Interpersonal Trauma and Depression Severity Among Individuals With Bipolar Disorder:

Findings From the Prechter Longitudinal Study of Bipolar Disorder

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ABSTRACT

Background: Experiences of interpersonal trauma, both in childhood and in adulthood, can affect the trajectory of bipolar disorder (BD). However, the degree to which childhood and/or adult trauma impacts the longitudinal trajectory of depression severity among individuals with BD actively receiving treatment remains unclear.

Methods: The effects of childhood trauma (Childhood Trauma Questionnaire) and adult trauma (Life Events Checklist) on depression severity (Hamilton Depression Rating Scale) were investigated in a treatment-receiving subsample with BD (*DSM-IV*) of the Prechter Longitudinal Study of Bipolar Disorder (2005–present). A mixed-effects linear regression model was used to assess the trajectory of depression severity over 4 years.

Results: Depression severity was evaluated in 360 participants, of whom 267 (74.8%) reported a history of interpersonal trauma. A history of childhood trauma alone (n = 110) and childhood and adult trauma combined (n = 108)—but not adult trauma alone (n = 49) —were associated with greater depression severity at the 2-year and 6-year follow-up assessments. However, the trajectory of depression severity (ie, change over time) was similar between participants with a history of childhood trauma, those with a history of adult trauma, and those with no history of interpersonal trauma. Interestingly, participants with a history of both types of trauma showed more improvement in depression severity (ie, from year 2 to year 4: $\beta = 1.67$, $P = .019$).

Conclusions: Despite actively receiving treatment for BD, participants with a history of interpersonal trauma—particularly childhood trauma—presented with more severe depressive symptoms at several follow-up assessments. Hence, interpersonal trauma may represent an essential treatment target.

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Bipolar disorder (BD) is associated with significant functional impairment and high premature mortality rates, primarily due to suicide.[1] To assist the development of effective and personalized interventions for the disorder, elucidating prognostic factors is valuable.[2] Experiences of interpersonal trauma, in both childhood and adulthood, are common among individuals with BD.[3,4] Interpersonal trauma in childhood (hereafter, "childhood trauma") is reported by approximately 50% of persons with BD,[5,6] while interpersonal trauma in adulthood (hereafter, "adult trauma") is evident in around 20%.[7–9] For the present study, interpersonal trauma is defined as encompassing abuse (physical, sexual, and emotional) as well as neglect (physical and emotional).[10]

Experiences of childhood or adult trauma alter the clinical presentation of BD, negatively affecting its complexity and severity.[11–14] As part of their recent meta-analysis, Agnew-Blais and Danese[15] highlighted relationships between childhood trauma and several clinical features of BD. For instance, they emphasized an association between childhood trauma and greater symptom severity, including more severe depressive symptoms, ie, bipolar depression.[15] Similarly, cross-sectional and longitudinal studies have found a relationship between adult trauma and bipolar depression.[13,16] However, there remains limited research exploring adult trauma—separately and combined with childhood trauma—as a predictor of depression severity among individuals with BD. This represents an important oversight because survivors of childhood trauma are known to be at an increased risk of experiencing interpersonal trauma in adulthood,[17–20] which potentially exacerbates the detrimental effects of childhood trauma.[20,21]

The severity of bipolar depression may have significant implications for its management.[22,23] Some evidence indicates that persons with BD who have experienced interpersonal trauma

Clinical Points

- Systematically screening patients with mood disorders like bipolar disorder for interpersonal trauma is necessary in clinical practice. This screening process may facilitate psychotherapeutic strategies that are specifically designed to assist patients with processing traumatic experiences to be incorporated into the treatment plan.
- In addition to employing trauma-focused interventions, it may be beneficial to target the likely psychological mechanisms that underlie the association between interpersonal trauma and depression severity when treating patients with bipolar disorder. However, more research is needed to fully elucidate these mechanistic pathways.

respond more poorly to pharmaco- and psychotherapy.[24–27] This body of literature is countered by research showing no association[28,29] or even an improved treatment response among survivors of interpersonal trauma.[30,31] Given these conflicting results, further investigation is required.[32] Moreover, there is a lack of studies focusing on interpersonal trauma and bipolar depression specifically. Finding new treatment targets for bipolar depression is particularly important as current intervention strategies are limited in efficacy.[2] The presentation of bipolar depression is heterogeneous, determined by not only biological but also environmental factors.[2] Considering the clinical relevance of interpersonal trauma, it may be a promising psychotherapeutic target in treating bipolar depression.[2,15,33] Therefore, the purpose of the current study was to explore the associations between childhood *and/or* adult trauma and the longitudinal trajectory of depression severity among individuals with BD actively receiving treatment.

METHODS

Data from the Prechter Longitudinal Study of Bipolar Disorder were accessed for the present study.[34] The Prechter Study, an ongoing open cohort study of individuals with all types of BD and healthy controls, is being conducted at the University of Michigan (2005 to present). The study received ethical approval from the Institutional Review Board of the University of Michigan. All participants provided written informed consent before participation. Full details of the study design can be found elsewhere.[34] Reporting of the present study was aided by the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[35]

Participants

Potential participants for the Prechter Study were assessed with the Diagnostic Interview for Genetic Studies (DIGS),[36] and diagnoses of BD were confirmed using a best estimate process completed by at least 2 doctoral-level clinicians (in accordance with the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition [*DSM-IV*] criteria).[37] For the present study, a subset of the Prechter Study cohort focusing on participants with BD (BDI, BDII, BD not otherwise specified, schizoaffective disorder [bipolar type]) who reported receiving treatment (eg, outpatient, inpatient, day treatment) at the 2-year follow-up assessment was selected. Participants reporting not to be in treatment and participants for whom treatment status could not be determined were excluded. Additionally, selected participants had completed measures of interpersonal trauma on entry to the Prechter Study.

Measures

For an overview of data used in the current study, including information pertaining to measures and assessment time points, see Table 1.

Diagnosis and demographics. The DIGS[36] is a detailed semi-structured clinical interview for the assessment of major psychiatric disorders, which has excellent interrater reliability for BD.[36] During the DIGS interview, demographic information was also collected.

Childhood trauma. Childhood trauma was assessed with the Childhood Trauma Questionnaire (CTQ).[38] The CTQ is a self-report instrument that comprises 28 items rated on a 5-point scale (1 = "never true when you were growing up"; 5 = "very often true when you were growing up") and 5 subscales (physical abuse, sexual abuse, emotional abuse, physical neglect, and emotional neglect). The CTQ has demonstrated good reliability and validity,[38–40] with emerging evidence of reasonable correlations with prospective measures of childhood trauma.[41] In line with previous studies,[24,25,29] we considered participants with a score of moderate severity on at least 1 subscale (physical abuse ≥ 10, sexual abuse ≥ 8, emotional abuse ≥ 13, physical neglect ≥ 10, emotional neglect ≥ 15)[42] as having experienced childhood trauma.

Adult trauma. Adult trauma was assessed with the Life Events Checklist (LEC).[43] The LEC is a self-report instrument that screens for exposure to 16 potentially traumatic events over participants' lives. For each event, participants indicated their level of exposure ("happened to me," "witnessed it," "learned about it"). In keeping with previous research,[13] we considered participants who reported that physical assault ("being attacked, hit, slapped, kicked, beaten up") and/or sexual assault ("rape, attempted rape, made to perform any type of sexual act through force or threat of harm") happened to them as having experienced adult trauma.

Clinical characteristics and treatment status. Clinical characteristics at approximately 2 years since the diagnostic interview were assessed with the Longitudinal Interval Follow-up Evaluation (LIFE).[44] The LIFE is a semi-structured interview designed for the assessment of the longitudinal course of psychiatric disorders. For example, information on the number of mood episodes, the number of suicide attempts, the number of hospitalizations, and the presence of affective psychosis and rapid cycling was recorded. Some information on the severity of mania (1 = "no impairment"; 4 = "incapacitation"), depression (1 = "no impairment"; 4 = "incapacitation"), suicidality (1 = "fleeting thoughts/passive wishes only"; 4 = "acted with intent to die/serious consequences"), and functional

Table 1. Overview of Data Used in the Current Study

Variable	Measure	Assessment			
		Entry	Year 2	Year 4	Year 6
Demographics	Diagnostic Interview for Genetic Studies[36]	✓			
Diagnosis	Diagnostic Interview for Genetic Studies[36]	✓			
Childhood trauma	Childhood Trauma Questionnaire[38]	✓			
Adult trauma	Life Events Checklist[43]	✓			
Clinical characteristics	Longitudinal Interval Follow-up Evaluation[44]		✓		
Treatment status	Longitudinal Interval Follow-up Evaluation[44]		✓		
Depression severity	Hamilton Depression Rating Scale[45]		✓	✓	✓

impairment (1 = "no loss of employment/marital status"; 4 = disabled, not living independently") was also collected. Finally, it was noted whether participants reported that they were currently in treatment (eg, outpatient, inpatient, day treatment) and which medications they were taking (eg, lithium, antipsychotic, anticonvulsant).

Depression severity. The severity of depressive symptoms was assessed with the Hamilton Depression Rating Scale (HDRS).[45] The HDRS is a clinician-rated scale that consists of 17 items measuring depressive symptoms experienced over the past week. The HDRS yields an overall score, which can range from 0 to 54: scores 8–16 correspond to mild depression, scores 17–23 to moderate depression, and scores ≥ 24 to severe depression.[46] On the HDRS, a score < 8 is considered a clinically meaningful indicator of remission from depressive symptoms[47]; a reduction of 11 points is considered a clinically meaningful change in depression severity.[48]

Statistical Analysis

All statistical analyses were conducted with the statistical open-source program R Version 4.1.0[49] and RStudio.[50] Participants were divided into 4 mutually exclusive groups: participants with no history of interpersonal trauma, participants with a history of childhood trauma, participants with a history of adult trauma, and participants with a history of both childhood and adult trauma.

Multinomial logistic regression models. To examine group differences in clinical characteristics at the 2-year follow-up assessment, we conducted a series of multinomial logistic regression models; participants with no history of interpersonal trauma were treated as the reference group. From each model, we obtained odds ratios (ORs) and their 95% confidence intervals (CIs).

Mixed model for repeated measures. To explore group differences in the longitudinal trajectory of depression severity, we performed a mixed-effects linear regression model utilizing a repeated measures approach (MMRM). Here, we included the fixed, categorical effects of participants' history of interpersonal trauma, follow-up year, and the trauma-by-year interaction, while adjusting for age and gender. HDRS data from the 2-year, 4-year, and 6-year follow-up assessments were analyzed. As for the multinomial logistic regression models, participants with no history of interpersonal trauma were used as the reference group. From the MMRM, we estimated β-coefficients (including 95% CIs).

Sensitivity analysis. We undertook a sensitivity analysis to investigate how our choice of group division affected differences in the longitudinal trajectory of depression severity. For this sensitivity analysis, participants were divided into 2 mutually exclusive groups: participants with no history of interpersonal trauma and participants with a history of any interpersonal trauma, and the MMRM—as specified above—was rerun.

RESULTS

The clinical characteristics of the 4 groups, as recorded at the 2-year follow-up assessment, are presented in Table 2 (N = 360). In comparison to participants with no history of interpersonal trauma, participants with a history of childhood trauma were older, were more likely to be female, were less likely to use lithium, and presented with poorer functioning and more severe depressive symptoms. On average, the depressive symptoms of participants with a history of childhood trauma were above the HDRS cutoff score for remission but in the mild range. Participants with a history of adult trauma were more likely to use a sedative, but there were no other statistically significant differences in clinical characteristics between participants with a history of adult trauma and those with no history of interpersonal trauma. Participants with a history of both childhood and adult trauma were older, were more likely to be female, were more likely to use an antidepressant and a sedative, and presented with poorer functioning and greater (albeit mild) depression severity—including a lower likelihood of being in remission from depressive symptoms—than participants with no history of interpersonal trauma.

Interpersonal Trauma and the Longitudinal Trajectory of Depression Severity

Using an adjusted MMRM, we compared the trajectory of depression severity across the 4 groups over time (see Figure 1). There were significant main effects of group (no trauma vs childhood trauma: $\beta = 2.73$, 95% CI = 1.08 to 4.38, $P = .001$; no trauma vs both traumas: $\beta = 3.59$, 95% CI = 1.91 to 5.27, $P < .001$) but not of time (see Table 3). In comparison to participants with no history of interpersonal trauma, participants with a history of childhood trauma and participants with a history of both childhood and adult trauma had significantly higher mean HDRS scores at the 2-year and 6-year follow-up assessments (all $P < .05$; see Figure 1); participants with a history of adult trauma did not

Table 2. Clinical Characteristics at the 2-Year Follow-up Assessment, Stratified by History of Interpersonal Trauma[a]

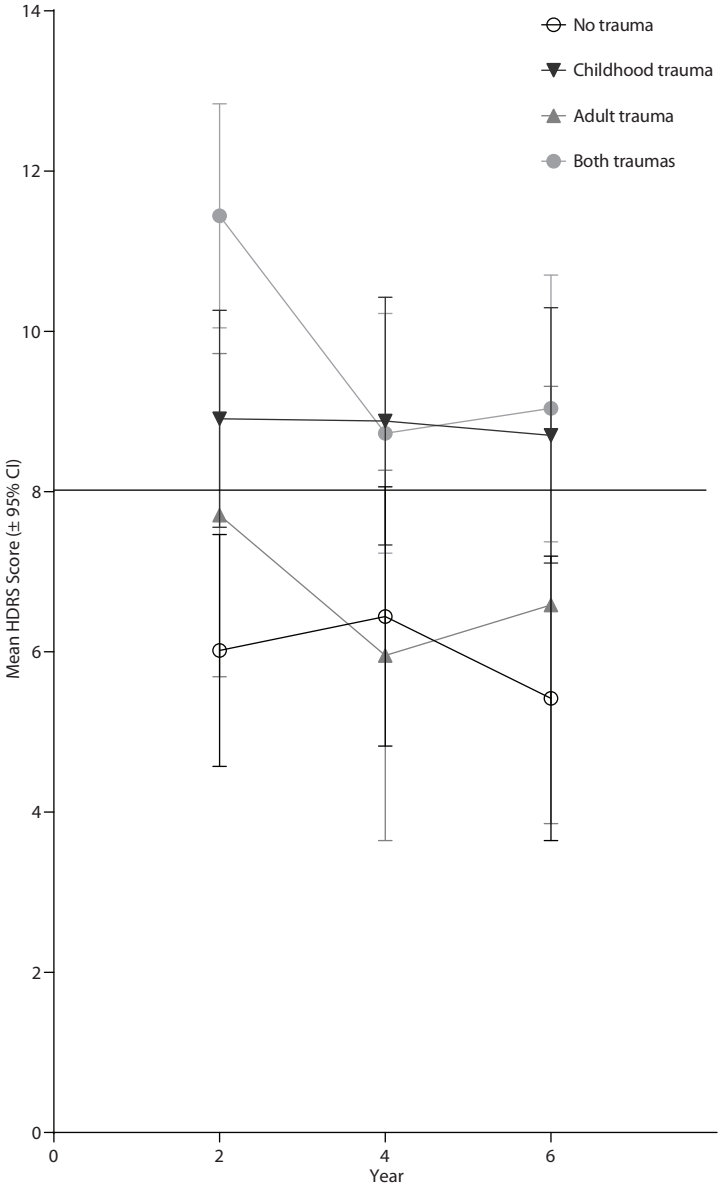
	No trauma	Childhood trauma	Adult trauma	Both traumas
n (%)	93 (25.8)	110 (30.6)	49 (13.6)	108 (30.0)
Age, mean (SD), y	49.5 (15.1)	54.3 (13.4)	52.3 (14.9)	55.5 (11.8)
OR (95% CI)	…	**1.03 (1.01 to 1.05)**	1.02 (0.99 to 1.04)	**1.03 (1.01 to 1.05)**
Gender (male), n (%)	40 (43.0)	30 (27.3)	13 (26.5)	25 (23.1)
OR (95% CI)	…	**0.50 (0.28 to 0.89)**	0.48 (0.22 to 1.02)	**0.40 (0.22 to 0.73)**
Diagnosis (bipolar I disorder), n (%)	64 (68.8)	75 (68.2)	35 (71.4)	69 (63.9)
OR (95% CI)	…	0.97 (0.54 to 1.76)	1.13 (0.53 to 2.42)	0.80 (0.44 to 1.44)
Lithium, n (%)	30 (32.3)	21 (19.1)	14 (29.2)	23 (21.3)
OR (95% CI)	…	**0.50 (0.26 to 0.94)**	0.86 (0.40 to 1.85)	0.57 (0.30 to 1.07)
Antipsychotic, n (%)	37 (39.8)	41 (37.3)	26 (54.2)	45 (41.7)
OR (95% CI)	…	0.90 (0.51 to 1.59)	1.79 (0.89 to 3.61)	1.08 (0.61 to 1.90)
Anticonvulsant, n (%)	55 (59.1)	50 (45.5)	25 (52.1)	62 (57.4)
OR (95% CI)	…	0.58 (0.33 to 1.01)	0.75 (0.37 to 1.51)	0.93 (0.53 to 1.63)
Antidepressant, n (%)	37 (39.8)	56 (50.9)	27 (56.2)	64 (59.3)
OR (95% CI)	…	1.57 (0.90 to 2.74)	1.95 (0.96 to 3.94)	**2.20 (1.25 to 3.88)**
Sedative, n (%)	23 (24.7)	38 (34.5)	21 (43.8)	42 (38.9)
OR (95% CI)	…	1.61 (0.87 to 2.97)	**2.37 (1.13 to 4.96)**	**1.94 (1.05 to 3.56)**
Stimulant, n (%)	9 (9.7)	9 (8.2)	7 (14.6)	10 (9.3)
OR (95% CI)	…	0.83 (0.32 to 2.19)	1.59 (0.55 to 4.58)	0.95 (0.37 to 2.45)
No. of manic episodes (LIFE), mean (SD)	0.3 (0.7)	0.6 (3.6)	0.1 (0.5)	0.6 (2.6)
OR (95% CI)	…	1.11 (0.88 to 1.40)	0.74 (0.38 to 1.45)	1.11 (0.88 to 1.40)
No. of hypomanic episodes (LIFE), mean (SD)	2.3 (4.6)	2.9 (7.4)	1.0 (1.7)	1.7 (3.3)
OR (95% CI)	…	1.02 (0.97 to 1.07)	0.90 (0.78 to 1.04)	0.97 (0.91 to 1.04)
No. of depressive episodes (LIFE), mean (SD)	1.4 (2.2)	2.3 (4.4)	1.1 (1.5)	2.2 (3.2)
OR (95% CI)	…	1.10 (0.99 to 1.23)	0.92 (0.74 to 1.13)	1.09 (0.98 to 1.22)
No. of suicide attempts (LIFE), mean (SD)	0.0 (0.1)	0.1 (0.3)	0.0 (0.2)	0.1 (0.3)
OR (95% CI)	…	2.33 (0.57 to 9.58)	1.73 (0.30 to 9.87)	2.68 (0.66 to 10.84)
No. of hospitalizations (LIFE), mean (SD)	0.2 (0.5)	0.2 (0.6)	0.3 (0.6)	0.4 (1.3)
OR (95% CI)	…	0.98 (0.66 to 1.45)	1.06 (0.68 to 1.66)	1.16 (0.83 to 1.63)
Affective psychosis (LIFE), n (%)	11 (13.4)	20 (21.7)	8 (20.5)	21 (23.6)
OR (95% CI)	…	1.79 (0.80 to 4.01)	1.67 (0.61 to 4.54)	1.99 (0.89 to 4.44)
Rapid cycling (LIFE), n (%)	14 (17.7)	11 (13.3)	3 (8.3)	18 (22.0)
OR (95% CI)	…	0.71 (0.30 to 1.67)	0.42 (0.11 to 1.57)	1.31 (0.60 to 2.85)
Severity of mania (LIFE), mean (SD)	1.3 (1.4)	1.1 (1.2)	1.0 (1.4)	1.4 (1.4)
OR (95% CI)	…	0.86 (0.70 to 1.07)	0.83 (0.63 to 1.11)	1.01 (0.82 to 1.24)
Severity of depression (LIFE), mean (SD)	2.0 (1.4)	2.4 (1.3)	1.8 (1.4)	2.4 (1.3)
OR (95% CI)	…	**1.27 (1.02 to 1.57)**	0.91 (0.70 to 1.19)	**1.27 (1.02 to 1.58)**
Severity of suicidality (LIFE), mean (SD)	0.8 (0.9)	1.0 (1.0)	0.6 (1.0)	1.0 (1.2)
OR (95% CI)	…	1.28 (0.97 to 1.69)	0.84 (0.57 to 1.24)	1.27 (0.96 to 1.68)
Severity of functional impairment (LIFE), mean (SD)	1.5 (0.8)	2.1 (0.9)	1.4 (0.9)	2.0 (1.0)
OR (95% CI)	…	**2.02 (1.45 to 2.82)**	0.87 (0.55 to 1.38)	**1.79 (1.28 to 2.50)**
Severity of depression (HDRS), mean (SD)	6.0 (5.9)	9.1 (7.2)	7.6 (6.3)	11.5 (7.9)
OR (95% CI)	…	**1.08 (1.03 to 1.13)**	1.05 (0.98 to 1.11)	**1.12 (1.07 to 1.18)**
Remission of depression (HDRS), n (%)	58 (69.0)	52 (54.7)	24 (55.8)	31 (35.2)
OR (95% CI)	…	0.54 (0.29 to 1.00)	0.57 (0.27 to 1.21)	**0.24 (0.13 to 0.46)**

[a]Odds ratios in bold are significant at $P < .050$. Sample sizes slightly vary due to missing data (see Supplementary Table 1).
Abbreviations: CI = confidence interval, HDRS = Hamilton Depression Rating Scale, LIFE = Longitudinal Interval Follow-up Evaluation, OR = odds ratio.

significantly differ in mean HDRS score from participants with no history of interpersonal trauma at the 2-year, 4-year, or 6-year follow-up assessments.

In addition to the significant main effects of group, there was 1 significant group × time interaction effect (year 2 vs year 4 × no trauma vs both traumas: $\beta = 1.67$, 95% CI = 0.27 to 3.07, $P = .019$); however, no other group × time interaction effect was significant (see Table 3). This indicates that participants with a history of both childhood *and* adult trauma showed significantly more improvement in depression severity from the 2-year to the 4-year follow-up assessment, as measured with the HDRS, than participants with no history of interpersonal trauma. These results additionally highlight that there was no statistically significant difference between participants with a history of childhood *or* adult trauma and participants with no history of interpersonal trauma in the longitudinal trajectory of depression severity on the HDRS. To note, participants with a history of childhood trauma showed only minimal change over the entire follow-up period (mean HDRS: year 2 = 9.1; year 4 = 8.9; year 6 = 8.7).

Figure 1. Mean HDRS Scores Across the Follow-up Period Stratified by History of Interpersonal Trauma[a]



[a]The horizontal line represents the cutoff score for remission from depressive symptoms (ie, HDRS < 8); scores above the line are all indicative of mild depression (ie, HDRS ≥ 8 and HDRS ≤ 16).
Abbreviations: CI = confidence interval, HDRS = Hamilton Depression Rating Scale.

Sensitivity analysis. The results pertaining to the main effects of group and time were robust to the sensitivity analysis (no trauma vs any trauma: $\beta = 2.66$, 95% CI = 1.21 to 4.11, $P < .001$); however, there were no significant group × time interaction effects (see Supplementary Table 3).

DISCUSSION

The purpose of this study was to examine the associations between childhood and/or adult trauma and the longitudinal trajectory of depression severity among individuals with BD receiving treatment. Approximately 75% of participants in the current subsample reported a history of any interpersonal trauma. Participants with a history of childhood trauma and participants with a history of both childhood and adult trauma presented with greater depression severity at several follow-up assessments. Note that these participants also presented with greater functional impairment at the 2-year follow-up assessment. In comparison to participants with no history of any interpersonal trauma, participants with a history of childhood trauma and participants with a history of adult trauma did not significantly differ in their trajectory of depression severity over the entire follow-up period.

Table 3. Results From the Adjusted Mixed-Effects Linear Regression Model[a]

	β	95% CI	*P*
Intercept	**7.08**	4.60 to 9.55	< .001
Age	−0.01	−0.06 to 0.03	.603
Gender	−1.26	−2.60 to 0.08	.065
Year 2 vs year 4	0.06	−0.95 to 1.06	.913
Year 4 vs year 6	0.55	−0.59 to 1.68	.346
No trauma vs childhood trauma	**2.73**	1.08 to 4.38	.001
No trauma vs adult trauma	0.57	−1.52 to 2.67	.590
No trauma vs both traumas	**3.59**	1.91 to 5.27	< .001
Year 2 vs year 4 × no trauma vs childhood trauma	0.02	−1.36 to 1.39	.982
Year 4 vs year 6 × no trauma vs childhood trauma	−0.41	−1.95 to 1.13	.601
Year 2 vs year 4 × no trauma vs adult trauma	0.94	−0.85 to 2.72	.303
Year 4 vs year 6 × no trauma vs adult trauma	−0.34	−2.46 to 1.78	.753
Year 2 vs year 4 × no trauma vs both traumas	**1.67**	0.27 to 3.07	.019
Year 4 vs year 6 × no trauma vs both traumas	0.14	−1.43 to 1.71	.860

[a]N = 360, including 743 observations. Coefficients in bold are significant at $P < .050$. The unadjusted results can be found in Supplementary Table 2.
Abbreviation: CI = confidence interval.

Although participants with a history of both childhood and adult trauma improved significantly more in depression severity from the 2-year to the 4-year follow-up assessment, this finding was not robust to the sensitivity analysis and may not represent a clinically meaningful improvement.[48]

Taken together, our findings highlight that even though participants with and without a history of interpersonal trauma showed comparable rates of improvement in symptom severity when receiving treatment, participants with a history of childhood trauma continued to present with greater depression severity. Importantly, a history of childhood trauma was related to more severe depressive symptoms separately from and combined with a history of adult trauma; a history of adult trauma alone, however, was unrelated to symptom severity. This implies that participants with a history of childhood trauma, specifically, did not recover to the same extent as participants with no history of interpersonal trauma. Thus, experiences of interpersonal trauma in sensitive/critical periods—such as childhood—may have long-lasting impacts on individuals' development and/or mental health. Although the psychological mechanisms that underlie the association between childhood trauma and depression severity in BD remain underresearched, several mechanistic candidates (eg, insecure attachment, treatment adherence, therapeutic alliance) have been suggested.[28,51–60]

Childhood Trauma, Adult Trauma, and Depression Severity

Our findings partially align with another longitudinal study that separately explored the effects of childhood and adult trauma on the severity of depressive symptoms in a sample of participants with BD. Among 109 first-admission patients, Neria et al[13] assessed depression severity 6 and 24 months after initial hospitalization. Similar to our study, Neria et al[13] were unable to find significant group differences in change in symptom severity over time. In contrast to our study, participants examined by Neria et al[13] with a history of adult trauma (but not childhood trauma) reported greater depression severity at the 6-month follow-up visit compared to participants with no history of interpersonal trauma. Notably, only 6 participants in Neria and colleagues'[13] sample had experienced both childhood and adult trauma, precluding the researchers from exploring the cumulative effect of both traumas.

Additionally, our results are partly consistent with the cross-sectional study by Maguire et al.[16] In a cohort of 60 participants with BD receiving mental health care, the researchers evaluated associations between both childhood and adult trauma and illness severity. Here, participants with a history of childhood trauma *and* participants with a history of adult trauma experienced more severe residual or interepisode depressive symptoms. Nevertheless, these studies by Neria et al[13] and Maguire et al[16] need to be interpreted cautiously as they rely on relatively small samples. Interestingly, our findings are also concordant with some studies that used interpersonal trauma as a unidimensional construct consisting of both childhood and adult trauma.[61,62] For instance, Daglas et al[61] reported that participants with a history of any interpersonal trauma experienced more severe depression 12 months following a first episode of psychotic mania. Like our findings, Daglas et al[61] highlighted that these participants had significantly poorer functioning.

Limitations

There are several limitations. Despite the reasonable size of our total sample, only a small subset of participants (n = 49) reported a history of adult trauma alone, potentially resulting in limited statistical power to detect group differences. Additionally, the majority of participants included in the current sample reported relatively mild depression, which means that our findings may not apply to populations with more severe symptoms. Furthermore, treatment details—including comprehensive data on type of treatment received (eg, pharmacotherapy only vs pharmacotherapy and psychotherapy)—were unavailable for most, primarily because these were self-reported data. Receiving (adjunctive) psychotherapy may be especially beneficial for individuals with BD who have a history of interpersonal trauma[63]; hence, it may be valuable to consider treatment type—as well as other treatment-related factors—as a moderator or

mediator of the effects of interpersonal trauma on clinical outcomes of BD in future research.

Moreover, the data on childhood trauma (assessed with the CTQ) and adult trauma (assessed with the LEC) were retrospectively collected, which may introduce recall bias and lead to underreporting. Nevertheless, the prevalence of interpersonal trauma in our study (74.2%) is similar to previously reported findings.[7] To note, the LEC is not specifically tailored to measure trauma experienced in adulthood but screens for lifetime exposure to trauma. Thus, some traumatic experiences from childhood may have been restated by participants when completing the LEC. Similarly, details about participants' history of interpersonal trauma (eg, age at exposure, frequency of exposure) are not collected with either the CTQ or the LEC. Given that exposure characteristics have been shown to moderate the effect of interpersonal trauma in participants with other serious mental illnesses,[64,65] they may also need to be considered in future clinical studies targeting BD.

Implications

Although all participants included in our sample actively received treatment for BD, participants with a history of interpersonal trauma—especially when experienced in childhood—reported more severe depressive symptoms than participants with no history of interpersonal trauma. Therefore, systematically screening patients with BD for interpersonal trauma appears necessary in clinical practice. This screening process would allow for psychotherapeutic strategies that are specifically designed to assist patients with processing traumatic experiences to be incorporated into the treatment plan. To note, several trauma-focused interventions, including eye movement desensitization and reprocessing therapy and trauma-focused cognitive behavior therapy,[66] are available; however, their usefulness in BD needs to be determined.[63] There remains a concerning paucity of evidence-based interventions for people with BD who have experienced interpersonal trauma. In addition, it may be beneficial to target psychological mechanisms that underlie the association between interpersonal trauma and depression severity when treating BD. To support novel treatment development, further studies investigating plausible mediators that can explain the relationship between interpersonal trauma and symptom severity, including depression severity, are urgently needed.

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Additional information: The datasets generated and/or analyzed during this study are not publicly available due to privacy restrictions but are available from the Prechter Longitudinal Study of Bipolar Disorder (prechter-data-request@med.umich.edu) on reasonable request.

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Supplementary Material

Article Title: Interpersonal Trauma and Depression Severity Among Individuals With Bipolar Disorder: Findings From the Prechter Longitudinal Study of Bipolar Disorder

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List of Supplementary Material for the article

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This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary Material

Supplementary Table 1. Number of participants with missing data for the clinical characteristics at the 2-year follow-up assessment, stratified by history of interpersonal trauma.

	No trauma	Childhood trauma	Adult trauma	Both traumas
n	93 (25.8)	110 (30.6)	49 (13.6)	108 (30.0)
Age	0	0	0	0
Gender (male)	0	0	0	0
Diagnosis (bipolar I disorder)	0	0	0	0
Lithium	0	0	1	0
Antipsychotic	0	0	1	0
Anticonvulsant	0	0	1	0
Antidepressant	0	0	1	0
Sedative	0	0	1	0
Stimulant	0	0	1	0
Number of manic episodes (LIFE)	8	8	7	13
Number of hypomanic episodes (LIFE)	5	10	6	12
Number of depressive episodes (LIFE)	4	6	5	10
Number of suicide attempts (LIFE)	5	7	5	11
Number of hospitalisations (LIFE)	4	7	5	10
Affective psychosis (LIFE)	11	18	10	19
Rapid cycling (LIFE)	14	27	13	26
Severity of mania (LIFE)	5	10	8	14
Severity of depression (LIFE)	6	10	6	14
Severity of suicidality (LIFE)	3	9	5	12
Severity of functional impairment (LIFE)	4	9	7	12
Severity of depression (HAM-D)	9	15	6	20
Remission of depression (HAM-D)	9	15	6	20

Abbreviations. HAM-D = Hamilton Depression Rating Scale; LIFE = Longitudinal Interval Follow-up Evaluation.

Supplementary Table 2. Results from the unadjusted mixed-effects linear regression model.

	β	**95% CI**	***p***
Intercept	**5.96**	4.76, 7.16	<.001
Year 2 vs. Year 4	0.06	-0.95, 1.06	.909
Year 4 vs. Year 6	0.54	-0.60, 1.68	.351
No Trauma vs. Childhood Trauma	**2.87**	1.24, 4.50	.001
No Trauma vs. Adult Trauma	0.79	-1.29, 2.87	.456
No Trauma vs. Both Traumas	**3.78**	2.14, 5.41	<.001
Year 2 vs. Year 4 x No Trauma vs. Childhood Trauma	0.02	-1.36, 1.40	.976
Year 4 vs. Year 6 x No Trauma vs. Childhood Trauma	-0.41	-1.96, 1.13	.600
Year 2 vs. Year 4 x No Trauma vs. Adult Trauma	0.90	-0.89, 2.69	.322
Year 4 vs. Year 6 x No Trauma vs. Adult Trauma	-0.38	-2.50, 1.75	.728
Year 2 vs. Year 4 x No Trauma vs. Both Traumas	**1.65**	0.25, 3.05	.021
Year 4 vs. Year 6 x No Trauma vs. Both Traumas	0.16	-1.41, 1.73	.844

Abbreviations. CI = Confidence Interval.
Note. N = 360, including 743 observations. Coefficients in bold are significant at $p < .050$.

Supplementary Table 3. Results from the sensitivity analysis.

	β	**95% CI**	***p***
Intercept	**6.86**	4.35, 9.37	<.001
Age	-0.01	-0.05, 0.04	.745
Gender	-1.26	-2.62, 0.10	.069
Year 2 vs. Year 4	0.06	-0.95, 1.07	.909
Year 4 vs. Year 6	0.55	-0.60, 1.69	.348
No Trauma vs. Any Trauma	**2.66**	1.21, 4.11	<.001
Year 2 vs. Year 4 x No Trauma vs. Any Trauma	0.82	-0.37, 2.00	.176
Year 4 vs. Year 6 x No Trauma vs. Any Trauma	-0.21	-1.55, 1.13	.754

Abbreviations. CI = Confidence Interval.
Note. N = 360, including 743 observations. Coefficients in bold are significant at $p < .050$.