Maintaining the brain's wiring in aging and disease

December 5 2008

Researchers at the Babraham Institute near Cambridge, supported by the Alzheimer's Research Trust and the Biotechnology and Biological Sciences Research Council (BBSRC), have discovered that the brain's circuitry survives longer than previously thought in diseases of ageing such as Alzheimer's disease. The findings were published today in the journal *Brain*.

Alzheimer's disease causes nerve cells in the brain to die, resulting in problems with memory, speech and understanding. Little is known about how the nerve cells die, but this new research has revealed how they first lose the ability to communicate with each other, before deteriorating further.

"We've all experienced how useless a computer is without broadband. The same is true for a nerve cell (neuron) in the brain whose wiring (axons and dendrites) has been lost or damaged," explained Dr Michael Coleman the project's lead researcher. "Once the routes of communication are permanently down, the neuron will never again contribute to learning and memory, because these 'wires' do not re-grow in the human brain."

But axons and dendrites are much more than inert fibre-optic wires. They are homes to the world's smallest transport tracks. Every one of our hundred billion nerve cells continuously shuttles hundreds of proteins and intracellular packages out along its axons and dendrites, and back again, during every minute of every day. Without this process, the wires

cannot be maintained and the nervous system will cease to function within a few hours.

During healthy ageing this miniature transport system undergoes a steady decline, but the challenges are immense. Axons up a metre long have to survive and function for at least eight or nine decades. Over this period, our homes will need rewiring several times, but in our brains the wires are all original, surviving from childhood. In Alzheimer's disease, axons swell dramatically, ballooning to 10 or 20 times their normal diameter. These swellings disrupt transport but not, it seems, completely. Enough material gets through the swellings to keep more distant parts of the axon alive for at least several months, and probably for a year or more. This is important because it suggests a successful therapy applied during this early period may not only halt the symptoms, but allow a degree of functional recovery.

"We've been able to look at whole nerve cells affected by Alzheimer's", said Dr Michael Coleman. "For the first time we have shown that supporting parts of nerve cells are alive, and we can now learn how to intervene to recover connections. This is very important for treatment because in normal adult life, nerve cell connections constantly disappear and reform, but can only do so if the supporting parts of the cell remain. Our results suggest a time window in which damaged connections between brain cells could recover under the right conditions."

This basic research gives hope over the longer term to the 700,000 people in the UK who live with dementia. Understanding how the brain responds to disease also tells us a lot about how it functions in all of us.

Source: Biotechnology and Biological Sciences Research Council