

# Experimental human model of migraine found redundant molecular pathways mediating migraine attacks

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Credit: Sasha Wolff/Wikipedia

A recent study published in the journal *Cephalalgia*, the official journal of the International Headache Society, reported an intriguing discovery. The study, entitled "Investigation of distinct molecular pathways in migraine induction using calcitonin gene-related peptide and sildenafil", was conducted by Dr. Samaira Younis and colleagues from the Danish Headache Center, Rigshospitalet Glostrup, University of Copenhagen, Denmark.

Previous clinical studies from the same research group using experimental human models have shown that at least two cellular signaling pathways are involved in [migraine attacks](#). One is mediated by increases in [cyclic adenosine monophosphate](#) (cAMP), which can be stimulated by infusing calcitonin gene-related peptide (CGRP) intravenously in patients, and the other one, the cyclic guanosine monophosphate (cGMP), which is upregulated under the actions of the inhibitor of phosphodiesterase-5 [sildenafil](#). The research question in this study was whether activation of these 2 different signaling pathways would yield distinct [migraine](#) attacks with regard their clinical characteristics.

Dr. Younis investigated the clinical characteristics of migraine attacks of 27 participants following intravenous injections of CGRP and oral administration of sildenafil. Attacks' pain localization and quality, as well as related symptoms such photophobia, phonophobia, nausea, aggravation by exertion, and triggers associated were compared between conditions in a double-blind, randomized, cross over design. Participants received both CRRP and sildenafil in two different days, separated by approximately 14 day in order to avoid drugs carry-over effect.

CGRP and sildenafil provoked migraine attacks in 67% and 89% of patients, respectively. In 63% of participants, both drugs provoked migraine attacks. There were no differences in the clinical characteristics of attacks, meaning that both drugs act through a

redundant molecular pathway. The finding concerning a more effective action of sildenafil in provoking migraine attacks "might be attributed to its more downstream effects, thus being closer to the common determinant compared to CGRP in the migraine initiating cascade", Dr. Younis explains. Additionally, The findings of this study will help researchers to search for "commonality of migraine attack initiation as it could prove a prospective cellular target for new preventive therapeutics", Dr. Younis concludes.

**More information:** Samaira Younis et al, Investigation of distinct molecular pathways in migraine induction using calcitonin gene-related peptide and sildenafil, *Cephalalgia* (2019). [DOI: 10.1177/0333102419882474](https://doi.org/10.1177/0333102419882474)

Provided by International Headache Society

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