



The Role of Childhood Trauma in Major Depressive Disorder: A Review of Pathophysiological and Psychopathological Aspects

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ABSTRACT

Major depressive illness can arise from a multitude of sources, such as a mix of hereditary variables, chemical alterations in the brain, stressful life events, and other environmental and psychosocial factors. Childhood trauma is a prevalent source of psychological distress and encompasses instances of abuse and neglect. This literature review seeks to investigate childhood trauma as a contributing factor to the emergence of major depressive disorder (MDD). Individuals with major depressive disorder (MDD) link childhood stress to atypical tissue structure. Prior research has identified alterations in the amplitude of low-frequency fluctuation (ALFF) in individuals with major depressive disorder (MDD) who have experienced childhood trauma. Researchers have specifically observed these changes in the left insula, right dorsal anterior cingulate cortex, bilateral amygdala, and orbitals. People with serious depressive disorders can use increased cortisol levels after waking up as a biological indicator. Childhood trauma frequently correlates with several signs of psychopathology, such as depression, somatization, and alexithymia. Alexithymia, a condition characterized by difficulty expressing emotions, can impede the recovery process in patients with significant depression. This difficulty in effectively conveying their feelings to mental health experts can delay the development of appropriate treatment plans and management strategies. In conclusion, childhood trauma contributes to the occurrence of major depressive disorder (MDD) and intensifies the frequency and severity of depressive symptoms.

1. Introduction

Major depressive disorder (MDD) is a serious mental condition characterized by profound feelings of sadness, loss of interest or joy in daily activities, and prolonged impairment of cognitive and physical function.^{1,2} This disorder usually lasts for several weeks or even months, and can significantly affect a person's quality of life. The main symptoms of major depressive disorder include prolonged feelings of sadness, loss of interest or enjoyment in previously enjoyed activities, significant changes in weight or appetite, sleep disorders such as insomnia or hypersomnia (excessive sleeping), prolonged feelings of tiredness or lack of energy, feelings of Unreasonable guilt or low self-esteem, difficulty concentrating, and thoughts of death or suicide.² Globally, depression is

considered the most widespread disease and can occur in every individual and every age group.³ This is an economic and financial burden because depression requires continuous pharmacological management and requires very high costs.⁴

Major depressive disorder can be caused by a complex of factors, including a combination of genetic factors, chemical changes in the brain, stressful life events, and other environmental and psychosocial factors.⁴ Childhood trauma is a common cause of psychological stress and includes experiences of abuse and neglect.⁵ Various studies have reported that childhood trauma can predict psychiatric disorders such as bipolar disorder, anxiety, substance use disorders, post-traumatic stress disorder, and MDD.⁶⁻
⁸ Childhood trauma may influence negative life events

in MDD patients.⁹ Individuals with a history of childhood trauma report more negative life events.¹⁰ This literature review aims to explore childhood trauma as a contributing factor to the occurrence of major depressive disorder.

Pathophysiology of major depressive disorder in patients with childhood trauma

Major depressive disorder (MDD) is a serious mental disorder that affects the sufferer's mood, interests, and cognitive function. Women are twice as likely to experience MDD as men.⁵ Compared with men, the impact of childhood trauma is more pronounced in women. Women also have more complex patterns of childhood trauma, and the female gender also plays a synergistic role with childhood trauma in certain mental disorders.¹¹

Childhood trauma is associated with abnormal tissue architecture in MDD patients. Previous studies have detected changes in amplitude low-frequency fluctuation (ALFF) in MDD with childhood trauma, including in the left insula, right dorsal anterior cingulate cortex, bilateral amygdala, and orbital.¹⁰ Neuroimaging studies conducted by Chen et al. reported an increase in ALFF in the middle frontal gyrus (MFG) left in MDD patients with childhood trauma compared with MDD patients without childhood trauma.⁵

Left MFG activation is associated with working memory, social information processing and social perception, memory retrieval, and emotion regulation. This area is also associated with rumination activity (rumination or repetitive thoughts regarding the past), which in turn increases an individual's risk of MDD.¹² Emotional rejection and abuse are thought to be related to depression, which is mediated by rumination activities.¹³ Additionally, abnormal left MFG activation in individuals with childhood trauma may repeatedly trigger traumatic memories and exacerbate rumination. This is what underlies the increased depressive symptoms in MDD patients with childhood trauma.

The association of MDD and childhood trauma

Childhood trauma is the most important environmental factor for several psychiatric disorders. Depressed patients with childhood trauma generally have more frequent symptom recurrence than depressed patients without trauma. According to the DSM-5, diagnostic and statistical manual of mental disorders-5 (DSM-5), psychological trauma refers to exposure to traumatic experiences, such as threatened or substantial physical violence, threatened or actual sexual violence, or circumstances related thereto. Childhood trauma is pathological and causes serious psychological and behavioral disorders such as poor emotional control, unstable interpersonal relationships, and lack of self-awareness. Unlike simple short-term anxiety, trauma usually lasts throughout the patient's life.¹⁴

Childhood trauma has several effects on a person's mental state. Traumatic experiences make patients more susceptible to depression and anxiety. People with a history of childhood sexual abuse experience significantly increased depression, higher suicide rates, and overall stress vulnerability, due to neurobiological factors, including hormonal changes. Additionally, childhood trauma is associated with intellectual dysfunction and cognitive deficits in childhood and adulthood, which are particularly relevant to difficulties in inhibitory control. Childhood trauma contributes to impulsivity or deficits in executive function in patients with psychiatric disorders. In addition, several studies have shown that childhood trauma is associated with affective lability or mood dysregulation in patients with borderline personality disorder or bipolar disorder.^{15,16}

Among the conditions listed above, negative childhood experiences are a potential risk factor for major depressive disorder (MDD), and a recent meta-analysis suggests that childhood abuse worsens the overall course and treatment outcome of MDD. Additionally, childhood trauma affects cognitive functions such as memory, and executive function in patients with MDD. Childhood trauma has a strong relationship with depressive symptoms. Previous

research by Hovens et al. stated that individuals with a history of childhood trauma are at risk of experiencing symptoms of depression rather than anxiety.¹⁷ In cases of severe childhood trauma, there is generally an increase in the severity of mood/cognitive, melancholy, general distress, and somatic depressive symptoms from all dimensions of depressive/anxiety symptoms. In other studies, it was stated that there were cognitive disorders typical of depression, such as disorders of judgment or decision-making.¹⁸ Beyond mood/cognitive symptoms, the most pronounced effects were seen on interpersonal sensitivity, previously found to be a significant risk factor for the development and worse course of depressive episodes.¹⁸

The long-term effects of childhood trauma on more severe and chronic manifestations of depressive/anxiety symptomatology may be explained by stress-induced changes in the brain, mind, and body. For example, exposure to abuse in childhood can change basic cognitive assumptions about oneself and others, which over time can become part of a person's personality. Traumatic experiences in childhood can irreversibly dysregulate the function of major body stress systems, in particular, the hypothalamic-pituitary-adrenal (HPA) axis and the immune-inflammatory system by chronically stimulating cortisol release and cortisol secretion. proinflammatory cytokines. This dysregulation can lead to more severe manifestations of depressive or anxiety symptoms and, especially, melancholic and somatic depressive symptoms. Increased engagement in health-defeating behaviors such as smoking or heavy alcohol/drug use in individuals with trauma is also noteworthy as poorer lifestyles have consistently been observed as a risk factor for poorer mental health outcomes in adulthood.¹⁴

Sustained activation of the stress system is also hypothesized to alter brain development in individuals with a history of childhood trauma.¹⁵ Consequently, various structural and functional brain changes, such as reduced network connectivity patterns associated with emotion regulation, decision-making, and self-

reflective processing, were observed, possibly associated with more negative cognitive schemas and worse symptomatology. Together, these psychological, behavioral, and biological changes may serve as potentially modifiable targets of interest for early prevention and intervention of more severe and chronic symptom manifestations in individuals with CT.

Correlation of cortisol levels in MDD patients with a history of childhood trauma

One of the biological markers of MDD is cortisol, an end product of the hypothalamic-pituitary-adrenal (HPA) axis. Cortisol is a stress hormone produced by the adrenal glands in response to stressful situations or stressors.¹⁹ Cortisol has an important role in the regulation of stress responses and various physiological functions of the body. In individuals with major depression, there is often dysregulation or dysfunction in the stress response system, including the bone marrow, hypothalamus, and cortisol-producing adrenal glands. This leads to an oversensitive or underresponsive stress response, which can contribute to the development of depression. Elevated cortisol levels can indicate excessive activation of the stress response system. Persistent high cortisol levels can have a negative impact on mental and physical health, including affecting mood and cognitive function.^{19,20}

Cortisol usually follows a daily pattern called the cortisol rhythm, with the highest levels in the morning and the lowest levels in the evening. In individuals with major depression, this cortisol rhythm can be disrupted, resulting in different patterns. For example, there can be abnormal increases or decreases in cortisol levels at certain times of the day. The hypothalamic-pituitary-adrenal (HPA) system regulates the production and release of cortisol in response to stress. In some individuals with major depression, the HPA may become inhibited, leading to a reduced cortisol response to stress. On the other hand, in some individuals, the HPA can become hyperactive, causing persistent increases in cortisol

production.²¹

Elevated post-awakening cortisol levels may serve as a biomarker for individuals with major depressive disorder. One study conducted in young adults found that total morning cortisol output was increased in individuals with childhood trauma when compared with individuals without childhood trauma.¹⁹ Measurement of cortisol levels may be performed as an additional diagnostic tool in evaluating HPA function in individuals with major depression but is not the only marker for diagnosing or treating this condition.²⁰ Treatment of major depression often involves an integrated approach involving psychological therapy and, in some cases, pharmacological treatment aimed at restoring the disturbed neurochemical balance.

Psychopathology in MDD patients related to history of childhood trauma

Alexithymia

Childhood trauma is often associated with later psychopathology, including depression, somatization, and alexithymia. Alexithymia is an emotional disorder characterized by difficulty in recognizing, describing, and differentiating one's own emotions. In individuals with alexithymia, they may have difficulty identifying the emotions they are experiencing, expressing emotions verbally, and understanding the relationship between emotional feelings and associated physical reactions.²² In cases of major depression, alexithymia can be an additional symptom that accompanies the main depressive disorder. People with major depression often experience feelings of sadness, loss of interest or excitement, changes in appetite or sleep, decreased energy, feelings of worthlessness, difficulty concentrating, and thoughts about death or suicide. Alexithymia in the context of major depression may worsen an individual's emotional experience, as they have difficulty identifying and expressing their feelings.

Alexithymia in major depression may hinder the recovery process, as individuals may have difficulty communicating their feelings to mental health professionals, which may hinder effective treatment

planning and management. Additionally, difficulties in recognizing and managing emotions can affect social and interpersonal relationships, as individuals with alexithymia may have difficulty understanding and responding to the feelings of others in an appropriate way. A study investigating the relationship between childhood trauma and alexithymia symptoms in MDD stated that there was an association between somatic symptoms in MDD and a history of childhood trauma. A history of physical abuse and emotional neglect correlates with symptoms of alexithymia. Overall, these studies suggest emotional abuse and neglect predict the emergence of alexithymia and somatization later in life.²²

Insomnia and dysfunctional attitudes

Insomnia is a common problem among MDD patients. According to previous research, the development and severity of insomnia are influenced by the experience of childhood trauma. In addition, negative life events and dysfunctional attitudes can also mediate these impacts. Insomnia symptoms are associated with more severe clinical symptoms in patients with MDD. Therefore, insomnia may be a reasonable treatment target for MDD because treating insomnia may improve depressive symptoms. If insomnia persists after treatment for depression, insomnia symptoms may predispose to depressive symptoms and residual insomnia is likely to lead to relapse of depression. Previous studies have shown that patients with MDD who experienced childhood trauma typically experience more sleep problems and more severe insomnia, and childhood trauma may be a predictor of insomnia in young MDD patients.²³

Childhood trauma usually refers to various forms of physical abuse and verbal or non-verbal psychological abuse before the age of 18. However, childhood trauma can affect MDD patients in early adulthood, suggesting that multiple factors may play a role in these effects over time. Negative life events refer to things that force a person to change, such as poor academic performance, the death of a good friend, and so on, which are considered social factors that can

explain the relationship between childhood trauma and insomnia. Negative life events are a common cause of stress in college student's lives, and depressed students reported more negative life events in the past 12 months than non-depressed students. Negative life events in the past year can predict the occurrence of insomnia. Individuals with MDD are more likely to have their sleep disrupted by life events than individuals without MDD. Childhood trauma may influence negative life events in MDD patients. Individuals with a history of childhood trauma report more negative life events. These findings suggest that negative life events may mediate the relationship between childhood trauma and insomnia. However, several studies clarify the role of negative life events experienced in the last 12 months of childhood trauma on the formation of insomnia in MDD.^{24,25}

Childhood trauma can cause dysfunctional attitudes. Dysfunctional attitudes are one of the core characteristics of depression, namely negative and biased attitudes about the self, the world, and the future. Dysfunctional attitudes are considered to be another important factor in the development of insomnia in MDD.²³ Dysfunctional attitudes are also linked to childhood trauma and negative life events. Dysfunctional attitudes are formed by people's cognitive deviation from reality that is gradually influenced by their negative experiences in childhood. Dysfunctional attitudes are activated when faced with stressors (negative life events), resulting in many negative, distorted, and extreme cognitive changes. Previous studies have revealed a correlation between childhood trauma, negative life events, and dysfunctional attitudes toward insomnia.^{23,24} However, few studies have simultaneously examined the relationship between childhood trauma, negative life events, dysfunctional attitudes, and insomnia. Childhood trauma, negative life events, and dysfunctional attitudes had an impact on insomnia after controlling for clinically significant depressive symptoms, which is similar to the results of several studies conducted on individuals with and without a history of MDD.

Previous studies also suggest that cognitive factors influence insomnia symptoms in MDD more than negative life events. Cognitive factors play an important role in inducing and maintaining insomnia. Dysfunctional attitudes are very common in patients with MDD and are one of the core characteristics of MDD. Currently, cognitive-behavioral therapy for insomnia (CBT-I) is used to treat insomnia in college students by changing dysfunctional attitudes about sleep. Additionally, a history of childhood sexual abuse was an important factor influencing sleep after controlling for depressive symptoms. Individuals with childhood trauma are associated with persistently increased activity of the hypothalamic-pituitary-adrenal (HPA) axis system. Stress caused by negative life events leads to activation of the HPA axis. Overactivity of the HPA axis is an important cause of insomnia in individuals with MDD.

Dysfunctional attitudes play a mediating role in childhood trauma or negative life events and insomnia. This pathway can be explained by physiological studies. Childhood trauma can affect brain structure (i.e., amygdala, prefrontal cortex, hippocampus) and atypical activation of some brain regions, including reduced activity in the prefrontal cortex and increased activity in the amygdala. The prefrontal cortex and amygdala play important roles in cognitive and emotional regulation. Potential mechanisms of dysfunctional attitudes in MDD are manifested by hypoactivation of the prefrontal cortex and hyperactivation of the amygdala. High amygdala activation can lead to negative emotional processing, low prefrontal cortex activation can lead to reduced amygdala inhibition so that the individual's attention remains on the negative stimulus and the individual remains in a negative state. Currently, several cognitive-related therapies have been used among young adults who experienced childhood trauma, such as developmentally adapted cognitive processing therapy for posttraumatic stress disorder symptoms following childhood trauma.

Negative life events may lead to more dysfunctional attitudes in patients with MDD. Negative life events

influence the activation state of the ventrolateral prefrontal cortex and subsequently influence cognitive function in depression. Prevention of childhood trauma may be considered in the prevention of insomnia. Negative life events and dysfunctional attitudes are mediators of the relationship between childhood trauma and insomnia. Lowering the threshold for negative life events may help depressed patients manage negative life events, and changing dysfunctional attitudes may be considered a treatment intervention for insomnia in the future. Screening for childhood trauma should be considered when treating insomnia in patients with MDD.²³⁻²⁵ Treatment for major depressive disorder may involve a combination of psychological therapy (such as cognitive behavioral therapy or interpersonal therapy) and pharmacological treatment (such as antidepressants). Psychological therapy helps individuals overcome negative thought patterns and develop strategies to deal with stress, while pharmacological treatment aims to regulate the chemical balance in the brain.

Electrophysiological changes associated with childhood trauma

The effects of childhood trauma can cause long-term changes in brain development.²⁶ Specifically, previous brain imaging studies have reported that childhood trauma is associated with structural changes in the frontal lobe and limbic system. In a voxel morphometry study, women who experienced stress early in life had less gray matter in the posterior precuneus than healthy controls.²⁶ Previous research suggests that childhood maltreatment is accompanied by physiological, hormonal, and biochemical changes that ultimately lead to changes in brain structure and function. These results further suggest that childhood trauma causes various structural changes in the brain.²⁷

The results of these changes can be determined through electroencephalography (EEG). EEG evaluation results can reflect the prognosis or severity of symptoms of various psychiatric disorders. Specifically, event-related potentials (ERPs) are a

neurophysiological tool used to indicate neural activity related to cognitive processes. Previous studies have shown that adolescents and adults who experienced childhood trauma show changes in Nogo ERP and frontal lobe activity sources, suggesting that impulsivity occurs due to dysfunction of these regions.²⁶ Meanwhile, a history of childhood trauma and depressive symptoms were associated with extensive regional brain networks and brain connectivity in MDD patients.

2. Conclusion

Childhood trauma contributes to the incidence of MDD and increases the recurrence and severity of depressive symptoms.

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