Concentrating on different aspects of pain leads to breakthrough in migraine genetics

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Migraine is the most common cause of episodic headache, and by far the most common neurological cause of a doctor's visit. It affects some 15% of the population, including some 41 million people in Europe, and places a considerable burden on healthcare in both the developed and the developing world.

During the last few years, great strides have been made in discovering common genes influencing the susceptibility to common diseases, such as diabetes, Crohn's disease and schizophrenia. However, no genes have yet been convincingly associated with migraine susceptibility, probably due to the high degree of variability of the disease phenotype combined with the lack of viable laboratory tests.

"To address this problem, we developed a new analysis technique concentrating on different symptoms of migraine", says Professor Aarno Palotie (University of Helsinki, Finland, and the Sanger Institute, Cambridge, UK). The new technique was used in the large international study including 1700 migraine patients and their close relatives from 210 Finnish and Australian migraine families. The Finnish families had been ascertained through neurology clinics, while the Australian families had been collected through a twin study. An initial genome-wide microsatellite study was followed up by an independent targeted replication study.

Researchers identified one gene locus on chromosome 10q23, which showed significant evidence of genetic linkage in both populations

studied as well as in the replication study. The gene locus was especially strongly linked to female migraineurs. “In a further analysis, two independent previous studies, one Finnish and one Australian, had detected the same locus, but in those studies the level of evidence had been just below significance, and thus the connection had so far been missed”, tells researcher Verneri Anttila from Palotie’s group.

This locus is thus linked to migraine in a total of 4000 migraineurs or their close relatives. “All of these findings depended on the newly discovered aspect of migraine genetics: different types of pain – such as pain that pulsates or pain that is unilateral – are more closely linked to specific genetic loci than general pain”, Palotie states.

In this study, researchers were able for the first time to convincingly demonstrate a genomic locus to be linked to migraine susceptibility in two diverse populations. This is especially interesting as Finland and Australia are genetically distant, and also as it tied together previous research, resulting in very robust evidence for pinpointing the susceptibility region.

“This study is the first international collaboration as well as the largest linkage study in migraine to date. It successfully applied new analysis strategies in detecting the locus and thus paved the way for subsequent large association studies”, Palotie and Anttila say. According them, this study gives new hope to deciphering the migraine pathways and therefore discovering targets for future treatments, as well as discovering the first migraine gene variants.

Source: University of Helsinki