

Multi-Mechanism of Migraine: Implications for Migraine Therapy Fact Sheet

Until recently, most clinicians believed that migraine was simply a vascular condition, induced by blood vessel dilation. Today, new insight suggests that the pathophysiology of migraine is much more complex. It is now thought that multiple mechanisms contribute to the onset of migraine, beginning long before a person feels any headache pain.

The multi-mechanistic approach to migraines holds that headache pain results from a chain of events that are both vascular *and* neurological. Migraine pain is induced not only by the widening of blood vessels, or vasodilation, but begins with inflammation, leading to pain reception, or nociception, and central and peripheral sensitization.

The Multi-Mechanistic Action of Migraine:

- ❖ **Inflammation** involves prostaglandins (hormone-like substances) and neuropeptides (molecules formed by the linking of amino acids) that result in vasodilation.
- ❖ **Vasodilation**, or widening of the blood vessels, activates pain receptors surrounding the brain called nociceptors.
- ❖ **Nociceptors**, or pain receptors, transmit pain signals to the higher centers of the brain, including the thalamus and cerebral cortex, *creating the first sensation of pain*
- ❖ **Peripheral sensitization**, resulting from activation of the nociceptors, leads to increased stimulation of the nerve cells in the trigeminal nerve. This prolonged stimulation of the main sensory nerve (trigeminal nerve) results in **central sensitization**.

This new understanding of the multi-mechanisms of migraines also explains why migraine sufferers may experience a variety of non-traditional migraine symptoms in addition to head pain and nausea or vomiting and sensitivity to light and sound. For example, stimulation of the trigeminal nerve may cause referral of pain to any of the nerve's three branches, resulting in sinus or facial pain. It can also cause a referral of pain to the sensory nerves of the posterior head and neck, resulting in neck pain.

Implications for Migraine Therapy

Current migraine-specific therapies do not fully address the multiple components of migraine pain – the inflammation, vasodilation, nociception, and peripheral and central sensitization.

Triptans treat migraines by preventing the release of inflammatory substances and pain transmitting signals. However, they do not address the inflammation, which has occurred long before a person feels pain and takes their medication, nor do they reverse central sensitization.

General pain relievers, like non-steroidal anti-inflammatory drugs (NSAIDs), do not target all of the known pain processes that occur during migraine.

There is a medical need for treatment that addresses multiple mechanisms of migraine.