Scottish Government Health Directorates Chief Scientist Office

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FOCUS ON RESEARCH

Cerebral and peripheral perfusion and reactivity in CADASIL: a longitudinal pilot study.

Researchers
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Aim
Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is the most common inherited cause of stroke. It affects young people, causing stroke and in many, a form of dementia. While it is known that the genetic fault causes problems with small blood vessels in the brain and elsewhere in the body, the very slow development of symptoms makes it difficult to test any potetial treatments. We undertook a study over 2 years to:

- Characterise the abnormalities in blood flow in the brain and the body in patients with CADASIL;
- compare changes in blood flow to clinical features of the disease;
- Determine how blood flow (or other) features change over time, and whether they predict disease progression.

Project Outline/Methodology
22 CADASIL patients were recruited to a 2 year study. Patients underwent a range of tests at baseline, then after 1 and 2 years. These included clinical assessments, tests on the blood flow in the brain by ultrasound and using an advanced MRI scanning method (Arterial Spin Labelling, or ASL), tests on blood flow in vessels in the body, detailed Neuropsychological testing, and Magnetic Resonance Imaging (MRI) scans of the brain to look at changes of the disease on brain structure and function.

Key Results
- Brain blood flow declines significantly in CADASIL patients over 1 year.
- In patients with cognitive impairment, changes in the communication between different parts of the brain can be measured.
- Impaired small vessel function in the brain and body is seen in patients with more evidence of brain damage (atrophy and lacunes).
- Large vessel damage (atherosclerosis and vessel stiffness) is also seen in these patients.
- Blood vessel responses to breathing carbon dioxide did not predict change over the period of one year.

Conclusions
Abnormalities in blood vessel function can be measured with the MRI ASL technique and may offer insight into progression of CADASIL, as well as other related conditions. The decline in blood flow seen over 1 year is significant and may offer a way of measuring change that could be valuable in clinical trials.

What does this study add to the field?
Vessels are known to be abnormal in CADASIL and brain damage such as lacunes is a major cause of disability. This study demonstrates abnormal small vessel function is associated with the development of this type of brain damage, and this warrants further assessment.

Implications for Practice or Policy
MRI ASL (with CO_2 challenge) is feasible in a clinical population of patients and may offer important pathophysiological insights, along with a potential role as a disease biomarker. The development of new lacunes was common and correlated with cognitive function. These offer potentially useful markers for disease progression.

Where to next?
Further scans require analysis and this will lead to further collaborative work with other centres. Researchers from Edinburgh, Australia and Denmark have already collaborated.
Studies in blood vessels obtained from CADASIL patients by gluteal biopsy are being studied to further understand the role of vessel dysfunction in CADASIL.

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