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RECEIVED 12 July 2025

ACCEPTED 26 September 2025

PUBLISHED 16 October 2025

CITATION

Zhu P, Wang Y, Xiang J, Gu J, Chen X,
Chen F, Zou L, Ai C, Qin K and Chen W
(2025) Multimodal MRI study of gray matter
and functional connectivity abnormalities in
adolescents with bipolar disorder.
Front. Psychiatry 16:1664729.
doi: 10.3389/fpsyt.2025.1664729

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Multimodal MRI study of gray matter and functional connectivity abnormalities in adolescents with bipolar disorder

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Background: Adolescent bipolar disorder (BD) is a severe psychiatric condition characterized by mood instability, with significant impacts on social and cognitive functioning. Clarifying the neural mechanisms underlying BD during adolescence may aid early diagnosis and treatment.

Methods: We conducted a multimodal neuroimaging study integrating functional and structural MRI data to investigate alterations in spontaneous neural activity (amplitude of low-frequency fluctuation (ALFF) and regional homogeneity (ReHo)), seed-based resting-state functional connectivity (rsFC), and gray matter volume (GMV) in 69 adolescents with BD and 42 matched healthy controls (HCs). ALFF and ReHo were used to identify local functional abnormalities. Overlapping brain regions were selected as seeds for rsFC analysis. Voxel-based morphometry (VBM) was performed to detect GMV differences. Correlations between imaging measures and clinical symptom scores (HAMD, HAMA, YMRS) were assessed.

Results: Compared to HCs, BD patients exhibited significant abnormalities in the ALFF within the default mode network (DMN) and the salience network (SN). ReHo was also altered in the SN. Seed-based rs-FC analysis revealed reduced connectivity between the right supramarginal gyrus and the left middle frontal gyrus, which are key nodes of the frontoparietal network (FPN). VBM analysis demonstrated decreased GMV in the left cerebellum. No significant correlations were found between imaging measures and clinical scale ratings.

Conclusions: Our findings suggest that adolescent BD is characterized by functional abnormalities within DMN and FPN, as well as cerebellar gray matter atrophy. Disrupted structure–function coupling in these regions may reflect possible neurobiological mechanisms underlying BD during adolescence.

KEYWORDS

bipolar disorder, resting-state functional magnetic resonance imaging, voxel- based morphometry, frontoparietal network, default mode network

1 Introduction

Bipolar disorder (BD) is a chronic and debilitating mood disorder characterized by recurrent episodes of mania and depression, with a substantial risk of suicide and functional impairment (1). The disorder imposes considerable individual and societal burdens due to long-term cognitive and emotional dysfunction (2). It is estimated that the incidence rate of BD accounts for approximately 1-2% of the global population. Moreover, in recent years, the age of onset of BD has been continuously advancing (3), and the misdiagnosis rate of diagnosis has also been increasing, early misdiagnosis may miss the best treatment time. Therefore, it is of clinical importance to elucidate the early neurobiological mechanisms underlying adolescent BD and to inform timely and targeted interventions.

Recent advances in the field of neuroimaging have enhanced our understanding of the neurophysiology of this disease (4). In particular, the application of resting-state functional magnetic resonance imaging (rs-fMRI), abnormal local spontaneous brain activity, and resting-state functional connectivity (rsFC) have been repeatedly observed in patients with BD (5, 6). Previous studies have shown that abnormal pathways in large-scale functional networks may be the basis of the pathophysiology of BD (7, 8). In these studies, functional magnetic resonance imaging (fMRI) studies showed that compared with healthy controls (HC), patients with BD had abnormal resting-state functional connectivity (rsFC) in the default mode network (DMN), frontal-parietal network (FPN), salience network (SN), and limbic network (7, 8).

Alterations in gray matter volume (GMV) are also of critical interest in the context of BD, given their relevance to cognition, affect regulation, and disease progression (9). Gray matter structures, including the cerebral cortex and subcortical nuclei, are essential for perceptual, motor, and higher-order cognitive processes (10). Voxel-based morphometry (VBM) provides an automated, objective whole-brain technique to detect subtle morphometric changes associated with psychiatric and neurological disorders (11). Meta-analytic evidence indicates reduced GMV in the left orbitofrontal cortex, right putamen, and right dorsolateral prefrontal cortex in youth with BD relative to healthy controls (12).

Multimodal techniques combining structural and functional methods may provide more useful information for clinical diagnosis. For instance, combining the cortical thickness and functional connectivity (FC) analysis of MDD patients, Spati et al. found that there were indications suggesting that thinning of prefrontal cortex (PFC) might impair the participation of anterior cingulate cortex (ACC) during depressive episodes (13). van et al. found that the cortical thickness of dorsomedial prefrontal cortex (dmPFC) could be used to predict the rsFC between dmPFC and the default mode network (14). The combination of VBM and FC has also been used to study schizophrenia (15), temporal lobe epilepsy (16), and Parkinson's disease (17).

In BD, emerging evidence suggests considerable neurobiological heterogeneity across clinical subgroups. Data-driven cognitive

subtyping has revealed distinct patterns of structural and functional brain alterations, including prefrontal cortical thinning, white matter abnormalities, and altered activation/connectivity in frontoparietal circuits (2, 18–20). Furthermore, two studies demonstrated different BD subgroups based on neural activation during emotion regulation, characterized by differential activation of the prefrontal cortex and amygdala (11, 21, 22). Together, these findings suggest that there is a connection between the changes in brain structure and function in BD and clinical and cognitive phenotypes, which can serve as potential therapeutic targets.

Taken together, these findings highlight the interplay between structural and functional brain alterations and clinical phenotypes in BD, underscoring their potential utility as biomarkers for diagnosis and treatment stratification. However, reliance on unimodal imaging approaches may constrain integrative, transdiagnostic research, as emphasized in the Research Domain Criteria (RDoC) framework promoted by the U.S. National Institute of Mental Health. Combining neuroanatomical and functional connectivity analyses offers a promising avenue for delineating structure–function relationships and refining pathophysiological models of BD (23).

Therefore, the present study aims to investigate alterations in both brain structure and function among adolescents with BD and examine the associations between neuroimaging findings and clinical symptoms. This approach seeks to clarify the underlying neural mechanisms of adolescent BD, inform early identification strategies, and ultimately contribute to reducing diagnostic delays and errors in this vulnerable population.

2 Methods

2.1 Participants

A total of 111 adolescents were recruited for this study, including 69 patients with BD from Taihe Hospital, Hubei University of Medicine, and 42 HCs from the local community. Due to excessive head movement, seven subjects (five BD patients and two HCs) were excluded from the final analysis. All patients met the diagnostic criteria of DSM-IV structured clinical interview (SCID), but in this study, we did not distinguish between BD-I and BD-II. The exclusion criteria are: (1) age below 10 or above 20 years; (2) history of alcohol or substance abuse; (3) any current or past neurological or medical condition affecting cognitive function; (4) history of head trauma with loss of consciousness; (5) contraindications for MRI; and (6) any current DSM-5 Axis I psychiatric disorder other than BD. In this experiment, the manic symptoms of all patients were evaluated using the Young Mania Rating Scale (YMRS). The Hamilton Depression Scale (HAMD) is used to assess the depressive symptoms of patients, and the Hamilton Anxiety Rating Scale (HAMA) assesses the anxiety symptoms of patients. This research adheres to the Declaration of Helsinki. The current research has been approved by the Institutional Review Committee of Shiyan Taihe Hospital

Affiliated to Hubei University of Medicine and Pharmacy. Written informed consent forms of all subjects were obtained before participating in this study.

2.2 fMRI data acquisition

All imaging data were collected using the GE 3T scanner at the Medical Imaging Center of Taihe Hospital in Shiyan City. Initially, the resting-state functional images were collected, followed by the T1 images. During the scanning process, the subjects were asked to try not to swallow or move their bodies, especially their heads. In the resting state, the subjects were also instructed to close their eyes, relax and stay awake. The resting-state functional images were collected using the echo planar imaging (EPI) sequence as follows: Axial scanning, repetition time (TR) = 2000ms, echo time (TE) = 30ms, flip angle = 52°, field of view (FOV) = 240 × 240 mm², matrix size = 80 × 80, number of layers = 62, layer thickness = 3.5 mm Voxel size = 2 × 2 × 2 mm³. T1 images were collected using the brain volume (BRAVO) sequence prepared by T1-weighted sagittal 3D magnetization, as shown below: TR = 7.4ms, TE = 30ms, flip angle = 12°, FOV = 256 × 256 mm², matrix size = 256 × 256, number of layers = 166, layer thickness = 1 mm, voxel size = 1 × 1 × 1 mm³.

2.3 fMRI data preprocessing

Resting-state fMRI data were preprocessed in the toolbox of (resting-state) brain imaging data processing and Analysis (DPABI v3.1) (24). The preprocessing steps include deleting the first five time points, slice timing, realignment, de-trend, removing the head movement effect (using the Friston 24-parameter model) (25), regression of nuisance covariates (white matter signal, cerebrospinal fluid signal, and global mean signal), normalizing the MNI space (using T1 images), and resampling (voxel size) = 2 × 2 × 2 mm³, spatial smoothing (6 mm full-width at half-maximum, applied to ALFF and rsFC analyses) and bandpass filtering (0.01–0.1 Hz, only applicable to ReHo and rsFC analysis). Furthermore, we use volume-based framewise displacement (FD) to quantify head movement (26). FD reflects the head movement from one volume to the next, and a volume with FD < 0.2 indicates a good point in time. The mean FD is calculated as the average of the sum of the absolute values of the differential realignment estimates at each time point (through backward differences) (27). If the number of good time points for the subjects is less than 160, the subjects will be excluded.

2.4 ALFF and ReHo calculation

Using the preprocessed resting-state fMRI data, we calculated the ALFF and ReHo values of each subject in DPABI v3.1. All values are calculated at the voxel level. Calculate the ALFF value using the signal strength in the low-frequency range (i.e., 0.01–0.1 Hz). The

ReHo value, also called the Kendall's coefficient of concordance (KCC), of the time series of a given voxel with its nearest neighbors (27 voxels were considered) was calculated to generate individual ReHo maps. Finally, the ALFF and ReHo maps of each subject were respectively converted into Z-score maps.

2.5 Functional connectivity analysis

This analysis was carried out in DPABI v3.1. The overlapping clusters exhibiting concurrent abnormalities in both ALFF and ReHo among patients with BD were selected as seeds for subsequent functional connectivity analysis. Specifically, clusters showing significant ALFF and ReHo alterations were first extracted to create masks, and their spatial overlap was identified as the seed regions. The average time series of the seed regions were extracted for each subject. Next, Pearson correlation coefficients were computed between the seed time series and the time series of every other voxel in the brain, resulting in a rsFC map for each individual. Finally, each subject's rsFC map was converted into a z-score map using Fisher's z-transformation to improve normality for further statistical analyses.

2.6 VBM analysis

We used the VBM8 (<http://dbm.neuro.uni-jena.de/vbm8>) toolbox in SPM12 (<http://www.fil.ion.ucl.ac.uk/spm>) software to analyze the T1-weighted images. First, check for artifacts in the image and adjust the source of the image to the front merge. Subsequently, the images were segmented into gray matter, white matter and cerebrospinal fluid maps, and then normalized to the standard Montreal Neuroscience Institute (MNI) space, with a voxel size of 1.5 × 1.5 × 1.5 mm³. After checking the data quality of the partitioned map, the gray matter map was further smoothed using an 8 mm full-width, semi-Gaussian kernel.

2.7 Statistical analyses

For the categorical variables of demographic and clinical data, we used chi-square tests for group comparisons. For continuous variables, we first performed a Shapiro–Wilk test to assess normality. If the variables follow a normal distribution, we use the two-sample t-test for group comparison. If the normal distribution is not followed, the Mann-Whitney U test is used to compare the differences between BD patients and HC patients. All statistical analyses were conducted using SPSS version 20.0.

For each functional measure (namely ALFF, ReHo and rsFC), the differences between the two groups were analyzed in SPM12. In these analyses, the two-sample t-test was used to control for age, gender and mean FD. Significance was determined using a voxel-level threshold of $p < 0.001$ (uncorrected) combined with cluster-level family-wise error (FWE) correction at $p < 0.05$. To further

TABLE 1 Demographic and clinical feature of participants.

Demographic	Bipolar disorder (N = 69)	HC (N = 42)	Statistics	P
Age	15(14, 16)	15.8(12, 19)	-0.977(Z)	0.329
Sex (male/female)	20/49	24/18	8.651(χ^2)	0.003
Age of onset	13.47 $\pm$ 1.638	NA	NA	NA
Duration of illness(m)	16.23 $\pm$ 14.571	NA	NA	NA
HAMD	30.5 $\pm$ 15	NA	NA	NA
HAMA	21.58 $\pm$ 10.5	NA	NA	NA
YMRS	14.6 $\pm$ 7.68	NA	NA	NA
Psychotic symptoms	58 ^a	NA	NA	NA
Physical symptoms	59 ^b	NA	NA	NA
Suicide consciousness	53 ^c	NA	NA	NA
Antipsychotic drugs	30 ^d	NA	NA	NA

NA, not applicable; HAMD, Hamilton Depression Scale; HAMA, Hamilton Anxiety Rating Scale; YMRS, Young Mania Rating Scale. ^{abcd}Representing the corresponding number of people.

examine associations between imaging markers and clinical symptoms, we performed Pearson correlation analyses between ALFF and ReHo values from significant clusters and clinical scores (HAMD, HAMA, and YMRS). A Bonferroni-corrected significance threshold of $p < 0.017$ ($0.05/3$) was applied.

For GMV, group differences in gray matter volume were examined using two-sample t-tests in SPM12, controlling for age, sex, and total intracranial volume. The significance level was set as a combination of uncorrected $P < 0.001$ at the voxel level and FWE correction $P < 0.05$ at the cluster level.

3 Results

3.1 Demographic and clinical characteristics

Table 1 summarizes the demographic and clinical data of all the subjects. We found that age did not follow a normal distribution (P

< 0.05). Therefore, the median and the upper and lower quartiles are used for representation. There was a significant difference in gender distribution between the BD group and the HC group ($\chi^2 = 8.651$, $p = 0.003$), among which the proportion of females was higher in the BD group. There was no significant difference in age between the two groups. (Table 1) Given the differences in gender distribution between the two groups (40.8% male in the BD group and 57.1% male in the HC group), gender was included as an independent covariate in the model in all secondary analyses to control its potential confounding effects. Meanwhile, age was also included in the analysis as a covariate (Table 1).

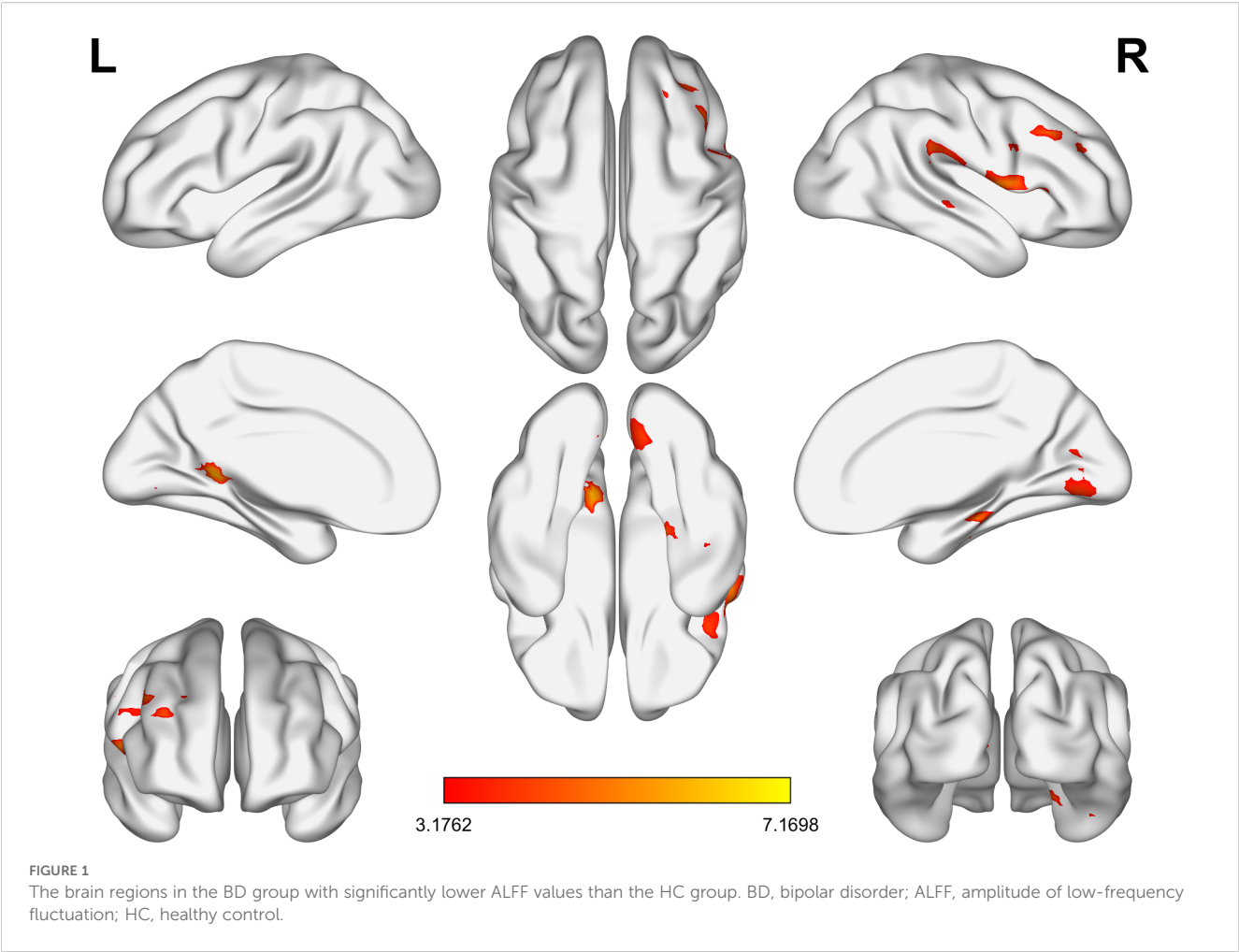
3.2 ALFF and ReHo analysis

Whole brain analysis revealed that in the BD group, the ALFF values in the right supramarginal gyrus, right lingual gyrus, right middle frontal gyrus, left posterior cingulate gyrus, and right parahippocampal gyrus were significantly increased (Table 2, Figure 1).

TABLE 2 Between-group differences in the ALFF analyses between the patients with BD and the healthy controls.

Brain region	Hemisphere	MNI coordinates	Peak T values	Cluster size	Cluster-level P_{FWE}
Patients > Controls					
Supramarginal gyrus	Right	48,-21,27	6.1856	468	<0.001
Lingual Gyrus	Right	6,-69,-3	4.8764	281	0.001
Middle Frontal Gyrus	Right	30,36,24	5.504	265	0.001
Posterior cingulate gyrus	Left	-12,-45,6	6.2056	200	0.003
Parahippocampal Gyrus	Right	15,-12,-15	7.1698	176	0.021

BD, bipolar disorder; ALFF, Amplitude of low-frequency fluctuation; MNI, Montreal Neurological Institute.



As for ReHo, in the BD group, the ReHo values of the right supramarginal gyrus and the left superior occipital gyrus were significantly increased, while those of the left superior frontal gyrus, the left parietal gyrus, the right parietal gyrus, the right middle frontal gyrus and the right middle temporal gyrus were significantly decreased (Table 3, Figure 2).

3.3 Seed-based rsFC analysis

The only overlapping region exhibiting concurrent ALFF and ReHo abnormalities in BD patients was located in the right supramarginal gyrus (185 voxels). Using this cluster as the seed (Supplementary Figure S1), we found decreased rsFC between the

TABLE 3 Between-group differences in the ReHo analyses between the patients with BD and the healthy controls.

Brain region	Hemisphere	MNI coordinates	Peak T values	Cluster size	Cluster-level P_{FWE}
Patients > Controls					
Supramarginal gyrus	Right	48,-21,27	5.1411	229	0.001
Superior occipital gyrus	Left	-21,-66,21	4.4698	89	0.001
Patients < Controls					
Superior Frontal yrus	Left	-3,33,-27	6.7245	813	<0.001
Superior parietal gyrus	Left	-48,-45,51	5.4273	795	<0.001
Superior parietal gyrus	Right	39,-63,51	5.8941	517	<0.001
Middle frontal gyrus	Right	45,24,48	4.9873	300	<0.001
Inferior temporal gyrus	Right	57,-60,-15	6.0793	175	0.003

BD, bipolar disorder; ReHo, regional homogeneity; MNI, Montreal Neurological Institute.

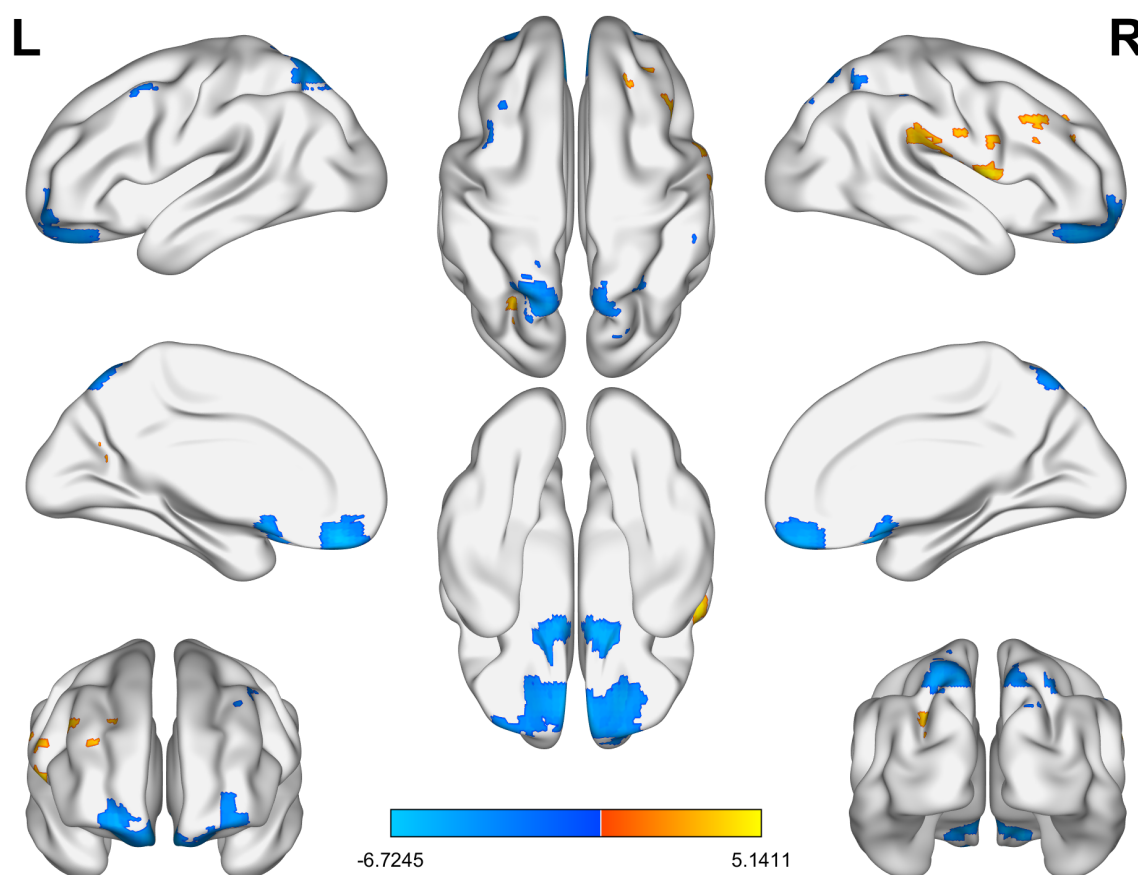


FIGURE 2

The brain regions with significant differences in ReHo values between the BD group and the HC group. Yellow indicates a significant increase and blue indicates a significant decrease. BD, bipolar disorder; ReHo, regional homogeneity; HC, healthy control.

right supramarginal gyrus and the left middle frontal gyrus (Table 4, Figure 3).

3.4 VBM analysis

Whole-brain analysis revealed that in the BD group, the gray matter volume in the left cerebellum was significantly reduced (Supplementary Table S2, Supplementary Figure S2). No regions showed increased gray matter volume.

3.5 Correlation analysis

We did not find a significant statistical correlation between the abnormal brain regions of ALFF and ReHo in the BD group and the total scores of HAMD, HAMA, and YMRS (all $P > 0.017$).

4 Discussion

In this article, we used two main functional indicators (ALFF and ReHo) to measure the spontaneous activities of local activity

connections to the network and functional connections. Our results show that in patients diagnosed with BD, significant increases in ALFF were observed in the left posterior cingulate gyrus and the right parahippocampal gyrus (key nodes in the DMN). In the BD group, increased ALFF was observed in both the right middle frontal gyrus and the right supramarginal gyrus, suggesting a possible compensatory mechanism in these regions. However, ReHo was significantly decreased in several FPN-related regions, including the left superior frontal gyrus, right middle frontal gyrus, right inferior temporal gyrus, and bilateral parietal gyrus, suggesting a decline in their internal functional integration ability. Furthermore, using the overlapping region of the right supramarginal gyrus (the key node in the FPN) as the seed point of rsFC, we found that the rsFC within the FPN decreased, specifically manifested as the reduction of rsFC between the right supramarginal gyrus and the left middle frontal gyrus. Furthermore, we found that the gray matter volume in the posterior cerebellar lobe of BD patients was atrophied.

We used two functional indicators and found that compared with the healthy control group, the ALFF and ReHo values of BD patients in the DMN were increased. The increase of ALFF indicates an increase in local BOLD signal fluctuations (28, 29). The increase of ReHo indicates an increase in the synchronization ability of the

TABLE 4 Between-group differences in the rsFC analyses between the patients with BD and the healthy controls.

Seed		Brain region	Hemisphere	MNI coordinates	Peak T values	Cluster size	Cluster-level P_{FWE}
185 voxels in the Supramarginal gyrus overlapped across ALFF and ReHo	Patients <Controls	Middle frontal gyrus	Left	-24,45,15	4.7608	908	<0.001

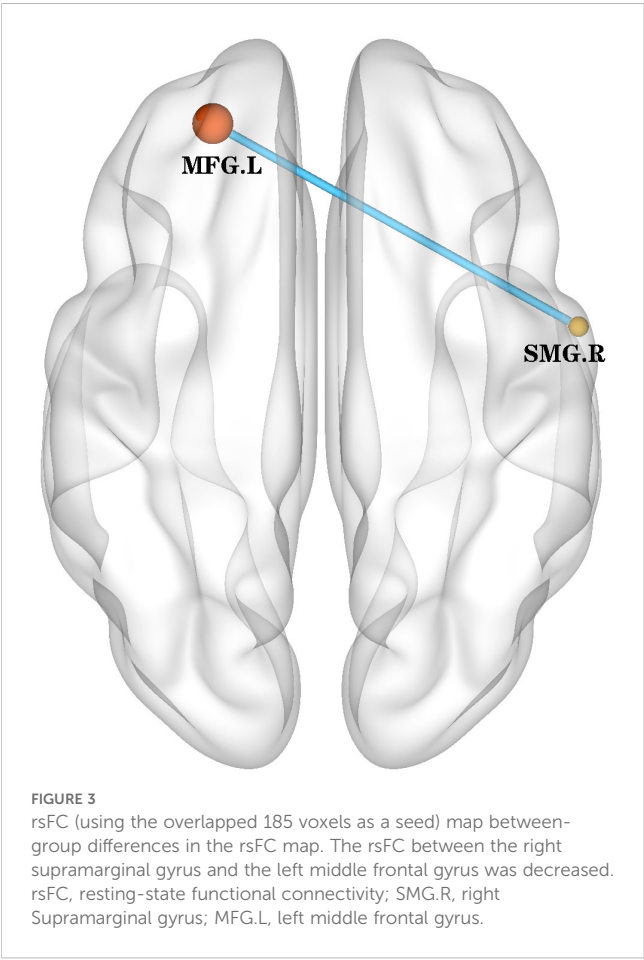
BD, bipolar disorder; ALFF, Amplitude of low-frequency fluctuation; ReHo, regional homogeneity; MNI, Montreal Neurological Institute

related voxels (30). Most previous studies have suggested that patients with BD mainly present with functional abnormalities in the inferior frontal gyrus, middle frontal gyrus, anterior central gyrus and insula, mainly belonging to FPN and DMN (31–34). These results are consistent with those of our study. All in all, past and present studies have repeatedly emphasized the importance of DMN and FPN during the stable period of BD, which may indicate that they are involved in this pathological process. Previous studies have found that the low connectivity between the anterior and posterior DMN in manic BD patients and HC patients may be related to the attention pattern of over-focusing on external stimuli at the expense of internal reflexes (35). However, using independent component analysis have found that there is no difference in rsFC of DMN between BD patients and HC patients during the clinical

remission period (36), and even there is no low connectivity in BD patients in remission (37, 38). This inconsistency might be caused by the heterogeneity of the samples, such as different types of BD or histories of mental illness. Abnormalities within the DMN are common, but they are reversed between the acute state and the remission state, which means that DMN injury is a characteristic of this disease and has different effects on BD individuals under different emotional states.

Subsequent rsFC analysis revealed that the connectivity of the left superior frontal gyrus and the left middle frontal gyrus (key nodes within the FPN network) in BD patients was low. Research reports indicate that compared with the control group, FC in the FPN of BD patients is reduced (39), which is consistent with our research results. However, Cipriani and Lu et al. found that, when it comes to the relationship between FPN and other networks, different studies gave completely opposite results. During the mitigation period, there was no significant difference between FPN and other networks (40, 41). However, a meta-analysis by Gong et al. observed low connectivity between FPN and DMN (42). On the contrary, Favre et al. reported an increase in the connection strength between FPN and DMN in BD with normal mood (43). The connection between FPN and DMN has not only been strengthened but also weakened. Our research has also found functional abnormalities of DMN, but no connection abnormalities between FPN and DMN have been found. This indicates that the inconsistent results may stem from the differences in the samples (such as BD subtypes, emotional states). In the future, a large amount of data will be needed for classification to further verify the results under different subtypes and different emotional states.

Whole-brain analysis revealed that BD presented a reduction in gray matter volume in the cerebellum. Previous studies have found that the volume of gray matter in the right cerebellum of BD patients is reduced (44), which is consistent with our research results. A topographic meta-analysis method used in functional neuroimaging studies indicates that this posterior cerebellar hemisphere region may be involved in higher-level tasks, including language and executive functions. With the activation of the posterior worm, the Crus I region, as part of the limbic circuit of the cerebellum, is also associated with emotion processing (45). A functional neuroimaging study on the cerebellum has shown that the reduction of FC in the cerebellum in BD patients involves the prefrontal lobe, cingulate gyrus, parietal lobe, temporal lobe, occipital bone and thalamic regions (46). Our study found that the ReHo of the left superior frontal gyrus, left parietal gyrus, right



parietal gyrus, right middle frontal gyrus and right middle temporal gyrus was significantly reduced. This might be a functional disorder caused by cerebellar atrophy, especially in the context of rapid neural development during adolescence.

Previous studies have indicated that the cerebellum can be functionally subdivided into distinct regions based on its connectivity with the cerebrum. The posterior lobe of the cerebellum is associated with cognition and is connected to associative areas such as the prefrontal cortex, whereas the anterior cerebellum may modulate sensorimotor cortical activity. Given the uniform cytoarchitecture of the cerebellar cortex across lobules (47), it has been proposed that the cerebellum regulates both sensorimotor and associative cortical regions in a comparable manner. Similar to lesions in sensorimotor areas of the cerebellum, which lead to motor impairments (48), abnormalities in cerebellar regions involved in executive function and emotional regulation may contribute to cognitive dysfunctions. This concept has been proposed to explain symptoms of psychiatric disorders such as schizophrenia and mood symptoms (48, 49).

A previous meta-analysis of numerous neuroimaging studies revealed aberrant functional connectivity between the DMN and the FPN, accompanied by gray matter alterations within these networks. Reduced gray matter volume suggests potential neuronal loss, providing a biological basis for the observed abnormalities in functional connectivity (7). It is well-established that structural impairment inevitably leads to functional deficits within neural circuits. Building on earlier research in BD demonstrating abnormal functional connectivity between the cerebellum and the frontal and temporal lobes as well as the thalamus, we hypothesize that cerebellar gray matter atrophy may share underlying neural mechanisms with the functional alterations observed between the DMN and FPN. This structure-function coupling might be an important biomarker for the occurrence of BD. In the future, it is necessary to combine the development of neuroscience to explore whether these abnormalities are related to the asynchronous development of the brain during adolescence.

In the analysis of clinical scales, we did not observe any significant correlations. Previous studies have indicated differences in gender and subtypes among patients with BD (50, 51). We speculate that this may be related to disease subtypes and patient gender. However, as we did not specifically investigate gender and disease subtypes, this represents a limitation of the present study.

Our study has several limitations that should be acknowledged. Firstly, there is heterogeneity in the emotional state of patients. In the future, more patients with the same emotional state need to be recruited to determine whether there are specific changes in the classification of disease subtypes. Secondly, and the use of drugs has not been strictly controlled, which may have a certain impact on the results. In future research, the types and dosages of drugs should be strictly controlled. Thirdly, We observed some misalignment in the image registration for part of the data, and future studies need to apply stricter registration standards to further validate the results.

5 Conclusions

This study provides novel insights into the neural underpinnings of adolescent bipolar disorder by combining ALFF, ReHo, rsFC, and GMV analyses. We demonstrated functional hyperactivity in DMN and limbic-related regions and reduced functional integration within the FPN. Furthermore, cerebellar gray matter atrophy may underlie broader functional disturbances observed in BD. Together, these multimodal findings support the notion that both functional and structural abnormalities are critical to the pathophysiology of adolescent BD. These alterations may serve as potential imaging biomarkers for early identification and intervention.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The current research has been approved by the Institutional Review Committee of Shiyan Taihe Hospital Affiliated to Hubei University of Medicine and Pharmacy. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

PZ: Conceptualization, Data curation, Formal Analysis, Methodology, Visualization, Writing – original draft, Writing – review & editing. YW: Data curation, Methodology, Software, Validation, Writing – original draft. JX: Data curation, Methodology, Software, Validation, Writing – original draft. JG: Data curation, Methodology, Software, Validation, Writing – original draft. XC: Data curation, Investigation, Supervision, Writing – original draft. FC: Data curation, Investigation, Supervision, Writing – original draft. LZ: Data curation, Investigation, Supervision, Writing – original draft. CA: Data curation, Investigation, Resources, Supervision, Writing – original draft. KQ: Conceptualization, Formal Analysis, Funding acquisition, Methodology, Visualization, Writing – review & editing. WC: Formal Analysis, Funding acquisition, Methodology, Project administration, Resources, Supervision, Visualization, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research and/or publication of this article. This study was funded by

Hubei Provincial Natural Science Foundation of China (Grant Nos. 2024AFB366 (KQ); 2023AFC033(WC)).

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Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fpsy.2025.1664729/full#supplementary-material>

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