Final report summary:

Do naturally produced new brain cells help repair stroke damage?

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

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Why did we fund this research?

Stroke remains the leading cause of acquired adult disability globally, despite advances in thrombolysis (clot busting drugs), which can help reduce disability for some. Half of all stroke survivors have residual deficits from their stroke, and up to 30% have permanent disability. 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 novel stroke treatments, a better understanding is required of both how the brain repairs itself after injury from stroke, and how potential treatments affect those processes involved.

The primary aim of this study was to investigate whether changes in blood flow, and chemicals associated with nerve cell changes following injury from stroke, could be measured reliably using MRI (magnetic brain imaging) brain scans. The brain region of particular interest was the intact area of the brain bordering the site of injury from stroke, which is where recovery starts. A secondary aim was to confirm the presence of a unique chemical signature associated with new-born brain cells (called neural progenitor cells) that had been reported by another group. This signal was considered to be indicative of recovery, with the size of the signal representing the number of new brain cells formed.

What did the researchers do?

The research was conducted by a research team at King’s College London which was led by its department of Clinical Neurosciences.

The first challenge was to develop an MR (magnetic resonance) imaging technique to reliably and accurately measure regional blood flow and chemicals in the brain on repeated testing. In addition, the imaging protocols needed to be patient friendly and comfortable, minimising their time spent in an MRI brain scanner so soon after a stroke.

MR techniques were developed with the participation of six volunteers for the measurement of blood flow in the brain (perfusion) and brain chemicals (metabolites). These included continuous arterial spin labelling (CASL) for the measurement of regional blood flow in the brain, and proton spectroscopy for the measurement of the following chemicals used as indicators of biological processes (biomarkers) in the brain: N-acetylaspartate (NAA) for the structural and functional integrity of brain cells; choline (Cho) involved in cell membrane synthesis and degradation; myo-inositol (mI) for the activity of cells that support and protect brain cells (called glial cells); glutamate and glutamine (Glx) for signal transmission between brain cells (neurotransmitters); creatine (Cr) for energy metabolism; and lactate and an MR signal at 1.28ppm (parts per million) thought to be indicative of new born (neural progenitor) cells.

The main experiment applied these brain imaging techniques to two groups of participants: 15 patients and 15 matched, healthy volunteer subjects. All participants underwent clinical assessments (disability with the NIHSS test, motor/movement function with the Fugl-Meyer test) and MRI brain imaging assessments two, six and twelve weeks after stroke onset. Each clinical assessment lasted about 30 minutes, and each imaging assessment took 60 minutes broken down into two 30 minute sessions.
What did the research find?

The research found that up to 12 weeks 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 decrease in the structural integrity and function of brain cells over time (indicated by decreased NAA concentrations), suggestive of progressive injury beyond the acute phase of stroke. There were also increases in regional blood flow, and concentrations of the chemicals choline, myo-inositol, creatine and lactate. These chemicals are biomarkers for processes that appeared to have a negative effect on recovery.

Greater blood flow and higher NAA concentrations at two weeks after stroke, and a reduced rate of NAA concentration loss between two and 12 weeks after stroke, were significantly associated with a better recovery of movement in patients at 12 weeks after stroke. This was recorded as higher Fugl-Meyer scores of motor recovery. 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.

The extent of a patient’s neurological deficit, motor impairment, or size of the brain area injured by stroke at two weeks after stroke, or changes in these between two and 12 weeks after stroke, were not associated with motor recovery at 12 weeks after stroke. This suggests them to be poor predictors of the recovery of a patient’s movement.

The 1.28 ppm signal that was intended to identify newly born nerve cells on MR imaging was found to be randomly located in the brain, and instead probably identified cells that had a high fat content.

What does this mean for stroke survivors?

Imaging techniques were developed to monitor brain processes involved in stroke recovery in real-time, in the early weeks after stroke. Such techniques could lead to new ways of understanding how the brain can recover after stroke, and ways to enhance recovery.
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