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Stroke association

Final report summary:

Predicting those most at risk of a stroke from a burst blood vessel in the brain

A UK wide clinical and genetic cohort study of aneurysmal subarachnoid haemorrhage

PROJECT CODE: TSA 2012/03

Why did we fund this research?

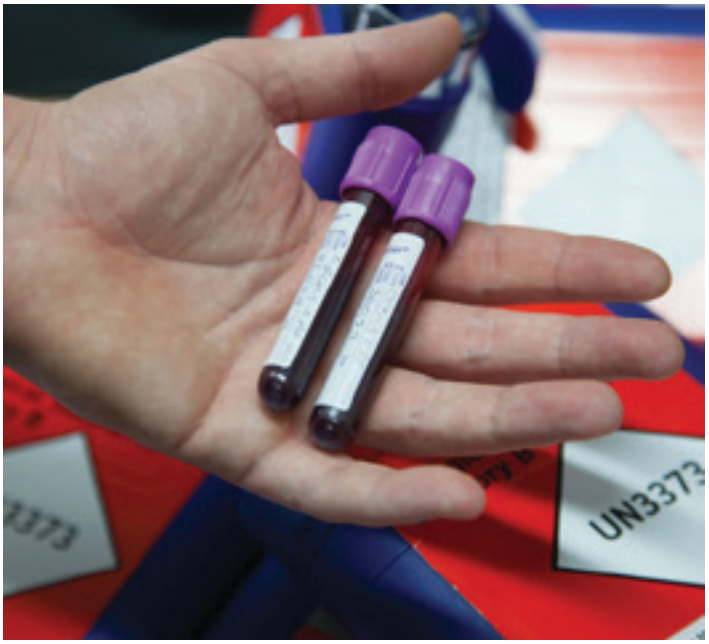
Bleeding (haemorrhage) in the brain can be caused by the rupture of an abnormal swelling in the wall of an artery called an intracranial aneurysm. This can cause a bleed on the surface of the brain, which is a devastating form of stroke known as subarachnoid haemorrhage (SAH).

SAH typically affects working age people between 50 and 65 years of age. Despite recent advances in treatment and management of the condition, about half of all cases of SAH still result in death or dependence. Those who do survive can experience a great deal of disability, and consequent hardship, when they are unable to return to work or find employment afterwards.

Economically, SAH results in a huge loss of potential life years of work and productivity and puts a strain on rehabilitative resources within the NHS.

It is therefore vital to detect those people who are likely to develop or harbour an existing intracranial aneurysm, and provide them with surveillance or treatment to prevent the devastating effects of SAH.

It is already known that there may be a genetic element predisposing people to the condition, as there are known family trees which have a large number of members affected by intracranial aneurysm. This has led to worldwide research into how intracranial aneurysms develop. Current knowledge of genetic risk factors suggest that many genetic variants of normal genes act together synergistically with clinical risk factors, such as high blood pressure and smoking, to predispose a person to having an intracranial aneurysm.



DNA used in the study is extracted from blood samples.

This project forms part of the on-going GOSH (Genetic and Observational Sub-arachnoid Haemorrhage) study led by researchers at University College London, who are part of the International Stroke Genetics Consortium (ISGC). The ISGC is collating results from all intracranial aneurysm research centres across the world.

The key aims of the GOSH study are to identify the genetic and clinical risk factors that lead to intracranial aneurysm: presence, rupture status, anatomy (size and location in the brain); identify the outcomes of a large UK cohort of people with the condition; and to collaborate internationally with colleagues in the same field of research.

The first project in the GOSH study started in 2009 and was funded by a Stroke Association grant (TSA 2008-07). It involved a comprehensive review and analysis of 61 studies associating genetic variations in people's DNA with their risk of intracranial aneurysm. The results were published in the medical journal, Neurology in 2013, and included the identification of a number of associations between people's genes and their likelihood of having an intracranial aneurysm. It was decided that further investigation was warranted in a large sample of people in the UK, with follow-on funding from the Stroke Association to do so.

The aims of this project (TSA 2012-03) were to further the GOSH work by looking more deeply into the most promising candidate genes associated with intracranial aneurysms. The project included the study of genetic changes called single nucleotide polymorphisms (SNPs).

During the project, the variations in 30 SNPs associated with intracranial aneurysm was assessed in a group of 1400 people in the UK with intracranial aneurysms, and also 1300 control participants for comparison. Preliminary analyses of the data are underway.

Data was also sent for analysis to collaborators at Yale University in the USA, the current world leaders in genetic aneurysm research.

At the end of the project, over 2,500 patients had been recruited to the wider GOSH study, across 20 centres in the UK. This makes the study the largest of its kind in the UK, and one of the largest in the world.

What did the research find?

SNPs were found within two genes called ACE and MMP2 that were significantly associated with intracranial aneurysms. The associations were strongest for ruptured aneurysms. Changes in these genes affect connective tissue, which suggests that abnormal changes in connective tissue contribute to intracranial aneurysm formation and rupture.

An analysis of the physical characteristics of study participants confirmed that high blood pressure and current smoker status are significantly associated with the presence of intracranial aneurysms.

If SNPs are related to the risk of future intracranial aneurysm rupture, findings from this project may have important implications for how to better manage patients who have the condition. This could include improved decision making regarding who should be treated to prevent SAH, and who should have their aneurysms put under surveillance (as treatment has its own risks).

The GOSH study is planned to continue with further work, analysing more genetic variants (in collaboration with Yale University and other aneurysm researchers throughout the world). It will investigate whether genetic variants are linked to the outcome from SAH.

What does this mean for stroke survivors?

The early findings from this study suggest that there may be a contribution from genetic and environmental risk factors that can lead to bleeding on the brain (subarachnoid haemorrhage) from a burst blood vessel in the brain (intracranial aneurysm).

Further outcomes of this work could lead to better predictions of which people with intracranial aneurysms should have them treated, and improve understanding of factors affecting outcome of subarachnoid haemorrhage.

We are the Stroke Association

The Stroke Association is the leading stroke charity in the UK. We believe in the power of research to save lives, prevent stroke and ensure that people make the best recovery they can after a stroke.

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