Genetic variant increases risk of common type stroke

EurekAlert

A genetic variant that increases the risk of a common type of stroke has been identified by scientists in a study published online in *Nature Genetics* today. This is one of the few genetic variants to date to be associated with risk of stroke and the discovery opens up new possibilities for treatment.

Stroke is the second leading cause of death worldwide (more than one in 10 of all deaths, and over six million deaths annually), and also in developed countries is a major cause of chronic disability. As the world's populations age the impact of stroke on wellbeing is likely to increase further.

Several different mechanisms underlie strokes. One of the most common types is when blood flow is impaired because of a blockage to one or more of the large arteries supplying blood to the brain large artery ischemic stroke. This accounts for over a third of all strokes.

Researchers from St George's, University of London and Oxford University, working with scientists from Europe, America and Australia, in one of the largest genetic studies of stroke to date, compared the genetic make-up of 10,000 people who had suffered from a stroke with 40,000 healthy individuals. The study was funded by the Wellcome Trust.

The researchers discovered an alteration in a gene called HDAC9 which affects a person's risk of large artery ischemic stroke. This variant occurs on about 10 per cent of human chromosomes. Those people who carry two copies of the variant (one inherited from each parent) have nearly twice the risk for this type of stroke compared to those with no copies of the variant.

The protein produced by HDAC9 is already known to play a role in the formation of muscle tissue and heart development. However, the exact mechanism by which the genetic variant increases the risk of stroke is not yet known. A better understanding of the mechanism could lead to new drugs to treat or prevent stroke; however, the researchers stress that this is still some way off.

Professor Hugh Markus, from St George's, University of London, who co-led the study says: "This discovery identifies a completely new mechanism for causing stroke. The next step is to determine in more detail the relationship between HDAC9 and stroke and see whether we can develop new treatments that reduce the risk of stroke. Interestingly, there are already drugs available which inhibit the HDAC9 protein. However, it is important that we understand the mechanism involved before trialling the effects of these drugs on stroke."

The researchers went on to show that the new variant does not have the same effect on the risk of other types of stroke which include bleeding in the brain (haemorrhagic stroke).

Professor Peter Donnelly, Director of the Wellcome Trust Centre for Human Genetics in the University of Oxford, who co-led the study, says: "Our study shows that the different subtypes of stroke could involve quite different genetic mechanisms. This is really fascinating, and if it holds up more generally, will move us closer to personalised medicine, where treatments and preventions can be tailored more precisely to individual patients."

Dr Peter Coleman, Deputy Director of Research at The Stroke Association, who funded collection of some of the samples used in this study, said:

"Over a third of strokes are caused by a blockage in one of the large blood vessels supplying blood to the brain (large artery stroke). Findings from this ground breaking study appear to show a genetic link which may affect a person's risk of large vessel stroke. Further study is needed, but this research could potentially lead to new methods of screening and prevention for large vessel stroke, and ultimately, new methods of treatment."

SOURCE [1]

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