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Large-scale genetic study provides new insight into the causes of migraine

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An international research consortium has identified almost 30 new genetic risk factors for common migraine. The results provide further

support for the theory that an abnormal function of the blood vessels of the brain is an important component in driving migraine attacks.

The results of the largest genetic study on migraine thus far were published online in the journal *Nature Genetics* today, June 20. The study was based on DNA samples of 375,000 European, American and Australian participants. Almost 60,000 of them suffer from migraine.

The researchers combined data from 22 genome-wide association studies including new data from around 35,000 migraine sufferers. From the millions of genetic variants analyzed, 38 independent genomic regions were shown to be associated with migraine. Only ten of these regions have been implicated in migraine susceptibility before.

The study was conducted by members of the International Headache Genetics Consortium including migraine research groups from Australia, Denmark, Estonia, Finland, Germany, Iceland, the Netherlands, Norway, Spain, Sweden, the UK and USA.

- Our consortium is devoted to uncovering the genetic causes of migraine and during the past few years we have been able to identify many risk variants. Yet, in this latest, large-scale study, tens of new genetic risk factors were discovered. Because all of these variants modify the disease risk only slightly, the effect could only be seen when this large amount of samples became available, said Professor Aarno Palotie, leader of the International Headache Genetics Consortium.

- We simply can't overstate the importance of international collaboration when studying genetics of complex, common diseases, continues Palotie who works as a Research Director at the Institute for Molecular Medicine Finland (FIMM), University of Helsinki, and is an associate member at the Broad Institute of MIT and Harvard.

Migraine is a debilitating disorder affecting around 1 in 7 people worldwide, but its molecular mechanisms remain poorly understood which makes developing new treatments challenging.

When the researchers took a closer look on the genomic areas pinpointed in the study, they noticed that most of them overlap with known genes. Interestingly, as many as nine of the genes have been previously associated with some vascular disease and four more are known to be involved in the regulation of vascular tone, supporting the importance of blood vessels in migraine attacks.

- These genetic findings are the first concrete step towards developing personalized, evidence-based treatments for this very complex disease. We doctors have known for a long time that migraine patients differ from each other and the drugs that work for some patients are completely inefficient for others, said Professor John-Anker Zwart from the Oslo University Hospital.

- In the future, we hope that this information can be utilized in dividing the patients into different genetic susceptibility groups for clinical drug trials, thus increasing the chances of identifying the best possible treatment for each subgroup, he continues.

- These interesting findings linking migraine with vascular dysfunction were generated using novel computational approaches that utilize and combine data from various international biological databases. Such datasets are invaluable in situations like this when tissue samples from patients are not readily available, underscoring the importance of data sharing, commented Dr. Benjamin Neale from the Broad Institute of MIT and Harvard.

More information: *Nature Genetics*, DOI: 10.1038/ng.3598

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