Stroke
Stroke and Cognitive Impairment
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26 June 2014

Stroke is responsible for 10.6% of all deaths worldwide, making it the second leading cause of death\(^1\). It is also a major cause of disability worldwide due to stroke survivors having impaired neurological function. Strokes account for 2-4% of total healthcare costs in the world, particularly in developed countries\(^2\). With increased awareness of stroke symptoms, the rate of survival is significantly increasing and even greater demands are being placed on healthcare systems. Stroke is a complex, multi-organ system disease that primarily affects the brain. There are many known risk factors for stroke including hypertension, diabetes, smoking, advanced age and sex\(^2\). Strokes are less common in pre-menopausal females than in age-matched males\(^3\). Genetics may also influence the risk of stroke, with stroke more likely to occur in those with a family history.

A stroke is classified as either ischemic or haemorrhagic\(^2\). An ischemic stroke is caused by an obstruction of brain arteries by a clot\(^3\), while a haemorrhagic stroke is caused by the rupture of a blood vessel\(^2\). Ischemic stroke accounts for approximately 80% of stroke cases and is the result of a blockage of a major brain artery by a blood clot, causing a disruption to blood supply\(^4\). This leads to a lack of oxygen and nutrients that are essential for brain cell function, resulting in the development of a central core of dead brain cells. The core is surrounded by an area of damaged but partially functional tissue that is potentially salvageable\(^5\). Salvage of this area is the main goal of therapeutic interventions that are designed to restore of blood flow and/or reduce further injury, in order to achieve less overall neurological deficit\(^2\).

Currently, the only approved treatment for an ischemic stroke is the use of a 'clot-busting' drug, which acts to break down a clot and enable blood flow to be returned to the brain\(^6\). However, it has a limited time of approved administration (<4.5 hours post-stroke) and largely due to the delay in diagnosis by CT scan, less than 12% of ischemic stroke patients are eligible to receive this treatment\(^6\). For this reason, a greater understanding of the underlying mechanisms of brain injury following stroke is desperately needed for the development of additional clinically useful treatment options.

Stroke survivors often experience cognitive impairment. In fact, cognitive impairments associated with one or more vascular disease states has a ~5% prevalence in people over the age of 65\(^7\). Vascular disease-associated cognitive impairment is encountered as milder cognitive impairments and may progress to dementia\(^8\). Therefore, it is conceivable that intervention following its early detection in patients with vascular disease may prevent such progression\(^9\). There is good evidence that a first-ever stroke increases the risk of cognitive impairment and, furthermore, that recurrent strokes promote the appearance of dementia seen in Alzheimer's Disease\(^10,11\).
Following ischemic stroke, there is a production of harmful oxygen radicals in the brain. When there is an excess production of oxygen radicals, the body’s ability to readily detoxify is compromised and a state of ‘oxidative stress’ results. This may promote regions of brain cell death, but may also promote the occurrence of pathological changes of AD\textsuperscript{12}. Apart from clinical stroke itself, vascular risk factors (such as hypertension, diabetes mellitus, and obesity) that develop from early to mid-life are associated with the later appearance of cognitive impairment and dementia\textsuperscript{12,13}. Over the lifespan there may be interplay between cerebrovascular disease or its risk factors that may initiate or promote the expression of clinical AD in later life\textsuperscript{13}. If vascular disease-associated cognitive impairment is to be effectively treated to halt any further progression to dementia, therapies to selectively target key pathological processes to safely restore the brain’s function will be required.

References: