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The common pathophysiology between migraine and cluster headache: a literature update

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Introduction

In accordance with the International Classification of Headache Disorders, migraine and cluster headache are two primary headaches that are distinguished clinically but share common pathophysiological mechanisms. These mechanisms are important for the pharmacological treatment of these disorders, including triptans and anti-CGRP monoclonal antibodies.

Objective

To investigate and update literature data on potential similar mechanisms involved in the pathology, structure, and neural physiology of migraine and cluster headache.

Method

The established inclusion criteria included articles published from 2016 to 2023, using the DeCS/MeSH descriptors "cluster headache," "migraine," and "pathophysiology." These terms were combined using the Boolean operator "AND" for searching the PubMed database. Following these criteria, eight articles were selected from a total of sixty-four results and subsequently analyzed for the purpose of this review.

Results

While the exact mechanisms underlying migraine and cluster headache are not yet fully understood, there are clear pathophysiological links between these two disorders involving the Trigeminovascular System (TVS), in which three key structures interact with cortical areas as well: the trigeminocervical complex, trigeminal autonomic reflex, and the hypothalamus. In the trigeminocervical complex, nociceptive fibers originating from the trigeminal ganglion and intracranial blood vessels in the meninges and cerebral arteries project signals to the Trigeminal Cervical Complex (TCC). These projections terminate on the neurons of the trigeminal brainstem nuclear complex, transmitting somatosensory information to the thalamus and hypothalamus.

These structures then reach cortical areas involved in pain processing. The trigeminal autonomic reflex is the connection between the trigeminal caudal nucleus and the superior salivatory nucleus, constituting a parasympathetic vasodilator pathway. Neurons from the superior salivatory nucleus project to cranial blood vessels, including the dura mater, directly contributing to the cranial autonomic symptoms found in cluster headache and up to 50% of migraine patients. Activation of this pathway induces dilation of intracranial vessels and a cascade of events that results in plasma protein extravasation, release of neuropeptides, and activation and sensitization of the trigeminal vascular system. Regarding the hypothalamus, specifically the paraventricular and lateral nuclei, it has significant connections in pain regulation in migraines and cluster headaches. This is evident through MRI studies that have shown increased gray matter volume in the hypothalamus during headache periods in cluster headache and migraine patients. Deep brain stimulation of the posterior hypothalamus has been used to treat refractory cluster headaches, with positive outcomes in about 60% of patients.

Conclusion

Understanding new conceptions about the physiopathological relationships between migraine and cluster headache is of fundamental importance for patient management by physicians and for the development of therapeutic mechanisms that provide a better quality of life for individuals suffering from these disorders.

Keywords: pathophysiology; cluster; migraine; update.