Stroke is the primary cause of disability among adults Australia, Europe, and the United States, and is the second leading cause of death worldwide, causing nearly 10 % of all deaths[1]. Every year around 40 000 Australian adults suffer from stroke, and about 30 % of these (that's around 12 000 people) die. Of those whole survive, around half are still permanently disabled 1 year later.

A stroke occurs as the result of a disruption of blood flow to the brain. This can be the result of a haemorrhage (known as haemorrhagic stroke), or a lack of blood flow (ischaemic stroke). The latter occurs when blood flow through the whole body is reduced (such as with a cardiac arrest) or because of a blockage (such as a thrombosis or embolism). Without appropriate blood flow to the brain, the brain tissue is deprived of oxygen and nutrients and cells die, potentially resulting in permanent neurological damage and even death.

After about 60 seconds without oxygen and nutrients, brain cells cease to function and over the next three to five hours, cell death ensues. With no oxygen and nutrients to fuel the brain, normally useful compounds such as glutamate build up and become toxic, allowing too much calcium to enter the cell. This calcium causes the cell to break down, stimulating enzymes that degrade the membranes, and interfering with the cells' energy production mechanisms. As the cell dies it can stimulate cells around it to take up more calcium, spreading the damage. The lack of oxygen and nutrients also causes the production of free radicals, which are toxic to the cell in large quantities. All this tissue disruption stimulates an immune response within the brain, which can further contribute to the damage.

Currently the best available treatment for an ischaemic stroke is to attempt to restore blood flow using "clot busters" such as recombinant tissue plasminogen activator, which is, unfortunately, useful only up to about 5 hours after the event. The faster blood flow is restored to the brain, the better off the patient will be. However, as described, cell damage and death can continue long after blood flow is restored and these clot busters do not treat the ongoing damage that occurs as a result of the original injury. There is currently no adequate drug treatment to prevent target the ischaemic damage that occurs in the days to weeks after reperfusion is established.

One potential candidate for treating stroke to prevent secondary damage is a hormone that is produced in the gut, ghrelin. Ghrelin is secreted from the gut when we are hungry. It acts in the brain to stimulate feeding pathways, encouraging us to eat and to reduce the amount of energy we use up. In addition to its role in stimulating food intake and encouraging weight gain, ghrelin is now thought to be protective against brain damage in a number of neurodegenerative diseases including Parkinson's and Alzheimer's diseases. Recent evidence from animal studies suggests giving ghrelin may also protect brain cells from injury and death after an ischaemic stroke. When rats are given ghrelin just prior to an ischaemic stroke, their infarct volume (primary damage) and cell death is less than if they are just given saline. Ghrelin probably does this by preventing cell 'suicide', the stimulation of enzymes and free radicals that will break down the cell. Ghrelin also increases the function of cell mitochondria, the machinery that produces the cell's energy, and it helps regulate the immune system to prevent excess inflammation in the brain.

Although initial animal studies are encouraging, it remains to be seen whether ghrelin can be useful in preventing damage after stroke in the clinic. Furthermore, our own findings suggest ghrelin may not be useful for all types of stroke. We have findings suggesting mice with no ghrelin may actually be better off after a cardiac arrest model of stroke than mice with normal ghrelin. Additional studies

are clearly necessary to investigate ghrelin's role in protecting the brain after stroke. However, the possibility remains that this hormone may be a new therapeutic agent in stroke recovery. If this proves to be the case, we may even be able to promote our own recovery from stroke in the short term just by going a little bit hungry.