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Adverse childhood experiences and migraine chronification: neurobiological mechanisms and clinical impact - a systematic review

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Introduction
Migraine is a highly prevalent and disabling neurological disorder associated with reduced quality of life. In recent years, adverse childhood experiences have been increasingly associated with the development of chronic pain conditions, including migraine, possibly through mechanisms involving central sensitization, neuroinflammation, and dysregulation of the stress response.

Objective
To analyze the impact of early-life trauma on the neurobiological vulnerability and clinical severity of migraine, considering its relationship with mechanisms of central sensitization and pain chronification.

Methods
This is a systematic review conducted using the PubMed, SciELO and LILACS databases, based on the PICO strategy, considering: population (patients with migraine), exposure (adverse childhood experiences), and outcome (development and chronification of migraine). The descriptors "migraine" AND "childhood trauma" OR "childhood adversity" were used. Initially, 37 articles were identified. After applying a 10-year publication filter and including only studies containing the descriptors in the title, 13 studies remained and were included in the final analysis.

Results
A higher prevalence of childhood trauma was observed among patients with chronic and refractory migraine, particularly in individuals with a history of emotional abuse, neglect, and early exposure to stress. In a Canadian cohort study involving adolescents, adverse childhood experiences were associated with a higher incidence of migraine during follow-up, as well as significant associations with anxiety and depressive symptoms. Another analysis found that patients with refractory chronic migraine had a significantly higher frequency of traumatic experiences compared to those with episodic migraine. Experimental models demonstrated that early-life stress induced hyperexcitability of brain networks, increased neuroinflammatory markers in the dura mater, and greater susceptibility to migraine-like behaviors. Furthermore, studies highlighted the possible involvement of central sensitization and hypothalamic-pituitary-adrenal axis dysregulation in the perpetuation of migraine attacks. Additionally, psychological factors such as insecure attachment, dissociation, anxiety, and depression acted as important mediators between childhood trauma and greater migraine severity, reinforcing the multifactorial nature of the disease.

Conclusion
Adverse childhood experiences were strongly associated with increased vulnerability to migraine chronification and greater clinical severity. Moreover, the presence of psychiatric comorbidities and therapeutic refractoriness in patients exposed to early trauma reinforces the need for a multidimensional approach to migraine management, with more individualized therapeutic strategies aimed at reducing pain chronification

Keywords:
Migraine
Central sensitization
Childhood trauma

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