The Specific Interaction of Lithium and Suicide History on Temporal Cortical Thickness in Bipolar Disorder

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Abstract: Background: Lithium, which exerts an antisuicidal effect in bipolar disorder (BD), was frequently reported to increase the grey matter in the temporal lobe. Suicide was also associated with brain structural abnormalities, including abnormalities in the temporal cortex. However, whether there exists an interactive effect of lithium treatment and suicide on the temporal cortex is still unknown. Methods: Our study recruited 165 BD patients (39 patients with suicide attempt history (SAH), 126 patients without SAH) and 147 healthy controls (HC), Structural imaging data were obtained by the Magnetic resonance imaging (MRI) of 3.0 Tesla, and were processed under the Freesurfer v6.0 software. We extracted eight thickness measurements from temporal cortex, including bilateral superior temporal gyrus, middle temporal gyrus, inferior temporal gyrus and transverse temporal cortex. General linear model was performed with eight thickness measurements with as dependent variables. Bonferroni correction for multiple comparisons of these measurements was applied to the results. Results: Compared to HC, BD without lithium treatment showed significantly decreased thickness in all measurements (all $P < 0.05$), while BD with lithium treatment only showed significant thinner left superior temporal and right superior temporal thickness (all $P < 0.05$). We found a significant SAH by lithium treatment interaction on left middle temporal thickness ($F = 9.172$, $P = 0.024$, Partial Eta Squared = 0.055), Post hoc tests with the Bonferroni correction revealed that in lithium-treated BD patients, left middle temporal thickness in patients with SAH were higher than patients without SAH. Interestingly, in the BD patients without lithium treatment, the patients with SAH had thinner middle temporal thickness compared to patients without SAH. Conclusions: This is the first study of the association between lithium therapy and suicidality on the temporal thickness in BD. We observed an increased effect of lithium on middle temporal thickness in BD patients with suicide history. Our result suggested that left middle temporal cortex might be a potential target for suicide therapy, as well as for monitoring the antisuicidal effect of lithium.

***Keywords*:** Lithium, bipolar disorder, temporal cortex, cortical thickness

1. Introduction

Bipolar disorder (BD) is one of the most severe chronic affective disorders with a worldwide prevalence rate of about 3%[1]. Additionally, BD is a lifelong disease with a high recurrence rate of about 90%, and approximately 30% of BD patients attempted to suicide during their lifetime[2, 3]. Managing suicide risk is crucial for BD patients, but the effectiveness of suicide-specific treatments remains unclear. Long-term lithium therapy, a key mood stabilizer, significantly reduces both attempted and completed suicide risk in BD patients[5, 6]. However, large-scale epidemiological studies indicate that antidepressant therapy, while effective in reducing suicide risk during acute mood episodes, does not significantly impact long-term suicide risk[4]. Additionally, only 47-60% of BD patients receiving lithium therapy experience therapeutic benefits, complicating the prediction of its efficacy[7-11]. Currently, there are no clinical markers to predict this specific response.

Given the high suicide risk and treatment uncertainty, identifying biomarkers to predict future suicidal behavior and evaluate treatment effectiveness is urgent[12]. Neuroimaging biomarkers are expected to provide clinicians with more possibilities to improve the assessment of suicide[13, 14]. Therefore, more and more studies are based on neuroimaging to discover potential biomarkers related to the clinical symptoms of BD, including neuroimaging markers closely related to BD suicidal behavior[12]. According to the functional and structural neuroimaging review, there were abnormalities of volume and thickness in prefrontal cortex (PFC)[15-18], superior temporal cortex (STC) and anterior cingulate cortex (ACC) as well as the dysfunction of the frontotemporal network in suicidal psychiatric patients[12]. More specifically, the brain regions associated with suicidal functional vulnerability include right anterior cingulate gyrus and posterior cingulate gyrus, and

the brain regions associated with suicidal structural vulnerability include left STC, rectal gyrus and caudate nucleus[19]. Interestingly, aInterestingly, the results of neuroimaging measurements of brain morphology in suicidal patients with bipolar affective disorder based on different methods are inconsistent.[20-22]. In conclusion, it is a suggestion that although more and more evidence is beginning to focus on the relationship between frontotemporal abnormalities and BD suicidal behavior, the results of the studies were still ambiguous or even opposite[23, 24], so we will also present our findings about this.

Actually, serveral studies attempted to use multifactorial models to explain suicidal symptoms in BD patients[6]. The frontotemporal cortex, which includes the aforementioned abnormal structures, can lead to a range of dysfunctions, such as mood regulation, cognitive control, response suppression, decision-making, monitoring, and memory[24-27]. These structural abnormalities are initially influenced by genetic and environmental factors. When exposed to environmental stressors, BD patients may experience stronger negative evaluations and emotional responses, fail to correctly understand (select-result) connections, lose emotional control, and exacerbate specific negative thoughts, potentially leading to despair and suicide[13, 21, 22, 28].Lithium has neurotrophic and neuroprotective effects on the above suicidal brain regions, which may be the mechanism of lithium for the treatment of BD suicide. In BD patients with lithium therapy, the integrity of GM and WM had a positive effect[29-30], suggesting the possibility of neurotrophic effects of lithium[32]. However, not all structural changes are associated with improvements in BD suicidal symptoms[24], necessitating the identification of therapeutic markers for lithium in treating BD suicidal behavior.

In the present study, our aim was to confirm the involvement of the temporal regions, especially the morphological effects of lithium therapy on temporal cortex in suicidal BD patients, and their potential as a marker of suicide efficacy.

2. Materials and methods

2.1 Participants

Our study was approved by the Institutional Review Board of the Affiliated Brain Hospital of Guangzhou Medical University (Guangzhou HuiAi Hospital), and all participants provided informed consent. The study included 166 BD patients (mean age 24.36 ± 7.27 years, 54.22% female) and 147 healthy controls (mean age 24.31 ± 4.83 years, 44.90% female). BD patients were divided into two groups: 60 receiving lithium (mean age 22.48 ± 6.29 years, 60.00% female) and 106 not receiving lithium (mean age 25.11 ± 7.24 years, 50.94% female). Additionally, BD patients were categorized into 40 with a history of suicide attempts (mean age 23.55 ± 6.15 years, 62.50% female) and 126 without (mean age 25.18 ± 7.24 years, 51.43% female). All participants underwent MRI scans and were assessed using the Structured Clinical Interview for DSM-IV (SCID) to confirm BD diagnosis, suicidal behavior, and medication use in BD patients, and to ensure no psychiatric or neurological disorders in healthy controls. BD patients were recruited from the inpatient and outpatient departments of Guangzhou HuiAi Hospital, while healthy controls were recruited from the local community. Exclusion criteria for all groups included severe neurological disease, current physical illness, history of brain injury, MRI contraindications, or left-handedness. Healthy controls were also excluded if they had any history of psychiatric or neurological disorders, psychiatric medication use, or substance/alcohol abuse. BD patients were excluded if they had a history of other psychiatric disorders. We collected data on education, suicidal behavior, BMI, HAM-D, YMRS, disease duration, and medication use for BD patients.

2.2 MRI acquisition and Image processing

MRI scans were performed after clinical structural interviews and clinical assessments. All image data were obtained from the 3. 0 Tesla MRI system (Philips Medical Systems, Achieva X series, Netherlands) of the Department of Radiology, Affiliated Brain Hospital of Guangzhou Medical University (Guangzhou Hui Ai Hospital). Participants were restricted from head movement and required to stay calm and awake as much as possible. High-resolution T1-weighted image thickness was collected using a sagittal T1-weighted 3D turbine field echo (T1W 3D TFE) sequence (field of view 256 x 256 mm2; repetition time 8. 2 ms; echo time 3. 8 ms; view matrix 256 x 256; slice) 1 mm).

Based on previous studies[23-25], we used Freesurfer software v. 5. 3. 0 (http://surfer.nmr.mgh.harvard.edu) to obtain cortical thickness measurements. Each hemisphere is divided into 34 regions[26]. The entire image processing includes intensity normalization; motion correction; removal of non-brain tissue; cortical surface reconstruction; automatic segmentation and automatic topological correction for cortical regions , subcortical gray matter(GM) and white matter(WM) volume structures; and triangular tessellation for WM/cerebrospinal fluid (CSF) boundary (pial surface) and the WM/GM interface[27-33]. The distance measurement between the GM and WM boundaries to the pial surface was calculated as the cortical thickness[24, 31]. We manually correct the images process by using the editing tools of Freesurfer if necessary. Based on previous studies, we extracted lateral Temporal lobe thickness measurements for each hemisphere as follows:

Superior temporal gyrus, Middle temporal gyrus, Inferior temporal gyrus, Transverse temporal cortex and Banks of the superior temporal sulcus.

2.3 Statistical analyses

We used IBM SPSS statistics (Version 25. 0) for statistical analysis. We used IBM SPSS statistical software (version 25. 0) for statistical analysis. Chi-square test and analysis of variance (ANOVA) were performed on demographic data and clinical differences (including medication use) in the BD group. The measurement of the thickness of the lateral temporal regions (Superior temporal gyrus, Middle temporal gyrus, Inferior temporal gyrus, Transverse temporal cortex, Banks of the superior temporal sulcus) was the dependent variable, the medication use (using Lithium vs Non-Lithium) and suicidal behavior (Suicide vs Non-suicide) for the two between-subject factors, gender and age were used as covariates to establish a general linear model (GLM). Post-hoc tests was performed between medication use and suicide history groups using the Bonferroni correction method. In addition, we compared the thickness of the lateral temporal regions between the three groups (BD Lithium, BD Non-Lithium, and healthy controls); as well as the three groups (BD with suicide history, BD Non-suicide history, and healthy controls). The dependent variables, covariates, and methods were the same.

3. Results

3.1 Demographic Characteristics

Study participants included 166 patients with BD (40 patients with a positive history of suicide attempts and 126 patients control without suicide attempt) and 147 HC patients. Demographic characteristics are shown in Table 1. No significant differences in gender and age were found across the three groups. In addition, no significant differences in BMI, education years and scale scores were found between SA patients and Non-SA BD patients.

3.2 Effect of Lithium Use

Compared with the healthy control group, there was no significant difference in the lithium treatment group, but the temporal cortex thickness in the non-lithium treatment group was significantly lower than HC. (table2)

3.3 Effect of Suicide Attempts

Demographic characteristics shows no significant in lithium use, but in order to avoid the effect of lithium treatment as much as possible, we measured with the above Demographic Characteristics, (sex and age $p<0.05$. Ham-D, YMRS, Education and BMI $p<0.05$). Compared with Non-SA BD patients, the Temporal thickness (left superior temporal, left middle temporal, inferior temporal) increased in patients with suicidal history. Compared with BD patients without suicide attempt, the cortical thickness of Temporal cortex (left superior temporal, left middle temporal, inferior temporal) were reduced, and Temporal cortex (transverse temporal) were increased in SA.

Demographic characteristics shows no significant in lithium use, but in order to avoid the effect of lithium treatment as much as possible, we measured the thickness of temporal cortex in patients with BD without lithium treatment. At the same time, the three groups were consistent with the above Demographic Characteristics, (sex and age $p<0.05$. Ham-D, YMRS, Education and BMI $p<0.05$). Compared with Non-SA BD patients, the Temporal thickness (left superior temporal, left middle temporal, inferior temporal) increased in patients with suicidal history. Compared with BD patients without suicide attempt, the cortical thickness of Temporal cortex (left superior temporal, left middle temporal, inferior temporal) were reduced, and Temporal cortex (transverse temporal) were increased in SA.

In addition, we measured the temporal cortical volume and thickness of these three groups. After covariance of age, sex and intracranial volume, Temporal cortex (superior temporal, middle temporal, inferior temporal) were smaller and left transverse temporal was larger in SA patients (table3). The same measurement method was applied to the group without Lithium treatment (table4).

Post-analysis showed that all P1 (P1 = Suicide-Non Suicide p-value) could not pass the conservative Bonferroni multiple comparison, and there was no significant difference between SAS and PC, but the differences between SAS and HC and the differences between PC and HC were different. The difference in the three groups were shown in Figure 1.

In addition, the correlation of structural indicators showed in Figure 2. The correlation between thickness and volume measurement was weak.

3.4 Main Analysis: Lithium-by-Suicide Interaction

We found a significant interaction between suicidal attempt and cortical thickness in BD patients treated with lithium (left middle temporal cortex (MTC)=0.003). In BD patients with lithium treatment, the left MTC and left pars opercularis

were thicker in SA patients than Non-SA patients. In BD patients without lithium treatment, the MTC was thicker in Non-SA patients.

Table 1. Demographic and clinical features of the participants (Mean±standard deviation (SD))

Variable	Suicide (n=40)	Non-Suicide (n=126)	HC (n = 147)	Statistic (p)
Sex (male/female)	15/25	61/65	81/66	4.154 (0.125)
Age *	23.550±6.148	24.357±7.268	24.313±4.834	0.291 (0.748)
HAM-D	5.175±6.004	3.246±4.678	NA	4.474 (0.036)
YMRS	5.051±6.992	3.256±6.264	NA	2.287 (0.132)
Education	12.150±3.167	12.159±3.340	14.054±2.523	16.028 (0.000)
BMI	22.555±3.885	22.464±3.292	20.655±2.881	5.731 (0.004)
Medication use(n)			NA	
Lithium	13 (32.5%)	47 (37.3%)	NA	0.303 (0.582)
Anticonvulsants	20	65		
Antidepressants	14	16		
Antipsychotics	28	92		
Anxiolytics	16	26		

Table 2. Comparisons of the thickness(TH) measurements on lateral temporal subregions by three groupings (Lithium/Non-Lithium/HC) (Mean±SD)

Region Measurements	BD		HC	F	P* value	P value		
	Non Li(n=106)	Li (n=60)				P1	P2	P3
Temporal cortex								
Lh superior temporal TH	2.786+0.160	2.828+0.169	2.916+0.129	24.610	0.000	0.795	0.000	0.000
Rh superior temporal TH	2.856+0.161	2.915+0.144	3.001+0.131	31.237	0.000	0.166	0.000	0.000
Lh middle temporal TH	2.858+0.142	2.903+0.147	2.939+0.133	9.491	0.001	0.541	0.000	0.103
Rh middle temporal TH	2.895+0.143	2.972+0.127	3.008+0.120	21.419	0.000	0.007	0.000	0.093
Lh inferior temporal TH	2.770+0.133	2.831+0.126	2.850+0.121	11.059	0.000	0.025	0.000	0.888
Rh inferior temporal TH	2.790+0.134	2.811+0.134	2.853+0.127	6.418	0.015	1.000	0.002	0.089
Lh transverse temporal TH	2.286+0.205	2.390+0.199	2.376+0.200	6.249	0.017	0.033	0.003	1.000
Rh transverse temporal TH	2.340+0.191	2.454+0.245	2.417+0.208	5.750	0.028	0.008	0.020	0.998

P1=lithium vs. Non lithium p-value; P2= HC vs. Non Lithium p-value; P3=HC vs. lithium p-value

aSurviving multiple comparison correction. All measurement covarying for sex, age, and intracranial volume as covariate.

Table 3. Comparisons of the thickness measurements on lateral temporal subregions by three grouping (Suicide/Non-Suicide/HC) (Mean±SD)

Region	L/R	BD		HC	F	P value	Post hoc		
		SAH (n=40)	NSAH (n=126)				P1	P2	P3
Temporal cortex									
Superior temporal	L	2.812+0.170	2.798+0.163	2.916+0.129	24.033	0.000	1.000	0.000	0.000
	R	2.897+0.161	2.870+0.156	3.001+0.131	29.726	0.000	0.850	0.000	0.000
Middle temporal	L	2.875+0.192	2.874+0.127	2.939+0.133	8.540	0.002	1.000	0.026	0.000
	R	2.936+0.175	2.919+0.131	3.008+0.120	16.640	0.000	1.000	0.009	0.000
Inferior temporal	L	2.796+0.150	2.791+0.128	2.850+0.121	7.490	0.005	1.000	0.116	0.001
	R	2.790+0.160	2.800+0.125	2.853+0.127	6.270	0.017	1.000	0.046	0.004
Transverse temporal	L	2.372+0.207	2.308+0.207	2.376+0.200	4.166	0.131	0.351	1.000	0.015
	R	2.455+0.194	2.358+0.221	2.417+0.208	4.155	0.133	0.043	1.000	0.072

P1= Suicide -Non Suicide p value; P2= HC- Suicide p value; P3=HC-Non Suicide p value

aSurviving multiple comparison correction. All measurement sex, age, and intracranial volume as covariate.

Table 4. Comparisons of the thickness measurements on lateral temporal subregions by three grouping without lithium treatment (Suicide/Non-Suicide/HC) (Mean±SD)

Region	L/R	BD		HC	F	P value	Post hoc		
		SAH (n=27)	NSAH (n=79)				P1	P2	P3
Temporal cortex									
Superior temporal	L	2.777+0.173	2.789+0.156	2.916+0.129	24.509	0.000	1.000	0.000	0.000
	R	2.868+0.169	2.851+0.158	3.001+0.131	29.48	0.000	1.000	0.000	0.000
Middle temporal	L	2.826+0.183	2.869+0.124	2.939+0.133	10.962	0.000	0.266	0.000	0.003
	R	2.904+0.181	2.892+0.129	3.008+0.120	20.924	0.000	1.000	0.001	0.000
Inferior temporal	L	2.753+0.153	2.775+0.125	2.850+0.121	11.031	0.000	1.000	0.002	0.000
	R	2.77+0.166	2.797+0.121	2.853+0.127	6.373	0.002	1.000	0.017	0.016
Transverse temporal	L	2.334+0.203	2.269+0.204	2.376+0.200	6.293	0.002	0.807	0.729	0.001
	R	2.394+0.139	2.322+0.203	2.417+0.208	5.233	0.006	0.445	1.000	0.004

P1= Suicide -Non Suicide p value; P2= HC- Suicide p value; P3=HC-Non Suicide p value

aSurviving multiple comparison correction. All measurement covarying for sex, age, and intracranial volume as covariate.

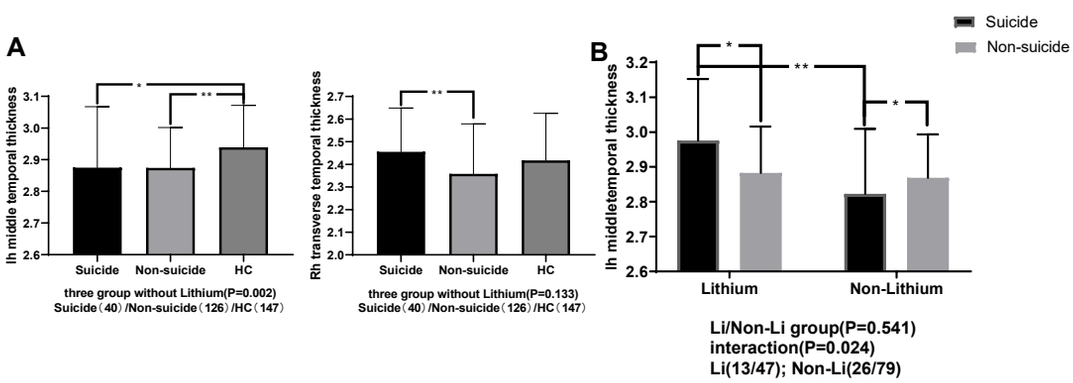

Figure 1. The difference in the three groups

Figure 1 (A) shows significant interaction between Li/Non-Li groupings and Suicide/Non-suicide groupings on the left middle temporal thickness and left pars opercularis thickness, * $p<0.05$.

In Figure 1 (B), (1) compared with HC, the left middle temporal volume of SA patients is significantly reduced, but there is no significant difference between PC; (2) compared with HC, the thickness of SA and PC is significantly reduced, but the difference in SA is more significant. (3) Compared with HC, there was no significant difference in the left transverse temporal volume and thickness in SA patients, and the PC group significantly decreased ($p <0.005$). See table 2 for corresponding statistics.

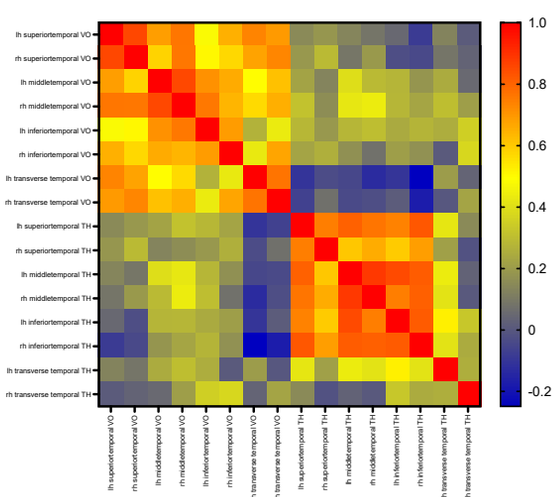

Figure 2. Correlation map between all magnetic resonance imaging measures for the four regions-of-interest

4. Discussion

As far as we know, this is the first study of the association between lithium therapy and the cortical thickness (TH) of middle temporal cortex (MTC) in BD patients with suicidal attempt history (SAH). We had three main findings: (1) Compared with HC, BD without lithium treatment showed significantly decreased thickness in all measurements (all $P < 0.05$), while BD with lithium treatment only showed significant thinner left superior temporal and right superior temporal TH (all $P < 0.05$). (2) Compared with BD patients without SAH, the TH of Temporal cortex (included left superior temporal, left middle temporal, inferior temporal) decreased. (3) There was a significant interaction between SAH and lithium treatment on left MTC TH ($F = 9.172$, $P = 0.024$, Partial Eta Squared = 0.055). Among lithium-treated BD patients, the thickness of left MTC in patients with SAH were thicker than patients without SAH. Interestingly, in the BD patients without lithium treatment, the thickness of left MTC in patients with SAH was thinner.

4.1 Reduced Cortical Thickness in BD

The reduced TH in the BD patients and the increased in lithium treatment group mentioned above were universally consistent with the results of study about bipolar disorder[1–4]. For example, the cross-sectional studies of structural abnormalities of BD reported significantly thinner CT of PFC and temporal cortex in BD patients than HC[44-51]. In addition, the studies of longitudinal cortical thickness showed that the temporal cortex was thinner in patients with BD than in HC[5]. In summary, the widespread frontotemporal cortical with thinning thickness in BD patient were consistent with present finding on the brain structure involved in emotional and cognitive regulation.

4.2 Abnormal structure in BD with SA

Because the suicide rate is much higher than the general population, it is helpful to find potential suicide markers in order to assess the suicide risk of BD patients. We provided CT and volume measurements (table3) of the frontotemporal lobe of BD, and observed the correlation between them (figure2). For the PFC region, structural damages of VLPFC, DLPFC and OFC are involved in the suicidal attempt of BD, including a reduction in cortical volume and thickness[28]. The reason why these findings were not completely consistent was not clear, but we provided some possible explanations. For example, sample size, intracranial volume correction, lithium or other treatments, different measurement methods (SPM/freesurfer) and structural indicators (area/volume/thickness) may lead to different or contrary results from previous studies. It is worth mentioning that the PFC study[14] showed a correlation between indicators measured by the SBM method. There was a high correlation between volume and area indicators, but thickness had a poor correlation with them. It could explain the reason why the CT of PFC increased but the volume decreased in our study, which also meant that CT and volume were two different phenotypes[30].

The possible explanation for the association between frontotemporal structural abnormalities and suicide is the dysfunction of the frontotemporal network. The prefrontal network FLN consisted of PFC (included DPFC, VPFC, OFC and MPFC), subcortical structures (included amygdala, hippocampus and so on) and ACC[41-43]. This connection is mainly involved in emotional regulation, responses to emotional and cognitive stimuli, stimulus value assessment, detection of adverse outcomes, risk decision-making and impulse control[13, 33, 40]. The structure of the temporal cortex connects with the prefrontal network and limbic system, and they participated in the functions mentioned above[25]. When stimulate by life stress, BD patients may have severely negative comments and emotional responses, and are unable to correctly understand the choice-outcome link. In the end, BD may not be able to control negative emotions and choose to commit suicide[8, 11, 14].

4.3 Lithium-by-Suicide Interaction

In our research, a significant interaction between suicidal behavior and lithium therapy was observed in the cortical thickness (CT) of the left middle temporal lobe. Specifically, the CT of the left middle temporal cortex (MTC) increased only in BD patients with suicidal attempts (SA). In BD patients without suicidal behavior, lithium carbonate treatment did not significantly alter cortical thickness. Similarly, in BD patients with non-suicidal attempts (Non-SA), there was no significant difference in cortical thickness between those treated with lithium and those who were not. Numerous studies have demonstrated that lithium is not only a key mood stabilizer but also offers a protective effect against suicide[26]. Long-term lithium therapy significantly reduced the risk of suicide attempt[48]. The left MTC and pars opercularis are integral to the frontotemporal network, and the connection between their structural abnormalities and suicidal behavior has been previously discussed. Importantly, these regions only exhibited significant changes in response to lithium treatment in BD patients with SA, suggesting that they may serve as potential therapeutic markers for lithium in treating suicidal symptoms in BD.

Lithium plays a important role in neurotrophic and neuroprotective effects through a variety of mechanisms. For example, (1) It attenuates apoptosis and enhances synaptic plasticity by promoting GSK3 phosphorylation and regulating tumor protein p53[47]. This process is abnormally active in the VPFC of suicidal BD[49]. (2) It enhances synaptic plasticity and promotes neuronal maturation and differentiation by increasing BDNF levels[48]. It also attenuates oxidative stress and neuropeptide inflammation during emotional attacks by regulating mitochondrial function, stress protein levels[48] and pro-inflammatory molecules levels[50]. (3) It improves mitochondrial dysfunction and repair neuronal plasticity by affecting the second messenger system, such as inhibiting Inositol monophosphatase and PKC, alleviating calcium regulation disorders and increasing the gene expression level of cAMP response element binding protein (CREB)[51].

4.4 Limitations

Lithium is considered a treatment for suicide, but no efficacy markers exist. Our study suggests that lithium-induced changes in the cortical thickness (CT) of the left middle temporal cortex (MTC) and pars opercularis may be potential brain imaging markers for suicidal behavior in BD, with potential clinical significance. However, these markers are far from being definitive efficacy indicators.[30].

Study limitations include variability in medication use, suicidal symptoms, and brain dysfunction improvements. Lithium dose and duration varied among BD patients, potentially affecting brain structure measurementse[23, 26]. Previous studies indicate that the number of suicide attempts and the lethality of suicidal behavior can influence brain structure abnormalities. As a cross-sectional study, we could not assess changes in suicidal symptoms following lithium treatment. It remains unclear whether lithium normalizes brain function and reduces suicidal symptoms. Our design also could not establish a causal relationship between these factors.

5. Conclusions

In summary, it is the first to study the efficacy response markers of lithium which prevent and treat the suicidal symptoms of BD. We believe that the structural abnormalities of the frontotemporal lobe are highly related to the suicidal behavior of BD, and lithium therapy normalizes these abnormal structures, which may be an important mechanism of lithium in the treatment of suicidal symptoms in BD. In addition, we provide evidence to support the cortical thickness of left middle temporal cortex and pars opercularis as potential markers of suicidal efficacy in the lithium treatment. It will ultimately help to evaluate and treat the suicidal symptoms of BD and reveal the mechanism of lithium therapy for suicidal BD.

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