

RESEARCH HIGHLIGHTS

STROKE

Mitochondrial DNA affects the risk of ischemic stroke

A large study published in *The Lancet Neurology* indicates that individuals who possess mitochondrial DNA subhaplogroup K have a markedly lower risk of stroke or transient ischemic attack (TIA) than people with one of the other main European mitochondrial DNA haplogroups. “This genetic effect is stronger than other previously identified genetic risk factors [for ischemic stroke],” states lead author Patrick Chinnery.

The heritability of ischemic stroke seems to be higher in women than in men, indicating that maternally inherited genetic factors, such as mitochondrial DNA, might influence the risk of developing this condition. Mitochondrial DNA can be subdivided into various classes—termed haplogroups—on the basis of its pattern of single nucleotide polymorphisms. Several small, and as yet unreplicated, studies have reported associations between different forms of ischemic stroke and various haplogroups.

To examine the possible relationship between variation in mitochondrial DNA and the risk of ischemic stroke, Chinnery and colleagues conducted a large case–control study that examined the distributions of the ten main European mitochondrial DNA haplogroups in two independent UK cohorts of patients with ischemic stroke or TIA ($n = 950$), a cohort of individuals with acute coronary syndromes ($n = 340$), and groups of healthy and disease controls ($n = 2,939$). The various haplogroups were determined

by means of a high-throughput genotyping technique.

The frequency of subhaplogroup K (a subgroup of haplogroup U) was found to be $\approx 50\%$ lower in all patients with ischemic stroke or TIA than in the acute coronary syndrome group, the healthy control group, or the healthy and disease control groups combined. A similar reduction in frequency was also observed when each cohort of patients with stroke or TIA was examined alone. In contrast to the change in frequency of subhaplogroup K, the frequencies of the other haplogroups did not vary across the groups. “To give you a flavor for the size of the effect, a 50% relative risk reduction, as with subhaplogroup K, is comparable to that which one would get in a clinical trial of aggressive blood pressure lowering [in ischemic stroke],” explains Peter Rothwell, one of the investigators.

According to the research team, the results of their study provide evidence that mitochondrial mechanisms might be involved in the etiology of ischemic stroke. Moreover, the researchers suggest that mitochondrial DNA could be used to identify individuals who are at risk of developing this condition.

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Original article Chinnery, P.F. *et al.* Mitochondrial DNA haplotypes and risk of transient ischaemic attack and ischaemic stroke: a genetic association study. *Lancet Neurol.* 9, 498–503 (2010)