken as covariates. Results with $P < 0.05$ (uncorrected) were considered statistically significant.

Results

Demographics and clinical characteristics

Demographic, clinical variables and the mean FD of the participants are presented in Table 1. There was no significant difference in the mean FD among SZ group, OCD group and HC group ($P > 0.05$). There were significant differences in age and education level among the three groups ($P < 0.05$), but not in sex ($P > 0.05$). The results of post-hoc analysis showed that the age of OCD group was lower than that of HC group, and the education level of SZ group was lower than that of HC group (Bonferroni, $P < 0.05$). The duration of disease in OCD group was significantly longer than that in SZ group ($P < 0.05$).

ALFF differences among the three groups

The results of ANCOVA analysis showed that there were significant differences among the three groups (voxel significance, $P < 0.001$; cluster significance, $P < 0.05$, FWE correction) in the right angular gyrus, the left superior temporal gyrus/insula/rolandic operculum, the left middle frontal gyrus/ precentral gyrus, the left postcentral gyrus, and the right supramarginal gyrus/inferior parietal lobule (**Figure 1A; Table 2**).

Post hoc t-tests ($P < 0.05$, Bonferroni correction) showed that compared to HC group, the ALFF values in the right supramarginal gyrus/inferior parietal lobule of the two patient groups were lower (SZ group: 1.07 ± 0.18 ; OCD group: 1.12 ± 0.15 ; Healthy group: 1.37 ± 0.29 , **Figure 2A**). Compared to HC group, patients with OCD had higher ALFF in the right angular gyrus (SZ group: 1.08 ± 0.26 ; OCD group: 1.60 ± 0.48 ; Healthy group: 1.17 ± 0.21 , **Figure 2A**) and the left middle frontal gyrus/precentral gyrus (SZ group: 0.75 ± 0.10 ; OCD group: 0.92 ± 0.20 ; Healthy group: 0.68 ± 0.12 , **Figure 2A**), and lower ALFF in the left superior temporal gyrus/insula/rolandic operculum (SZ group: 0.76 ± 0.16 ; OCD group: 0.60 ± 0.11 ; Healthy group: 0.75 ± 0.14 , **Figure 2A**) and the left postcentral gyrus (SZ group: 1.49 ± 0.50 ; OCD group: 1.00 ± 0.29 ; Healthy group: 1.28 ± 0.40 , **Figure 2A**). Compared to OCD group, the ALFF values of SZ group in the left superior temporal gyrus/insula/rolandic operculum and the left postcentral gyrus

were significantly higher, while those in the right angular gyrus and the left middle frontal gyrus/precentral gyrus were significantly lower (**Figure 2A**).

ReHo differences among the three groups

As for the ReHo, ANCOVA showed significant differences in the right angular gyrus/middle occipital gyrus (voxel significance, $P < 0.001$; cluster significance, $P < 0.05$, FWE correction) (**Figure 1B; Table 2**) among the three groups. Compared with HC group, the ReHo values of the right angular gyrus/middle occipital gyrus (SZ group: 1.23 ± 0.20 ; OCD group: 1.47 ± 0.17 ; Healthy group: 1.32 ± 0.11 , **Figure 2B**) were significantly higher in OCD group, whereas those were significantly lower in SZ group ($P < 0.05$, Bonferroni correction).

DC differences among the three groups

Analysis of ANCOVA showed that there were significant differences in DC of the right lingual gyrus/calcarine fissure and surrounding cortex and the right inferior parietal lobule/angular gyrus among the three groups (**Figure 1C; Table 2**). Compared to HC group, the DC values in the right inferior parietal lobule/angular gyrus (SZ group: 1.03 ± 0.21 ; OCD group: 0.83 ± 0.21 ; Healthy group: 0.76 ± 0.18 , **Figure 2C**) were significantly higher in SZ group and significantly lower in the right lingual

gyrus/calcarine fissure and surrounding cortex (SZ group: 1.21 ± 0.28 ; OCD group: 1.28 ± 0.28 ; Healthy group: 1.51 ± 0.22 , **Figure 2C**) in both SZ and OCD group. Compared to OCD group, the DC values of SZ group were significantly higher in the right inferior parietal lobule/angular gyrus ($P < 0.05$, Bonferroni correction).

Correlation with clinical scores

In SZ group, the ALFF values in the left postcentral gyrus were positively correlated with PANSS positive subscale score ($r = 0.588$, $P = 0.013$, uncorrected, **Figure 3A**) and PANSS general psychopathological subscale score ($r = 0.488$, $P = 0.047$, uncorrected, **Figure 3A**), respectively. The ALFF values in the left superior temporal gyrus/insula/rolandic operculum of patients with OCD were positively correlated with compulsion subscale score ($r = 0.463$, $P = 0.030$, uncorrected, **Figure 3B**) and total score of Y-BOCS ($r = 0.5713$, $P = 0.005$, uncorrected, **Figure 3B**).

Discussion

To the best of our knowledge, this work is the first attempt to directly compare the intrinsic brain functional alterations in treatment-naïve patients with SZ and OCD by adopting multiple imaging parameters. Compared to using any one of the parameters alone, the combination of the three methods may yield a valid and comprehensive

pathophysiological framework in brain studies [60, 61]. In the present study, there were significant differences among healthy controls, patients with SZ and OCD respectively in the values of ALFF, ReHo and DC in a series of brain regions. Our results showed that compared with patients with SZ and HC, patients with OCD had significantly higher ALFF in the right angular gyrus and the left middle frontal gyrus/precentral gyrus, and significantly lower ALFF in the left superior temporal gyrus/insula/rolandic operculum and the left postcentral gyrus, but there was no significant difference in ALFF of the above-mentioned brain regions between SZ group and HC group. Compared to HC group, the ALFF values in the right supramarginal gyrus/inferior parietal lobule of the two patient groups were lower. The ReHo values of the right angular gyrus/ middle occipital gyrus in OCD group were significantly higher than those in HC group, while those in SZ group were significantly lower than those in HC group. Compared with HC group, the DC values in the right inferior parietal lobule/angular gyrus were significantly higher in SZ group, and significantly lower in the right lingual gyrus/calcarine fissure and surrounding cortex in both SZ and OCD group. The exploratory correlation analyses showed that the ALFF values of specific brain regions were related to the clinical symptoms of the patients with SZ and OCD respectively.

ALFF alterations in patients with SZ and OCD

ALFF was supposed to reflect the intensity of regional spontaneous neuronal activity [62]. Previous studies have found that patients with OCD generally have abnormalities in the brain areas within the cortico-striato-thalamo-cortical (CSTC) circuits, whereas increasing abnormalities have also been found in the brain regions outside the CSTC circuits. This study found that patients with OCD displayed abnormal spontaneous neural activities in the brain regions outside the CSTC circuits, such as the parietal lobe, temporal lobe, occipital lobe, and prefrontal lobe, which was consistent with the results of previous studies [23, 28, 30]. The results of this study did not demonstrate the damage of spontaneous brain activities in the common CSTC circuits such as the orbitofrontal lobe, thalamus, and anterior cingulate gyrus in patients with OCD, which may be related to the difference of sample size and research methods. Our findings provide broader evidence that brain regions outside the CSTC circuits are involved in the pathophysiology of OCD.

The inferior parietal lobule, including the supramarginal gyrus and angular gyrus, is a major network hub of the human brain and plays an important role in a wide range of behaviors and functions from bottom-up perception to social cognition. It plays an important role in many networks, including frontoparietal control network, default

mode network (DMN), ventral attention network, and cingulo-opercular network. Several studies have reported changes in connectivity in these networks in patients with OCD [63, 64]. It was reported that patients with OCD have abnormalities in the inferior parietal lobule, reflecting a lack of cognitive flexibility, which may be associated with the repetition of obsessive-compulsive symptoms and behaviors [65]. Previous reviews suggested that the inferior parietal lobule may play an important role in SZ [66]. The impairment of the inferior parietal lobule in patients with SZ mainly affects their body image, sensory integration, self-concept, and executive function [66]. We observed that the ALFF values in the right supramarginal gyrus/inferior parietal lobule of the two patient groups were lower than those in HC group, and the ALFF values in the right angular gyrus in patients with OCD were significantly higher than those in HC group, suggesting that the local spontaneous brain activities in the inferior parietal lobule were impaired in both patient groups.

ReHo alterations in patients with SZ and OCD

ReHo reflects neural functional synchronization in local brain regions [20, 67]. Compared with HC group, the ReHo values of the right angular gyrus/middle occipital gyrus were significantly higher in OCD group and lower in SZ group. The angular gyrus is located in the parietal lobe and is mainly related to skill learning, attention, and

working memory [68]. These present findings are compatible with the previous functional alterations results. Niu et al [69]. demonstrated that higher ReHo values were found in the left angular gyrus in patients with OCD. Nierenberg et al [70]. found that the volume of the left angular gyrus in patients with new-onset schizophrenia was smaller than that in healthy subjects and proposed that the angular gyrus may be the neuroanatomical substrate of the expression of SZ. The occipital cortex is considered to play an important role in early visual processing, such as visual hallucinations and object-recognition defects [71]. Fan et al. found that patients with OCD had higher ALFF in the right middle occipital gyrus [72]. Moreover, the occipital cortex was also demonstrated to play an important role in OCD by several previous studies [72, 73]. Yu et al [74]. reported lower ReHo in the occipital lobe in patients with SZ. Therefore, the distinct patterns of ReHo values in the right middle occipital gyrus, which were lower in patients with SZ and higher in patients with OCD, respectively, may indicate differently impaired visual processing in the two different diseases, which is compatible with the previous findings on the eye movements characteristics of patients with SZ and OCD [75].

DC alterations in patients with SZ and OCD

DC reflects the role and importance of the nodes or brain regions in the brain networks [22, 23]. Both patients' groups showed lower DC in the right lingual gyrus/calcarine fissure and surrounding cortex in the current study. The lingual gyrus and calcarine fissure and surrounding cortex are located in the occipital lobe and are closely related to visual information processing. The lingual gyrus, an important part of the visual recognition network, plays a role in mediating visual word processing and analyzing the complex features of visual forms, and participates in emotion perception during facial stimulation, especially facial recognition [76]. Several studies have observed structural or functional abnormalities of the lingual gyrus or occipital lobe in patients with SZ and OCD [9, 77-80]. The meta-analysis of Gao et al. [77] showed structural abnormalities in the lingual gyrus in drug-free patients with SZ. Moreira et al. [9] observed that patients with OCD displayed reduced functional connectivity within and between visual and sensorimotor networks. The authors of the present study believe that these results are consistent with the hypothesis that occipital/parietal deactivation is one of the mechanisms of OCD phenotype. Based on this current study, we speculate that the lower DC in the right lingual gyrus/calcarine fissure and surrounding cortex may contribute to the visual processing deficits in SZ and OCD. This study also found that the DC values of the right inferior parietal lobule/angular gyrus in SZ group were

significantly higher than those in HC group, whereas there was no significant difference in DC value of these brain areas between OCD group and HC group. We speculate that the resting state of the inferior parietal lobule in Patients with SZ is highly vigilant, which may be attributed to the impairment of executive function and cognitive function.

Among these present findings, the abnormalities of ALFF, ReHo and DC in the angular gyrus were especially noticeable. Recent researches have suggested that the angular gyrus is responsible for complex mental phenomena and processes, such as understanding visual and audio inputs [81], interpreting languages [82], retrieving memories [83], and maintaining consciousness [84]. Moreover, the angular gyrus has been demonstrated to be one of the overlapping regions between the default mode network and social brain networks [85]. Schilbach et al. [85] proposed that the physiological “baseline” of the human brain is linked to the psychological “baseline”, the predisposition human beings have for considering social cognition as the default mode of thought. Concerning SZ and OCD, previous studies have revealed that the functional integration with the right angular gyrus was significantly correlated with sustained attention in both SZ and OCD patient samples [86]. Our data provide empirical evidence about the angular gyrus, whose abnormal spontaneous activities may play an important role in the pathophysiological mechanisms of SZ and OCD.

The positive correlation between ALFF and clinical symptoms severity in patients with SZ and OCD

Our findings showed that the ALFF values in the left postcentral gyrus were positively associated with the severity of clinical symptoms expressed by positive subscale score and general psychopathological subscale score on the PANSS in patients with SZ, and the values of ALFF in the left superior temporal gyrus, insula, and rolandic operculum were positively associated with the severity of clinical symptoms presented by compulsion subscale score and total score on the Y-BOCS in patients with OCD. These present findings are compatible with the previous studies. Qiu et al. [87] reported that abnormal gray matter density in the left postcentral was found, and the abnormal gray matter density in the left postcentral gyrus was associated with RSS, a specific eye movement index of schizophrenia, which is related to the integration of several perceptual/cognitive processes, including selective and sustained attention, and working memory [88-90], reflecting the clinical hallucination severity of schizophrenia [91]. As for OCD, the superior temporal gyrus was documented to be specifically associated with social anhedonia in OCD [92]. Moreover, greater recruitment of the left superior temporal gyrus was found in pediatric Patients with OCD than healthy controls

during combined symptom provocation, which suggested the involvement of the temporal poles in pediatric OCD during symptom provocation [93].

The limitations of our research

The present study has some potential limitations. First, the sample size used for imaging analyses in this study is relatively small, which may limit the value of the research. For example, due to the limitation of the sample size, difficulties in respectively subdividing patients of SZ and OCD into different groups based on symptoms or subtypes increased, resulting in a lack of full consideration of the heterogeneity of the sample. Second, we carefully excluded the influence of confounding factors such as antipsychotic medication in this study. However, the disadvantage is that the three groups of subjects in our present study are unevenly matched in terms of the number of participants, age and education level. In addition, it was reported that different standardized procedures may affect the re-test reliability of ALFF, ReHo and DC [67]. Finally, the present research is a cross-sectional study, and it's better to further adopt longitudinal studies to explore the changes in patients' brain function before and after treatment based on this study, which may be more helpful to the clinic.

Conclusions

In summary, our data demonstrated various patterns of altered spontaneous brain activities in the resting state between treatment-naïve patients with SZ and OCD. Moreover, the exploratory correlation analyses showed that the ALFF values of specific brain regions were related to the clinical symptoms of patients with SZ and OCD respectively. Convergent findings for abnormalities of the angular gyrus suggested this brain region may play an important role in the pathophysiological mechanisms of SZ and OCD. The distinct patterns of intrinsic brain activity were found in the two diseases that are usually reported to share neurobiological abnormalities and genetic characteristics, which may reveal that SZ and OCD have different underlying neurobiological mechanisms.

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Abbreviations

SZ: schizophrenia; OCD: obsessive-compulsive disorder; fMRI: resting-state functional magnetic resonance imaging; ALFF: The amplitude of low-frequency fluctuation; ReHo: regional homogeneity; DC: degree of centrality; HC: healthy control

group; PANSS: Positive and Negative Syndrome Scale; Y-BOCS: Yale-Brown Obsessive-Compulsive Scale; rs-fMRI: Resting-state functional magnetic resonance imaging; BOLD: blood oxygen level-dependent; KCC: Kendall's coefficient of concordance; FC: functional connectivity; CSTC: cortico-striato-thalamo-cortical; dlPFC: dorsolateral prefrontal cortex; IOG: inferior occipital gyrus; OFC: orbitofrontal cortex; HARS: Hamilton Anxiety Rating Scale; 24-HDRS: 24-item Hamilton Rating Scale for Depression; TR: time repetition; TE: time echo; FOV: field of view; MNI: Montreal Neurological Institute; FWHM: full-width half-maximum; mean FD: Jenkinson's mean framewise displacement; FEW: family-wise error; ANOVA: one-way analysis of variance; ANCOVA: Analysis of Covariance; SPSS: Statistical Package for the Social Sciences; DMN: default mode network.

Authors' contributions

LT and ZZ designed the study. HH, XZ, SW, and HL contributed to the acquisition of the data. XY, LQ, LT analyzed the data and drafted the manuscript. All authors contributed to and have approved the final version for publication.

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Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committee of Wuxi Mental Health Center, Nanjing Medical University, China. All participants provided written informed consent.

Consent for publication

Not applicable.

Competing interests

505 The authors declare that they have no conflicts of interest in this work.

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826

827 **Table1**

828 Demographic, clinical and head-motion characteristics of the samples in this study.

Variables	HC (n = 60)	OCD (n = 27)	SZ (n = 22)	Statistics (F/ χ^2 / T/Z/H)	P value
Age (years)	32.87±10.78 ^a	26.89±8.15	33.41±11.03	3.65	0.029 ^{*c}
Education(years)	14.02±3.72	13.26±2.96	10.77±4.74	5.94	0.004 ^{*d}
Sex (M/F)	38/22	21/6	11/11	4.12	0.128 [#]
Disease duration(years)	-	3.00(1.00, 6.00) ^b	1.29(0.17,3.25)	-2.61	0.009 ^{&}
PANSS positive score	-	-	27.18±4.63	-	-
PANSS negative score	-	-	19.82±5.14	-	-
PANSS general score	-	-	46.50±7.58	-	-
PANSS total score	-	-	93.50±12.39	-	-
Y-BOCS score					
Obsession score	-	12.33±3.87	-	-	-
Compulsive score	-	8.70±2.95	-	-	-
Total score	-	21.04±5.93	-	-	-
HARS score	-	14.00(12.00,19.00)	-	-	-
24-HDRS score	-	16.30±7.83	-	-	-
Mean FD	0.07(0.06,0.12)	0.08(0.05,0.12)	0.07(0.05,0.10)	0.95	0.623 [∇]

829 **Note:** ^a Values are presented as mean ± SD.830 ^b Values are presented as median (first quartile, third quartile).831 ^{*}, one-way ANOVA ; [#] , χ^2 test; [&],Mann–Whitney U test; [∇],Kruskal–Wallis test.832 ^c Post-hoc analysis showed that Patients with OCD differed significantly from controls
833 (Bonferroni, $P < 0.05$).834 ^d Post-hoc analysis showed that Patients with SZ differed significantly from controls
835 (Bonferroni, $P < 0.05$).836 $P < 0.05$ is considered significant.837 **Abbreviations:** HC, healthy controls; OCD, patients with obsessive-compulsive
838 disorder; SZ, patients with schizophrenia; PANSS, Positive and Negative Syndrome
839 Scale; HARS, the Hamilton Anxiety Rating Scale; 24-HDRS, the 24-item Hamilton
840 Rating Scale for Depression; Y-BOCS, the Yale-Brown Obsessive-Compulsive Scale;
841 Mean FD, mean framewise displacement.

842

843

844 Table2

845 The ALFF, ReHo and DC clusters with significant between-group differences (Cluster-level P_{FWE}

Feature	Index	Cluster size	Brain regions	side	BA	MNI coordinate			Peak F
						x	y	z	
ALFF	1	47	Angular gyrus	R	39	42	-51	30	29.20
	2	40	Superior temporal gyrus	L	48	-45	-36	24	8.77
			Insula	L	48	-36	-18	15	11.20
			Rolandic operculum	L	48	-36	-27	18	10.85
	3	37	Middle frontal gyrus	L	9	-36	9	51	21.84
			Precentral gyrus	L	6	-36	3	42	12.08
	4	37	Postcentral gyrus	L	4	-24	-30	66	11.39
	5	33	Supramarginal gyrus	R	2	45	-33	39	13.06
			Inferior parietal lobule	R	2	48	-36	51	11.96
ReHo	1	105	Angular gyrus	R	39	42	-51	30	40.14
			Middle occipital gyrus	R	19	39	-72	33	18.76
DC	1	105	Lingual gyrus	R	18	12	-87	-12	17.18
			Calcarine fissure and surrounding cortex	R	17	6	-78	3	8.32
	2	49	Inferior parietal lobule	R	40	54	-57	48	14.42
			Angular gyrus	R	39	60	-57	30	10.19

846 < 0.05 when voxel-level threshold was $P < 0.001$).

847 Abbreviations: BA, Brodmann area; MNI, Montreal Neurological Institute; R, right; L, left; ALFF,

848 amplitude of low-frequency fluctuation; ReHo, regional homogeneity; DC, degree centrality.

849

Figure 1

Significant differences in ALFF, ReHo and DC among healthy controls, patients with schizophrenia and obsessive-compulsive disorder.

854 (A). Brain regions with significant differences (cluster-level $P_{\text{FWE}} < 0.05$ when the voxel-level
855 threshold was $P < 0.001$) of the amplitude of low-frequency fluctuation among healthy controls,
856 patients with schizophrenia and obsessive-compulsive disorder.

857 (B). Brain regions with significant differences (cluster-level $P_{\text{FWE}} < 0.05$ when the voxel-level
858 threshold was $P < 0.001$) of the regional homogeneity among healthy controls, patients with
859 schizophrenia and obsessive-compulsive disorder.

860 (C). Brain regions with significant differences (cluster-level $P_{\text{FWE}} < 0.05$ when the voxel-level
861 threshold was $P < 0.001$) of the degree of centrality among healthy controls, patients with
862 schizophrenia and obsessive-compulsive disorder.

863 Notes: The colored bars show F values.

864 Abbreviations: L, left; R, right; ALFF, amplitude of low-frequency fluctuation; ReHo, regional
865 homogeneity; DC, degree centrality

Figure 2

Histogram plots illustrate the mean ALFF/ReHo/DC values of the clusters showing significant differences among the healthy controls, patients with schizophrenia and obsessive-compulsive disorder.

(A). The mean ALFF values in the ANG.R, STG.L/INS.L/ROL.R, MFG.L/PreCG.L, PoCG.L, and SMG.R/IPL.R among the three groups.

(B). The mean ReHo values in the ANG.R/MOG.R among the three groups.

(C). The mean DC values in the ING.R/CAL.R and IPL.R/ANG.R.

Error bars reflect the SD.

Abbreviations: HC, healthy controls; OCD, patients with obsessive-compulsive disorder; SZ, patient with schizophrenia; ALFF, amplitude of low-frequency fluctuation; ReHo, regional homogeneity; DC, degree centrality; ANG.R, right angular gyrus; STG.L/INS.L/ROL.R, left superior temporal gyrus/insula/rolandic operculum; MFG.L/PreCG.L, left middle frontal gyrus/precentral gyrus; PoCG.L, left postcentral gyrus, SMG.R/IPL.R, right supramarginal gyrus/inferior parietal lobule; ANG.R/MOG.R, right angular gyrus/middle occipital gyrus;

884 ING.R/CAL.R, right lingual gyrus/ calcarine fissure and surrounding cortex; IPL.R/ANG.R, right
885 inferior parietal lobule/ angular gyrus.
886

Figure 3:

Scatter plots show the relationships between the ALFF values and the clinical symptoms in patients with schizophrenia and obsessive-compulsive disorder.

(A). The ALFF values of the left postcentral gyrus of patients with SZ were positively correlated with the scores of PANSS general pathology scale and positive subscale; (B). The ALFF values in the left superior temporal gyrus/insula/rolandic operculum brain area of patients with OCD were positively correlated with compulsion subscale scores and the total scores of Y-BOCS.

Abbreviations: PANSS, Positive and Negative Syndrome Scale; Y-BOCS, the Yale-Brown Obsessive-Compulsive Scale; ALFF, amplitude of low-frequency fluctuation; PANSS-P, PANSS positive score; PANSS-G, PANSS general psychopathological score; Y-BOCS -C, Y-BOCS compulsive score; YBOCS-T, Y-BOCS total score; PoCG.L, left postcentral gyrus; STG.L/INS.L/ROL.R, left superior temporal gyrus/insula/rolandic operculum; R^2 , the coefficient of determination.

Figures

Figure 1

Significant differences in ALFF, ReHo and DC among healthy controls, patients with schizophrenia and obsessive-compulsive disorder. (A) Brain regions with significant differences (cluster-level PFWE < 0.05 when the voxel-level threshold was $P < 0.001$) of the amplitude of low-frequency fluctuation among

healthy controls, patients with schizophrenia and obsessive-compulsive disorder. (B). Brain regions with significant differences (cluster-level PFWE < 0.05 when the voxel-level threshold was $P < 0.001$) of the regional homogeneity among healthy controls, patients with schizophrenia and obsessive-compulsive disorder. (C). Brain regions with significant differences (cluster-level PFWE < 0.05 when the voxel-level threshold was $P < 0.001$) of the degree of centrality among healthy controls, patients with schizophrenia and obsessive-compulsive disorder. Notes: The colored bars show F values. Abbreviations: L, left; R, right; ALFF, amplitude of low-frequency fluctuation; ReHo, regional homogeneity; DC, degree centrality

Figure 2

Histogram plots illustrate the mean ALFF/ReHo/DC values of the clusters showing significant differences among the healthy controls, patients with schizophrenia and obsessive-compulsive disorder.

(A). The mean ALFF values in the ANG.R, STG.L/INS.L/ROL.R, MFG.L/PreCG.L, PoCG.L, and SMG.R/IPL.R among the three groups. (B). The mean ReHo values in the ANG.R/MoG.R among the three groups. (C). The mean DC values in the ING.R/CAL.R and IPL.R/ANG.R. Error bars reflect the SD. Abbreviations: HC, healthy controls; OCD, patients with obsessive-compulsive disorder; SZ, patient with schizophrenia; ALFF, amplitude of low-frequency fluctuation; ReHo, regional homogeneity; DC, degree centrality; ANG.R, right angular gyrus; STG.L/INS.L/ROL.R, left superior temporal gyrus/insula/rolandic operculum; MFG.L/PreCG.L, left middle frontal gyrus/precentral gyrus; PoCG.L, left postcentral gyrus, SMG.R/IPL.R, right supramarginal gyrus/inferior parietal lobule; ANG.R/MoG.R, right angular gyrus/middle occipital gyrus; ING.R/CAL.R, right lingual gyrus/ calcarine fissure and surrounding cortex; IPL.R/ANG.R, right inferior parietal lobule/ angular gyrus.

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Scatter plots show the relationships between the ALFF values and the clinical symptoms in patients with schizophrenia and obsessive-compulsive disorder. (A). The ALFF values of the left postcentral gyrus of patients with SZ were positively correlated with the scores of PANSS general pathology scale and positive

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