

**Final report summary :**

**Do naturally  
produced new brain  
cells help repair  
stroke damage?**

Harnessing cellular processes to repair neurological damage in patients with stroke.

## Why did we fund this research?

Stroke remains a leading cause of acquired adult disability globally<sup>(1)</sup>, despite advances in thrombolysis (clot busting drugs), which can help reduce disability for some<sup>(2)</sup>. Although stroke rehabilitation can make a significant difference to recovery, the search is on for treatments that can reduce the burden of stroke even further. In order to develop new stroke treatments, a better understanding is required of both how the brain repairs itself after injury from stroke, and how potential treatments affect the processes involved in brain repair.

The main aim of this study was to investigate whether changes after stroke in brain blood flow (perfusion) and brain cell chemicals (metabolites) can be measured reliably using MRI (magnetic resonance imaging) brain scans. If so, they may be used as indicators of biological processes (biomarkers) of brain recovery after stroke. The brain region of particular interest was the intact area of the brain bordering the site of damage caused by the stroke, which is where recovery starts. A second aim was to confirm the presence of a unique chemical signature on the MRI brain scans previously linked to new-born brain cells (called neural progenitor cells). The size of this chemical signature was thought to be representative of the number of new brain cells formed<sup>(3)</sup>. If successful, the study could open up new ways of using MRI brain scans to monitor recovery from stroke and assess the effectiveness of potential stroke treatments.

## What did the researchers do?

The first challenge was to develop MRI techniques to accurately measure regional blood flow and chemicals in the brain which would be reliable on repeat testing. Techniques used included continuous arterial spin labelling (CASL) for the measurement of regional blood flow in the brain, and proton spectroscopy for the measurement of chemicals that might be used as biomarkers. The chemicals were chosen to show a variety of brain cell properties including: the structural and functional integrity of brain cells; the making and degradation of cell walls (membranes) ; activity

of cells that support and protect brain cells (glial cells); signal transmission between brain cells (neurotransmitters); energy metabolism of cells; and the chemical signature thought to be indicative of new born (neural progenitor) cells.

In addition, the way the imaging was conducted needed to be patient friendly and comfortable, minimising the time patients spent in an MRI brain scanner so soon after a stroke.

The main experiment applied the brain imaging techniques developed in the first part of the study to two groups of participants: 15 stroke patients and 15 matched, healthy volunteer subjects to be used for comparison (control group). All participants underwent clinical assessments of their disability level and movement (motor function) which each lasted about half an hour. Disability was measured with the National Institute of Health Stroke Scale (NIHSS), which is a standard tool used to assess a stroke survivor's level of impairment. Movement was measured with the Fugl-Meyer Assessment for stroke patients with one-sided weakness (hemiplegia), testing their arm and leg weakness, balance, sensation and joint range of motion and pain.

All participants had MRI brain imaging assessments two, six weeks and three months after having a stroke. Each imaging assessment took one hour broken down into two half-hour sessions.



## What did the research find?

Up to three months after stroke, many blood flow and chemical changes took place in the intact areas of the brain bordering the site of recovery. In these regions, there was a gradual drop over time in the structural integrity and function of brain cells, suggestive of stroke damage. There were also rises in blood flow, and concentrations of chemical processes that appeared to have a negative effect on recovery. However, greater regional blood flow between two weeks and three months after stroke were significantly associated with a better recovery of movement at three months after stroke, as measured by higher scores on the Fugl-Meyer Assessment.

These results suggest that preservation of brain cell integrity may be the most important factor in promoting brain rewiring (plasticity) and recovery in stroke patients.

When measured at two weeks after stroke, the extent of a patient's disability (NIHSS score), movement (Fugl-Meyer Assessment) or size of the brain area damaged by stroke were not associated with motor recovery (improved movement) at three months after stroke. Furthermore, changes measured between two weeks and three months after stroke in these measures were also not associated with improved movement at three months after stroke, suggesting them to be poor predictors of the recovery of a patient's movement.

There was no suggestion of new born brain cells (neural progenitor cells) being detected by the MRI imaging, and hence no suggestion that recovery might occur through this process.

This study suggests that MRI imaging of metabolic processes in the brain offers insight into some of the underlying repair processes involved in the early stage recovery from stroke, and into potential biomarkers to enable researchers to predict recovery.

## References

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- 3) Manganas LN, Zhang X, Li Y, et al. Magnetic resonance spectroscopy identifies neural progenitor cells in the live human brain. *Science*. 2007, 318(5852):980-5.

### What does this mean for stroke survivors?

Imaging techniques were used to monitor brain processes involved in stroke recovery in the early weeks after stroke. These could lead to new ways of understanding how the brain can recover after stroke and potential ways to predict and enhance recovery.

## 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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