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A Systematic Review of Childhood Trauma and Cognitive Functioning in Individuals with Major Depressive Disorder (MDD) or Bipolar Disorder (BD)

Mobina Poormolaie[1], Saeedeh Zomorodi[2*]

[1] MA student, Department of Clinical Psychology, West Tehran Branch, Islamic Azad University, Tehran, Iran.
[2] Assistant Professor, Department of Psychology, West Tehran Branch, Islamic Azad University, Tehran, Iran.

*** Corresponding author email address**: mobina.por80@gmail.com

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A B S T R A C T

Purpose: This study aims to systematically investigate the relationship between childhood trauma and cognitive functioning in individuals diagnosed with Major Depressive Disorder (MDD) or Bipolar Disorder (BD).

Methods and Materials: This study employed a systematic review approach, analyzing peer-reviewed English-language articles published between 2020 and 2025. A three-stage screening protocol was used: removal of duplicate records, evaluation of relevance to the research domain, and inclusion based on direct response to the research question. Comprehensive database searches were conducted using a combination of keywords related to childhood trauma, cognitive function, and mood disorders. Inclusion criteria required that studies involve participants aged 18 or older with a confirmed diagnosis of MDD or BD, assess objective cognitive outcomes, and establish a relationship with childhood trauma. Fifteen eligible studies were identified and analyzed based on variables such as study design, population characteristics, assessment tools, and outcomes.

Findings: The included studies provided consistent evidence of significant associations between adverse childhood experiences (ACEs)—particularly emotional abuse and neglect—and structural and functional brain changes, including reduced gray matter, disrupted white matter integrity, and altered connectivity in regions involved in emotional regulation. These neural alterations were linked to impairments in memory, attention, executive functioning, and processing speed. Biological findings highlighted elevated levels of inflammatory markers (e.g., IL-6, TNF-α, CRP) and immune system dysregulation in individuals with childhood trauma histories. The cognitive effects and inflammatory responses varied across diagnostic groups, with some findings more pronounced in BD. Moderating factors such as family functioning, education, and medication type also influenced cognitive outcomes.

Conclusion: This review underscores the critical role of childhood trauma in shaping cognitive deficits in mood disorders and calls for trauma-informed, multidisciplinary treatment strategies.

Keywords: *Childhood trauma, cognitive functioning, major depressive disorder, bipolar disorder, systematic review*

1. Introduction

Cognitive impairments are recognized as one of the core features of mood disorders such as Major Depressive Disorder (MDD) and Bipolar Disorder (BD) (Rock et al., 2014; Zuckerman et al., 2018). These impairments manifest across various domains, including occupational or academic performance, psychosocial functioning, and interpersonal relationships (Depp et al., 2012). Even after mood symptoms subside, cognitive and functional impairments often persist (Porter et al., 2015; Semkovska et al., 2019), and early evidence indicates that the presence of cognitive impairments increases the likelihood of symptom recurrence (Majer et al., 2004; Schmid & Hammar, 2013). However, cognitive dysfunctions are not universally present in all individuals with mood disorders, and their severity ranges from non-existent to severe (Douglas et al., 2018; Douglas & Porter, 2012). A better understanding of the contributing factors to cognitive impairments in mood disorders may aid in developing personalized interventions to improve cognitive performance.

Childhood trauma refers to adverse events occurring before the age of 18. These events may include physical or emotional abuse, neglect, sexual abuse, witnessing violence, or other serious problems within the family environment (Barczyk et al., 2023; Congia et al., 2022). Childhood trauma is described under various terms, including early life stress, adverse childhood experiences (ACEs), child maltreatment, or abuse and neglect. ACEs have been linked to poorer physical and mental health outcomes in adulthood (Kalmakis & Chandler, 2015; Taylor et al., 2011). Individuals who have experienced trauma during childhood are at greater risk of developing depression in adulthood, with the condition tending to be more prolonged (Bektaş, 2025; Harb et al., 2025) and less responsive to treatment (Yang, 2025; Zhang, 2025). In this context, a large meta-analysis found that higher levels of childhood trauma were associated with a greater likelihood of developing depression and with elevated depressive symptom scores (Humphreys et al., 2020). Similarly, a systematic review and meta-analysis of childhood trauma and clinical outcomes in individuals with BD revealed that a history of childhood trauma was linked to increased severity and recurrence of mania, depression, and psychosis, higher rates of comorbid disorders, faster cycling, and more frequent suicide attempts (Agnew-Blais & Danese, 2016).

Childhood trauma has also been associated with poorer cognitive performance in adulthood. This has been observed in both clinical and healthy populations across a range of cognitive domains, including working memory (Goodman et al., 2019; Masson et al., 2015), executive functioning, attention (Lu et al., 2017; Masson et al., 2015), psychomotor speed (Masson et al., 2015), and general intelligence (Masson et al., 2015). This association is not unexpected, as childhood trauma has been linked to alterations in the structure, function, and connectivity of key brain areas involved in cognition, such as the prefrontal cortex, hippocampus, and amygdala, as well as changes in white matter integrity, particularly in the corpus callosum.

Therefore, investigating the effects of childhood trauma on cognitive functioning in adults with mood disorders through systematic review and meta-analysis is essential and multidimensional. Firstly, prior research on the effects of childhood trauma on mood disorders and cognitive functioning has produced mixed findings. Some studies report strong negative impacts of trauma on mental health and cognition, while others report inconsistent results. These discrepancies may stem from methodological differences or limited sample sizes in previous research. This study seeks, through systematic review, to synthesize these findings and provide a more comprehensive analysis of the existing data. Secondly, given the increasing prevalence of mood disorders and related cognitive problems in society, gaining a more accurate understanding of the impact of childhood trauma on these issues holds particular significance. As existing studies have often employed varying methodologies and yielded divergent outcomes, a meta-analytic approach is necessary to unify these findings. This can help clarify the mechanisms through which childhood trauma affects cognitive functioning and ultimately inform the development of preventive and therapeutic strategies. Moreover, the methodological strength of this approach lies in its capacity to aggregate and analyze findings from multiple independent studies, making it a valuable innovation. Accordingly, the present study was conducted to systematically examine the associations between reported exposure to childhood trauma and cognitive functioning in individuals diagnosed with Major Depressive Disorder (MDD) or Bipolar Disorder (BD), aiming to answer the following research question:

What are the results of the systematic review regarding the associations between reported exposure to childhood trauma and cognitive functioning in individuals with Major Depressive Disorder (MDD) or Bipolar Disorder (BD)?

2. Methods and Materials

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This study employed a systematic review to examine the associations between childhood trauma and cognitive functioning in individuals diagnosed with Major Depressive Disorder (MDD) or Bipolar Disorder (BD). A systematic review focuses on a clearly formulated question or topic and analyzes the findings of prior research in a structured and logical manner. As a second-order analytical method, systematic review collects and synthesizes previous research findings, identifies gaps in the literature, and lays the groundwork for future studies. Accordingly, the present research utilizes a systematic review approach to investigate relevant studies. The systematic review protocol consisted of three phases: the first involved identifying keywords related to the research topic across various databases; the second established a database structure including inclusion and exclusion criteria; and the third involved data entry, summary table creation, and data analysis.

In line with the study objective, the researchers undertook various steps. First, a broad range of related terms was extracted through a literature review and selected for database searches. Reputable indexing databases were then identified. The search was conducted using keywords such as “childhood trauma,” “adverse childhood experiences,” “child maltreatment,” “early life stress,” “physical abuse,” “emotional and sexual abuse,” and “neglect” in combination with terms like “cognitive,” “neurocognitive,” or “neuropsychological,” and also with “depression” or “bipolar.” Additionally, articles were selected based on the following criteria:

- Inclusion of samples diagnosed with Major Depressive Disorder (MDD) or Bipolar Disorder (BD) according to standard diagnostic criteria (e.g., DSM or ICD classifications);
- Participant age of 18 years or older;
- Inclusion of healthy control participants in the study;
- Articles must be written in English;
- Studies must assess objective cognitive functioning at least once and link it to childhood trauma in MDD or BD participants, either by (1) comparing cognitive performance in patients with and without trauma history, or (2) using correlation or regression analyses to examine the relationship between trauma severity and cognitive performance.

The primary reasons for exclusion were as follows:

- Use of emotion-based cognitive assessments;
- Inclusion of psychiatric samples that did not isolate mood disorder diagnoses.

3. Findings and Results

In total, 53 articles were initially identified from the databases. Researchers then manually removed duplicate entries indexed in multiple databases. Titles were reviewed, and those unrelated to the topic were excluded, leaving 41 articles. Abstracts of these remaining articles were reviewed, and 14 were removed due to irrelevance, leaving 27 articles. Upon full-text examination, 15 articles were ultimately selected as directly relevant to the research questions, and the rest were excluded. The researchers did not restrict the publication date range and aimed to include all available studies. For each article, information was extracted regarding the authors’ names, year of publication, study method, research instruments, study location, population, target groups, and key findings.

Figure 1

Flowchart Diagram

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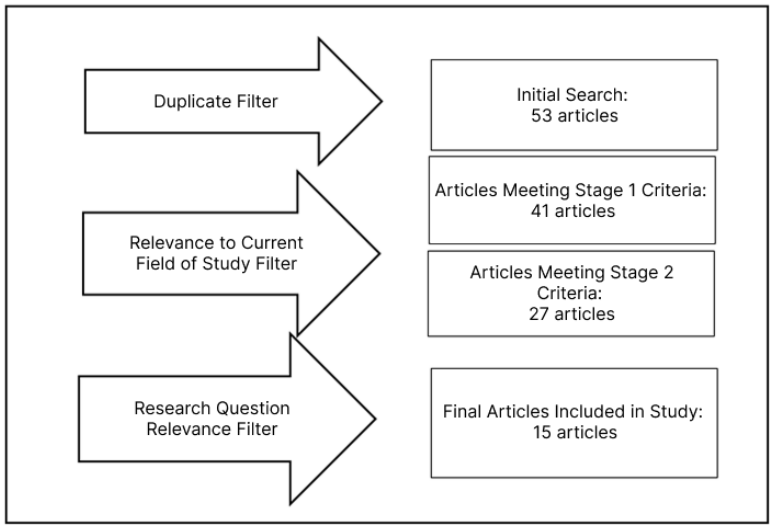

Accordingly, 15 international articles from credible databases aligned with the research topic were extracted and summarized in Table 1, organized by author, year, study type, and article title. As observed, among the 15 studies included: 2 were published in 2020, 4 in 2022, 3 in 2023, 4 in 2024, and 2 in 2025. These represent 13.33% in 2020, 26.66% in 2022, 20.00% in 2023, 26.66% in 2024, and 13.33% in 2025, respectively.

Table 1

Overview of Included Studies

No.	Reference	Study Type	Sample Size	Article Title
1	(Riemann et al., 2024)	Multiple Regression	839 (443 single-episode MDD, 331 recurrent MDD, 65 BD)	Borderline Personality Traits in Relation to Childhood Trauma in Unipolar and Bipolar Depression
2	(Jørgensen et al., 2023)	Correlation	Healthy controls, MDD with and without cognitive impairment, BD	Childhood Trauma and Cognitive Impairments in Recovered Bipolar Patients
3	(Du et al., 2024)	Pearson Correlation & Mediation Analysis	562 patients with depression, 204 healthy controls	Family Functioning as a Mediator Between Childhood Trauma and Depression Severity
4	(Miao et al., 2022)	Correlation	72 patients, 30 healthy controls	Childhood Trauma History and Abnormal Brain Metabolism in Drug-Free Adults with MDD
5	(Yoon Park et al., 2023)	Correlation	787 patients, 734 general population	Childhood Trauma and Resilience in Patients with Mood Disorders
6	(Lai et al., 2025)	Correlation	503 MDD patients, 503 controls	Trauma Exposure as a Risk Factor for MDD: A Case-Control Study
7	(Jiaa & Lubetkin, 2020)	-	-	Impact of Adverse Childhood Experiences on Quality-Adjusted Life Expectancy in the U.S. Population
8	(Nguyen & Shaw, 2020)	Multiple Linear Regression	263 participants	Etiology of Subclinical Narcissism: Roles of Adverse Childhood Experiences and Parental Overvaluation
9	(Maed et al., 2024)	-	30 patients, 20 healthy controls	T Cell Activation and Regulatory T Cell Reduction in Severe MDD: Effects of Relapse and Childhood Trauma
10	(Congia et al., 2022)	Correlation	42 patients, 40 healthy controls	Cognitive Impairment, Childhood Trauma, Inactivity, and CRP in Major Affective Disorders
11	(Palomo et al., 2024)	Systematic Review	-	Clinical, Demographic, and Environmental Predictors of Bipolar Relapse: A Systematic Review
12	(Porcu et al., 2022)	Correlation	Smokers and non-smokers	Childhood Trauma, Biomarkers, and Mood Symptoms in Bipolar Smokers and Non-Smokers
13	(Poletti et al., 2022)	Correlation	200 participants	Long-Term Effects of Childhood Trauma: Role of White Matter Inflammation in Mood Disorders
14	(Barczyk et al., 2023)	Systematic Review	-	Childhood Trauma and Cognitive Functioning in Mood Disorders: A Systematic Review
15	(Zhang et al., 2025)	Correlation	90 patients, 94 healthy individuals	Effects of Childhood Trauma on Cognitive Performance in BD Patients

According to Table 1, Reimann et al. (2024), in a multivariate regression study, found a strong association between adverse childhood experiences—especially emotional neglect—and borderline personality traits

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(Riemann et al., 2024). In the same vein, Jørgensen et al. (2023) reported that cognitive impairment in bipolar patients is associated with a specific pattern of structural brain changes that may be influenced by developmental factors such as childhood trauma. The observed differences in various brain regions may form a neural basis for cognitive differences among subgroups of patients (Jørgensen et al., 2023). Similarly, Dou et al. (2024) concluded that childhood trauma has both direct and indirect effects—via family functioning—on the severity of depression in mood disorder groups. Miao et al. (2022) also emphasized that early childhood trauma has long-lasting effects on brain metabolism in drug-free adult MDD patients (Miao et al., 2022).

Furthermore, Yoon Park et al. (2023) acknowledged that all individuals with a history of childhood trauma demonstrated lower levels of resilience. Specifically, emotional abuse and emotional neglect had the strongest association with reduced resilience, standing out compared to other forms of childhood trauma. The negative association between childhood trauma and resilience was more pronounced in the healthy control group than in the MDD group, and individuals with mood disorders exhibited a different pattern in this relationship. Thus, adverse childhood experiences may disrupt the capacity for psychosocial adaptation (Yoon Park et al., 2023).

Lai et al. (2025) further found that exposure to childhood trauma (CT) and stressful life events (SLEs) were each independently associated with an increased risk of developing MDD, and this association remained even after controlling for confounding variables (Lai et al., 2025). Jia and Lubetkin (2020) affirmed that adverse childhood experiences are characterized by various forms of psychological, physical, and sexual abuse, as well as dysfunctional family environments, such as parental mental illness or substance abuse (Jiaa & Lubetkin, 2020). Similarly, findings from Nguyen and Shaw (2020) indicated that childhood trauma is a predictor of narcissism in adulthood (Nguyen & Shaw, 2020).

In a 2024 study, Maed et al. concluded that adverse childhood experiences lead to abnormal immune activation, with an increase in cytotoxic T cells, effector T cells, and B cells with autoimmune potential, alongside a decrease in regulatory T cells, which play a crucial role in controlling immune responses. These immune system alterations are considered key mechanisms in the development of depression. The findings suggest that the broadening of depressive symptoms and increase in suicidal behavior stem from autoimmune processes, which are themselves the result of childhood trauma and the progressive sensitization of the immune system. In other words, the more adverse experiences a person has in childhood, the more their immune system is prone to inflammatory and autoimmune responses, ultimately contributing to depressive symptoms and suicidal ideation. This mechanism partly explains why individuals with a history of abuse or neglect are more likely to suffer from treatment-resistant depression (Maed et al., 2024).

In another study, Congia et al. (2022) found that outpatients with BD engaged in less physical activity during leisure time compared to the control group. High-sensitivity C-reactive protein (hs-CRP) levels ≥5 mg/L were significantly associated with a history of physical and sexual abuse in childhood and with poorer cognitive functioning in mood disorders, particularly in BD (Congia et al., 2022).

Palomo et al. (2024), in a study based on 58 eligible articles, reported that risk factors for bipolar relapse include clinical and psychiatric history (e.g., family history, personal history, earlier onset, lower global functioning, and cognitive impairment), as well as sociodemographic variables (e.g., unemployment, low educational level, poor social adjustment, and stressful life events), and substance-related factors. These findings highlight the need for a multifaceted approach in the management of mood disorders (Palomo et al., 2024).

Porcu et al. (2022) found that bipolar smokers with elevated leptin levels had significant associations with a history of childhood trauma, more severe depression and anxiety symptoms, and changes in metabolic components. These findings suggest that leptin levels may serve as an important biomarker in bipolar smokers, with childhood trauma potentially influencing the course of illness via changes in leptin and related metabolic disruptions, which may in turn explain part of the mechanism linking smoking to symptom exacerbation (Porcu et al., 2022).

Poletti et al. (2022), in their study, showed that adverse childhood experiences (ACEs) were associated with higher levels of peripheral inflammatory markers—such as IL-2, IL-17, bFGF, IFN-γ, TNF-α, CCL3, CCL4, CCL5, and PDGF-BB—but only in patients with BD. Specifically, elevated CCL3 and IL-2 levels were associated with reduced fractional anisotropy (FA) in white matter, indicating a potential link between inflammation and structural brain changes (Poletti et al., 2022).

Finally, Barczyk (2023), in a systematic review titled *Childhood Trauma and Cognitive Functioning in Mood*

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Disorders, found a consistent association between childhood trauma and cognitive deficits in mood disorders. This association may manifest differently depending on the phase of illness (acute vs. stable) (Barczyk et al., 2023). Zhang et al. (2025) also reported that the prevalence of abuse and neglect in childhood was significantly higher in the BD patient group than in healthy controls (HC). Their findings showed that mood stabilizer use was positively associated with verbal abilities, while antipsychotic use negatively impacted attention in these patients. Emotional abuse in childhood was found to impair immediate memory, and both the number of illness episodes and valproate dosage were inversely related to total RBANS (Repeatable Battery for the Assessment of Neuropsychological Status) scores. In contrast, educational attainment and mood stabilizer use were positively correlated with RBANS scores (Zhang et al., 2025). These results underscore the importance of carefully considering the cognitive effects of medications and of paying close attention to prognostic factors such as trauma history and educational level when treating bipolar patients.

4. Discussion and Conclusion

The present study is the result of a systematic review of 15 peer-reviewed English-language articles published between 2020 and 2025, aimed at exploring the association between childhood trauma and cognitive functioning in individuals diagnosed with Major Depressive Disorder (MDD) or Bipolar Disorder (BD).

Numerous studies have examined the profound and multidimensional impacts of adverse childhood experiences (ACEs) on the trajectory of mood disorders. Findings strongly indicate that childhood trauma—particularly emotional neglect and abuse—is associated with both structural and functional brain alterations. These changes include reduced gray matter volume in the prefrontal cortex and hippocampus, disrupted white matter integrity, and abnormalities in neural circuits involved in emotional regulation. From a cognitive perspective, these neural changes are linked to persistent impairments in memory, attention, processing speed, and executive functioning. Notably, the patterns of these changes differ between individuals with BD and MDD, suggesting distinct pathophysiological mechanisms across these disorders.

From a biological standpoint, childhood trauma leads to chronic immune activation and elevated levels of inflammatory markers such as IL-6, TNF-α, and CRP. This chronic inflammatory state is associated not only with exacerbation of mood symptoms but also with impaired cognitive function through its effects on neuroplasticity. Research has shown that these inflammatory effects may be more pronounced in patients with BD and are further influenced by factors such as cigarette smoking and metabolic changes, including elevated leptin levels. Additionally, childhood trauma disrupts immune system balance, including a decrease in regulatory T cells and an increase in effector T and B cells with autoimmune potential—changes that may contribute to the development of treatment-resistant forms of mood disorders.

Several factors can moderate these associations. Family functioning is recognized as a key protective factor, where better family cohesion and adaptability can buffer the negative consequences of childhood trauma. Conversely, factors such as low educational attainment, unemployment, and exposure to stressful life events can exacerbate the effects of early trauma. Importantly, pharmacological treatments also influence cognitive outcomes; for example, mood stabilizers may have a protective effect on cognitive functions, whereas some antipsychotic medications may negatively impact attention and other cognitive domains.

These findings have significant implications for clinical practice. First, they highlight the necessity of routine screening for childhood trauma in clinical assessments. Second, they suggest that treatment for affected individuals should be multifaceted, incorporating pharmacological interventions (e.g., anti-inflammatory agents), trauma-focused psychotherapies, and cognitive rehabilitation. Third, they underscore the importance of considering social factors such as family support and education level in treatment planning. Ultimately, these studies emphasize the need for developing personalized interventions based on each patient's biological profile and developmental history. Future research should further examine targeted interventions, such as immune-modulating therapies and novel brain stimulation techniques, to improve cognitive outcomes in these populations.

A core objective of systematic review is to identify knowledge gaps and offer directions for future research. Accordingly, longitudinal studies with extended follow-up periods are needed to assess the impact of adverse childhood experiences on brain development from childhood through adulthood, monitor inflammatory and neurocognitive changes across time, and evaluate the effects of early interventions in preventing long-term consequences. Additionally, integrated interdisciplinary research combining genetic data, neuroimaging, cognitive

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assessments, and simultaneous measurement of inflammatory markers, metabolic shifts, and neurocognitive performance should be pursued. Furthermore, targeted intervention studies are required to assess the effectiveness of anti-inflammatory treatments in patients with trauma histories, examine the impact of combining specialized psychotherapies with pharmacological treatments, and conduct randomized controlled trials on cognitive-behavioral interventions.

Moreover, stratified research based on subgroups should be undertaken to investigate gender differences in response to childhood trauma, differentiate the effects of various trauma types (emotional, physical, and sexual), and identify predictors of treatment response. There is also a need to develop innovative assessment technologies, including the use of artificial intelligence for analyzing neuroimaging patterns and digital tools for real-time symptom tracking. Such research efforts could enhance understanding of underlying mechanisms, facilitate the development of more precise diagnostic tools, and contribute to the design of personalized treatment strategies.

Authors' Contributions

All authors significantly contributed to this study.

Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

Transparency Statement

Data are available for research purposes upon reasonable request to the corresponding author.

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Declaration of Interest

The authors report no conflict of interest.

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Ethical Considerations

Not applicable.

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