

Search for this author in: Google Scholar
Diana Carolina Esguerra Sánchez 1
María Virginia Pinzón Fernández 2
Luisa Fernanda Zúñiga-Cerón 3
Luisa Fernanda Mahecha Virgüez 4
Diana Lorena Cepeda Riascos 5
Jhan Sebastián Saavedra-Torres 6

INFORMATION CIRCULAR: Updates in Migraine.

About the authors:
1- Medical- Medical Cooperative University of Colombia, Faculty of Medicine, Health Research Group (GIS) - Popayán - Colombia.
2- Bacteriology, Esp. Education, Master's Degree in Public Health, PhD candidate in Medical Anthropology, Full Professor at Universidad del Cauca.
3- Student of medicine – Universidad Nacional de Colombia, Faculty of Medicine, Laboratory of the Field Corporation (DLC), Health Research Group (GIS) - Popayán - Colombia.
4- Nurse, Universidad del Cauca, Faculty of Health Sciences, Department of Nursing, Health Research Group (GIS) - Popayán - Colombia.
5- Medical, Pontificia Universidad Javeriana (Cali), Health Research Group (GIS) of the University of Cauca, Popayán - Colombia.
6 - Student of medicine - Universidad del Cauca, Faculty of Health Sciences, Department of Internal Medicine, Corporación del Laboratorio al Campo (DLC), Health Research Group (GIS) - Popayán - Colombia.

Updates in Migraine: Department of Physiological Sciences

The International Headache Society defines migraine as a recurrent primary headache disorder resulting in attacks that last 4-72 hours.

Migraine is a common, disabling neurological disorder characterized by multiple phases: premonitory, aura, headache, postdrome, and interictal (1-5).

Migraine is a common disabling primary headache disorder. Many epidemiological studies have documented its high prevalence and socio-economic and personal impacts. In the Global Burden of Disease Study 2010 (GBD2010), it was ranked as the third most prevalent disorder in the world. In the Global Burden of Disease Study 2015 (GBD2015), it was ranked third–highest cause of disability worldwide in both males and females under the age of 50 years (1-5).

Approximately one-third of migraine attacks are preceded by aura.

Migraine without aura is a clinical syndrome characterized by headache with specific features and associated symptoms. In approximately one-third of individuals with migraine, some attacks are associated with an aura phase, comprised of visual, sensory, and language or brainstem disturbances (1-5).

Migraine with aura is primarily characterized by the transient focal neurological symptoms that usually precede or sometimes accompany the headache. Some patients also experience a prodromal phase, occurring hours or days before the headache, and / or a postdromal phase following headache resolution. Prodromal and postdromal symptoms include hyperactivity, hypoactivity, and depression, cravings for particular foods, repetitive yawning, fatigue and neck stiffness and/or pain (1-5).

The disorder may be categorized according to the frequency of attacks; episodic migraine is defined as headache occurring on 1-14 days per month, whereas chronic migraine is diagnosed in those who experience headache on ≥15 days per month, at least 8 days of which fulfill criteria for migraine with or without aura (5-8).

One proposal is that migraine triggers, such as stress, awakening, or other changes in physiological or emotional homeostasis, activate nociceptive pathways through increased parasympathetic tone (8-10)

Other pathways may also play a role in the provocation of migraine by stress. Sympathetic outflow into the meninges involving norepinephrine release has been shown in preclinical models to contribute to pronociceptive signaling through actions on dural afferents and dural fibroblasts (6-10)

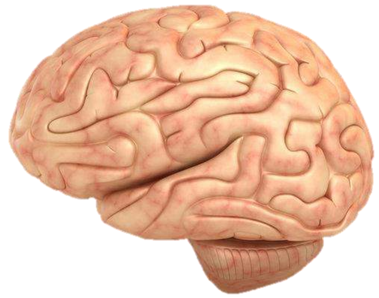
The characteristic throbbing pain of migraine headache is widely accepted to be the result of trigeminovascular pathway activation (11).

The trigeminovascular pathway conveys nociceptive information from the meninges to the central areas of the brain, and subsequently to the cortex. Nociceptive fibers originating from the trigeminal ganglion innervate the meninges and large cerebral arteries (11,12)

Consult reports : https://www.ichd-3.org/1-migraine/

Conflicts of interests
None stated by the authors
Financing
None stated by the authors.

Updates in Migraine



The activation of migraine pain begins peripherally when nociceptive neurons that innervate the dura mater are stimulated and release vasoactive neuropeptides such as calcitonin gene-related peptide (CGRP) and pituitary adenylate cyclase-activating polypeptide-38, causing signaling along the trigeminovascular pathway – the extent to which arterial vasodilatation, mast cell degranulation and plasma extravasation are involved remains unclear (11).

In a prospective study of the time course of aura and headache symptoms, it was found that many patients reported migraine symptoms such as nausea (51%), photophobia (88%), phonophobia (73%), and headache (73%) during the aura phase, and 11% reported the headache as starting simultaneously with the aura (14).

Neurophysiological studies have shown that the migraine brain is characterized by general neuronal hyperexcitability. Evoked and event-related potential studies have shown increased excitability in patients with migraine in response to a wide range of stimuli including visual, somatosensory, and auditory, as well as brainstem reflexes in response to nociceptive stimuli (15).

The first genetic association with migraine to be identified was familial hemiplegic migraine (FHM), a rare form of migraine that is inherited in an autosomal dominant pattern. Se caracteriza por ataques de migraña acompañados de una debilidad motora unilateral transitoria (16).

The genes identified for FHM all encode for proteins that ultimately modulate the availability of glutamate at synaptic terminals, thus increasing neuronal excitability (16).

Most people with migraine have never used acute prescription medications for migraine attacks

While there have been significant advances in our knowledge of the complex mechanisms involved in migraine pathophysiology, there remains an unmet need for more effective treatments for the disease.

While many aspects of migraine pathophysiology remain unclear, a great deal of research has been conducted over recent years to increase our understanding of the complex processes involved in all stages of the migraine attack, which has subsequently informed the identification of therapeutic targets.

An interesting study that will be presented at the AHS meeting relates to the problem of undertreatment of acute migraine. As background, the pathophysiology of migraine is associated with activation of the trigeminovascular system and neuropeptide release, including- the calcitonin gene-related peptide (CGRP).

As with acute therapies, little overall change has occurred in migraine preventive therapy since 2012. Beta blockers, tricyclic antidepressants, anticonvulsants including topiramate and divalproex sodium, onabotulinum toxin A (for chronic migraine), and flunarizine (outside the USA) continue to be standard therapies for migraine prevention (17).

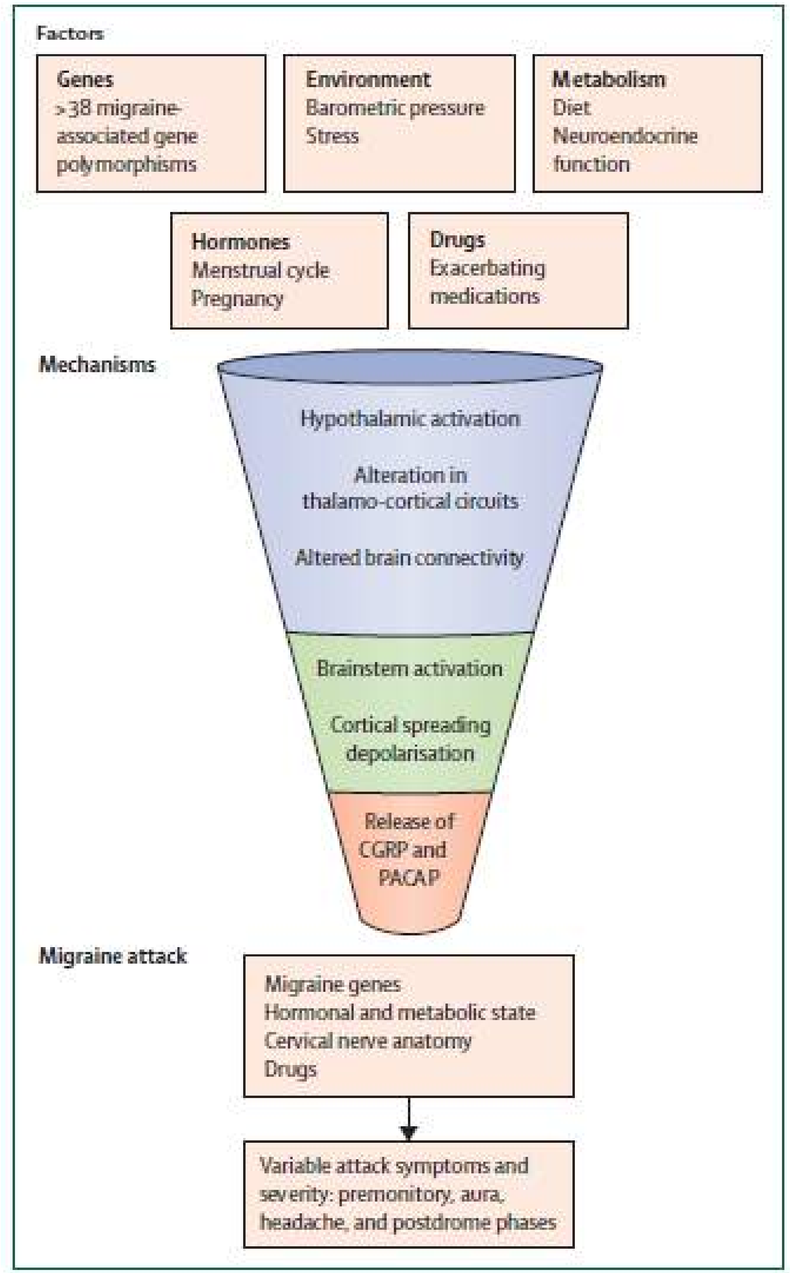
Recommended Reading: A Phase-by-Phase Review of Migraine Pathophysiology. https://doi.org/10.1111/head.13300

Conflicts of interests
None stated by the authors
Financing
None stated by the authors.



INFORMATION CIRCULAR: Updates in Migraine.

Contributing factors and mechanisms of a migraine attack: A wide range of factors can contribute to the initiation of an attack, with variable mechanisms leading to a migraine attack. The clinical features of a migraine attack then diverge on the basis of genetic, anatomical, and other factors. CGRP=calcitonin gene-related peptide. PACAP=pituitary adenylate cyclase-activating polypeptide (17).



The pathophysiology of migraine: implications for clinical management : Lancet Neurol 2018; 17: 174–82

World Health Organization → **Headache disorders**

https://www.who.int/news-room/fact-sheets/detail/headache-disorders

- Migraine most often begins at puberty and most affects those aged between 35 and 45 years.
- It is more common in women, usually by a factor of about 2:1, because of hormonal influences.
- It is caused by the activation of a mechanism deep in the brain that leads to release of pain-producing inflammatory substances around the nerves and blood vessels of the head.
- Migraine is recurrent, often life-long, and characterized by recurring attacks.

Yet, many of those troubled by headache do not receive effective care. For example, in the United States of America and the United Kingdom, only half of those identified with migraine had seen a doctor for headache-related reasons in the previous 12 months, and only two-thirds had been correctly diagnosed. Most were solely reliant on over-the- counter medications.

Search for this author in: Google Scholar
Diana Carolina Esguerra Sánchez 1
María Virginia Pinzón Fernández 2
Luisa Fernanda Zúñiga-Cerón 3
Luisa Fernanda Mahecha Virgüez 4
Diana Lorena Cepeda Riascos 5
Jhan Sebastián Saavedra-Torres 6

INFORMATION CIRCULAR: Updates in Migraine.

REFERENCES

1. Stovner L, Hagen K, Jensen R, et al. The global burden of headache: A documentation of headache prevalence and disability worldwide. *Cephalalgia.* 2007;27:193-210.
2. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition (beta version). *Cephalalgia.*2013;33:629-808.
3. Russo AF. Calcitonin gene-related peptide (CGRP): A new target for migraine. *Annu Rev Pharmacol Toxicol.* 2015;55:533-552.
4. Goadsby PJ, Holland PR, Martins-Oliveira M, Hoffmann J, Schankin C, Akerman S. Pathophysiology of migraine: A disorder of sensory processing. *Physiol Rev.* 2017;97:553-622.
5. Burstein R, Jakubowski M. Unitary hypothesis for multiple triggers of the pain and strain of migraine. *J Comp Neurol.* 2005;493:9-14.
6. Katsarava Z, Manack A, Yoon MS, et al. Chronic migraine: Classification and comparisons. *Cephalalgia.* 2011;31:520-529.
7. Burstein R, Noseda R, Borsook D. Migraine: Multiple processes, complex pathophysiology. *J Neurosci.* 2015;35:6619-6629.
8. Wei X, Yan J, Tillu D, et al. Meningeal norepinephrine produces headache behaviors in rats via actions both on dural afferents and fibroblasts. *Cephalalgia.* 2015;35:1054-1064.
9. Noseda R, Burstein R. Migraine pathophysiology: Anatomy of the trigeminovascular pathway and associated neurological symptoms, CSD, sensitization and modulation of pain. *Pain.* 2013;154: S44-S53.
10. Nakamura-Craig M, Gill BK. Effect of neurokinin A, substance P and calcitonin gene related peptide in peripheral hyperalgesia in the rat paw. Neurosci Lett. 1991;124:49-51.
11. Amin FM, Hougaard A, Schytz HW, et al. Investigation of the pathophysiological mechanisms of migraine attacks induced by pituitary adenylate cyclase-activating polypeptide-38. Brain. 2014;137:779-794.
12. Charles A, Hansen JM. Migraine aura: New ideas about cause, classification, and clinical significance. Curr Opin Neurol. 2015;28:255-260.
13. Bigal ME, Lipton RB. Clinical course in migraine: Conceptualizing migraine transformation. Neurology. 2008;71:848-855.
14. Hansen JM, Lipton RB, Dodick DW, et al. Migraine headache is present in the aura phase: A prospective study. Neurology. 2012;79:2044-2049.
15. Magis D, Lisicki M, Coppola G.Highlights in migraine electrophysiology: Are controversies just reflecting disease heterogeneity? Curr Opin Neurol.2016;29:320-330.
16. Ferrari MD, Klever RR, Terwindt GM,Ayata C, van den Maagdenberg AM.Migraine pathophysiology: Lessons from mouse models and human genetics. Lancet Neurol. 2015;14:65-80.
17. Andrew Charles; Headache 2- The pathophysiology of migraine: implications for clinical management : Lancet Neurol 2018; 17: 174–82

Conflicts of interests
None stated by the authors
Financing
None stated by the authors.