Why the brain is more reluctant to function as we age

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New findings, led by neuroscientists at the University of Bristol and published this week in the journal *Neurobiology of Aging*, reveal a novel mechanism through which the brain may become more reluctant to function as we grow older.

It is not fully understood why the brain's cognitive functions such as memory and speech decline as we age. Although work published this year suggests cognitive decline can be detectable before 50 years of age. The research, led by Professor Andy Randall and Dr Jon Brown from the University's School of Physiology and Pharmacology, identified a novel cellular mechanism underpinning changes to the activity of neurones which may underlie cognitive decline during normal healthy aging.

The brain largely uses electrical signals to encode and convey information. Modifications to this electrical activity are likely to underpin age-dependent changes to cognitive abilities.

The researchers examined the brain's electrical activity by making recordings of electrical signals in single cells of the hippocampus, a structure with a crucial role in cognitive function. In this way they characterised what is known as "neuronal excitability" — this is a descriptor of how easy it is to produce brief, but very large, electrical signals called action potentials; these occur in practically all nerve cells and are absolutely essential for communication within all the circuits of the nervous system.

Action potentials are triggered near the neurone's cell body and once produced travel rapidly through the massively branching structure of the nerve cell, along the way activating the synapses the nerve cell makes with the numerous other nerve cells to which it is connected.

The Bristol group identified that in the aged brain it is more difficult to make hippocampal neurones generate action potentials. Furthermore they demonstrated that this relative reluctance to produce action potential arises from changes to the activation properties of membrane proteins called sodium channels, which mediate the rapid upstroke of the action potential by allowing a flow of sodium ions into neurones.

Professor Randall, Professor in Applied Neurophysiology said: "Much of our work is about understanding dysfunctional electrical signalling in the diseased brain, in particular Alzheimer's disease. We began to question, however, why even the healthy brain can slow down once you reach my age. Previous investigations elsewhere have described age-related changes in processes that are triggered by action potentials, but our findings are significant because they show that generating the action potential in the first place is harder work in aged brain cells.

"Also by identifying sodium channels as the likely culprit for this reluctance to produce action potentials, our work even points to ways in which we might be able modify age-related changes to neuronal excitability, and by inference cognitive ability."

More information: The research, entitled 'Age-related changes to Na+ channel gating contribute to modified intrinsic neuronal excitability' by Andrew D Randall, Clair Booth and Jon T Brown, is published in the journal *Neurobiology of Aging* and funded by Pfizer who are long-standing collaborators with Randall and Brown. The paper is available to download: www.sciencedirect.com/science/ … ii/S0197458011005756

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