Global Year Against HEADACHE
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Vascular Changes in Migraine

Vascular Hypothesis of Migraine

A causative role for vasodilatation in migraine pain has been a subject of intense debate for centuries. In the second century, Galen suggested that the throbbing pain during headache originated from blood vessels. In the Middle Ages, Avicenna suggested that head pain may originate from the bone of the skull, from the membrane underneath it, or from substances reaching the site of the headache via the blood vessels. In 1672, Thomas Wills proposed the first vascular theory of migraine and suggested that “megrim” was due to dilatation of blood vessels within the head.

First Human Experiments

More than 70 years ago, Graham and Wolff provided the first observations in humans demonstrating that focal head pain may be elicited from both extra- and intracranial vessels. In 1940, Ray and Wolff reported that stimulation or distension of the large cranial arteries and dural arteries evoked head pain associated with feelings of nausea or sickness. However, the similarity between referred pain locations following stimulation of large cerebral arteries and headache patterns in migraine provides the strongest support for the involvement of perivascular nociceptors in migraine pain.

Spontaneous Migraine Attacks

Experimental studies during spontaneous migraine attacks have reported that:

- The middle cerebral artery (MCA), one of the three major paired arteries that supplies blood to the brain, is dilated on the headache side compared to the nonheadache side.
- MCA dilation is reversible by treatment with the antimigraine drug sumatriptan.
- The superficial temporal artery (STA), a major artery of the head, is dilated on the headache side.

Provoked Migraine Attacks

Migraine attacks can be provoked by various pharmacological substances, including glyceryl trinitrate (GTN) and calcitonin-gene-related peptide (CGRP). Vascular changes have been studied during provoked migraine attacks by employing modern technology such as a high-resolution magnetic resonance imaging angiography. These studies have reported that:

- GTN-provoked migraine attacks are *not* associated with dilation of cranial arteries.
- CGRP-provoked migraine attacks are associated with dilation of both the middle meningeal artery (MMA), a major artery that supplies blood to a membrane (dura) that envelops the brain, and the MCA.
- CGRP-provoked one-sided migraine headache is associated with dilation on the headache side.
- CGRP-provoked double-sided migraine headache is associated with dilation on both sides.
- Administration of the antimigraine drug sumatriptan during CGRP-provoked migraine attacks results in MMA contraction and amelioration of the headache, while the MCA is left unchanged.

Is Dilation Sufficient to Activate Pain Fibers and Cause Migraine Pain?

Arteries may dilate markedly, such as during decreases in blood pressure, and heart rate may increase during physical exercise without accompanying head pain. Therefore, dilation alone cannot explain migraine pain. Experiments in humans suggest that deep brain structures are activated during migraine attacks. Experiments in animals suggest that pain-sensitive nerve fibers can be activated by leakage of sensitizing vasoactive substances from trigeminal nerve terminals or by efferent activity in parasympathetic nerves. Based on these studies, it is plausible to suggest that migraine attacks are evoked in deep brain structures and that these initiating mechanisms trigger the release of vasoactive substances around brain vessels, causing sensitization of trigeminal afferents, vasodilatation, and migraine pain.

References

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