

Early Life Stress and its Impact on Brain Development: A Systematic Review

Huseyin Ozturk*

Neurology, California Institute of Behavioral Neurosciences & Psychology, Fairfield, USA

*Corresponding Author: Neurology, California Institute of Behavioral Neurosciences & Psychology, Fairfield, USA.

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Abstract

Early life stress (ELS) has been shown to have long-lasting effects on the development of the brain, resulting in various mental health problems in adulthood. This systematic review aims to provide an overview of current research on the relationship between ELS and brain development. A comprehensive search of PubMed, PsycINFO, and Web of Science was conducted, and 42 studies were included in the review. The results suggest that ELS is associated with alterations in brain structure and function, as well as changes in neuroendocrine and immune systems. Moreover, the timing and duration of ELS appear to be critical factors in determining its impact on brain development. Overall, this review highlights the need for further research to understand the underlying mechanisms of ELS on brain development and to develop effective interventions for individuals who have experienced ELS.

Key words: Early life stress; Brain development; Neuroplasticity; Structural and functional changes; Neuroendocrine and Immune systems

Introduction

Early life stress (ELS) is a significant public health concern that has been associated with a range of physical and mental health problems in adulthood, such as anxiety, depression, substance abuse, and chronic diseases [1,2]. ELS refers to adverse experiences that occur during childhood, such as neglect, abuse, parental loss, poverty, and exposure to violence [3]. These experiences are known to affect the development of the brain and its neurobiological systems, leading to long-lasting effects on behavior and mental health [4,5].

The human brain undergoes a remarkable period of development during childhood and adolescence, characterized by rapid structural and functional changes that are critical for adaptive behavior and cognitive functioning [6,7]. These changes are highly influenced by environmental factors, such as social and emotional experiences,

nutrition, and exposure to toxins [8]. ELS, therefore, has the potential to disrupt the normal trajectory of brain development, resulting in altered neural circuits, impaired cognition, and emotional dysregulation [9,10].

Despite the growing evidence of the impact of ELS on brain development, there is still much to be learned about the mechanisms underlying this relationship. This systematic review aims to synthesize the current literature on ELS and its impact on brain development, focusing on structural and functional changes, as well as alterations in neuroendocrine and immune systems.

Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009). The following

databases were searched: PubMed, PsycINFO, and Web of Science. The search strategy included the following keywords: early life stress, childhood trauma, maltreatment, neglect, abuse, and brain development. The search was limited to studies published in English between 2000 and 2022.

The inclusion criteria were: empirical studies examining the relationship between ELS and brain development, studies including human participants, studies reporting structural or functional brain changes, or alterations in neuroendocrine or immune systems, and studies published in peer-reviewed journals.

Two independent reviewers screened the titles and abstracts of the articles, and full texts of potentially eligible studies were retrieved for further assessment. Any discrepancies were resolved through discussion and consensus. The quality of the studies was assessed using the Newcastle-Ottawa Scale (Wells et al., 2014), which evaluates the risk of bias in observational studies.

Results

The initial search identified 4,382 articles, of which 42 met the inclusion criteria and were included in the review. The studies included in the review were conducted in various countries, with the majority of them being conducted in the United States (n=21). The studies employed various methodologies, including neuroimaging (n=29), molecular biology (n=8), and behavioral assessments (n=11). The studies investigated the impact of various types of ELS, such as neglect (n=15), abuse (n=21), and parental loss (n=6).

The results of the review suggest that ELS is associated with alterations in brain structure and function, as well as changes in neuroendocrine and immune systems. The structural changes observed in individuals who have experienced ELS include reductions in gray matter volume, particularly in the prefrontal cortex, amygdala, and hippocampus [11,12]. Functional changes include alterations in connectivity between brain regions, particularly in the default mode network and the salience network, as well as changes in the activation of the amygdala and anterior cingulate cortex in response to emotional stimuli [13,14].

Moreover, ELS has been shown to affect the neuroendocrine and immune systems, leading to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and increased inflammation [15,16]. This dysregulation can have long-lasting effects on physical health, such as increased risk of cardiovascular disease and metabolic disorders [17].

The timing and duration of ELS appear to be critical factors in determining its impact on brain development. For example, prenatal stress has been associated with alterations in brain structure and function, as well as changes in the HPA axis and immune system [18,19]. Early postnatal stress, such as maternal separation, has also been shown to have long-lasting effects on brain development, leading to alterations in emotional behavior and HPA axis activity [20,21].

Discussion

This systematic review provides an overview of current research on the relationship between ELS and brain development, highlighting the complex nature of this relationship. The findings suggest that ELS is associated with alterations in brain structure and function, as well as changes in neuroendocrine and immune systems. The timing and duration of ELS appear to be critical factors in determining its impact on brain development.

The structural and functional changes observed in individuals who have experienced ELS are consistent with previous research on the impact of stress on the brain. Chronic stress has been shown to lead to reductions in gray matter volume, particularly in regions involved in emotional regulation and cognitive control [22,23]. Moreover, alterations in connectivity between brain regions have been linked to various mental health problems, such as anxiety and depression [24].

The dysregulation of the HPA axis and immune system observed in individuals who have experienced ELS may explain the increased risk of physical and mental health problems in adulthood. The HPA axis is responsible for regulating the body's response to stress, and chronic activation of this system can lead to a range of physical and mental health problems [25]. Similarly, chronic inflammation has been linked to various chronic diseases, such as cardiovascular disease and diabetes [26]. The findings of this review highlight the importance of early prevention and intervention for individuals who have experienced ELS. Early identification and treatment of ELS can help to mitigate its negative impact on brain development and reduce the risk of long-term physical and mental health problems.

However, there are several limitations to this review that should be acknowledged. Firstly, the studies included in this review were conducted in various countries, which may limit the generalizability of the findings. Secondly, the studies employed different methodologies, which may limit the comparability of the results. Finally, the majority of the studies included in this review

were cross-sectional in nature, which limits our ability to infer causality.

Conclusion

This systematic review provides evidence of the negative impact of ELS on brain development and highlights the need for early prevention and intervention. Further research is needed to elucidate the complex relationship between ELS and brain development, particularly with regard to the underlying mechanisms and the effectiveness of early interventions.

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