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Difference in resting-state fractional amplitude of low-frequency fluctuation between bipolar depression and unipolar depression patients

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Abstract. – OBJECTIVE: To investigate the difference in fractional amplitude of low-frequency fluctuation (fALFF) of localized brain activities in the resting-state between bipolar depression and unipolar depression patients and to find biological markers that differentiate the two groups of patients.

PATIENTS AND METHODS: Thirteen patients with bipolar depression, 15 patients with unipolar depression, and 16 healthy control subjects that were matched in age and years of education were subjected to 3.0 T resting-state functional magnetic resonance scans. The values of whole brain fALFF were calculated and statistical analysis was performed.

RESULTS: The fALFF-values of the right inferior temporal gyrus, left cerebellar posterior lobe, right middle temporal gyrus, left inferior frontal gyrus/insula, right inferior frontal gyrus/insula, left lingual gyrus and right middle temporal gyrus of the three groups showed significant differences ($p < 0.05$). Compared with the healthy control (HC) group, the fALFF-values of the unipolar depression (UD) patient group significantly increased in the right superior temporal gyrus, left insula, left inferior frontal gyrus, right inferior frontal gyrus, right supramarginal gyrus and right medial frontal gyrus but significantly decreased in the right medial occipital gyrus, left frontal lobe, right superior parietal lobule; the fALFF-values of the bipolar depression (BD) patient group significantly decreased in the left cerebellum posterior lobe, right lingual gyrus, left lingual gyrus, right middle temporal gyrus, left middle temporal gyrus, and left superior frontal gyrus and significantly increased in the right inferior frontal gyrus and left insula compared to those of the HC group; compared with those of the UD group, the fALFF-values of the BD group significantly decreased in the left middle occipital gyrus, right middle temporal gyrus, left middle frontal gyrus, and left medial frontal gyrus.

CONCLUSIONS: The brain activities of BD and UD patients in the resting-state exhibit abnormalities, which differ between the two groups of patients.

Key Words:
Unipolar depression, Bipolar depression, Resting-state, Functional magnetic resonance, Fractional amplitude of low- frequency fluctuation.

Introduction

Bipolar depression (BD) and unipolar depression (UD) are two common types of affective disorder. The differential diagnosis of these conditions continues to be based on the symptomatology and the course of the disease. BD and UD are similar symptomologies, such as depressed mental state, thinking slow, volitional activity drops, and so on. Although mania or hypomania is a defining feature of BD patients, the presence of subthreshold manic symptoms can be observed in both disorders during a depressive episode. This leads to a difficulty in distinguishing BD from UD patients as they have the same diagnostic criteria for the first depressive episode[1]. Studies[2] have shown that nearly 60% of BD patients were initially misdiagnosed as UD. Therefore, it is of particular importance to find objective biomarkers that distinguish BD and UD, so that bases for early diagnosis and correct treatment of the two diseases can be found.

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Functional magnetic resonance imaging (fMRI) is a noninvasive research tool that has been widely used in the study of psychiatric disorders in recent years. Task-state fMRI has been used to compare BD and UD. It has been shown that when facing grief and fear scenarios, BD patients are more prone to activate the left amygdala[3] but to reduce the top-down effective connection between the left ventral midline prefrontal cortex and amygdala when in pleasant situations[4]. Some researchers have argued that activity in the ventral and dorsal sides of the prefrontal cortex of UD patients is much lower[5], while that in the anterior and back of cingulate gyrus of UD patients is significantly elevated compared with that of BD patients[5]. Relative to investigations of task-state fMRI[6], studies that directly compare BD and UD using resting-state fMRI have been rare, although some studies have found that the amplitude of low-frequency fluctuation (ALFF) values of BD patients in the left superior parietal lobule and the posterior of left insula are higher than those of UD patients while also exhibiting increased ALFF-values in the anterior dorsal of the right insula. However, ALFF is sensitive to physiological noise, whereas fractional amplitude of low-frequency fluctuations (fALFF) can effectively inhibit nonspecific signals of the cisternal area, reduce physiological noise interference and improve the sensitivity and specificity of the detection of spontaneous brain activities[7]. Therefore, in this work, the resting-state functional magnetic resonance method was employed to compare the fALFF-values of UD and BD patients.

Patients and Methods

Patients

The patients were recruited from outpatients and inpatients admitted to the psychiatric clinics of the Second Affiliated Hospital of Zhejiang University, China, from September 2011 to September 2016. The patients were diagnosed by two clinically experienced psychiatrists (both above the rank of attending physician) using the structured clinical interview method for DSM-IV-IR axis I-disorders. Subjects in the healthy control (HC) group were recruited through advertisement. All subjects were right-handed.

Thirteen patients were included in the BD group, based on the following inclusion criteria: (1) compliance with the diagnosis standard for bipolar depression of "The Diagnostic and Statistical Manual of Mental Disorders (the 4th edition)" (DSM-IV); (2) of Han Chinese and Chinese nationality; (3) right-handed; (4) 18-50 years of age; (5) score > 21 points on the 24-item Hamilton Depression Scale (HAMD-24); and score < 5 points on the Young Manic Rating Scale (YMRS). Exclusion criteria were as follows: (1) brain organic mental disorders; (2) substance-induced mental disorders; (3) serious physical illness; (4) a history of electrotractive treatment; and (5) MRI contraindications.

Fifteen patients were included in the UD group, based on the following inclusion criteria: (1) compliance with the diagnosis standard for unipolar depression of "The Diagnostic and Statistical Manual of Mental Disorders (the 4th edition)" (DSM-IV); (2) of the Han Chinese and Chinese nationality; (3) right-handed; (4) 18-50 years of age; (5) score > 21 points on the HAMD-24; and score < 5 points on the Young Mania Rating Scale (YMRS). Exclusion criteria were as follows: (1) brain organic mental disorders; (2) substance-induced mental disorders; (3) serious physical illness; (4) a history of electrotractive treatment; and (5) MRI contraindications.

Sixteen gender-, age- and education-matched subjects were included in the HC group, based on the following inclusion criteria: (1) 18-50 years of age; (2) not been diagnosed with disorders, according to DSM-IV-IR axis I or DSM-IV-IR axis II; (3) no family history of mental illness; (4) does not suffer from any disease or has not taken any drug within one month before the scan; and (4) score < 7 points on the HAMD-24, and score < 5 points on the YMRS.

This study was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Zhejiang University Medical College. All subjects or their family members voluntarily participated in the study and signed the informed consent agreement.

Methods

Magnetic Resonance Data Acquisition

A GE SIGNA 3.0T magnetic resonance imager was used to acquire brain structure and function images of subjects. At the time of scanning, subjects were awake, with their eyes closed and head fixed, and were quietly lying on the examination bed without performing any specific cognitive tasks. They were informed that they should try to avoid systemic thinking activities. The scan

sequence and parameters were as follows. Anatomical images were obtained using fast spoiled gradient echo (FSPGR) with the following parameters: TR = 5 ms, TE = 1.1 ms, TI = 400 ms, flip angle = 15°, slice thickness = 1.2 mm, interval = 0 mm, FOV = 240 mm × 240 mm, and matrix = 256 × 256. A total of 136 slices were acquired from the whole brain, with a scanning time of 5 min 50 s. Images of brain structures not found with significant abnormalities were acquired through a resting-state functional scan, which was conducted using the spin echo-echo planar imaging (SE-EPI) sequence with the following scan parameters: TR/TE = 2000 ms/30 ms, FOV = 240 mm × 240 mm, matrix = 64 × 64, and slice thickness = 4 mm. A total of 185 images were acquired in a scan time of 6 min.

Data Processing

1. **Data preprocessing:** sequences of the first 10 time points of the scan were discarded to eliminate the impact of signal instability of the machine, and data of the subsequent 175-time points were used in the analysis, in which the image data format was converted using DCM-2NII software. Following head movement correction, slice-time correction and covariant regression using Data Processing Assistant for Resting-State fMRI (DPARSF) software, the imaging data were normalized through spatial autocorrelation at the standard spatial resolution of 3 mm × 3 mm × 3 mm and the Gaussian smoothing of 6 mm × 6 mm × 6 mm. To avoid abnormal signals caused by large head movements, only subjects with a horizontal head movement < 2 mm and a rotational head movement < 2° were included in the subsequent analysis.
2. **fALFF analysis**: The DPARSF software was used to eliminate linear drift of the above images, and the extraction of square roots was performed on the power spectrum of signals under 0.01-0.08 Hz to obtain the ALFF-value. Then ALFF-values in the range were added together and divided by the total of ALFF-values in the range of 0.01-0.25 Hz, resulting in the fALFF-value. Bandpass filtering of 0.01-0.08 Hz was then performed to avoid the effect of physiological noise, such as heart rate, respiratory rhythm, etc. The whole brain voxel was normalized by dividing the fALFF-value of each voxel by the mean of the ALFF-values of the whole brain signals.

Statistical Analysis

SPM8 software was used to perform Analysis of Variance (ANOVA) on the three groups of subjects, and a pair-wise sample *t*-test was conducted on the basis of differences in the brain regions. AlphaSim correction was performed, using a Monte Carlo simulation, and a cerebral region with single voxel $p < 0.01$, continuous voxel number > 18, and corrected $p < 0.01$ was defined as exhibiting a statistically significant difference.

Results

The general Behavioral Data and the Evaluation of The Disease Status of Each Group

Following analysis using SPSS 18 statistics software (SPSS Inc., Chicago, IL, USA), no significant differences were found in gender, age, years of education and HAMD scores among the three groups ($p > 0.05$) (Table I).

ANOVA of the Brain fALFF-values of the Three Groups

The brain regions that showed statistically significant differences in fALFF-values among the three groups were as follows: right inferior temporal gyrus, left cerebellar posterior lobe, right middle temporal gyrus, left inferior frontal gyrus/insula, right inferior frontal gyrus/insular, left lingual gyrus, and right middle temporal gyrus ($p < 0.05$) (Table II and Figure 1).

Table I. Comparison of general information and the HAMD scores of the three groups of subjects.

Item	BD group (n = 13)	UD group (n = 15)	HC group n = 16)	χ^2/*F*-value	*p*-values
Gender (Male/Female)	7/6	7/8	6/10	0.786	0.675
Age (years)	31.2 ± 10.5	37.9 ± 7.1	27.8 ± 8.3	0.893	0.588
Years of education (years)	13.2 ± 2.7	13.9 ± 3.2	14.3 ± 2.8	0.503	0.609
HAMD score	32.9 ± 7.3	34.2 ± 3.8		2.786	0.107

Note: HAMD is the Hamilton Depression Scale.

Table II. ANOVA of the brain fALFF-values of the three groups.

Brain region	Brodmann area	MNI coordinate of peak point (x, y, z)	*K*-value	*F*-value of peak point
Right inferior temporal gyrus	20	54-6 -42	46	14.613
Left posterior cerebellar lobe		-39 -75 -21	76	11.457
Right middle temporal gyrus	21	48 -9 -18	33	9.635
Left inferior frontal gyrus/insular	47	--3915-6	69	13.271
Right inferior frontal gyrus/insular	47	3915-3	56	9.704
Left lingual gyrus	17	-12 -93 -9	33	12.802
Right middle temporal gyrus	19	24 -84 6	135	13.768

Note: The peak point is the point that shows the most significant difference; MNI is the Montreal coordinate system; K-value is the continuous voxel value; *F*-value: a positive value indicates an increased fALFF-value, while a negative value indicates a decreased fALFF-value.

Difference in Brain fALFF-values Between the BD, UD and HC Groups

Based on the one-way ANOVA results, which show a significant difference compared with the HC group, the UD group showed higher fALFF-values in the right superior temporal gyrus, left insula, left inferior frontal gyrus, right inferior frontal gyrus, right supramarginal gyrus, and right medial frontal gyrus but lower fALFF-values in the right middle occipital lobe, left frontal lobe, and right superior parietal lobule (Table III and Figure 2). Compared with the HC group, the BD group exhibited lower fALFF-values in the left cerebellum posterior lobe, right lingual gyrus, left lingual gyrus, right middle temporal gyrus, left middle temporal gyrus, left

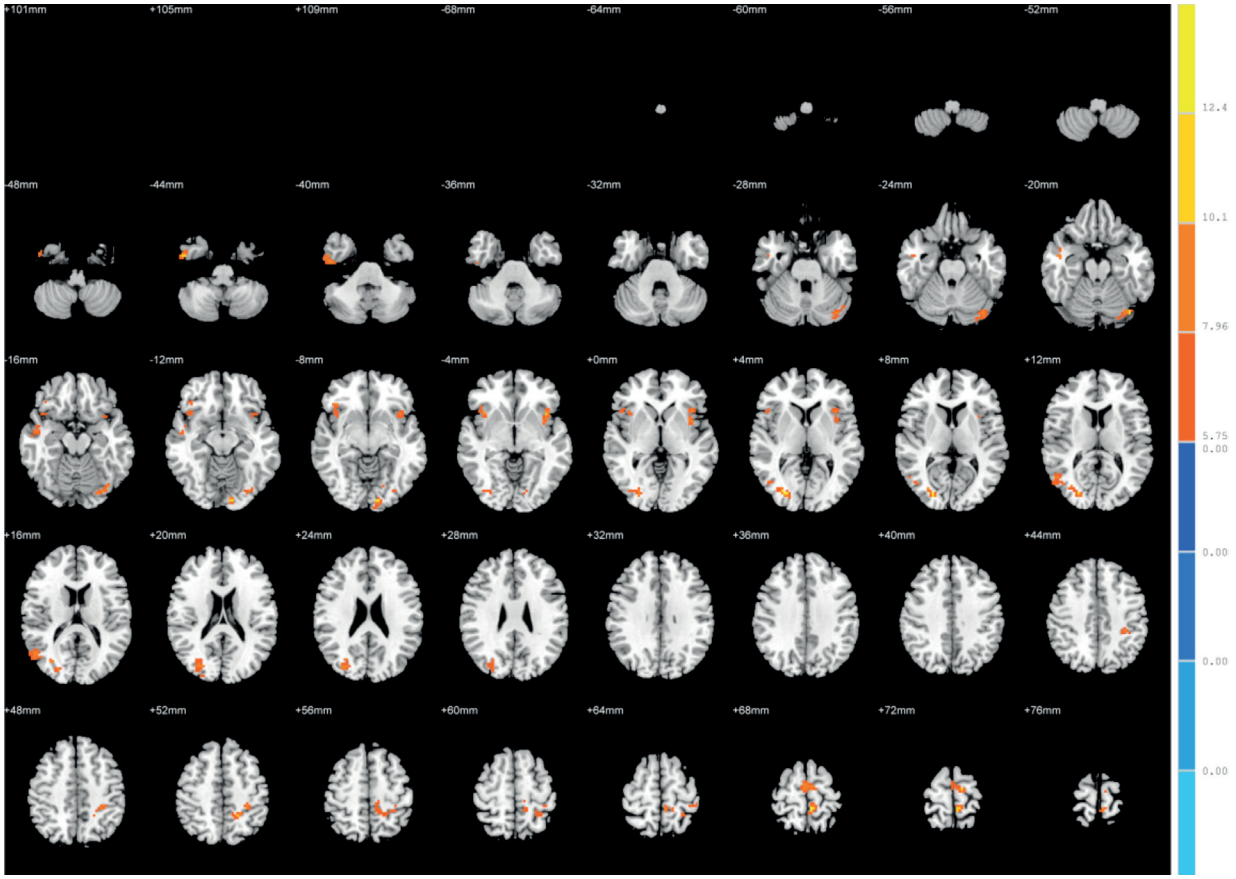

Figure 1. ANOVA result of brain fALFF-values of the BD, UD and HC groups. The color bar on the right represents *F*-values: red and yellow indicate an increase, while blue and green indicate a decrease.

Table III. Brain regions of the UD group that exhibited different cerebral fALFF-values from those of the HC group.

Brain region	Brodmann area	MNI coordinate of peak point (x, y, z)	*K*-value	*F*-value of peak point
Right superior temporal gyrus	21	48 -6 -21	64	3.800
Left insula	13	-42 -12 6	Gt;	3.668
Left inferior frontal gyrus	47	--39 15 -6	82	5.050
Right inferior frontal gyrus	47	39 15 -3	91	4.276
Right middle occipital gyrus	18	24 -84 9	90	-4.764
Right superior frontal gyrus	40	60 -54 30	44	3.759
Right medial frontal gyrus	9	3 45 21	84	3.813
Left parietal lobe	7	-18 -48 54	189	-4.573
Right top lobular	7	15 -66 54	36	-5.333

Note: The peak point is the point that shows the most significant difference; MNI is the Montreal coordinate system; *K*-value is the continuous voxel value; *F*-value: a positive value indicates an increased fALFF-value, while a negative value indicates a decreased fALFF-value.

superior frontal gyrus but higher fALFF-values in the right inferior temporal gyrus and left insular ($p < 0.05$) (Table IV and Figure 3). Compared with the UD group, the BD group showed lower fALFF-values in the left middle occipital gyrus, right middle temporal gyrus, left middle frontal gyrus, and left medial frontal gyrus (Table V and Figure 4).

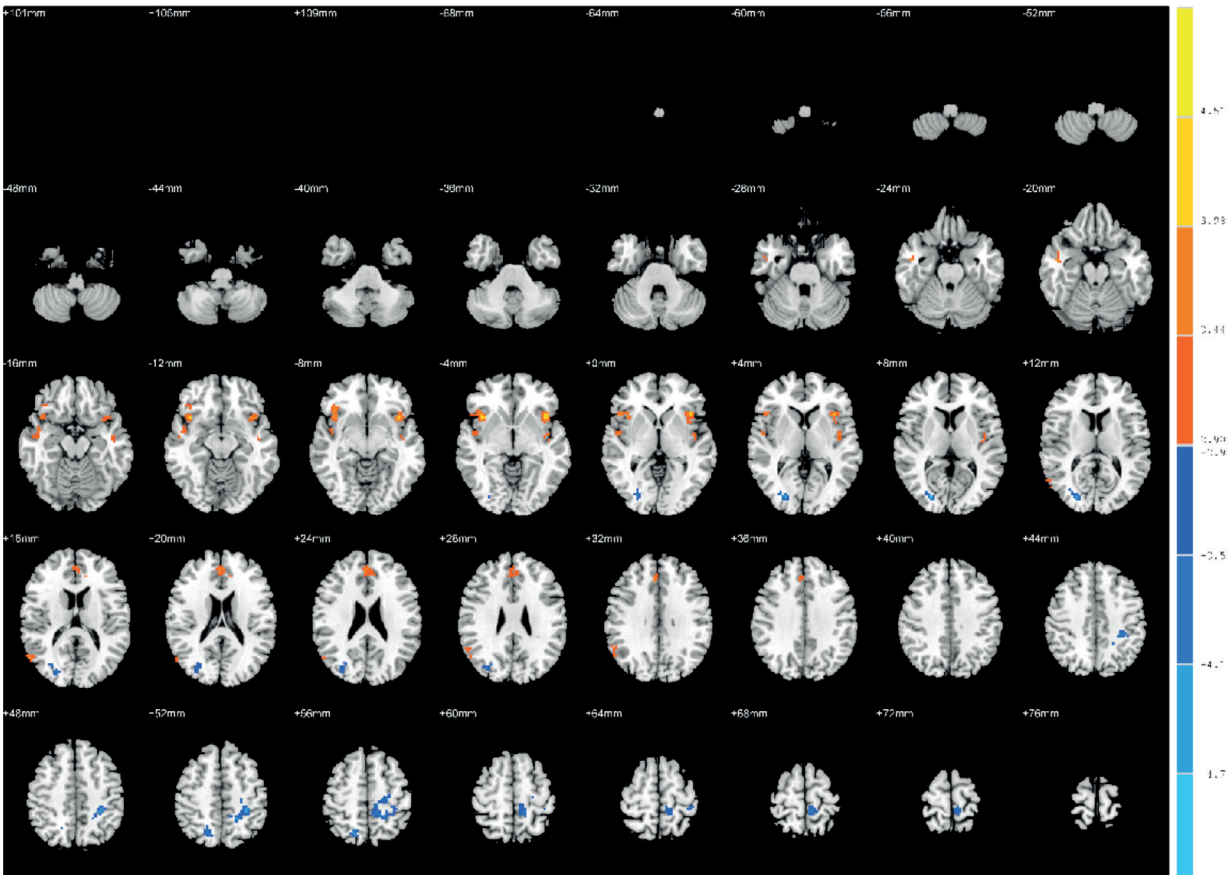

Figure 2. The two-sample *t*-test results for the fALFF-values of the UD and HC groups. The color bar on the right represents *t*-values: red and yellow indicate that the UD group > the HC group, while blue and green indicate that the UD group < the HC group.

Table IV. Brain regions of the BD group that exhibited different cerebral fALFF-values from those of the HC group.

Brain region	Brodmann area	MNI coordinate of peak point (x, y, z)	*K*-value	*F*-value of peak point
Right inferior temporal gyrus	20	54 -6 -42	61	4.948
Left cerebellar posterior lobe	–	-39 -75 -21	149	-4.756
Right lingual gyrus	18	12 -84 -15	57	-3.792
Left lingual gyrus	18	-9 -93 -9	50	-3.999
Left insula	13	-36 6 -3	30	4.151
Right middle temporal gyrus	19	27 -84 3	227	-4.451
Left middle temporal gyrus	39	-45 -66 9	32	-4.099
Left superior frontal gyrus	6	-12 -15 72	76	-4.421

Note: The peak point is the point that shows the most significant difference; MNI is the Montreal coordinate system; *K*-value is the continuous voxel value; *F*-value: a positive value indicates an increased fALFF-value, while a negative value indicates a decreased fALFF-value.

Discussion

At present, although the diagnosis of BD episode and UD episode symptomology standard is the same, research shows that the relevant clinical characteristics of the two diseases have sometimes differences. Following features of depressive episode patients may alert to be bipolar depression: onset early (first depressive episode age < 25); the frequencies of depression attack (5 or higher); the attack time of duration is short; family history of bipolar disorder first-degree

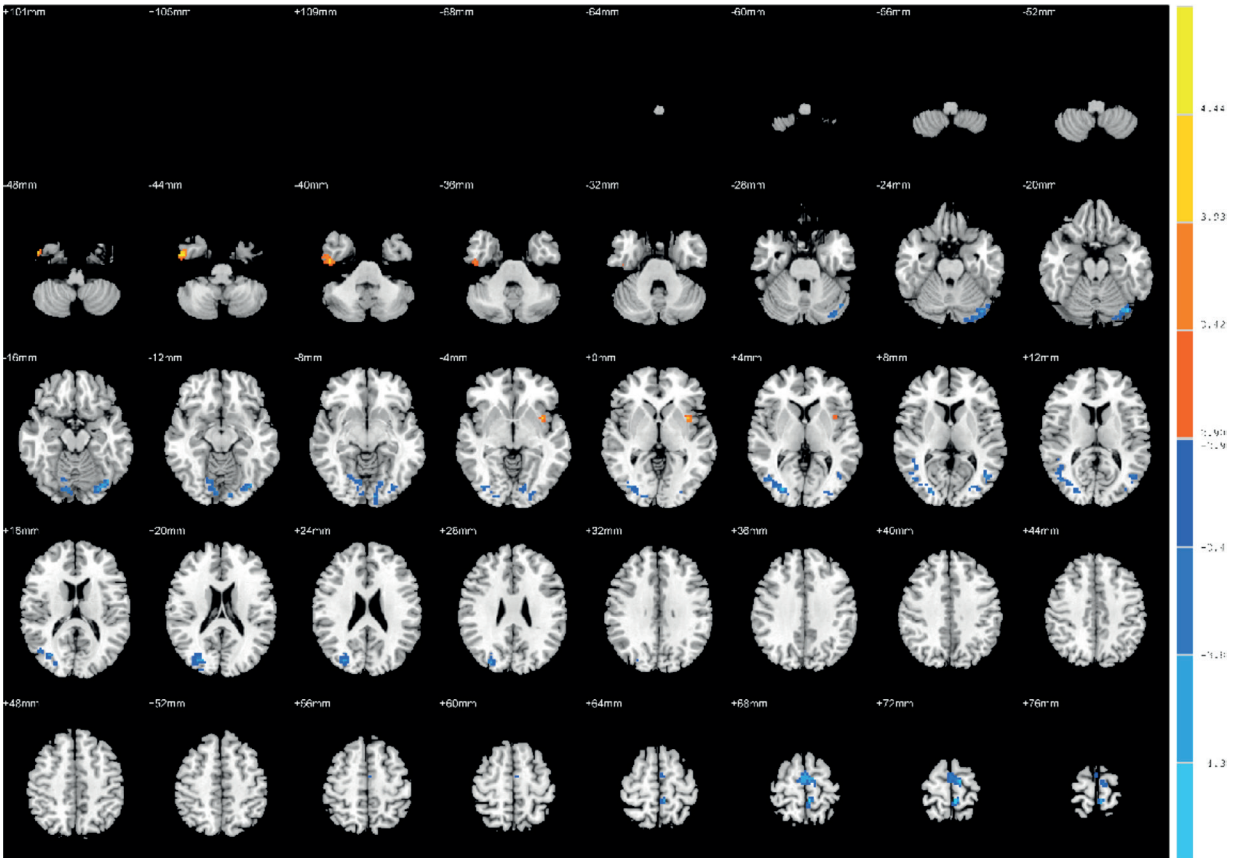

Figure 3. The two-sample t-test results for the fALFF-values of the BD and HC groups. The color bar on the right represents *t*-values: red and yellow indicate that the BD group > the HC group, while blue and green indicate that the BD group < the HC group.

Table V. Brain regions of the BD group that exhibited different cerebral fALFF-values from those of the UD group.

Brain region	Brodmann area	MNI coordinate of peak point (x, y, z)	*K*-value	*F*-value of peak point
Left middle occipital gyrus	18	-39 -75 -18	51	-3.6652
Right middle temporal gyrus	19	51-63 15	74	-4.3784
Left middle frontal gyrus	9	-48 21 36	33	-3.5243
Left medial frontal gyrus	6	-6 -15 69	50	-3.5352

Note: The peak point is the point that shows the most significant difference; MNI is the Montreal coordinate system; *K*-value is the continuous voxel value; *F*-value: a positive value indicates an increased fALFF-value, while a negative value indicates a decreased fALFF-value.

relatives; before the disease attacks has emotional exuberant and (or) cycle temperament and (or) borderline personality disorder; seasonal mood changes; always poor efficacy of antidepressant treatment and (or) rapid change of mood and (or) after treatment of mania or hypomania induced; sleep too much and (or) daytime sleepiness; bulimia or increase body quality; psychomotor retardation; some psychotic symptoms; postpartum depression. These suggest that the BD and UD have differences in the function of the brain[8].

Our study indicates that brain regions that exhibited significantly different fALFF-values among the BD, UD, and HC groups were as follows: right inferior temporal gyrus, left posterior cerebellar lobe, right middle temporal gyrus, left inferior frontal gyrus/insula, right inferior frontal gyrus/insula, left lingual gyrus, and right middle temporal gyrus. Brain regions of the BD group that showed significantly lower fALFF-values than those of the UD group were as follows: left middle occipital gyrus, right middle temporal gyrus, left middle frontal gyrus, and left medial frontal gyrus.

We found that the fALFF-value of the left middle occipital gyrus of the BD group was much

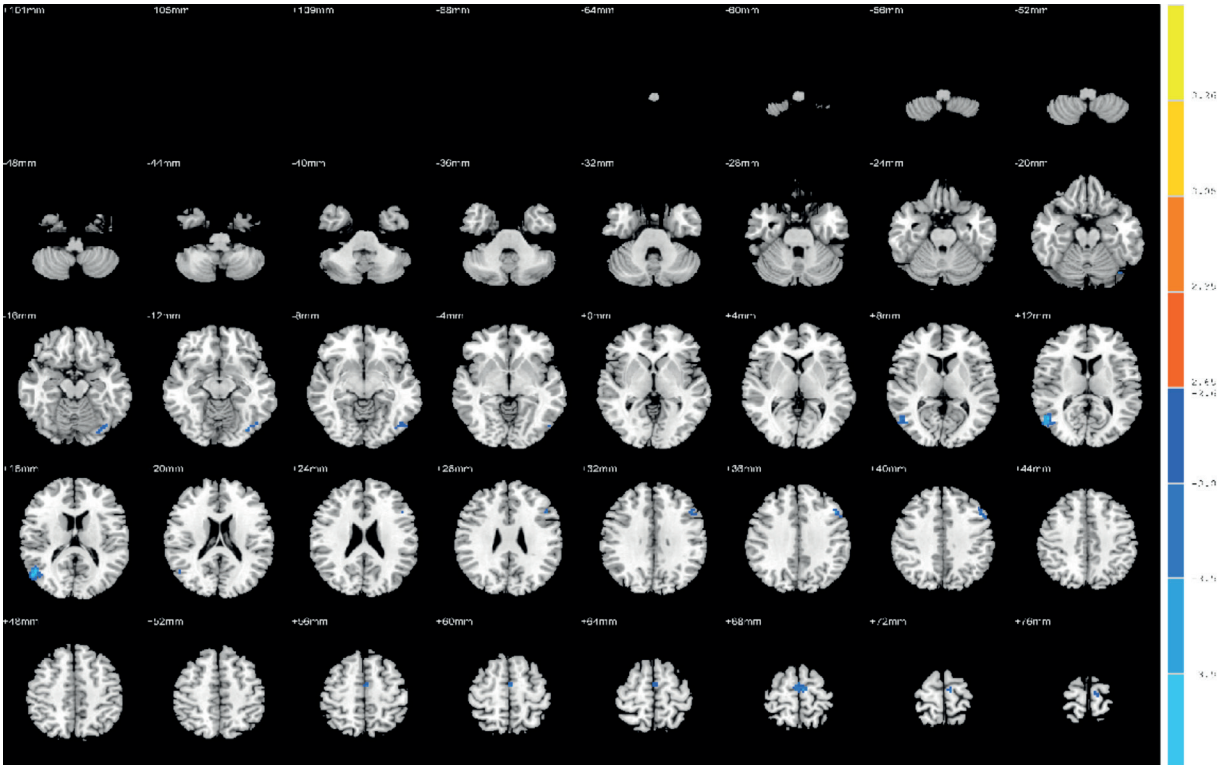

Figure 4. The two-sample t-test results on the fALFF-values for the BD and UD groups. The color bar on the right represents the *t*-value: red and yellow indicate that the BD group > the UD group, while blue and green indicate that the BD group < the UD group.

lower than that of the UD group; Liang et al[9] found that local consistency of the left occipital lobe of UD and BD patients was significantly different from that of the normal population and that the ALFF-value of the right middle occipital gyrus of patients with late-onset UD decreased[10]. As the visual cortex, the occipital lobe is mainly involved in visual formation and functional activities of visual perception. In the processing and synthesis of visual information, the occipital lobe is extensively linked with other regions of the two lobes and plays an important role in the process whereby visual information is integrated with information gathered by auditory and other sensory systems. It, therefore, participates in neuropsychological activities, such as attention, visual memory, visual-motor, motor speech, etc[11]. When patients are in a depressive episode, they exhibit weaker cortical functions in processing visual information of external positive stimuli in the resting-state than is shown by healthy controls. The weaker cortical functions are reflected in reductions in neuropsychological activities, such as execution, attention, visual memory, emotional processing, etc. Clinically, they manifest such symptoms as lowered attention, motor block, etc. In clinical investigations, it has been observed that BD patients indeed show retardation symptoms more frequently than UD patients[12].

Our work also revealed that the right middle temporal gyrus of the BD group differed from that of the UD group; Liu et al[13] found that differences in the medial temporal lobe and subcutaneous structures between UD and BD patients were rather common. Structural MRI investigations have shown that temporal lobe volume, cortical thickness and surface area of BD patients differed from those of the healthy group[13]; some studies have demonstrated abnormal activation of the middle temporal lobe and basal ganglia during emotional processing of BD patients (regardless of current emotional state)[14]; Liu et al[13] found that the ALFF-value of the temporal gyrus of BD patients differed from that of healthy individuals and postulated that the right middle temporal gyrus of BD patients may be involved in emotional processing, showing a more significant difference from healthy individuals than UD patients. The temporal gyrus is part of the limbic system and is associated with emotional processing and cognitive function; it is involved in the regulation of cognitive and emotional activities, and the decreased information transmission efficiency in the nerve loop would result in a failure to suppress the generation of negative emotions by the prefrontal limbic system, ultimately manifesting in persistent negative emotional experience[15].

We also observed that fALFF-values of the left middle frontal gyrus and left medial frontal gyrus of the BD group were much lower than those of the UD group. The middle frontal gyrus is an important part of the dorsolateral prefrontal cortex and is closely linked to executive functions, such as working memory, abstract reasoning, and cognitive flexibility[16]. Functional abnormalities in the dorsolateral prefrontal cortex have commonly been seen in BD patients[2,17] and UD patients[18]. This is likely associated with the pathogenesis common to BD depression and depressive disorder. Resting-state MRI researches, using the functional connectivity method[19, 20], found that the functional connectivity between the dorsolateral prefrontal cortex and medial frontal cortex of BD patients weakened and that BD patients without drug treatment showed reduced functional connectivity between the bilateral of the medial prefrontal cortex. The medial frontal gyrus is an important part of the medial prefrontal cortex, responsible for processing self-related emotional information, including emotional processing and episodic memory extraction[21,22]. In this report, we showed that fALFF-values of the left middle frontal gyrus and left medial frontal gyrus of the BD group were even lower than those of the UD group, suggesting functional connectivity abnormalities in various cerebral regions of BD and UD patients and that BD patients may exhibit more executive dysfunction and negative emotional processing than UD patients, which is consistent with clinical manifestations[23].

We also found inconsistencies with some previous studies. Wei et al[24] observed that the fALFF-value of the left anterior callosal gyrus of the UD group was higher than that of the HC group; the fALFF-values of the bilateral of the superior medial frontal gyrus and the middle of the left callosal gyrus of the BD group were higher than those of the HC group; the fALFF-values of the right middle orbitofrontal gyrus, right anterior callosal gyrus and bilateral medial frontal gyrus of the UD group were significantly lower than those of the BD group. Lu et al[25] found that fALFF-values of the left quadrate lobe, left parietal lobule and bilateral occipital gyrus were lower than those of the HC group, while those of the bilateral caudate nucleus and left globus pallidus of the BD

group were higher than those of the HC group. Xu et al[26] found that the brain regions with significantly elevated ALFF-values in BD patients are concentrated in the prefrontal cortex, insula, and putamen and extend to the ventral striatum, while the ALFF-value of the lingual gyrus in BD patients is significantly reduced. Liu et al[6] demonstrated that the ALFF-values of the left parietal lobule and posterior of the left insula of BD patients are significantly reduced, whereas that of the right anterior dorsal insula is significantly increased. These discrepancies may be associated with differences in sample size, the type of disease, the division of age groups and the method of analysis.

Conclusions

In this study, the fALFF method was used to analyze differences in patients with BD and UD and revealed that BD patients show differences from UD patients in cerebral functions and activities in the left middle occipital gyrus, right middle temporal gyrus, left middle frontal gyrus and left medial frontal gyrus, suggesting that these differences in brain activity can be used as specific indicators to distinguish between BD and UD patients and provide a new criterion for the identification of patients. Additionally, it may provide a basis for the study of the pathophysiological mechanisms of BU and UD patients and a reference for the potential development of future biological markers. Nevertheless, there are some limitations to this work, including a small sample size and the fact that drugs were taken by some subjects during the study. As there is still no consensus on the effects of drugs on the results of functional magnetic resonance[27], we cannot completely rule out that the use of drugs may impact the results. In the future, more in-depth investigations should be conducted on larger samples of patients without drug treatment.

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Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) Fierro M, Bustos A, Molina C. Differences in subjective experience Between Unipolar and Bipolar Depression. Rev Colomb Psiquiatr 2016; 45: 162-169.
2) Rive MM, Mocking RJ, Koeter MW, van Wingen G, de Wit SJ, van den Heuvel OA, Veltman DJ, Ruhé HG, Schene AH. State-dependent differences in emotion regulation between unmedicated bipolar disorder and major depressive disorder. JAMA Psychiatry 2015; 72: 687-696.
3) Almeida JR, Versace A, Hassel S, Kupfer DJ, Phillips ML. Elevated amygdala activity to sad facial expressions: a state marker of bipolar but not unipolar depression. Biol Psychiatry 2010; 67: 414-421.
4) Almeida JR, Versace A, Mechelli A, Hassel S, Quevedo K, Kupfer DJ, Phillips ML. Abnormal amygdala-prefrontal effective connectivity to happy faces differentiates bipolar from major depression. Biol Psychiatry 2009; 66: 451-459.
5) Taylor TJV, Clark L, Furey ML, Williams GB, Sahakian BJ, Drevets WC. Neural basis of abnormal response to negative feedback in unmedicated mood disorders. Neuroimage 2008; 42: 1118-1126.
6) Liu CH, Ma X, Wu X, Li F, Zhang Y, Zhou FC, Wang YJ, Tie CL, Zhou Z, Zhang D, Dong J, Yao L, Wang CY. Resting-state abnormal baseline brain activity in unipolar and bipolar depression. Neurosci Lett 2012; 516: 202-206.
7) Zou QH, Zhu CZ, Yang Y, Zuo XN, Long XY, Cao QJ, Wang YF, Zang YF. An improved approach to detection of amplitude of low-frequency fluctuation (ALFF) for resting-state fMRI: fractional ALFF. J Neurosci Methods 2008; 172: 137-141.
8) Marchand WR. Recognizing and treating bipolar disorder. Hosp Physician 2003; 39: 21-30.
9) Liang MJ, Zhou Q, Yang KR, Yang XL, Fang J, Chen WL, Huang Z. Identify changes of brain regional homogeneity in bipolar disorder and unipolar depression using resting-state FMRI. PLoS One 2013; 8: e79999.
10) Guo W, Liu F, Xue Z, Gao K, Liu Z, Xiao C, Chen H, Zhao J. Decreased interemispheric coordination in treatment-resistant depression: a resting-state fMRI study. PLoS One 2013; 8: e71368.
11) Petersen SE, Fox PT, Posner MI, Mintun M, Raichle ME. Positron emission tomographic studies of the cortical anatomy of single-word processing. Nature 1988; 331: 585-589.
12) Galvão F, Sportiche S, Lambert J, Amiez M, Musa C, Nieto I, Dubertret C, Lepine JP. Clinical differences between unipolar and bipolar depression: interest of BDRS (Bipolar Depression Rating Scale). Compr Psychiatry 2013; 54: 605-610.
13) Liu CH, Li F, Li SF, Wang YJ, Tie CL, Wu HY, Zhou Z, Zhang D, Dong J, Yang Z, Wang CY. Abnormal baseline brain activity in bipolar depression: a resting state functional magnetic resonance imaging study. Psychiatry Res 2012; 203: 175-179.

14) Jiang X, Zhou QT, Yan Q, Wang F. Altered regional homogeneity in bipolar depression: resonance imaging study. Journal of China Medical University 2016; 45: 305-308.

15) Chen JH, Yao ZJ, Zhao K, Yan R, Hua LL, Jia FN, Wei QX, Lu Q. The global efficiency of brain white matter networks in the unipolar and bipolar depression patients and its relationship with the clinical features. Chinese Journal of Psychiatry 2015; 48: 271-278.

16) Porcaro C, Medaglia MT, Thai NJ, Seri S, Rotshtein P, Tecchio F. Contradictory reasoning network: an EEG and FMRI study. PLoS One 2014; 9: e92835.

17) Singh MK, Chang KD, Mazaika P, Garrett A, Adleman N, Kelley R, Howe M, Reiss A. Neural correlates of response inhibition in pediatric bipolar disorder. J Child Adolesc Psychopharmacol 2010; 20: 15-24.

18) Tekin S, Cummings JL. Frontal-subcortical neuronal circuits and clinical neuropsychiatry: an update. J Psychosom Res 2002; 53: 647-654.

19) Favre P, Baciu M, Pichat C, Bougerol T, Polosan M. fMRI evidence for abnormal resting-state functional connectivity in euthymic bipolar patients. J Affect Disord 2014; 165: 182-189.

20) Wang Y, Zhong S, Jia Y, Zhou Z, Zhou Q, Huang L. Reduced interhemispheric resting-state functional connectivity in unmedicated bipolar II disorder. Acta Psychiatr Scand 2015; 132: 400-407.

21) Brunoni AR, Boggio PS, De Raedt R, Benseñor IM, Lotufo PA, Namur V, Valiengo LC, Vanderhasselt MA. Cognitive control therapy and transcranial direct current stimulation for depression: a randomized, double-blinded, controlled trial. J Affect Disord 2014; 162: 43-49.

22) Harvey PO, Fossati P, Pochon JB, Levy R, Lebastard G, Lehéricy S, Allilaire JF, Dubois B. Cognitive control and brain resources in major depression: an fMRI study using the n-back task. Neuroimage 2005; 26: 860-869.

23) Switalska J. Cognitive functioning in depression and the course of bipolar affective disorder. Psychiatr Pol 2013; 47: 239-253.

24) Wei QX, Yao ZJ, Yan R, Wei MB, Lu Q. Study on fractional amplitude of low-frequency fluctuation in male patients with unipolar and bipolar depression. Chinese Journal of Behavioral Medicine and Brain Science 2015; 24: 791-794.

25) Lu D, Jiao Q, Zhong Y, Gao W, Xiao Q, Liu X, Lin X, Cheng W, Luo L, Xu C, Lu G, Su L. Altered baseline brain activity in children with bipolar disorder during mania state: a resting-state study. Neuropsychiatr Dis Treat 2014; 10: 317-323.

26) Xu K, Liu H, Li H, Tang Y, Womer F, Jiang X, Chen K, Zhou Y, Jiang W, Luo X, Fan G, Wang F. Amplitude of low-frequency fluctuations in bipolar disorder: a resting state fMRI study. J Affect Disord 2014; 152-154: 237-242.

27) Passarotti AM, Sweeney JA, Pavuluri MN. Differential engagement of cognitive and affective neural systems in pediatric bipolar disorder and attention deficit hyperactivity disorder. J Int Neuropsychol Soc 2010; 16: 106-117.