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Effects of Early Psychological Trauma on Limbic System Structure and Function

Erken Dönem Psikolojik Travmaların Limbik Sistem Yapısı ve İşlevi Üzerindeki Etkileri

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ABSTRACT

This paper aims to review the subtypes of childhood trauma and its effects on brain structures and function, especially the hippocampus and amygdala within the limbic system, in the context of clinical psychology. For this purpose, original articles published between 1996 and 2024 were systematically searched in major databases such as PubMed, PsycArticles, Web of Science, and Google Scholar using keywords such as early childhood trauma, psychological trauma, limbic system, hippocampus, amygdala, and neuroimaging. The articles were initially screened based on their titles, and those meeting the search criteria, including study population, investigated brain regions, and types of traumas, were further assessed for relevance. Ultimately, 136 articles were selected and discussed in this review. Trauma experiences in early life can have a significantly negative influence on a person's psychological health by causing neurodevelopmental impairments, especially in the limbic system. While it is understood that trauma influences how individuals think, behave, and feel, the results of neuroimaging studies reveal variations in the amygdala and hippocampus based on different trauma subtypes. These changes merit deeper investigation in future research to fully understand the reasons behind the diverse findings in existing literature.

Anahtar sözcükler: Psychological trauma, childhood trauma, limbic system, hippocampus, amygdala

ÖZ

Bu makale psikolojik travmanın ne olduğunu (türlerini de içerecek şekilde) ve erken travmatik deneyimlerin, özellikle limbik sistem içerisindeki hipokampüs ve amigdala olmak üzere, yetişkin insan beyni yapılarını nasıl etkilediğini klinik psikoloji bağlamında derlemeyi amaçlamaktadır. Erken dönem travma, psikolojik travma, çocukluk çağı travması, limbik sistem, hipokampus, amigdala ve nörogörüntüleme gibi anahtar kelimeler kullanılarak 1996 ile 2024 yılları arasında yayımlanan orijinal makaleler, PubMed, PsycArticles, Web of Science ve Google Scholar gibi önemli veri tabanlarında sistemli bir şekilde taranmıştır. Makaleler ilk olarak başlıklarına göre taranıp, ardından araştırma popülasyonu, incelenen beyin bölgeleri ve travma türleri gibi arama kriterlerini karşılayan çalışmalar incelenmiştir. Sonuç olarak, bu derlemede toplamda 136 makale seçilmiş ve tartışılmıştır. Yaşamın erken dönemlerindeki travma yaşantıları, özellikle limbik sistemde olmak üzere, nörogelişimsel hasarlara sebep olarak bireylerin psikolojik sağlık durumları üzerinde önemli olumsuz etkilere sahip olabilmektedir. Travmanın insanların düşünüş, davranış ve hissediş biçimlerini etkilediği bilinse de alan yazındaki birbiriyle çelişen bulguların kaynağını anlayabilmek adına, nörogörüntüleme çalışmalarının bulgularının amigdala ve hipokampüs özelinde farklı travma türleriyle ilişkili olarak nasıl değişkenlik gösterdiği gelecekte yapılacak çalışmalarda daha detaylı şekilde araştırılmalıdır.

Keywords: Psikolojik travma, çocukluk çağı travması, limbik sistem, hipokampüs, amigdala

Introduction

Exposure to trauma during childhood is quite common, and as a result, a significant portion of children have the potential to be affected by traumatic experiences at some point during their developmental processes, which adversely affects various areas of daily life (Copeland et al. 2018). Although numerous studies have been conducted on the effects of psychological traumas on mental health (Kessler et al. 2010), the impact of traumas on the brain and the importance of this subject remain a critical issue that requires in-depth examination. Various approaches and methodologies have been utilized to investigate the effects of traumas experienced in early childhood on the developing brain and the related changes in the structure and function of certain brain regions during development and adulthood. Despite this, there are missing and contradictory neuroimaging findings about the affected brain regions, abnormalities in the brain structures under discussion, and the

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relationships between types of traumas. However, converging findings related to brain structures considered as part of the limbic system are noteworthy. Therefore, the purpose of this review is not only to address significant gaps in the current literature but also to provide a more consistent and comprehensive summary of findings related to the limbic system associated with specific trauma subtypes.

For this purpose, original articles published between 1996 and 2024 have been researched in leading databases (e.g., PubMed, PsycArticles, Web of Science, Google Scholar, etc.) using keywords such as “early childhood trauma, psychological trauma, limbic system, hippocampus, amygdala, and neuroimaging”. The articles were selected based on their titles, and those meeting the research criteria (study population, investigated brain regions, and types of traumas) were deemed appropriate for this review. Although the present work does not fulfil the characteristics of a traditional systematic review, the authors have made an effort to adhere as much as possible to the PRISMA 2020 guidelines, aiming to provide a comprehensive and objective overview of the identified subject. Consequently, 136 articles related to the present works objective are discussed in this study.

This review article commences with an overview on various subtypes of early psychological traumas. Subsequently, the article aims to analyse the detrimental effects of early traumatic experiences on the limbic system, and their complex relationships with psychiatric disorders. By this, the review article untangles inconsistent findings from different studies, highlights the effects of early life traumatic experiences on neurodevelopment, and consequently, points to the impact of the limbic systems disruptions on an individual's psychological health.

Psychological Traumas

Diagnostic and Statistical Manual of Mental Disorders (APA 2013) defines traumatic situations as exposure to actual or threatened death, injury, sexual violence, or threats; direct exposure to or witnessing of traumatic events; learning about trauma experiences of close family members or friends; and repeated or extreme exposure to the aversive details of traumatic events (APA 2013). Briere and Scott (2006) stated that the traumatic nature of an event stems from an individual's inadequate coping capacity at that moment, leading to persistent psychological symptoms and subsequently severe distress.

Encountering or witnessing psychological traumas such as natural disasters, earthquakes, floods, abuse, neglect, assault, accidents, and the diagnosis of life-threatening diseases particularly during early childhood, exacerbates the severity of psychological effects (Öztürk 2020). Childhood trauma is used to describe the psychological harm caused by significant, unexpected, and damaging events that subjects face during their early lives (Felitti et al. 2010). Considering that childhood traumas have profound effects on the individuals' belief systems and shape their perceptions of the world and other people (Spalletta et al. 2020), such traumas, along with the chronic stress stemming from early traumatic experiences, lead to lasting negative mental and physical outcomes in individuals (Van der Kolk 2007, Dannlowski et al. 2012). Consequently, individuals exposed to childhood traumas become more vulnerable to psychopathologies (Van der Kolk et al. 1991).

Types of Early Psychological Trauma

Childhood traumas can arise from various events and are divided into two main categories: neglect and abuse. Following this basic division, each main category includes subcategories such as emotional and physical neglect, as well as physical, emotional, and sexual abuse (Bernstein et al. 2003, APA 2013). A summary of each subcategory and an introduction to the concept of complex trauma will be presented in the following section right before a detailed examination of their effects on the adult brain is provided.

Emotional, Sexual and Physical Abuse

The intentional use of force that can lead to injury of a child or adolescent, such as beating, shaking, burning, or kicking, is defined as physical abuse (CDCP 2022). Situations where parents or other caregivers display demeaning behaviors towards children and adolescents, call them insulting nicknames, belittle them, adopt hostile attitudes, make excessive and inappropriate demands, or show aggressive behaviors are considered emotional abuse (CDCP 2022).

Negative judgments on mental disorders, excessive pressure applied for disciplinary purposes, intimidation, threats, excessive control, boundary violations, imposing age-inappropriate heavy responsibilities on the child (for example, expecting them to contribute to the family's finances), preventing the child from forming social

relationships and socializing, involving the child in family conflicts, and holding the child responsible for familial problems are various examples of emotional abuse (Hopper et al. 2018).

Childhood sexual abuse encompasses exposing children and adolescents to sexual acts that they are not fully capable of comprehending (Modelli et al. 2012). APA (2013) defines child sexual abuse as any sexual act involving a child that is performed by a parent, caregiver, or another individual responsible for the child for the purpose of sexual gratification. The World Health Organization listed characteristics of sexual abuse and states that the abuse is often carried out by people in the child's immediate surroundings and whom the child trusts, that the abuser typically attempts to gain the child's trust with the aim of concealing the abuse, and that physical force or violence is rarely used (WHO 2022). However, it has been noted that the abuse can continue over extended periods, such as several weeks or months, and that instances of repeated sexual abuse have increased over the time (Mathews et al. 2024).

Emotional and Physical Neglect

Neglect is defined as the failure to meet the physical, emotional, social, and cognitive needs of children and adolescents to an adequate extent (APA 2013). Examples of emotional neglect include the caregiver's physical absence from the child's life due to various reasons such as health issues, workload, military duty, chronic mental health problems, alcohol or substance use, developmental challenges, or incarceration. Additionally, ignoring the child's emotional needs, avoiding the child, limiting interaction with the child by isolating oneself for extended periods, or leaving the child in uncertainty about when the caregiver will return are also considered forms of emotional neglect (Hopper et al. 2018). Ignoring the significance of a medical condition, failing to cover medical expenses, or underestimating the severity of the child's health condition are further examples of physical neglect (Valles et al. 2019).

Type I, Type II and Complex Trauma

The absence of agreement on how to define complex trauma has presented difficulties for researchers, as definitions may prioritize different aspects such as the quantity and types of traumatic events, the developmental stages during which they occur, or the resulting symptoms (Weathers and Keane 2007). According to Terr (1991) traumas can be further classified into two subtypes. Type I traumas are characterized by a single event that presents continuous and permanent challenges to the child's developmental process. Severe illness or injury, road accident, hospitalisation, life threatening illness, diagnosis or perceived life-threatening illness and traumatic loss can be shown as examples of Type I traumas (The Trauma Practice 2024). Type II traumas are often prolonged and recurring experiences, commonly occurring within interpersonal relationships, or involving close attachment figures during childhood (The Trauma Practice 2024). According to Terr (2003), Type II traumas tend to be repeated and long-standing experiences which often manifested as an absence of feeling, a sense of rage an unremitting sadness. Lastly, clinicians and researchers working on childhood trauma and maltreatment have proposed another potential subtype of trauma known as complex trauma (Courtois 2004).

Although the concept of complex trauma was defined by Courtois in 2004, it is considered quite "new" in this field. In the literature, the term "complex trauma" is used to refer to “crossover type conditions” by Terr (2003). This classification was explained as the coexistence of Type T and Type II trauma features (Terr 2003). According to another definition, complex trauma can be described as long-term traumatic life experiences that occur in the early years of life and often involve interpersonal relations such as sexual abuse, physical violence, bullying, persistent and negative changes in care systems, and exposure to societal violence (Ceyhan and Alkar 2023). Kliethermes et al. (2014) described complex trauma as a repetitive and prolonged traumatic experience that impairs primary caregiving relationships and transpires during critical stages of brain development. Complex traumas are distinct from traumas that occur as isolated events because they emerge in a continuous and prolonged manner, including significant stages of life, such as childhood and adolescence (Terr 2013). Studies focusing on measuring complex trauma are not as common as those for other subtypes of trauma. This may be due to the lack of surveys, which will be discussed later.

Trauma and the Brain

Previous research has exposed the relationship between traumatic experiences in childhood and mental health and deviant behaviors through studies examining the effects of traumatic experiences on brain structure and function (Maier et al. 2020, Popovic et al. 2020, DeCross et al. 2022). These studies showed that exposure to

childhood traumatic experiences affects one's developmental processes, behavior, and spiritual life through its impact on the nervous system (Dannlowski et al. 2012, Agorastos et al. 2019, McLaughlin et al. 2019). Consequently, the recent literature describes various ways on how exposure to various kinds of trauma changes the brains' structure and function and thereupon how an individual perceives and reacts to the world. To better understand these mechanisms and identify potential target areas for treatment, the following sections will discuss and summarize recent findings about the distinctive effects of traumatic childhood experiences on the structure and function of the still-developing brain.

Effects of Trauma-Induced Stress on the Brain's Structure and Function

As mentioned at the beginning of this review, psychological trauma encompasses a range of subtypes that can have various effects on the brain. Physical abuse (for example, hitting the head) reasonably leads to traumatic brain injury and results in abnormalities in the structure and functionality of specific brain regions such as the amygdala, hippocampus, temporal lobe, and prefrontal cortex (Bremner et al. 1997, Weber and Reynolds 2004). These abnormalities can cause altered behavior and emotional disorders. On the other hand, passive forms of abuse that do not involve physical contact, such as emotional and physical neglect, similarly can have serious effects on the nervous system and behavior (Weber and Reynolds 2004). A possible mediator of this may be changes in mechanisms related to the stress response. It has been observed that traumatic experiences cause changes in interconnected brain circuits and hormonal systems involved in managing and regulating stress (Nemeroff 2004).

The exposure to any potentially dangerous and life-threatening event naturally sets in motion the activity of brain regions involved in the stress response controlled by the brainstem and the limbic system, specifically the hypothalamus-pituitary-adrenal (HPA) axis, including the amygdala, the hypothalamus and also the hippocampus (Murphy et al. 2022). To ensure the individual's survival, this response enables an individual to react to the stressor with a fight or flight response, facilitated by the release of stress hormones such as cortisol and adrenaline/noradrenaline into the bloodstream. However, exposure to a single intense or repeated negative event can damage regulatory brain regions (McEwen et al. 2016) and, as a result, cause long-term dysregulation of the nervous system (Heim and Nemeroff 2001, Aas et al. 2019, Begemann et al. 2023). Stress leads to a temporary disruption of the homeostatic balance in the body (Trauelsen et al. 2015) and, depending on the intensity of the exposure and the life stage at which it occurs, has been associated with numerous structural and functional changes in the nervous system (Teicher et al. 2004, Nemeroff 2016).

In situations of chronic stress, and when it is not possible to escape or fight off stressful stimuli, cortisol levels fail to decrease to normal levels (Aguilera and Liu 2012). This process leads to functional and structural changes in the hippocampus (Bremner and Vermetten 2012) and the amygdala (Nogovitsyn et al. 2022). Similarly, neurobiological abnormalities such as neuroendocrine disturbance (in the serotonin, catecholamine, and endogenous opioid systems) have been significantly associated with early life traumas (van der Kolk 2007). Such immunometabolic changes can be permanent, leaving the still-developing child's brain particularly vulnerable (Perry 2002). These changes can lead to neurodevelopmental problems (Hoover 2020) and long-term effects on the adult brain (Orellana et al. 2023). The persisting stress response, for example due to an abusive parent, not only increases the sensitivity of brain regions that usually regulate the stress response but also weakens neural connections (Cook et al. 2009, Du et al. 2019). Furthermore, it causes neural loss through the decreased release of neurotrophic factors in other brain regions (Aas et al. 2019, Kershner 2020). The repeated activation of the stress response leads to toxicity for the neural tissue, as well as adverse effects on the immune system (Lee et al. 2022) and disruptions in the connections between limbic structures and the prefrontal cortex (Silveira et al. 2020). This results in cognitive dysfunctions, including thinking, planning, decision-making, memory, and learning disabilities (Hakamata et al. 2021).

According to Briere and Scott (2006), these effects on the brain can impact memory and information processing and disrupt trauma victims' capacity to regulate their social and psychological responses to stress through the impairment of the HPA axis (Nemeroff 2004, Perry and Szalavitz 2017). Despite reports of generally weakened neural connections, continuous exposure to fear- and anxiety-inducing events actually strengthens the connectivity of specific neural circuits that regulate these responses (Tottenham et al. 2011). Some studies discuss this aspect under the concept of resilience (Feder 2009, Ashy et al. 2020) and in terms of the development of mechanisms for coping with traumatic or stressful events later in life (Southwick and Charney 2012). However, its primary effect is a sensitivity and heightened state of alertness towards threats, which persists even if it is not overtly apparent to others.

Developmental Aspects

According to the neurosequential model proposed by Perry (1998), the brain's organization develops in a bottom-up and inside-out manner, meaning in a sequential and hierarchical fashion. Much of the brain's critical structural organization occurs during early childhood. Therefore, while systems crucial for immediate survival develop first, the organization and full development of brain areas related to higher cognitive functions, such as emotional and behavioral regulation, take longer (Murphy et al. 2022). In the use-dependent organization of the developing child's brain, repetitive sensory experiences shape neural system organization for optimum development and organization of brain function (Weber and Reynolds 2004). The dramatic effects of extreme neglect during critical developmental periods have been reported by Perry (2002), who documented significantly lower weight, enlarged ventricles, and cortical atrophy in a severely neglected 3-year-old child when compared with a matched healthy control.

The reviewed literature indicates that childhood trauma alters plasticity processes throughout developmentally critical periods, subsequently affecting the structural and functional interactions of cortical and subcortical neural networks (Holz et al. 2023). Furthermore, current findings suggest that early life traumas leave lasting marks (Agorastos et al. 2019) and lead to impairments in brain structure and function in trauma victims, often causing a discrepancy between developmental and chronological age (Perry 2002).

Trauma and Limbic System

Studies examining the neurodevelopmental outcomes of childhood maltreatment have largely focused on the impact on various structures within the limbic system (Teicher et al. 2003). The limbic system comprises brain structures that form a complex network responsible for the regulation of emotions, memory, and motivation. Among these structures are the hippocampus, associated with memory function; the hypothalamus, regulating the stress response; and the amygdala, playing a significant role in the regulation and processing of emotions.

Structural and Functional Changes in the Amygdala

Structural Changes: Amygdala

The amygdala is a part of the limbic system that plays a critical role in encoding emotional memories and learning the significance of emotional stimuli (Davis and Whalen 2001). Additionally, the amygdala is responsible for the formation of conditioned fear responses and autonomic reactions that can be encoded in early memory (Joseph 1996).

Following early childhood trauma experiences, structural or functional abnormalities can be observed in the amygdala. In particular, amygdala hypertrophy was reported in children who have experienced neglect (Tottenham et al. 2010) or moderate maternal disengagement (Lupien et al. 2011) while physical or sexual abuse were mostly unrelated (Bremner et al. 1997, Woon et al. 2008) early in life. Other studies have demonstrated that psychological stressors resulting from abuse and neglect can increase the volume of the amygdala through the formation of new spines on pyramidal cells. Teicher and Samson (2013) have noted that increased amygdala volumes are observed in individuals with experiences of emotional and physical neglect in childhood. Dannlowski et al. (2012) specifically tested the relationship between childhood abuse and amygdala reactivity in 148 non-clinical participants using an emotional face matching paradigm. The researchers reported strong positive relationships between childhood traumas and amygdala reactivity, even when recent life stressors, current depression, anxiety symptoms, or sociodemographic factors were controlled for. Other studies reported increased amygdala volumes in subjects who had depressed mothers in their childhood and accordingly faced emotional and physical neglect (Lupien et al. 2011).

Beyond that there are studies that claim there is no difference in amygdala volumes between children who have experienced abuse and neglect and those who have not been subjected to any maltreatment (Lupien et al. 2009). At the same time, some research reported a decrease in the amygdala volume and its association with stress sensitivity mechanisms in participants diagnosed with major depressive disorder (MDD) who have past trauma experiences (McLaughlin et al. 2019). Other studies have also found negative relationships between childhood traumas and amygdala volumes (Souza-Queiroz et al. 2016), and further identified bilateral reductions in hippocampus and amygdala volumes in PTSD groups compared to control groups (Ahmed-Leitao et al. 2016). Another significant study conducted by Nogovitsyn et al. (2022) has revealed that smaller amygdala sizes, especially in basal regions, are more common in participants with higher trauma levels. This study also highlights that, among childhood traumas, sexual and physical abuse were selectively affecting he subregions of the

amygdala. Despite the fact that none of the subjects at the time of evaluation matched the requirements for a clinical diagnosis, abuse-related abnormalities in the right basal area, nevertheless, mediate the intensity of depression and anxiety symptoms (Nogovitsyn et al. 2022).

These inconsistent findings related to amygdala volume highlights the necessity of examining the types of traumas experienced and the ages of exposure more carefully. By this, the literature will gain more robust and reliable findings for the better understanding of the impact of trauma experience on the amygdala structure.

Functional Changes: Amygdala

While volumetric studies may be divergent, functional studies mostly report increased activity in the amygdala associated with childhood maltreatment. In a meta-analysis of 32 fMRI studies (Saarinen et al. 2021), childhood abuse was shown to be associated with greater bilateral amygdala activation in response to sad faces. The exaggerated response of the amygdala to emotional faces in adolescents exposed to various traumatic experiences in the past, including physical and sexual abuse as well as neglect, has been reported by Maheu et al. (2010), Tottenham et al. (2011), Garrett et al. (2012), Ganzel et al. (2013), and van den Bulk et al. (2016); similarly, the long-term effects of trauma on amygdala functionality in adults who have experienced childhood trauma have been demonstrated by Dannlowski et al. (2013), van Harmelen et al. (2013), and Ross et al. (2021). In light of these findings, it is considered that the lack of reliable information or reduced perceptions of safety in the early years may shape the relevant structures, and that these individuals may respond to danger through aberrant amygdala activity (Tottenham et al. 2010).

While the studies mentioned above are task-based MRI studies, resting-state MRI offers the opportunity to measure minor fluctuations in the activity of brain networks during rest. Luo et al. (2022) have examined the relationships between amygdala-based functional networks and childhood abuse, depression, and anxiety. They found a strong negative correlation between the resting-state functional connectivity of the left amygdala and the anterior insula with childhood abuse, indicating negative relationships between them. The relationship between structural and functional changes in the amygdala has been extensively studied not only in connection with trauma but also with emotional dysregulation seen in many other psychiatric disorders (Ahmed-Leitao et al. 2016, Ashy et al. 2020). For instance, Kebets et al. (2021) found increased neural variability in parts of the fronto-limbic network, including regions such as the amygdala, hippocampus, and prefrontal cortex (PFC). Another network-based approach on brain activity patterns was conducted by Ireton et al. (preprint, Psyarxiv 2023). This study performed a meta-analysis of 14 studies on children with trauma experience and reported aberrant activity patterns in the Default Mode/Affective Network/posterior insula and Central Executive Networks. This difference was found regardless of the presence of a diagnosed post-traumatic stress disorder (PTSD). PTSD, anxiety disorders such as social phobia and other specific phobia types (Lanius et al. 2010), mood disorders such as unipolar and bipolar depression (Dannlowski et al. 2014) and lastly borderline personality disorder are some other disorders where aberrant amygdala activity and structure have been reported to be crucial in the development of the diseases.

Structural and Functional Changes in the Hippocampus

Another critical limbic area that has been the focus of recent research is the hippocampus, a region known for its importance for the formation of declarative, spatial, and contextual memory (Holz et al. 2023). The hippocampus is among the first regions affected by the damages caused by chronic stress such as neuronal excitability, neurogenesis, and dendritic remodelling. This sensitivity stems from its susceptibility to stress-induced increases in circulating glucocorticoids and excitatory amino acids (McEwen 2010, 2016). Furthermore, the hippocampus plays a significant role in psychopathology, especially in anxiety and related disorders (Teicher et al. 2013). Teicher et al. (2004) have suggested that both, the hippocampus and the parahippocampal gyrus, could play critical roles in anxiety and related disorders, which may be due to the excessive noradrenergic effects originating from the locus coeruleus on the hippocampus. The hippocampus plays a critical role in the inhibitory control within the HPA-Axis. It is also vital for cognitive functions and the verbal aspects of fear and stress learning (Heim et al. 2004).

Structural Changes: Hippocampus

Recent research has scrutinized the relationship between childhood traumas and hippocampal volumes (Dannlowski et al. 2012, Maier et al. 2020, DeCross et al. 2022). Clinical studies focusing on the effects of abuse experienced at an early age on the hippocampus have yielded conflicting results. Stein (1997) identified a significant reduction in the left hippocampal volume in adults with childhood traumatic experiences, particularly

those with PTSD or dissociative identity disorder. On the other hand, a study by Rao et al. (2010) observed reduced hippocampal volume in depressive women with a history of childhood abuse, whereas no such volume reduction was detected in women who were equally depressive but had not experienced childhood traumas. Rao et al. (2010) reported that a smaller hippocampal volume might play a mediating role between childhood traumas and depression. Additionally, another study by Bremner et al. (1997) found that adult women diagnosed with borderline personality disorder (BPD) who had experiences of abuse or neglect in childhood showed approximately a 16% reduction in hippocampal volume on both sides. Hippocampal volume has also been reported to be decreased in studies related to major depressive disorder (MDD) and depression in children (Barch et al. 2019). Similarly, smaller hippocampal volumes have been observed in MDD patients who have experienced childhood trauma compared to those who have not (Heim et al. 2001). Janiri et al. (2019) investigated the complex interactions of past childhood trauma and the volumes of subfields of the hippocampus in individuals with borderline personality disorder and healthy control groups. The results generally showed that the volumes of the hippocampal subfields are smaller in the group with borderline personality disorder; however, patients with borderline personality disorder who experienced childhood trauma had larger volumes of the hippocampal subfields compared to the control groups (Janiri et al. 2019).

In contrast, no significant difference in hippocampal volume was detected between children diagnosed with posttraumatic stress disorder (PTSD) who had been abused and healthy control groups (De Bellis et al. 1999). Similarly, a study conducted by Carrion et al. (2001) reported no significant differences in hippocampal volumes between children subjected to abuse and healthy control groups. On the other hand, in another investigation involving 165 patients, it was documented that hippocampal and amygdala volumes in females varied according to the transdiagnostic psychopathological dimensions of trauma (Sambuco et al. 2023). More recently, research by Badura-Brack et al. (2020) examined the impact of gender on trauma and brain volume. The study identified significant interactions between gender and trauma in children. A reduction in hippocampal and parahippocampal region volumes was observed in male children exposed to trauma, mirroring the outcomes of studies in adults. Conversely, it was observed that female children exposed to trauma had larger volumes in limbic regions compared to control groups.

Differences in limbic lobe volume can be influenced not only by gender but also by genetic and epigenetic factors. Womersley et al. (2020) investigated the role of oxytocin receptor variants in the relationship between childhood trauma effects and brain volume in women diagnosed with anxiety disorders. They found that the rs2254298 allele had an interaction effect between emotional neglect and decreased left hippocampal volume, and also determined that amygdala volumes were associated with the rs2254298 allele. The role of oxytocin in the development of trauma-related disorders has also been examined by Flanagan and colleagues (2019), who, in a complementary manner to the findings of Womersley et al. (2020), found that intranasal oxytocin played a significant role in the reactivity of the amygdala during the processing of frightening faces in PTSD related to the severity of childhood trauma (Flanagan et al. 2019).

Functional Changes: Hippocampus

Functional and structural changes in the hippocampus affect cognitive abilities such as memory function. Hakamata et al. (2021) discovered significant relationships between childhood trauma, semantic-related memory, and functional connections in limbic areas. While decreased functional connectivity between the hippocampus and medial PFC was associated with trauma scores, the functional connectivity was increased between lateral and anteromedial PFC and extrastriate cortex. The increased functional connectivity further mediated the relationship between trauma scores and semantic-associate memory, most likely affected by hyposecretion of cortisol (Hakamata et al. 2021). The relationship among childhood trauma, functional connectivity and executive functions have been further studied, in particular in relation to the development of alcohol abuse (Silveira 2020). In their study, the association between childhood trauma and executive dysfunctions was mediated by dispersed functional connectivity from hub regions in the bilateral dorsal anterior cingulate cortex, right anterior insula, right intraparietal sulcus, and bilateral pre- and postcentral gyri. The discovered network changes were also promising predictors for future alcohol abuse in the follow-ups.

Structural and Functional Changes in the (Pre)Frontal Lobe

By establishing extensive connections with other brain regions, the prefrontal cortex participates in thinking processes, regulates our emotions, and controls behaviors. The development of this region continues until early adulthood, making its structural and functional development process highly vulnerable to traumatic damages. Early childhood emotional maltreatment was repeatedly associated with reduced medial PFC volume in adults (Underwood et al. 2019) and functioning of prefrontal-limbic circuit (Herringa et al. 2013). One of the

fundamental reasons for functional abnormalities in the limbic circuit could be the changes in the volumes of limbic structures and observed reductions in the integrity of white matter (WM) tracts that connect these structures to each other. The uncinate fasciculus (UF), one of these tracts, is among the long-range fiber tracts that connect distant gray matter regions in the brain. As the UF directly connects the orbitofrontal cortex to the anterior temporal lobes through a bidirectional pathway, abnormalities in this tract can lead to impairments in memory, language, or social -emotional processing (Von Der Heide et al. 2013). Additionally, due to its location in the human brain, the prefrontal cortex (PFC) is sensitive to damages stemming from head traumas. Therefore, traumatic brain injury cases are commonly related with damage to white matter as well (Johnson et al. 2015). One of the roles of the prefrontal cortex (PFC) in trauma-related pathologies is the abnormal amygdala-PFC functional connectivity, which is often reported in comparison to control groups, especially in conditions such as major depressive disorder (MDD) (Tang et al. 2013, Wu et al. 2020). Popovic et al. (2020) reported that various childhood traumas, including sexual abuse and emotional trauma, affected the gray matter volumes in prefronto-cerebellar, limbic, and sensory networks. A whole-brain morphometric meta analyses carried out by Tymofiyeva et al. (2022) found increased volume in the left brain hemispheres areas involved in motor functions and language production such as the left precentral gyrus, the left inferior frontal gyrus, left fibers of the body of corpus callosum, and left postcentral gyrus, while they found decreased brain volume in regions involved in language processing and/or sensory processing such as the bilateral cerebellum, bilateral middle temporal gyrus, left rostrum of corpus callosum, and bilateral supramarginal gyrus for subjects with traumatic past when compared to controls. The researchers suggest that these findings reflect the increased sensory sensitivity and hypervigilance observed in adolescents as a result of childhood trauma. Bounoua et al. (2022), in a study focusing on the morphometric features of the amygdala and orbitofrontal cortex (OFC), not only identified a positive correlation in the volume of these connected structures but also demonstrated that this condition could modify the specific characteristics of Cluster B personality disorders. These findings indicate that the OFC-amygdala circuit may act as a fundamental anatomical pathway through which childhood trauma sustains emotional dysregulation in adulthood and increases the risk of developing personality disorders (Bounoua et al. 2022). On the other hand, a study conducted by Begemann et al. (2023), which compared healthy controls, bipolar disorder patients, and schizophrenia patients, found decreased gray matter volumes in the right medial orbitofrontal, paracentral, superior frontal regions, and the left precentral area in participants with trauma experience; however, no such reduction was detected in subcortical areas. In a study conducted by Begemann et al. (2023), a comparison among healthy controls, bipolar disorder patients, and schizophrenia patients revealed decreased gray matter volumes in the right medial orbitofrontal, paracentral, superior frontal regions, and the left precentral area in participants with a history of trauma; however, no such reduction was identified in subcortical areas. These studies indicate that changes in brain structure can provide significant insights for understanding and treating psychiatric disorders.

Finally, the heterogeneity of studied trauma categories and types makes it difficult to create a coherent picture. However, there is evidence to suggest that different traumas indeed have distinct effects on brain structure and function. Li and colleagues (2022) were able to map differences in functional connectivity density (FCD) of diverse brain regions with 4 distinct trauma subtypes. The identified regions corresponded to the sensorimotor, cingulum, accumbens, insula, and frontal-parietal areas, as well as in regions within the default mode network, regions that also corresponded with cognitive functions. The capability to associate different trauma subtypes with specific neural changes and affected areas offers critical insights for the risk analysis of psychiatric disorders and the development of targeted treatment strategies.

Childhood Trauma and Its Relationship with Psychopathologies

Experiences of both neglect and abuse at a young age cause significant impairment, especially in the structures of the limbic system. Considering the critical roles the limbic system plays in emotion regulation, learning, and motivation, its impairment can lead to both psychological and physical illnesses (Keyes et al. 2012). For instance, these early traumas experienced during brain development are recognized as risk factors for the onset of various mental disorders and are considered precursors to stress-related mental and physical illnesses, as well as reduced life expectancy (Holz et al. 2023). More specifically, traumatic experiences during childhood have been associated with various psychological disorders, including depression, anxiety, somatic disorders, schizophrenia, and bipolar disorder. The psychological difficulties and disorders frequently observed in individuals exposed to traumatic events in childhood reflect certain neurodevelopmental changes in a context where the development of the human brain is dependent on the complex interaction between genetic potential and the environment (Weber and Reynolds 2004), with traumatic experiences functioning as stress factors. For instance, it is reported that particularly traumatic experiences and high stress levels during childhood negatively affect brain

development, lead to a series of persistent disorders, and trigger depression, which is closely associated with suicide (Bains and Abdijiadid 2021). Alvarez et al. (2011) reported that suicide rates among patients with bipolar disorder, schizophrenia, and schizoaffective disorder who experienced trauma in childhood are nearly three times higher than those patients without traumatic experiences in childhood, further emphasizing that childhood trauma serves as a significant factor in the prognosis of severe psychiatric disorders. In addition to mental and psychotic disorders, it is indicated that traumatic experiences in childhood also predict somatic symptoms (Eilers et al. 2023). Furthermore, Özturk and Derin (2020) suggested that individuals exposed to neglect and abuse in childhood are hindered in developing a stable and social self-concept. The hindered social identity development due to early trauma leads to relationship problems in adulthood and encounters with a series of social problems (Nurius et al. 2015).

From this perspective, when examining mood and anxiety disorders specifically, studies have shown that nearly half of the patients with bipolar disorder have experienced traumatic events in childhood, and when childhood trauma is present, the prognosis is worse, and suicide attempts are more frequent (Garno et al. 2005). Conus et al. (2010) also noted that these patients are more likely to attempt suicide even during treatment. Furthermore, in a study investigating the relationship between childhood traumas and psychopathology, it was reported that depression, anxiety disorders, and alcohol misuse are more common in individuals exposed to trauma in childhood (Herrenkohl et al. 2013). Similarly, Spataro et al. (2004) demonstrated a strong association between childhood sexual abuse and both anxiety and mood disorders. The results of the study by Dias et al. (2015) indicated that emotional abuse experienced during early developmental periods is the strongest predictor of interpersonal sensitivity and depression. It was also found that depression could be predicted by a history of sexual abuse (Chen et al. 2010). Horesh and Iancu (2010) also demonstrated a significant relationship between traumatic life events in childhood and the development of both unipolar and bipolar disorders, showing that stressful life events are predictors of both the first depressive and manic episodes. In another similar study, stressors such as traumatic experiences were shown to play a significant role in mood disorders like bipolar disorder, indicating that stress can trigger mood episodes, thereby leading to relapse (Altman et al. 2006). Additionally, Brietzke et al. (2012) proposed that the interaction between traumatic events and the development of bipolar disorder is complex, depending on various factors such as timing and individual differences.

When considering psychotic disorders, Read et al. (2005) highlighted that sexual and physical abuse in childhood is highly prevalent among patients. It has also been shown that patients with psychotic disorders who have experiences of physical or sexual abuse in childhood are more likely to have a co-occurring psychiatric disorder (Conus et al. 2010). Similarly, when examining childhood trauma and its developmental impacts, it has been reported that childhood traumas predict dissociative experiences in adulthood (Sar 2018). According to another study, emotional abuse experienced during early developmental periods strongly predicts paranoid ideation, which is commonly experienced in psychotic disorders (Dias et al. 2015). Janssen et al. (2004) discovered that traumatic experiences in childhood predict the development of positive symptoms of psychosis, such as hallucinations and delusions. Nettelbladt et al. (1996), in their study, showed that patients with schizoaffective disorder reported significantly higher rates of sexual and physical abuse compared to matched control groups. Similarly, another study found more than three times the prevalence of childhood sexual abuse among schizophrenia patients (Wurr and Partridge 1996). Despite numerous findings indicating a strong relationship between various types of psychotic disorders and a history of sexual abuse, Bendall et al. (2008) have argued that in order to better understand this relationship, it is necessary to examine different types of traumas including physical and emotional neglect and abuse, in addition to sexual abuse. Moreover, it is significant that the presence of multiple types of childhood traumatic experiences has been shown to be a greater risk factor for the development of many psychiatric disorders (Teicher et al. 2006, Kisely et al. 2018).

Future Research Areas and Clinical Impacts

As emphatically noted by Brietzke et al. (2012), traumatic experiences do not always produce the same outcomes for everyone, making this a significant topic of discussion in the context of resilience, gene-environment interactions, and epigenetics, as well as the harmful effects of early psychological traumas on the brain. For example, new approaches are attempting to explore the gene x brain x environment relationship and have found that the catechol-O-methyltransferase (COMT) Val158Met polymorphism might have a significant modulatory function through structural and functional changes in the orbitofrontal cortex and language networks, as well as anxiety levels (Tian et al. 2020) or its impact on the hippocampus associated with aggressive behaviors (Wang et al. 2023). In another study, Tian et al. (2021) discuss the relationship between childhood trauma questionnaire scores, BDNF Val66Met polymorphism, and anxiety scores, finding its association with brain plasticity involving emotion regulation. These new perspectives on genetic polymorphisms allow for a better

understanding of their effects on limbic responses and prefrontal-limbic connectivity. This situation also influences how responses to traumatic events (Feder et al. 2009) may play a role in resilience.

Resilience has been defined both as a response outcome to stressful life events and as a trait that makes individuals less vulnerable to the harmful effects of psychological trauma. For instance, a study examining this distinction found that both resilience as a trait and as a response outcome mediate the relationship between early trauma and psychological disorders (Philippe et al. 2011). Additionally, researchers have emphasized that this finding is only valid for specific trauma subtypes. This situation applies to emotional abuse and neglect, and physical neglect, with the mediation effect being much weaker for physical and sexual abuse. These results further underscore the necessity of conducting research on specific trauma subtypes in the context of their harmful effects on the brain. In their research, Ashy et al. (2020) demonstrated that the relationship between early traumatic experiences and psychopathology is mediated by limbic dysfunction, but resilience regulates this relationship, functioning as a protective factor. Teicher et al. (2006) have argued that this relationship between limbic dysfunction and childhood traumas has a biological basis in terms of harboring an increased stress response system against adverse environments. Thus, considering the role of the limbic system in processing and regulating emotions and that resilience is largely concerned with the ability to regulate difficult emotions such as shame, guilt, and fear, it can be said that disorders in the structure and function of the limbic system have a tremendous impact on resilience (Ashy et al. 2020).

Neuroplasticity-A Protector?

While observing all the negative effects of trauma on the structure and function of one of the brain's most complex organs, the ability of the brain and neural networks to heal and restructure using plasticity mechanisms should not be forgotten or underestimated. Neuroplasticity can be defined as the brain's ability to change its structure in response to environmental stimuli (Klorer 2005). Thus, therapeutic success largely depends on the brain's responsiveness and changes in mistrained neural circuits. Some studies have shown the neurological healing effects of creative therapies such as dance/movement, music, drama, and art, which often impact at a non-verbal level involving the limbic system basal ganglia and other areas (Lusebrink 2010, Garrett 2020), while others discuss the effects of trauma-focused cognitive-behavioral therapy (Spiegel et al. 2022) on neuroplasticity and the reduction of trauma-related symptoms.

When examining individuals resilient to traumatic experiences, it is observed that these individuals possess larger volumes of gray and white matter in their hippocampi and have more connections between limbic structures and the central executive network (Moreno-López et al. 2020). Researchers also noted that these differences enhance the ability of resilient individuals to regulate their emotions through medial prefrontal cortex-limbic regulation, decrease activation in the hippocampal area when faced with emotional faces, and increase stress habituation in the amygdala. Therefore, the critical factor for resilience may be the very specific ability of neuroplasticity and gene polymorphisms. As previously mentioned, maltreatment during early childhood can increase neuroplasticity in the prefrontal cortex by creating a need to cope with stress, which in turn defends against the adverse effects of future stressful events (Southwick and Charney 2012). Alongside effective regulation of the stress response, prefrontal regulation can be another significant moderator for resilience (Southwick and Charney 2012).

Conclusion

Maltreatment in any form during childhood is associated with significant impairments in critical brain regions within the limbic system, such as the amygdala and hippocampus, and these impairments are evident even decades into adulthood. Childhood traumas possess characteristics that can affect an individual's entire life. Anatomical studies have shown a connection between childhood traumas and a decrease in hippocampus volume (Rao et al. 2010, Dannlowski et al. 2012) and an expansion of amygdala volume; however, irregular hippocampus and amygdala volumes have been depicted in patients with borderline personality disorder, hence the findings are complex (Tottenham et al. 2010). Based on studies discussed in this review, while some findings suggest a decrease in amygdala volume and an increase in hippocampus volume, the results of other studies may contradict these findings. Therefore, these conflicting findings could be due to different reasons such as the method of measuring traumatic experiences and the nature of the trauma experienced. Upon reviewing the literature, it is observed that the classification, definitions, and the experiences within these definitions used for childhood traumas vary. While some research uses the term "childhood traumas," others refer to "early life stress" or "adverse childhood experiences." The absence of a standard definition in the field of psycho-traumatology and

the existence of many different types of psychotraumas can be seen as a reason for the differing views in research. Another possible reason is the different effects that various types of childhood traumas can have on the human brain. Therefore, future studies focusing on the differences between childhood neglect and abuse and their specific subtypes will be more effective. For example, one study demonstrated that exposure to childhood emotional abuse is the most significant predictor of having paranoid thoughts, depression, and interpersonal sensitivity (Dias et al. 2015). More research examining the effects of different childhood trauma subtypes on the adult brain should be conducted in the future to understand the different mechanisms.

Additionally, there are a very limited number of surveys used to measure traumatic experiences, such as the Childhood Trauma Questionnaire (CTQ) and the Structured Clinical Interview for DSM (SCID); however, both methods do not include specific traumas such as witnessing someone's death, being diagnosed with a life-threatening illness, experiencing war, being an immigrant, or being exposed to political and cultural traumas. Therefore, while all these different experiences belong to the definition of psychological trauma, they constitute different subcategories within this definition. The conflicting findings mentioned in the literature within this review may result from the lack of inventories to specify these subtypes.

This point is also significant in clinical practice because treatment effects are likely to be greater when the treatment is tailored to the specific trauma subcategory and aligned with the concept of gene-environment interactions. While victims of childhood trauma can access many different treatment approaches, progressive clinical research is expected to distinguish clear neurobiological focuses for intervention and indicators for treatment selection in light of early developmental, genetic, and clinical characteristics. Consequently, more studies are needed to obtain more specific information on different childhood trauma subcategories and how they affect the human brain.

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