

# Scientists identify two new genes involved in hemiplegic migraine

March 2 2023

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QUT and Dutch scientists have identified two new genes involved in hemiplegic migraine, a rare, debilitating subtype of migraine that causes weakness along one side of the body during the aura phase.

Distinguished Professor Lyn Griffiths, Director of the QUT Center for Genomics and Personalized Health, and scientists from Leiden University in the Netherlands, used genome sequencing methods to implicate a role for the two genes and published their findings in *Molecular Neurobiology*.

"Hemiplegic [migraine](#) (HM) is a severe subtype of migraine, usually inherited dominantly in families, where people experience significant weakness or paralysis on one side of their body, along with other serious migraine symptoms," Professor Griffiths said.

"Using [genome](#) sequencing methods, we implicated two genes, CACNA1H and CACNA1I, which are ion channel genes involved in controlling calcium levels in the brain and potentially affecting neurotransmitter release.

"Research suggests that HM, may be regarded as a complex disorder with multiple [genetic factors](#). Already there are three known causally implicated genes for familial hemiplegic migraine.

"It has also been hypothesized that a complex disorder can be the result of an accumulation of genetic variants in a disease pathway, where the crossing of a certain threshold leads to disease."

Professor Griffiths said current evidence indicated that complex traits were likely to be underpinned by a combination of both common and rare variants.

"Our study found that hemiplegic migraine was associated with an increased burden of mutations in the number of variants in the CACNA1H and CACNA1I genes

"These genes can modify HM disease risk, which supports the

hypothesis that the disease may have complex heritability, in addition to the strictly single gene forms.

"This study adds to our knowledge of the modification of risk by mutations in several other genes previously identified in some HM patients. These genes implicated in HM are mainly associated with disorders of transport of various substances across brain membranes."

Professor Griffiths said [a previous study](#) published in *Frontiers in Molecular Neuroscience*, investigated the role of identified mutations in the CACNA1I gene and confirmed that there were functional effects of CACNA1I variants on electrophysiological properties.

"These studies investigated five implicated mutations and showed numerous functional alterations across the channels, further suggesting that variants identified in CACNA1I could play a causative or contributory role in HM."

**More information:** Neven Maksemous et al, Whole Exome Sequencing of Hemiplegic Migraine Patients Shows an Increased Burden of Missense Variants in CACNA1H and CACNA1I Genes, *Molecular Neurobiology* (2023). [DOI: 10.1007/s12035-023-03255-5](https://doi.org/10.1007/s12035-023-03255-5)

Provided by Queensland University of Technology

Citation: Scientists identify two new genes involved in hemiplegic migraine (2023, March 2) retrieved 18 April 2024 from <https://medicalxpress.com/news/2023-03-scientists-genes-involved-hemiplegic-migraine.html>

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