

2005 Jul;49(1):65-76.

doi: 10.1016/j.brainresrev.2004.11.006.

The role of mast cells in migraine pathophysiology

[Theoharis C Theoharides](#) ¹, [Jill Donelan](#), [Kristiana Kandere-Grzybowska](#), [Aphrodite Konstantinidou](#)

Affiliations

- PMID: **15960987**
- DOI: [10.1016/j.brainresrev.2004.11.006](https://doi.org/10.1016/j.brainresrev.2004.11.006)

Abstract

Mast cells are critical players in allergic reactions, but they have also been shown to be important in immunity and recently also in inflammatory diseases, especially asthma. Migraines are episodic, typically unilateral, throbbing headaches that occur more frequently in patients with allergy and asthma implying involvement of meningeal and/or brain mast cells. These mast cells are located perivascularly, in close association with neurons especially in the dura, where they can be activated following trigeminal nerve, as well as cervical or sphenopalatine ganglion stimulation. Neuropeptides such as calcitonin gene-related peptide (CGRP), hemokinin A, neurotensin (NT), pituitary adenylate cyclase activating peptide (PACAP), and substance P (SP) activate mast cells leading to secretion of vasoactive, pro-inflammatory, and neurosensitizing mediators, thereby contributing to migraine pathogenesis. Brain mast cells can also secrete pro-inflammatory and vasodilatory molecules such as interleukin-6 (IL-6) and vascular endothelial growth factor (VEGF), selectively in response to corticotropin-releasing hormone (CRH), a mediator of stress which is known to precipitate or exacerbate migraines. A better understanding of brain mast cell activation in migraines would be useful and could lead to several points of prophylactic intervention.

Similar articles

- [Stress-induced intracranial mast cell degranulation: a corticotropin-releasing hormone-mediated effect.](#) Theoharides TC, Spanos C, Pang X, Alferes L, Ligris K, Letourneau R, Rozniecki JJ, Webster E, Chrousos GP. *Endocrinology*. 1995 Dec;136(12):5745-50. doi: 10.1210/endo.136.12.7588332. PMID: 7588332
- [Neuroendocrinology of mast cells: Challenges and controversies.](#) Theoharides TC. *Exp Dermatol*. 2017 Sep;26(9):751-759. doi: 10.1111/exd.13288. Epub 2017 Apr 2. PMID: 28094875 Review.
- [PACAP-38 infusion causes sustained vasodilation of the middle meningeal artery in the rat: possible involvement of mast cells.](#) Bhatt DK, Gupta S, Olesen J, Jansen-Olesen I. *Cephalalgia*. 2014 Oct;34(11):877-86. doi: 10.1177/0333102414523846. Epub 2014 Feb

21. PMID: 24563332

- [Morphological and functional demonstration of rat dura mater mast cell-neuron interactions in vitro and in vivo.](#) Rozniecki JJ, Dimitriadou V, Lambracht-Hall M, Pang X, Theoharides TC. Brain Res. 1999 Dec 4;849(1-2):1-15. doi: 10.1016/s0006-8993(99)01855-7. PMID: 10592282
- [Mast cell involvement in the pathophysiology of migraine headache: A hypothesis.](#) Levy D, Burstein R, Strassman AM. Headache. 2006 Jun;46 Suppl 1:S13-8. doi: 10.1111/j.1526-4610.2006.00485.x. PMID: 16927959 Review.

[See all similar articles](#)

Cited by 70 articles

- [Headache as a Cardinal Symptom of Coronavirus Disease 2019: A Cross-Sectional Study.](#) Membrilla JA, de Lorenzo Í, Sastre M, Díaz de Terán J. Headache. 2020 Nov;60(10):2176-2191. doi: 10.1111/head.13967. Epub 2020 Sep 28. PMID: 32989732 Free PMC article.
- [Autism and Migraine: An Unexplored Association?](#) Vetri L. Brain Sci. 2020 Sep 6;10(9):615. doi: 10.3390/brainsci10090615. PMID: 32899972 Free PMC article. Review.
- [RAR-related orphan receptor A: One gene with multiple functions related to migraine.](#) Farahani S, Solgi L, Bayat S, Abedin Do A, Zare-Karizi S, Safarpour Lima B, Mirfakhraie R. CNS Neurosci Ther. 2020 Dec;26(12):1315-1321. doi: 10.1111/cns.13453. Epub 2020 Sep 5. PMID: 32892507 Free PMC article.
- [Mast cell-mediated neuroinflammation may have a role in attention deficit hyperactivity disorder \(Review\).](#) Song Y, Lu M, Yuan H, Chen T, Han X. Exp Ther Med. 2020 Aug;20(2):714-726. doi: 10.3892/etm.2020.8789. Epub 2020 May 25. PMID: 32742317 Free PMC article. Review.
- [Investigation of sumatriptan and ketorolac trometamol in the human experimental model of headache.](#) Ghanizada H, Al-Karagholi MA, Arngrim N, Mørch-Rasmussen M, Metcalf-Clausen M, Larsson HBW, Amin FM, Ashina M. J Headache Pain. 2020 Feb 24;21(1):19. doi: 10.1186/s10194-020-01089-3. PMID: 32093617 Free PMC article. Clinical Trial.

[See all "Cited by" articles](#)