Many migraines may have a common genetic basis

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Computer-generated artwork illustrating a migraine. Credit: Adrian Cousins,Wellcome Images.

(Medical Xpress) -- A study into the genetic basis of many common forms of migraine has identified three variants that suggest that most forms of migraine have a shared genetic foundation, regardless of how they manifest in the people who have them.

Migraine affects up to 20 per cent of the population and is defined as being 'with aura' (where the migraine is preceded by symptoms such as visual disturbances, slurred speech or numbness), or 'without aura', where the migraine starts without any warning.

Although migraine has an inheritable component, until recently the only genetic variants associated with the condition were for rare forms of the condition where just one gene had altered - known as 'rare variants'.

Little is known about the genetic basis of more common forms of

migraine that are believed to be due to many factors, including variants that affect a number of chemical processes in brain. In September 2010, genome-wide association studies revealed the first common variant associated with migraine and showed it was associated with a chemical communication system in nerves in the brain known as the glutamate signalling pathway. This current study has applied a similar approach to identify more areas of the genome that might have an effect on common forms of migraine.

The research team compared the genomes of more than 8000 people who have migraines with 37 000 individuals who are migraine-free. To achieve this scale, the study combined data from two large migraine research initiatives, the US-based Women's Genome Health Study and the European-based International Headache Genetics Consortium with two smaller studies from the Netherlands and Germany.

By conducting a genome-wide association study (GWAS), the researchers were able to zoom in on variants that could increase susceptibility to migraine. The study found three genetic variants that were equally associated with migraines with aura and migraines without aura.

"Most forms of migraine are likely to be due to a number of affected pathways working in concert," explains Dr Tobias Kurth, senior author of the study from INSERM, France as well as Brigham and Women's Hospital, Harvard Medical School, Boston. "This study has found three areas of the human genome that are associated with migraine at the population level that are shared by people who have attacks with aura and without aura. It offers the possibility that migraines may be due to disturbances in signalling pathways that are common to all forms of the condition. Our work will stimulate more targeted research to unveil more precise mechanisms of these genes."

Two of the variants identified by the study are clearly associated with migraines only - affecting the genes LRP1 and TRPM8, with the variant affecting TRPM8 appearing to be more prevalent in women. By contrast, the third variant that affects the gene PRDM16 appears to have a function in both migraines and non-migraine headaches, but the pathway it affects is unknown. The targets of these variants both confirm current thinking on the causes of migraine and shed new light on a mechanism not previously linked to the condition.

"By associating a variant that affects the gene LRP1 with common migraines, this confirms that the glutamate signalling pathway is involved in the development of migraines," says Professor Aarno Palotie, Senior Group Leader at the Wellcome Trust Sanger Institute and one of the authors of the study. "This agrees with our previous study where we identified the first variant associated with common migraine, which also affected the glutamate signalling pathway. The second variant appears to affect the gene TRPM8, which is expressed in neurons and encodes a sensor for pain."

"The third variant has yet to be linked to any particular signalling pathway and elucidating its role should provide further knowledge of why people experience the symptoms they do with migraines."

More information: Chasman DI et al. Genome-wide association study reveals three susceptibility loci for common migraine in the general population. *Nat Genet* 2011 [epub ahead of print]

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