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Review

Is Schizophrenia Influenced by Childhood Trauma - A Review Article

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ABSTRACT

About 1% of people suffer from schizophrenia (SCZ), a serious neuropsychiatric illness and 20 million people worldwide suffer from the same. Excessive dopamine release is the pathophysiology behind this. There are numerous environmental factors that have been connected to various clinical manifestations of schizophrenia spectrum disorders, such as childhood hardship, substance misuse and usage, minority and ethnicity status, birth season, urbanity, and pregnancy and perinatal issues. The term "childhood adversity," often known as "childhood trauma" (ChT), refers to painful life events such as physical, sexual, or emotional abuse or neglect. Though there are various factors pertaining to the development of schizophrenia childhood traiuma is found to be an important factor for the development as well as affecting the disease progression and treatment rates. But this is often neglected during assessment and in prevention. Hence this research focuses on the relationship between childhood trauma and schizophrenia.

Keywords: Schizophrenia; Childhood trauma; Adverse childhood experience; Schizotypal personality disorder

Introduction

About 1% of people suffer from schizophrenia (SCZ), a serious neuropsychiatric illness[1] and 20 million people worldwide suffer from the same. Positive, negative, and cognitive symptoms are frequently found in SCZ cases. Positive symptoms align well with auditory hallucinations and mental disorders. Both psychological and cognitive symptoms are present, including learning and concentration problems as well as social disengagement and flat affect in the negative symptoms[2]. It has been suggested that defective genes and environmental variables interact to cause the symptoms of schizophrenia, which is considered a neurodevelopmental illness. According to the dopamine hypothesis, the hyperfunction of dopamine D2 receptor neurotransmission in the limbic and subcortical brain regions is linked to positive symptoms. Neurotransmission from the D1 receptor is hypoactive, which adds to the negative and cognitive symptoms of schizophrenia[3]. There are beliefs about the involvement of various natural environmental elements in the development of SCZ, despite the fact that the incidence of SCZ is higher in family members of affected persons. Because multiple exposures are involved, the neurodevelopmental hypothesis of schizophrenia supports the idea that the cause of schizophrenia is a combination of hereditary features and environmental exposures that occur during development, starting in infancy and continuing into adolescence[4]. Although twin studies found a heritability of about 60-80% for schizophrenia[5]. According to the two-hit model, a neurodevelopmental issue in the perinatal

stage may result in neural circuit failure and stress sensitivity at critical brain times; later, the disorder may be triggered by psychosocial stress or substance misuse, for example[6]. In addition, when exposed to stresses such as increased alertness and anxiety, schizophrenia patients react emotionally more strongly than non-psychiatric controls[7].

Childhood adversity, or childhood trauma (ChT), is the term used to describe traumatic life events including physical, sexual, or emotional abuse or neglect. Adverse childhood experiences (ACEs) are defined as long-term exposure to environmental stressors during early developmental stages. These include living in a household where there is continuing substance misuse, experiencing interpersonal loss, and being mistreated as a youngster. Experiencing parental death, divorce, or mental illness before the age of 17 is considered interpersonal loss[8-10]. A growing array of literature connects ChT to inflammation, suggesting that inflammation may play a role in the pathophysiology of trauma-related psychopathology[10]. Those who eventually develop schizophrenia have earlier cognitive deficits in childhood, even though psychotic symptoms usually start in the 18–25 age range. This suggests that cognitive deficiencies are a sign of aberrant neurodevelopment, especially when early developmental adversity is taken into account[11]. The primary stress neuroendocrine system in the body, the hypothalamus-pituitary-adrenal (HPA) axis, is dysregulated as a neurobiological result of stress sensitization. The HPA axis is involved in the adrenal glands' synthesis of the stress hormone cortisol[12]. Stress-induced HPA axis activity heightens stress-induced striatal dopamine release and mesolimbic regions' dopamine sensitization[13].

To predict and eventually decrease the development of these disorders in adulthood, it is necessary to first determine the impact that adverse life events experienced during childhood play in psychotic disorders. Though there are various factors about the development of schizophrenia childhood trauma is found to be an important factor for the development as well as affecting the disease progression and treatment rates. However, this is often neglected during assessment and in prevention. Hence this research focuses on the relationship between childhood trauma and schizophrenia.

The purpose of this review is to provide an overview of the role that ChT plays in the onset of schizophrenia and to go into further depth about this idea.

Pathophysiology of Schizophrenia

The pathophysiology of schizophrenia is primarily driven by anomalies in neurotransmitters, including glutamate, gamma-aminobutyric acid (GABA), dopamine, and serotonin. The finding that dopamine D2 receptor blockers effectively reduced psychotic symptoms led to the inadvertent discovery of the relationship between dopamine and schizophrenia[14]. It is thought that there is an excess of dopamine in the mesolimbic pathway, which links the limbic regions to the ventral tegmental area. This could contribute to the positive symptoms of schizophrenia. Decreased dopamine levels in the mesocortical pathway, which links the cortex and ventral tegmental area, may be the source of negative symptoms and cognitive deficits. Different pathophysiological mechanisms underlie the positive and negative symptoms of schizophrenia, according to these studies. Moreover, the nigrostriatal pathway is tied to extrapyramidal motor side effects brought on by D2 receptor blockers, whereas the tuberoinfundibular pathway is linked to the hyperprolactinemia observed with D2 receptor blocker treatment[15]. The interaction of glutamate, GABA, and dopamine is essential for controlling the activity of both excitatory and inhibitory interneurons in cortical circuits. Studies conducted after death reveal that schizophrenia is associated with changes in the microstructure and functionality of these microcircuits. These results have led investigators to investigate the possibility of focusing not just on the dopaminergic pathway but also on the glutamate and GABA signalling pathways for more potent therapeutic approaches in schizophrenia[16]. The schematic representation of the pathophysiology of schizophrenia is shown in **(Figure 1)**[17].

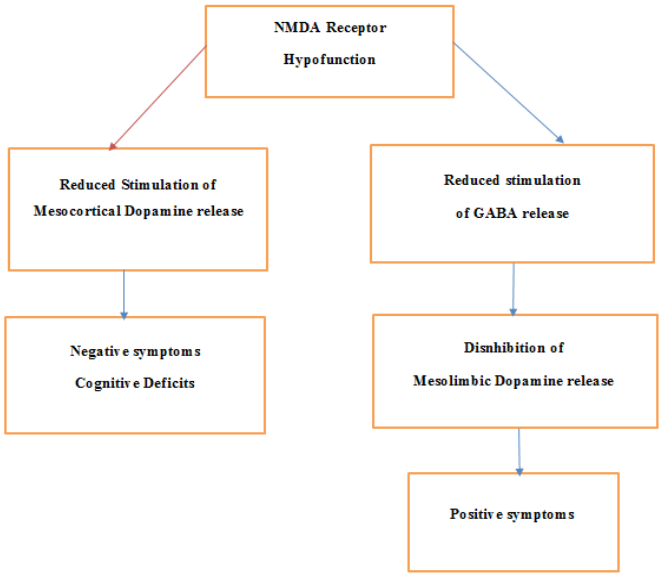

Figure 1: The schematic representation of the pathophysiology of schizophrenia.

Genomics of Schizophrenia

Although schizophrenia has been better described as an underpinning multifactorial aetiology with a complex polygenic genetic architecture, genetic epidemiology investigations have demonstrated that schizophrenia is substantially heritable. Evidence has been presented in favour of the involvement of several environmental factors that may contribute to the aetiology of schizophrenia, as well as frequent and unusual genetic variations linked to the development of the disorder[18]. while more than 100 genetic risk loci for schizophrenia have been found by recent genome-wide association studies (GWAS), their total contribution to the risk of schizophrenia is minimal. Furthermore, it has been proposed that the polygenic risk score could help identify the relationship between intermediate phenotypes, like the structural changes in the brain that occur in schizophrenic individuals, and schizophrenia. Furthermore, five CNV areas associated with schizophrenia have been revealed to contain genes that were found to express differently in schizophrenia, according to a recent systematic review of research using copy number variants (CNVs). With a 25-fold increase in the chance of developing schizophrenia, the 22q11.2 deletion syndrome is the most thoroughly studied CNV linked to an elevated risk of schizophrenia[19] and people with SCZ also have higher peripheral FKBP5 expression. However, beyond genetic susceptibility, epigenetics also plays a crucial role in the development of schizophrenia. The interaction of genetic and environmental factors during the foetal to developmental stages can potentially impact and alter the psychopathological course

of the illness. Additionally, other post-developmental factors may influence the onset of schizophrenia through an epigenetic mechanism. These factors are known as epigenetic factors[20,21].

Aspects of Trauma in Childhood

The capability of a caregiver to provide a safe and healthy environment is directly proportional to the quality of a child's attachment style. A child's relationship with the caregiver plays a vital role in early attachment style formation. Children with responsive caregivers develop secure attachments and are more open to seeking support when faced with difficulties. On the other hand, children with unreliable caregivers who fail to care for their needs tend to develop an avoidant and resistant attachment style, learning to be emotionally self-reliant at an early age. Childhood exposure to violence can have negative long-term effects on one's emotional, physical, and mental well-being. The different ways of childhood trauma are depicted in **(Figure 2)**[22].

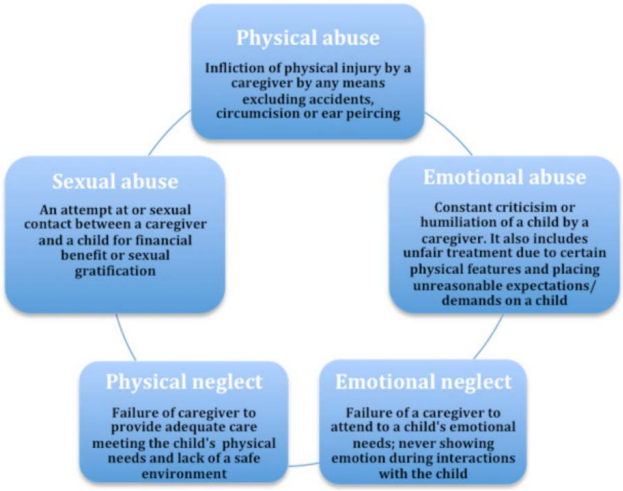

Figure 2: The different ways of childhood trauma.

Discussion

Though various theories have been postulated for the pathophysiology of schizophrenia there is a gap in the literature regarding the environmental effects on the developing brain which leads to the disease. Differential clinical presentations of schizophrenia spectrum disorders have been linked to several environmental factors, including childhood adversity, substance use and abuse, minority and ethnicity status, birth season, urbanity, and pregnancy and perinatal problems[23].

Childhood Trauma and its Effect on the Developing Brain

Severe stress, or ChT, can leave people in susceptible mental states and increase their risk of developing mental health conditions like SCZ. Numerous studies show that ACEs increase the likelihood of psychosis and SCZ development. Higher levels of ChT cause more heightened positive, general, and depressed symptoms as well as worse global functioning in ultra-high-risk (UHR) persons. Individuals at UHR frequently have histories of emotional abuse, physical abuse, emotional neglect, and sexual abuse[24]. Findings were found in a recent South African study investigating the connection between childhood trauma and SCZ. One physical or emotional trauma experience did not significantly correlate with schizophrenia. However, those who experienced more than two of these traumas had a higher chance of developing schizophrenia, indicating that, even in rare cases, physical and emotional childhood adversity does not always raise the risk of schizophrenia. However, the likelihood and intensity of sexual assault increase after just one incident[25].

Relationship between Childhood Trauma and Schizophrenia in Genetic Approach

A gene called FKBP5 is connected to the hypothalamic-pituitary-adrenal (HPA) axis' stress response. Notably, the FKBP5 gene plays a role in the development of SCZ when subjected to acute or prolonged stress. Increased cortisol secretion in ChT-positive schizophrenic patients points to a link between ChT and the dysfunction of the HPA axis in SCZ[26]. In addition to the interaction between genes and environmental factors, specifically ChT, studies have also shown a direct correlation between symptoms of schizophrenia-type disorder (SCZ) and the genetic component brain-derived neurotrophic factor (BDNF) Val66Met polymorphism. A typical observation in SCZ is the loss of volume in brain regions such as the hippocampus. When glucocorticoids are used as a stress inducer in animal models, there is a reduction in hippocampal BDNF levels after both acute and long-term stress. When used in medical treatments, cortisol can exacerbate symptoms. SCZ patients exhibit a flattened reactivity to stress and lower thresholds than controls during and after stress exposure, supporting that SCZ patients have a significant impairment in their stress response. It's interesting to note that teenagers who are very susceptible to SCZ have elevated cortisol levels at rest, which can be attributed to environmental factors such as emotional abuse from family members and a poor self-image[27,28].

Chemical Changes with Childhood Trauma

ChT always exhibits modification on the HPA axis. People who have experienced maltreatment as children have hyperactivity of the axis, which changes dopamine levels, the autonomic nervous system, the shape of the brain, and neural function, all of which raise the risk of developing psychosis. Individuals who experienced childhood hardship showed increased striatal dopamine function, suggesting a link between associative striatum elevation and psychogenic stress, particularly physical and sexual abuse[29]. As previously mentioned, the primary theory about the pathogenesis of SCZ is that dopamine overstimulates the brain's D2 receptors. Research suggests that one important aspect of SCZ is stress sensitization, which lowers the sensitivity threshold in SCZ patients. Stress can trigger the HPA axis, which makes dopamine in the mesolimbic area more sensitive and increases dopamine release in the striatum[30].

Brain Anatomical and Physiological Links to Childhood Trauma

In schizophrenia patients, emotional neglect was inversely correlated with grey matter volume overall and, more especially, with the volume and density of the dorsolateral prefrontal cortex, which was predictive of disorganization. It's interesting to note that in cases of schizophrenia, there have been reports of additive effects of childhood trauma and being a BDNF met carrier on volume reduction in the hippocampal subregions of CA2/3 and CA4/dentate gyrus. Abuse in childhood has been linked to both decreased hippocampus volume and elevated amygdala reactivity[31]. Childhood trauma was linked to activity of the dorsomedial prefrontal cortex, precuneus, and posterior cingulate gyrus in patients with schizophrenia during a theory-of-mind task that mirrored social cognition. Furthermore, patients who experienced significant degrees of physical and/or sexual abuse as children have reduced connections between the amygdala and the posterior cingulate/precuneus region[32].

Conclusions

This review expands on the research that is currently accessible by recognizing the potential for hardship experienced throughout childhood and adolescence to manifest into adulthood. However, a resilience-promoting environment-that is, an environment that integrates interventions to increase a positive outcome, despite adversities, to implement wellbeing-is frequently absent from many mental health services, despite the recovery-oriented approach that is necessary for the management of schizophrenic patients.

In recent times, acknowledging personal life experiences has demonstrated advantageous effects on the treatment of many mental illnesses. The main goal of this study is to highlight how crucial it is to assess patients holistically, taking into account the impact of their past experiences on the emergence of present symptoms. Research points to the brain's neurobiological reactions to trauma as a risk factor for SCZ development. To demonstrate the realistic potential of neurological effect regulation, it will be imperative in further trials to assess the advantages of early trauma detection and the accessibility of early support. Finding a beneficial effect on neurobiology ought to motivate additional primary care physicians to include early trauma screening in child wellbeing visits. In a perfect world, early identification of adversity in individuals would result in the prompt introduction of resources that help address mental and emotional dysregulations; this might be a crucial step in reducing the annual diagnostic rate and severity of schizophrenia in the general population.

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References

1. Jablensky A. Schizophrenia: Recent epidemiologic issues. Epidemiol Rev 1995;17:10-20.
2. Stępnicki P, Kondej M, Kaczor AA. Current concepts and treatments of schizophrenia. Molecules 2018;23(8):2087.
3. Syed AB, Brasic JR. The role of lumateperone in the treatment of schizophrenia. Ther Adv Psychopharmacol 2021;11.
4. Kesby JP, Eyles DW, McGrath JJ, Scott JG. Dopamine, psychosis and schizophrenia: the widening gap between basic and clinical neuroscience. Transl Psychiatry 2018;8:30.
5. Sullivan PF, Kendler KS, Neale MC. Schizophrenia as a complex trait: evidence from a meta-analysis of twin studies. Arch Gen Psychiatry 2003;60(12):1187-1192.
6. Schmitt A, Malchow B, Hasan A. Falkai P. The impact of environmental factors in severe psychiatric disorders. Front Neurosci 2014;8:19.
7. Docherty NM, St-Hilaire A, Aakre JM, Seghers JP. Life events and high-trait reactivity together predict psychotic symptom increases in schizophrenia. Schizophr Bull 2009;35(3):638-645.
8. Bhavsar V, Boydell J, McGuire P, et al. Childhood abuse and psychotic experiences - evidence for mediation by adulthood adverse life events. Epidemiol Psychiatr Sci 2019;28:300-309.
9. Beal SJ, Wingrove T, Mara CA, Lutz N, Noll JG, Greiner MV. Childhood adversity and associated psychosocial function in adolescents with complex trauma. Child Youth Care Forum 2019;48(3):305-322.
10. Devi F, Shahwan S, Teh WL, et al. The prevalence of childhood trauma in psychiatric outpatients. Ann Gen Psychiatry 2019;18:15.
11. Sheffield JM, Karcher NR, Barch DM. Cognitive deficits in psychotic disorders: a lifespan perspective. Neuropsychol Rev 2018;28(4):509-533.
12. Holtzman CW, Trotman HD, Goulding SM, et al. Stress and neurodevelopmental processes in the emergence of psychosis. Neuroscience 2013; 249:172-191.
13. van Winkel R, Stefanis NC, Myin-Germeys I. Psychosocial stress and psychosis.A review of the neurobiological mechanisms and the evidence for gene-stress interaction. Schizophr Bull 2008;34:1095-1105.
14. Marder SR, Cannon TD. Schizophrenia. N Engl J Med 2019;381(18):1753-1761.
15. Robison AJ, Thakkar KN, Diwadkar VA. Cognition and Reward Circuits in Schizophrenia: Synergistic, Not Separate. Biol Psychiatry 2020;87(3):204-214.
16. Lavretsky H. History of Schizophrenia as a Psychiatric Disorder. In: Clinical Handbook of Schizophrenia. New York, Guilford Press 2008;3-12.
17. Dawe GS, Hwang EH, Tan CH. Pathophysiology and animal models of schizophrenia. Ann Acad Med Singapore 2009;38(5):425-426.
18. Owen MJ, Sawa A, Mortensen PB. Schizophrenia. Lancet Lond. Engl ٣٨٨;٢٠١٦:86-97.
19. Merikangas AK, Shelly M, Knighton A, et al. What Genes Are Differentially Expressed in Individuals with Schizophrenia? A Systematic Review. Mol. Psychiatry 2022;27:1373-1383.
20. Radua J, Ramella-Cravaro V, Ioannidis JPA, et al. What Causes Psychosis? An Umbrella Review of Risk and Protective Factors. World Psychiatry 2018;17(1):49-66.
21. Smigielski L, Jagannath V, Rossler W, Waltiza S, Grunblatt E. Epigenetic mechanisms in schizophrenia and other psychotic disorders: A systematic review of empirical human findings. Mol. Psychiatry 2020;25(8):1718-1748.
22. Zeanah CH, Humphreys KL. Child abuse and neglect. J Am Acad Child Adolesc Psychiatry 2018;57:637-644.

23. Pence AY, Pries LK, Ferrara M, et al. Gender Differences in the Association between Environment and Psychosis. Schizophr. Res 2022;243:120-137.

24. Popovic D, Schmitt A, Kaurani L, et al. Childhood trauma in schizophrenia: current findings and research perspectives. Front Neurosci 2019;13:274.

25. Sallis HM, Croft J, Havdahl A, et al. Genetic liability to schizophrenia is associated with exposure to traumatic events in childhood. Psychol Med 2021;51(11):1814-1821.

26. Stramecki F, Misiak B, Frydecka D. The role of the interaction between the fkbp5 gene and stressful life events in the pathophysiology of schizophrenia: A narrative review. Arch Psychiatry Psychother 2020;3:7-16.

27. Bi XJ, Lv XM, Ai XY, et al. Childhood trauma interacted with BDNF Val66Met influence schizophrenic symptoms. Medicine (Baltimore) 2018;97(13):0160.

28. Kauppi K, Westlye LT, Tesli M, et al. Polygenic Risk for Schizophrenia Associated with Working Memory-Related Prefrontal Brain Activation in Patients with Schizophrenia and Healthy Controls. Schizophr Bull 2015;41(3):736-743.

29. Egerton A, Valmaggia LR, Howes OD, et al. Adversity in childhood linked to elevated striatal dopamine function in adulthood. Schizophr Res 2016;176(2):171-176.

30. Gabínio T, Ricci T, Kahn JP, et al. Early trauma, attachment experiences and comorbidities in schizophrenia. Trends Psychiatry Psychothe 2018;40:179-184.

31. Aas M, Haukvik UK, Djurovic S, et al. Interplay between childhood trauma and BDNF val66met variants on blood BDNF mRNA levels and hippocampus subfields volumes in schizophrenia spectrum and bipolar disorders . J Psychiatr Res 2014;59:14-21.

32. Quide Y,Ong XH, Mohnke S, et al. Childhood trauma-related alterations in brain function during a Theory-of-Mind task in schizophrenia. Schizophr Res 2017;189:162-168.