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Editorial

The choroid plexus and its role in headaches

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In recent years, the choroid plexus (ChP) and its role in cerebrospinal fluid (CSF) production and regulation of intracranial pressure have garnered significant attention from researchers investigating the mechanisms underlying headaches (1,2). Studies on the morphology and physiology of ChP and its relationship with intracranial pressure are crucial for understanding and treating headaches associated with CSF flow alterations (2–6).

This edition highlights the ChP through a featured short communication presenting morphology views from a cadaver specimen and detailed electron microscopy anatomical visuals. These images provide unique insights into its morphology, role in CSF dynamics, and potential involvement in headache pathophysiology, setting the stage for further exploration of this vital yet underexplored structure.

The International Headache Society (IHS) classifies headaches into approximately 200 types and subtypes, divided into three major groups: primary headaches, secondary headaches, and cranial neuralgias (7). The ICHD-3 provides detailed classifications for headaches associated with intracranial pressure disorders, offering clear diagnostic criteria for idiopathic intracranial hypertension, secondary intracranial hypertension, cerebrospinal fluid hypotension, and other conditions that affect intracranial pressure. Among these, several headaches are closely linked to ChP and its role in CSF production (5,7–9).

Pharmacological treatments for headaches often work by reducing CSF production, thereby decreasing intracranial pressure and relieving symptoms (4,10). Conversely, headaches can arise from excessive accumulation of CSF, leading to increased intracranial pressure, or from abnormally low CSF volume within the cranial cavity, underscoring the complex relationship between CSF dynamics and headache pathophysiology (3,11). Medications such as acetazolamide and topiramate, non-pharmacological interventions like weight loss, and surgical procedures such as shunts and venous stenting are key approaches in severe cases. Additionally, emerging therapies target molecular pathways in ChP and investigate the role of hormones in CSF regulation (6,12).

Under normal conditions, an adult human produces approximately 450 mL of CSF daily. This fluid is essential for maintaining intracranial homeostasis, cushioning the brain, and protecting it from mechanical damage (11). However, disruptions in CSF production or absorption, often associated with ChP, can result in conditions such as idiopathic intracranial hypertension, spontaneous intracranial hypotension, and other CSF-related disorders, many of which present headache as a primary symptom.

Morphology of the choroid plexus

Despite its critical role in CSF production, relatively little has been published about the detailed morphology of the human choroid plexus. This structure resides within the ventricular system, occupying the lateral, third, and fourth ventricles of the brain. It comprises a network of blood vessels enveloped by a specialized epithelial layer that actively secretes CSF, playing a key role in intracranial homeostasis.

In 2023, we presented electron microscopy images of the ChP at the Brazilian Headache Congress in Santos (13). These images, derived from an adult cadaver specimen, revealed intricate details of its microstructure, including villi, microvilli, and cilia. Such visualizations contribute to a deeper understanding

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of the choroid plexus's morphology and its potential involvement in various neurological disorders, including headaches. However, the microstructure, function, and pathological variations of this vital organ remain areas ripe for further exploration, underscoring the need for continued research into its role in health and disease.

To further illustrate these findings, this edition features an image article presenting the choroid plexus through two complementary perspectives: an anatomical view from a cadaver specimen and detailed electron microscopy visuals highlighting its morphology and intricate microstructures, providing a deeper understanding of its potential pathological variations.

The role of CSF in brain support

The CSF, primarily produced by the choroid plexus, is critical in cushioning the brain and protecting it from mechanical trauma during everyday movements such as running, jumping, or sudden head turns (11). Without this protective layer, the gelatinous brain tissue would risk colliding with rigid intracranial surfaces, resulting in damage. A significant reduction or absence of CSF, as seen in conditions like spontaneous intracranial hypotension, often leads to orthostatic headaches, where pain worsens when the individual is upright and is alleviated when lying down.

Conversely, excessive CSF accumulation, as occurs in hydrocephalus or idiopathic intracranial hypertension, leads to increased intracranial pressure, causing diffuse, pressure-like headaches. The intricate balance of CSF production, circulation, and absorption, regulated in large part by ChP, is therefore crucial for maintaining neurological function and preventing headache disorders (1,10,11).

Future directions

The ChP remains an underexplored tissue, with many unanswered questions regarding its role in health and disease. Its contribution to CSF dynamics and potential involvement in headache disorders represents an exciting frontier for future research. Advances in imaging techniques, molecular biology, and neuropathology hold promise for unraveling the ChP's intricate structure and function.

With growing interest in CSF-related headaches, further studies are essential to clarify how alterations in the structure and morphology of the ChP, as well as CSF production, contribute to headache pathophysiology. This knowledge could pave the way for targeted therapies that modulate CSF dynamics, providing new treatment options for patients with refractory headaches.

By bridging the gap between basic science and clinical practice, translational research has the potential to unlock the ChP role as both a diagnostic and therapeutic target in headache medicine. This is just the beginning of a promising journey, with future discoveries to deepen our understanding of the intricate relationships between the brain, CSF, and headache disorders.

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