

Wednesday, 17 May 2017

World-first breakthrough study by Prince of Wales Hospital identifies cause of delirium

A world-first study by Prince of Wales Hospital (POWH), has identified a breakthrough in the cause of delirium.

Using Positron Emission Tomography (PET) scans, the *Fluoro-2-deoxyglucose positron emission tomography in delirium study* (study), shows abnormal and disordered glucose metabolism of the brain as the leading cause of delirium.

Delirium is a neuropsychiatric syndrome, mostly affecting older people in hospital. Signs and symptoms of delirium include acute confusion, fluctuating altered attention and alertness, often with hallucinations. It has the same death rate as a heart attack, however the causes of delirium are largely unknown.

Glucose is the essential fuel supplying energy to the brain. The brain is two per cent of the body by weight, however consumes 20 per cent of the body's supply of glucose. When the brain is unable to metabolise glucose efficiently, brain function deteriorates causing delirium.

Previous international studies of fluid surrounding the brain (cerebrospinal fluid biochemistry) have shown unexpected abnormal glucose metabolism. However, this study has discovered the final common pathway to the cause of delirium.

Leading this study, Associate Professor Gideon Caplan, Director of Geriatric Medicine, Prince of Wales Hospital, said this research found widespread, reversible decreases in brain metabolism, referred to as cortical hypometabolism; and posterior cingulate cortex (PCC) brain hypometabolism during delirium.

"We know that many problems, such as infections, drugs, surgery, and injuries can trigger delirium, but we did not understand how all of these different conditions can lead to the same neurological presentation," A/Professor Caplan said.

"In 10 years of delirium research at Prince of Wales Hospital, we have found the answer to a 2,500 year old mystery - what is happening in the brain during delirium. This breakthrough now informs us as to where to aim our therapeutic interventions to treat, and hopefully to beat delirium; and has the potential to assist in the development of treatments for delirium."

In examining glucose metabolism of the brain as part of this study, particular emphasis was on the PCC, a key region of the brain which is concerned with attention - a central feature of delirium.

The study confirms that through abnormal glucose metabolism, the parts of the brain connected with attention, executive function and cognitive function (such as memory), are impaired in delirium as they are not metabolising glucose correctly.

However, the motor cortex part of the brain, which allows people to move their arms and legs, are metabolising normally, or are, at times, overactive.

Of the participants studied, 13 participants (eight of which were female with a median age of 84 years old) were scanned during delirium. Six participants were scanned again after their episode of delirium had ceased.

PET scans of participants with delirium were compared with post-delirium brain PET scans using NeuroQ – a software specifically designed to analyse PET scans. The same study participants were rescanned two to three months later.

On visual analysis, cortical hypometabolism was evident in all of the study participants during delirium and improved after their episode of delirium. Using NeuroQ, glucose metabolism was higher post-delirium in the whole brain and bilateral PCC, compared to during delirium.

The findings of the study showed the extent of the reversible decrease in glucose metabolism seen with delirium is equal in magnitude to the average decrease in glucose metabolism seen in a year in a person with Alzheimer's dementia.

People with dementia also show a decrease in glucose metabolism, however with a different pattern, and the decrease is not reversible.

Evidence increasingly shows that the mental and physical impacts of delirium linger, and can have devastating long term effects.

It is estimated that one in four people over 65 are admitted to hospital in Australia with delirium. There are currently no licensed treatments for delirium in hospital wards or emergency departments (ED).

A/Professor Caplan said as well as increased mortality rates in older people, there is a higher rate of nursing home placement - twice than those seen without delirium.

“There are no licensed treatments for delirium that we can use in the ED or on the wards. We need to understand what is happening in delirium to be able to find treatments for it,” A/Professor Caplan said.

“This study will lead to a better prognosis and reduced mortality, particularly in dementia patients, for people admitted to hospital with delirium around the world.”

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