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# Association of childhood trauma, social support, cognition, and suicidality in females with bipolar disorder

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## Abstract

**Background** Bipolar disorder (BD) is a severe mental disorder with heavy disease burden. Females with BD are special populations who suffer a lot from childhood trauma, social support, cognitive deficits, and suicidality. In this study, the relationship among childhood trauma, social support, and clinical symptoms of BD was investigated and the risk factors for suicidality were explored in female patients with BD.

**Methods** This study included 57 drug-naïve female BD patients, 64 female BD patients with long-term medication, and 50 age-matched female healthy controls. Childhood trauma, social support, clinical symptoms, cognition, and suicidality (suicide ideation, suicide plan, suicide attempt, suicide frequency) were measured with scales.

**Results** Compared with healthy controls, females with BD showed higher levels of childhood trauma and suicidality, and lower levels of social support and cognitive deficits. In the drug-naïve BD group, social support mediated the relationship between childhood trauma and insomnia symptoms (indirect effect:  $ab=0.025$ ). In the BD with long-term medication group, mania symptom was associated with suicide plan ( $OR=1.127, p=0.030$ ), childhood trauma was associated with suicide attempt ( $OR=1.088, p=0.018$ ), and years of education ( $OR=0.773, p=0.028$ ), childhood trauma ( $OR=1.059, p=0.009$ ), and delayed memory ( $OR=1.091, p=0.016$ ) was associated with suicide frequency ( $OR=1.091, p=0.016$ ).

**Conclusions** This study provides initial evidence that social support partially explains the relationship between childhood trauma and clinical symptoms in females with BD. Additionally, mania symptoms, childhood trauma, and delayed memory were risk factors for suicidality. Interventions providing social support and improving cognitive function may be beneficial for females with BD who are exposed to childhood trauma and with high suicide risk.

**Keywords** Bipolar disorder, Female, Childhood trauma, Social support, Cognition, Suicidality

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## Introduction

Bipolar disorder (BD) is a severe mental disorder characterized by recurrent mood episodes, including depressive and manic/hypomanic episodes [1]. Patients with BD have low-quality lives, such as comorbidities [2], impaired psychosocial functioning [3], low employment [4], and suicide ideation and suicide attempts [5]. Females with BD are important and special populations who may need more attention. Partial S reviewed that females with BD are characterized by late age of onset, seasonality, atypical presentation, high degree of mixed episodes, and a high frequency of medical and psychiatric co-morbidity [6]. In addition, women shoulder the burden of bearing children, and the reproductive period of life is strongly influenced by BD [6]. Moreover, a recently published study reported that females with BD were overlooked by their mothers during their upbringing [7]. All these factors may aggravate the disease condition and make treatment extremely challenging in females with BD.

Early-life stress, including childhood trauma, can disturb the development of the brain and thus increase the risk of mental illness [8]. It was found that BD patients with childhood trauma showed greater symptom severity [9], and increased risk of nonsuicidal self-injury [10]. Wrobel et al. reported that depressive symptoms in BD patients were positively associated with childhood trauma [11]. A meta-analysis of Agnew-Blais et al. also reported that depressive, manic, and psychotic symptoms of BD were all positively associated with childhood trauma, and the number of depressive and manic episodes was also positively associated with childhood trauma [12]. Colic et al. found that females with BD experienced more severe childhood trauma than males with BD [13]. Although researchers have recognized the role of childhood trauma in bipolar disorder, most studies were conducted in BD patients with medication, and there is a lack of literature comparing self-report childhood trauma between drug-naïve BD patients and those with medication.

Social support is a protective factor for mental health. Studies have shown that low social support worsens the outcome of BD and causes a high caregiver burden [14]. Some researchers proposed that fully understanding the role of social support in BD could provide information on prevention and treatment [15]. Compared with males, females were more sensitive to low social support [16] and tended to seek and obtain social support when faced with environmental stressors [17]. Therefore, females with BD may benefit more from social support interventions [18]. Additionally, some studies have found that social support was associated with mood symptoms and could mediate the negative impact of childhood trauma on mood symptoms [19, 20]. However, there is a gap in the understanding of the interaction between childhood

trauma and social support in drug-naïve patients with BD and comparing this interaction between drug-naïve BD patients and BD patients with medication.

Cognitive deficits of BD patients were widely reported in a range of domains, including attention, verbal learning, and mental flexibility [21]. Zhang et al. reviewed that cognitive dysfunction is one important parameter implicated in suicidality [22], but Gilbert et al. did not find the association between cognition and suicide attempt [23]. Xu et al. reported that there was a difference in domains of cognition between male and female BD patients [24]. And there may be different neurobiological mechanisms underlying suicide ideation and suicide attempt [22]. Considering gender and different categories of suicidality in the relationship between cognitive deficits and suicidality may make development in the treatment and prevention of suicidality.

It was reviewed that the annual suicide rate in BD was approximately 0.9% [25]. One study found that BD patients with suicide attempts were more likely to be females [26]. More importantly, Rowe et al. reported that both childhood trauma and social support served as predictors of suicide ideation [20]. However, few studies explored childhood trauma, social support, and suicidality independently in female patients. Identifying the risk factors of suicidality for females with BD may help improve clinical outcomes.

In this study, childhood trauma, social support, cognition, and suicidality were compared in drug-naïve female BD and BD patients with long-term medication. Furthermore, the role of social support in the relationship between childhood trauma and clinical symptoms were explored. More importantly, the predictors of suicidality including suicide ideation, suicide plan, suicide attempt, and suicide frequency were explored.

## Methods

### Participants

A total of 121 female patients with BD were recruited from the Department of Psychiatry of Second Xiangya Hospital of Central South University, Changsha, China. The patients were divided into two patient groups: the drug naïve BD group and BD with long-term medication. The inclusion criteria for BD patients were: (1) aged 15–50 years, female; (2) meet the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), and diagnosed with BD by at least one psychiatrist at or above the deputy director level using MINI-International Neuropsychiatric Interview Mini diagnostic interview (M.I.N.I.); (3) willing to participate and signed informed consent. Additionally, the drug naïve BD group should not have use of previous and current psychotropic drugs, and the BD with long-term medication group should have a long-term medication

for at least 6 months. Fifty-three female healthy controls (HCs) were recruited from nearby communities and universities by advertisements and screened for psychiatric disorders. The participants of the HC group should have never been diagnosed with any psychiatric disorder and should not have a family history of psychiatric disorders. Three of the 53 HCs were excluded because they had a family history of psychiatric disorders. The exclusion criteria for all participants were: (1) a history of craniocerebral trauma or diagnosed with neurological or organic mental diseases; (2) complicated with other psychiatric diagnoses, such as general anxiety disorder, panic disorder, obsessive-compulsive disorder, posttraumatic stress disorder, major depressive disorder, and so on; (3) a history of psychoactive substance abuse; (4) presence of severe physical diseases such as cardiovascular diseases; (5) pregnancy or lactation.

This study was approved by the Ethics Committee of Second Xiangya Hospital of Central South University. All subjects were informed and fully understood the study and each subject provided a written informed consent.

### Materials

Demographic data were collected from all participants. The duration of illness of BD patients was collected by using the M.I.N.I. Clinical scales, including the Young Mania Rating Scale (YMRS) [27], 17-item Hamilton Depression Rating Scale (HDRS-17) [28], and 14-item Hamilton Anxiety Scale (HAMA-14) [29] were used to assess the manic, depressive, and anxiety symptoms of BD patients, respectively (based on the performance of patients over the past seven days). The subjects in the HC group were carefully screened with M.I.N.I. for DSM-5 to exclude the presence of psychiatric diseases.

Athens Insomnia Scale (AIS) is an internationally recognized self-measurement of sleep quality. It is simple, concise and easy to use, with a total of 8 items, each divided into four levels: 0, 1, 2, and 3, indicating from none to severe [30]. The total score of AIS ranges from 0 to 24, and a total score greater than 6 suggests the presence of insomnia.

Childhood Trauma Questionnaire (CTQ) is a maltreatment inventory that examines childhood growth experiences before age 16. The Chinese version of CTQ short-form (CTQ-SF) [31] was used in this study. It consists of 3 validity items and 25 clinical items which were divided into five clinical subscales: emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect [32]. Each item is rated from 1 to 5 points, representing never, occasionally, sometimes, often, and always, respectively. All the subscale scores meet the following criteria: emotional abuse < 13 points, physical abuse < 10 points, sexual abuse < 8 points, emotional neglect < 15 points, and physical neglect < 10 points

means to be free of any form of childhood trauma. As long as one subscale score does not meet the above criteria, it is considered to exist childhood trauma.

Social support was measured in all participants using the Social Support Rating Scale (SSRS). The SSRS contains 10 selective items, 3 for objective support, 4 for subjective support, and 3 for utility of this support [33]. Higher scale scores represent higher levels of social support. A total score of < 20 is generally considered to receive less social support, 20–30 is considered to have general social support, and 30–40 is considered to have satisfactory social support.

The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) [34] and the Stroop Color-Word Test (Stroop test) were used to measure cognitive function. The RBANS contains 12 subtests which makes up 5 age-adjusted indexes: immediate memory, visuospatial, language, attention, and delayed memory. The Stroop test contains Stroop word, Stroop color, and Stroop color-word.

Suicidality were assessed through self-report questionnaire. Suicide ideation was assessed with a standard question: “Have you ever had thoughts of committing suicide?” with a binary response option “Yes” and “No”. Suicide plan was assessed with a standard question: “Have you ever made a suicide plan?” with a binary response option “Yes” and “No”. Suicide attempt was evaluated with a standard question: “Have you ever tried committing suicide?” with a binary response option “Yes” and “No”. If participants respond positive to these questions, they would continue to be asked about the method, frequency, and further relevant details on the attempts of suicide. Suicide frequency was recorded with a four-level response option “0 time”, “1 time”, “2 times”, and “3 or more times”.

### Statistical analysis

The Statistical Package for Social Sciences (SPSS) version 25.0 (IBM, Chicago) was used for data analysis and Microsoft Power Point was used for graphing. The data were first checked for normality by one-sample Kolmogorov–Smirnov test and quantile-quantile plot (Q-Q plot). Continuous variables were shown as mean (SD), categorical variables were shown as N (%). Variables with skewed distribution were compared by Kruskal-Wallis H and normally distributed variables were compared by One way ANOVA among three groups. Categorical variables were compared by chi-square tests. Two sample *t*-tests were used to compare normally distributed variables between drug-naïve BD and BD with long-term medication groups. The statistically significant level was set to  $p < 0.05$  (two-tailed). Post-hoc tests were Bonferroni corrected.

Partial correlation analysis was conducted to analyze the pairwise correlations among childhood trauma, clinical symptoms, and social support to control for education and duration of illness in BD patients. Significant variables were included in Binomial Logistic Regression Analysis (Input) to explore the predictors of suicide ideation, suicide plan, and suicide attempt, and included in Ordinal Logistic Regression Analysis (Input) to explore the predictors of suicide frequency. Multi-collinearity was checked to rule out any association between independent variables.

Bootstrapped Mediation analyses were performed using PROCESS version 3.4 procedure in SPSS ([www.afhayes.com](http://www.afhayes.com)) [35]. Total CTQ was entered as a predictor (X), total scale scores of symptoms (HDRS, HAMA, YMRS, and AIS) were entered as outcome variables (Y), and total SSRS was entered as a mediating variable (M) in

the mediation model. Total CTQ predicts total SSRS via a path represented by *path a*. Total SSRS predicts clinical symptoms via a path represented by *path b*. The mediation effect (indirect effect) is the cross product of *a* and *b*. The direct effect (*path c'*) represents the relationship between total CTQ and clinical symptoms after controlling for total SSRS in the model. The total effect is the effect of total CTQ on the clinical symptoms without the influence of total SSRS. The number of bootstrap samples was 5000, and years of education were served as covariates in the analysis.

**Results**

**Demographic and clinical characteristics**

Table 1 shows that there was no difference in age and age of onset among three groups. Both drug-naïve BD and BD with long-term medication group had lower years of

**Table 1** Demographic and clinical data of all participants

	1. Drug naïve BD (n=57)	2. BD with long-term medication (n=64)	3. HCs (n=50)	F/t/H/ $\chi^2$	p	Post-hoc
Age (year)	22.68 (5.12)	24.11 (6.60)	24.24 (2.88)	1.527	0.220 <sup>a</sup>	-
Age of onset	19.89(5.51)	18.73(4.70)	-	1.250	0.214 <sup>b</sup>	-
Education (year)	14.14 (2.25)	14.00 (2.72)	16.12 (1.73)	14.045	<0.001 <sup>a</sup>	1, 2<3
Family history of mental illness (n, %)	17 (29.82%)	23 (35.94%)	0	0.509	0.476 <sup>d</sup>	
Duration of illness	2.29 (2.79)	5.37 (3.99)	-	4.972	<0.001 <sup>b</sup>	-
HDRS	22.51 (6.08)	13.17 (8.28)	-	7.122	<0.001 <sup>b</sup>	-
HAMA	28.04 (7.09)	16.34 (10.77)	-	7.121	<0.001 <sup>b</sup>	-
YMRS	14.21 (7.37)	9.98 (6.11)	-	3.446	0.001 <sup>b</sup>	-
AIS	11.54 (5.03)	7.08 (3.67)	4.24 (2.93)	45.861	<0.001 <sup>a</sup>	1>2>3
<b>Childhood trauma</b>						
Emotional abuse	12.51 (4.70)	9.88 (4.45)	5.88 (1.29)	66.018	<0.001 <sup>c</sup>	1>2>3
Physical abuse	7.81 (4.65)	6.22 (2.72)	5.22 (0.79)	25.075	<0.001 <sup>c</sup>	1>2>3
Sexual abuse	6.84 (3.06)	6.17 (2.72)	5.12 (0.39)	17.275	<0.001 <sup>c</sup>	1, 2>3
Emotional neglect	16.49 (5.44)	14.98 (5.53)	9.74 (4.67)	23.881	<0.001 <sup>a</sup>	1, 2>3
Physical neglect	11.04 (4.51)	9.80 (3.82)	7.57 (1.87)	12.510	<0.001 <sup>a</sup>	1, 2>3
CTQ total	54.68 (17.05)	47.05 (14.51)	33.50 (7.02)	31.965	<0.001 <sup>a</sup>	1>2>3
<b>Social support</b>						
Objective support	6.61 (2.44)	7.89 (2.62)	8.66 (2.32)	20.895	<0.001 <sup>c</sup>	1<2, 3
Subjective support	13.51 (3.81)	16.98 (4.12)	20.04 (3.94)	36.419	<0.001 <sup>a</sup>	1<2<3
Degree for support utilization	6.28 (2.10)	7.14 (1.67)	8.74 (1.70)	24.542	<0.001 <sup>a</sup>	1<2<3
SSRS total	26.46 (6.56)	32.02 (6.48)	37.44 (6.07)	39.441	<0.001 <sup>a</sup>	1<2<3
<b>Suicide</b>						
Ideation (n, %)	55 (96.49%)	56 (87.50%)	13 (26.00%)	77.929	<0.001 <sup>d</sup>	1, 2>3
Plan (n, %)	34 (59.65%)	36 (56.25%)	0	49.829	<0.001 <sup>d</sup>	1, 2>3
Attempt (n, %)	44 (77.19%)	48 (75.00%)	4 (8.00%)	66.565	<0.001 <sup>d</sup>	1, 2>3
Frequency (n, %)				72.740	<0.001 <sup>d</sup>	
0	11 (19.30%)	17 (26.56%)	45 (90.00%)	-	-	1, 2>3
1	5 (8.77%)	11 (17.18%)	4 (8.00%)	-	-	-
2	15 (26.32%)	18 (28.13%)	0	-	-	1, 2>3
3 or more	26 (45.61%)	18 (28.13%)	1 (2.00%)	-	-	1, 2>3

(a) One-way ANOVA; (b) Two sample t test; (c) Kruskal-Wallis H; (d) Chi-square test

Post-hoc: Bonferroni corrected. BD, Bipolar disorder; HC, healthy control; HDRS, Hamilton Depression Rating Scale; HAMA, Hamilton Anxiety Scale; YMRS, Young Mania Rating Scale; AIS, Athens Insomnia Scale; CTQ, Childhood Trauma Questionnaire; SSRS, Social Support Rating Scale

**Table 2** Cognitive function in all participants

	1. Drug naïve BD (n=57)	2. BD with long-term medication (n=64)	3. HCs (n=50)	F	p	Post-hoc
Immediate memory	39.41 (9.11)	38.16 (9.43)	48.60 (4.75)	25.748	<0.001	1, 2<3
Visuospatial	33.64 (4.02)	34.11 (2.90)	36.78 (1.95)	15.669	<0.001	1, 2<3
Language	28.259 (4.620)	27.555 (5.33)	33.76 (4.64)		<0.001	1, 2<3
Attention	70.63 (10.24)	69.48 (9.20)	78.40 (6.66)	15.847	<0.001	1, 2<3
Delayed memory	47.27 (6.55)	46.59 (8.34)	54.28 (3.76)	21.699	<0.001	1, 2<3
RBANS total	219.21 (26.08)	215.90 (25.79)	251.82 (14.10)	39.427	<0.001	1, 2<3
Stroop word	100.80 (16.99)	94.70 (17.74)	121.22 (16.24)	35.854	<0.001	1, 2<3
Stroop color	69.41 (15.97)	65.42 (15.04)	85.10 (11.44)	28.116	<0.001	1, 2<3
Stroop color-word	38.79 (10.98)	37.97 (9.55)	50.24 (9.22)	25.283	<0.001	1, 2<3
Stroop total	209.00 (38.86)	198.09 (36.77)	256.56 (28.29)	41.905	<0.001	1, 2<3

BD, bipolar disorder; RBANS: Repeatable Battery for the Assessment of Neuropsychological Status

**Table 3** Correlation of symptoms, childhood trauma, and social support in drug naïve BD patients

n = 57	1	2	3	4	5	6
	r					
1. HDRS	1	-	-	-	-	-
2. HAMA	0.744**	1	-	-	-	-
3. YMRS	0.006	0.196	1	-	-	-
4. AIS	0.602**	0.570**	0.161	1	-	-
5. CTQ total	0.401*	0.508**	0.134	0.427*	1	-
6. SSRS total	-0.353*	-0.355*	0.036	-0.378*	-0.341*	1

\*\*  $p < 0.001$ ; \*  $p < 0.05$ ; All correlation coefficients were controlled for years of education and duration of illness

BD, Bipolar disorder; HDRS, Hamilton Depression Rating Scale; HAMA, Hamilton Anxiety Scale; YMRS, Young Mania Rating Scale; AIS, Athens Insomnia Scale; CTQ, Childhood Trauma Questionnaire; SSRS, Social Support Rating Scale

education than HC group. Comparing to the drug-naïve BD group, BD with long-term medication group showed lower scores of HDRS, HAMA, and YMRS scores.

For AIS, emotional abuse, physical abuse, and CTQ total among the three groups, the drug-naïve BD group showed the highest scores, BD with long-term medication group showed the second scores and the HCs group showed the lowest scores. For objective support, the drug-naïve BD group showed lower scores than the BD with long-term medication group and the HCs group. For subjective support, degree for support utilization, and SSRS total, the drug-naïve BD group showed the lowest scores, BD with long-term medication group showed the second scores and the HCs group showed the highest scores.

Comparing to the HCs group, the drug-naïve BD group and the BD with long-term medication group showed higher proportions of suicide ideation, suicide plan, suicide attempt, and suicide frequency. Comparing to cognition of the HCs group, the drug-naïve BD group, and the BD with long-term medication group showed lower scores in immediate memory, visuospatial, language, attention, delayed memory, RBANS total, Stroop word, Stroop color, Stroop color-word, and Stroop total scores (Table 2).

**Associations among childhood trauma, social support, clinical symptoms, cognitive function and suicidality**

In the drug-naïve BD group, after controlling for years of education and duration of illness, CTQ and SSRS total scores were correlated with each other, and both CTQ and SSRS total scores were correlated with HDRS, HAMA, and AIS scores ( $p < 0.01$ , shown in Table 3). However, correlations between suicidality and CTQ/SSRS total scores were not found.

In the BD with long-term medication group, after controlling for years of education and duration of illness, no correlation between CTQ and SSRS total scores was found. Suicide plan was correlated with age, years of education, HAMA, YMRS, and SSRS total scores. Suicide attempt was correlated with age, years of education, YMRS, and CTQ total scores. Suicide frequency was correlated with age, years of education, duration of illness, HAMA, YMRS, AIS, CTQ total, SSRS total scores, and delayed memory (Table 4).

**Mediation of social support on the association between childhood trauma and clinical symptoms**

The mediation of social support on the association between childhood trauma and AIS scores after controlling for years of education and duration of illness was significant in the drug-naïve BD group (Fig. 1). The results revealed a significant positive indirect effect of CTQ total score on AIS via SSRS total score (standardized indirect

**Table 4** Correlations of childhood trauma, social support, clinical symptoms, and suicidality in BD patients with long-term medication

n = 64	Suicide ideation	Suicide plan	Suicide attempt	Suicide frequency
	<b>r</b>			
Age	-0.237	-0.352**	-0.285*	-0.372**
Education	-0.242	-0.300*	-0.311*	-0.363**
Duration of illness	-0.180	-0.146	-0.157	-0.328**
HDRS	0.004	0.092	0.011	0.177
HAMA	0.210	0.272*	0.231	0.331*
YMRS	0.160	0.328**	0.277*	0.297*
AIS	0.242	0.168	0.159	0.261*
CTQ total	0.046	0.201	0.263*	0.343**
SSRS total	-0.099	0.321**	-0.173	0.296*
Delayed memory	0.172	0.189	0.160	0.349**

Spearman correlation analysis; All correlation coefficients were controlled for years of education and duration of illness; \*\*  $p < 0.01$ ; \*  $p < 0.05$

effect on AIS  $ab = 0.025$ , 95% bootstrap CI 0.001 to 0.067). The mediation of social support on the association between childhood trauma and other clinical symptoms was not significant in the drug-naïve BD group.

The mediation of social support on the association between childhood trauma and clinical symptoms was not significant in the BD with long-term medication group.

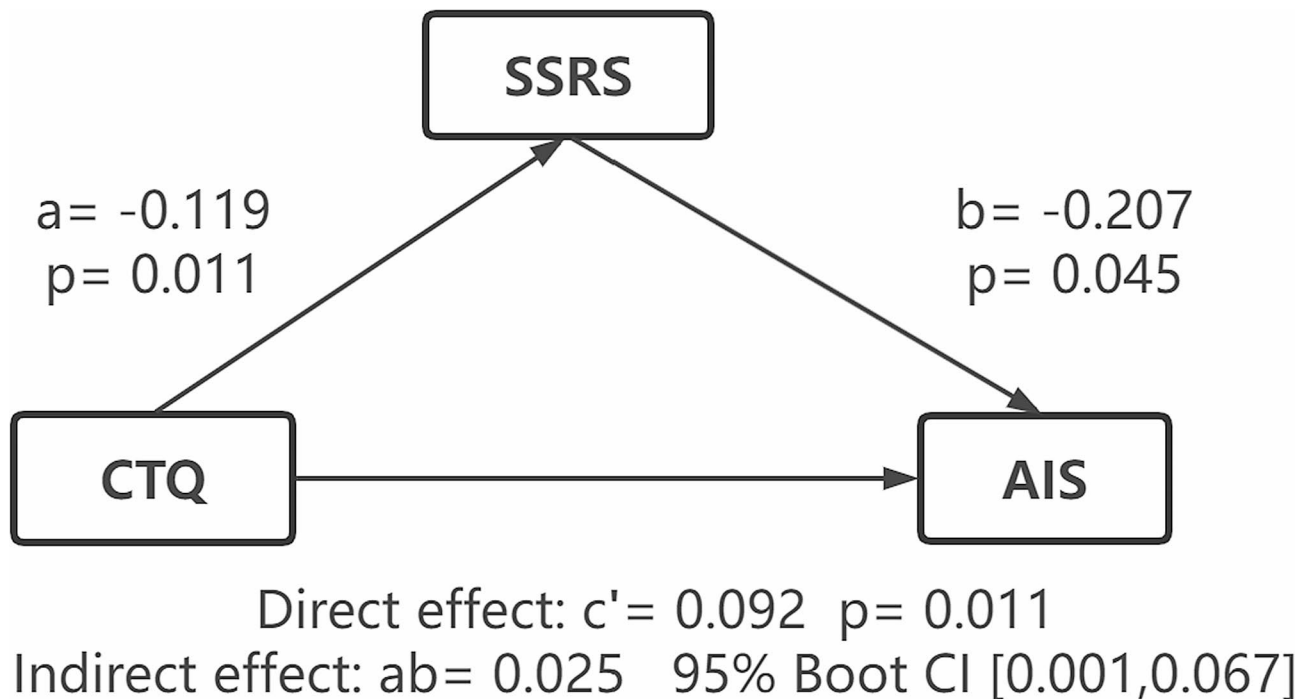
**Predictors of suicidality in BD patients with long-term medication**

In the BD with long-term medication group, suicide plan and suicide attempt were correlated with age (suicide plan:  $r = -0.352$ ,  $p = 0.004$ ; suicide attempt:  $r = -0.285$ ,  $p = 0.022$ ) and years of education (suicide plan:  $r = -0.300$ ,  $p = 0.016$ ; suicide attempt:  $r = -0.311$ ,  $p = 0.012$ ), respectively. And suicide frequency was correlated with age ( $r = -0.372$ ,  $p = 0.003$ ), education ( $r = -0.363$ ,  $p = 0.003$ ), and duration of illness ( $r = -0.328$ ,  $p = 0.008$ ). Therefore, age and years of education were included in the Binomial Logistic Regression Analysis, and age, years of education, and duration of illness were included in the Ordinal Regression Analysis.

YMRS was a risk factor for suicide plan, and CTQ was a risk factor for suicide attempt. For suicide frequency, years of education was a protective factor, whereas CTQ and delayed memory were risk factors (Table 5).

**Discussion**

We found high levels of childhood trauma, high proportions of suicidality, low social support, and cognitive deficits in drug-naïve and long-term medication female BD patients. Compared to drug-naïve BD patients, long-term medication BD patients showed higher social support and lower childhood trauma, but cognitive deficits and proportions of suicidality were similar. Furthermore, we built two different models in drug-naïve and long-term



**Fig. 1** Mediation effect of social support dimensions on the correlation between childhood trauma and Insomnia in drug-naïve BD patients. Years of education and duration of illness were served as covariates. BD, Bipolar Disorder; CTQ, Childhood Trauma Questionnaire; SSRS, Social Support Rating Scale; AIS, Athens Insomnia Scale

**Table 5** Predictors of suicidality using ordinal logistic regression in BD patients with long-term medication

	OR (95% CI)	P
<b>Suicide plan</b>		
Age	0.916 (0.818, 1.025)	0.126
Education	0.970 (0.762, 1.237)	0.808
HAMA	0.980 (0.917, 1.047)	0.548
YMRS	1.127 (1.012, 1.256)	0.030*
SSRS total	0.941 (0.851, 1.039)	0.229
<b>Suicide attempt</b>		
Age	0.903 (0.799, 1.021)	0.103
Education	0.787 (0.570, 1.085)	0.144
YMRS	1.067 (0.947, 1.202)	0.289
CTQ total	1.088 (1.014, 1.167)	0.018*
<b>Suicide frequency</b>		
Age	0.956 (0.851, 1.074)	0.448
Education	0.773 (0.615, 0.973)	0.028*
Duration of illness	0.960 (0.791, 1.165)	0.681
HAMA	1.008 (0.942, 1.080)	0.814
YMRS	1.064 (0.968, 1.169)	0.200
AIS	0.916 (0.753, 1.115)	0.382
CTQ total	1.059 (1.014, 1.104)	0.009*
SSRS total	0.957 (0.871, 1.050)	0.353
Delayed memory	1.091 (1.016, 1.172)	0.016*

\*  $p < 0.05$ 

medication BD patients, respectively. In the drug-naïve BD patients, social support served as a mediator in the relationship between childhood trauma and AIS. In the long-term medication BD patients, insomnia symptoms, childhood trauma, and cognition served as the predictors of suicidality.

#### Social support as a mediator between childhood trauma and clinical symptom

Traumatic life events are risk factors for BD, and childhood trauma can exert a lasting effect on mental health [36]. As a stressor, childhood trauma may participate in the pathogenesis of BD via the following mechanisms: (1) altering the developmental progression of the brain; (2) systemic inflammation; (3) alterations in hypothalamic-pituitary-adrenal (HPA) axis function, and disturbance of corticotropin-releasing factor (CRF) neural systems; and (4) genetic influence, such as expression of HPA axis genes, single nucleotide polymorphic gene variants (SNPs) [37].

Social support can be interpreted as a person who is loved, cared for, esteemed, and participates in a network of mutual obligations [38]. The Social Convoy Model provides a conceptual framework that social support provided by parents in early childhood yields a “secure base” and a “safe haven” when faced with stress in subsequent life [39]. And the benefit of social support is prominent in female people [18]. When faced with chronic stress, perceived social support was uniquely related to depression,

anxiety, and stress symptoms [40]. The mechanisms by which social support impacts health and well-being are unclear. However, the response to stress was found to be a potential target of social support.

In our study, social support was a mediator between childhood trauma and AIS in the drug-naïve BD patients. A previous study reported that objective support of social support was negatively related with insomnia in major depressive disorder [41]. And it was also reported that a greater degree of childhood trauma was associated with poor sleep health [42]. Our result was consistent with these studies, and we first built this model in drug-naïve BD patients. However, we did not find this model exist in BD patients with long-term medication as previous studies did. In both patients with BD and major depressive disorder, it was also found that social support was a mediator of the relationship between childhood trauma and depression severity [20, 43]. We also did not find this mediation of social support between childhood trauma and depression in our study. These differences could be explained by race, culture, and previous studies excluding the patients with current active suicidal ideation, and age under 18 years old [20].

Treatment strategies targeting social support may serve as effective ways to promote the relief of clinical symptoms and reduce caregiver burden [14]. Mindfulness-based stress reduction (MBSR) program was effective in reducing psychological distress, involving improvement of social support [44]. In addition, online programs which provide web platforms, online support groups and online forums could improve social support by increasing interpersonal contacts and professional communications [45]. One meta-analysis reported that BD patients may benefit from the combination of pharmacotherapy and psychotherapy [46]. By component network meta-analysis, they further found that some specific psychotherapy components delivered in a family or group format was more effective in reducing recurrences than in an individual format [46], suggesting the positive effects of social support. Previous studies have reported that psychosocial treatment could improve total and relationship functioning, life satisfaction, and decrease of time from mood episodes in BD patients [47, 48]. However, current interventions targeting social support are still relatively few, let alone those applied in the field of mental illness.

#### Predictors of suicidality

Childhood trauma as a predictor of suicide ideation was previously reported in BD patients [20]. Hippocampus is a brain region which is closely related with cognitive function. Johnston et al. reported that suicide attempters with BD showed significant reductions of gray matter volume in hippocampus when compared to nonattempters with BD [49]. Atrophy of hippocampus is associated with

cognitive decline, such as memory [50]. Autobiographical memory, long-term memory and working memory, but not short-term memory, were found to be associated with suicide attempt [51]. In line with these evidences, our results found both childhood trauma and delayed memory could predict suicide frequency but did not find the associated between cognition and suicide attempt in BD patients with long-term medication. BD disease itself, and female patients may explain the differences.

Suicide is regard as a cognitive disorder, and there are some evidences of efficacy of cognitive treatment in suicidality. Self-help mindfulness-based cognitive therapy was effective in reducing suicide ideation of depressive patients, and this effect could last for 3 months [52]. Roberge et al. reported that brief cognitive behavioral therapy could reduce suicide risk by changing cognitive flexibility, which is defined by measures of hopelessness and suicide beliefs. In youth with BD, one study reported that Child- and Family-Focused Cognitive Behavioral Therapy was as effective as psychotherapy treatment-as-usual in reducing likelihood and intensity of suicide ideation[53]. The association between cognition and suicidality found in our study explains why cognitive treatment is effective for suicidality.

There are several limitations in this study. Firstly, this study only included female patients with BD and lacked male patients with BD, which limited the generalization of conclusions to the whole BD population and could not reveal the differences in associations among childhood, social support, cognition, and suicidality between male and female patients with BD. Secondly, the mediation analysis applied in this study predicts a longitudinal process. However, this is a cross-sectional study, and we could not unveil a causal relationship among childhood trauma, social support, and clinical symptoms in BD. The disease itself may also influence social support [15]. Long-term follow-up studies are beneficial to validate the hypothesized model in this study. Thirdly, although we used an age-matched clinical control group, this study is limited by the small sample size. Finally, the assessment of childhood trauma and social support of all participants was based on self-report, which may make the data we obtained somewhat subjective. Moreover, the mood state could influence the retrospective reports of childhood trauma [54]. And we did not evaluate BD in first degree relatives of the patients, which may be a factor that influences the way parents bring up their children. Therefore, there may be some bias in the data used in this study.

## Conclusion

In our study, females with BD showed high levels of childhood trauma and suicidality, as well as low levels of social support and cognitive deficits. The low levels of social support may buffer the negative effect of high levels of

childhood trauma on insomnia in BD. Insomnia symptom, childhood trauma, and delayed memory may be predictors of suicide risk in BD patients with medication.

## Abbreviations

BD	Bipolar disorder
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
M.I.N.I	MINI-International Neuropsychiatric Interview Mini diagnostic interview
YMRS	Young Mania Rating Scale
HDRS-17	17-item Hamilton Depression Rating Scale
HAMA-14	14-item Hamilton Anxiety Scale
AIS	Athens Insomnia Scale
CTQ	Childhood Trauma Questionnaire
SSRS	Social Support Rating Scale
SPSS	Statistical Package for Social Sciences
HPA	axis hypothalamic-pituitary-adrenal axis
CRF	corticotropin-releasing factor
SNPs	single nucleotide polymorphic gene variants
MBSR	Mindfulness-based stress reduction

## Acknowledgements

We thank all subjects who participated in this study. And we thank Dr. He Jingqi for suggestions on amendments to the draft.

## Author contributions

M.Y. wrote the original draft. J.L. and Y.F. did data collection and methodology of this study. G.W. and M.L. did formal analysis. J.C. contributed to review and editing of the draft. J.L. provided the conceptualization of this study, and M.Y. revised the manuscript. All authors contributed to the study and approved the submitted version.

## Funding

This work was supported by grants from the National Natural Science Foundation of China (Grant numbers 81971258, 81270019, 81501163), and Fundamental Research Funds for Central Universities of the Central South University (Grant number 2021zzts390).

## Data availability

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

## Declarations

### Ethics approval and consent to participate

This study was approved by the Ethics Committee of Second Xiangya Hospital of Central South University. All subjects were informed and fully understood the study, and each subject and their parents/legal guardians provided a written informed consent.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

Received: 30 August 2023 / Accepted: 11 March 2024

Published online: 02 April 2024

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