Researchers put brains together for clearer picture of Alzheimer's cause

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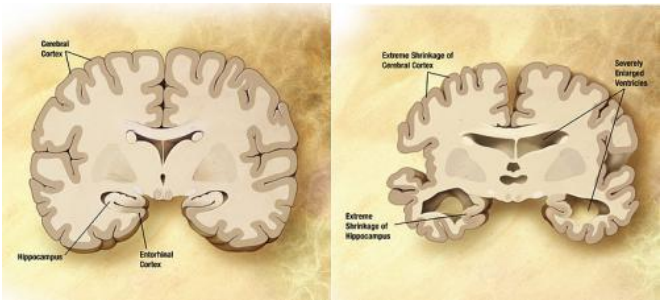

Diagram of the brain of a person with Alzheimer's Disease. Credit: Wikipedia/public domain.

It's an unfortunate fact that the Alzheimer's brain gives up most of its chemical secrets only after the patient has died.

But what if the deceased brain could be made to work with the living brain to shed light on the causes and prevention of Alzheimer's disease?

That is what UTS analytical chemist Dominic Hare is aiming for with his ongoing research into the role played by iron in the development and progress of this increasingly common neurodegenerative disease.

Dr Hare led a team in an international pilot study that for the first time measured and mapped the absolute levels of iron in the white and grey matter of Alzheimer's brains, compared with healthy brains. The findings have just been published in the journal *NeuroImage*.

"We are investigating how to use the brains of deceased patients to improve what we can see in living patients," says Dr Hare, who is also a researcher at the Florey Institute of Neuroscience and Mental Health in Melbourne.

"With deceased brains, we can push the boundaries of discovery to develop better ways of exploring the living brain and understanding what we see.

"It's like reverse engineering: to understand what's happening in the living brain it's often necessary to use the deceased brain to conduct experiments that aren't possible otherwise."

Imaging technology used by collaborator Erika Raven, a PhD candidate at the US National Institute for Neurological Disorders and Stroke and Georgetown University, is able to extract data from sections of the brain that were previously inaccessible. It was combined with a novel technique developed at UTS that uses phosphorus to boost visibility of iron in the brain.

"Our imaging method – called laser ablation inductively coupled plasma-mass spectrometry – functions like a microscope for metals, allowing you to see how elements such as iron are distributed at the near-cellular level," says Dr Hare.

Ms Raven says magnetic resonance imaging (MRI) is highly sensitive to iron "but not so great in detecting iron in grey or white matter".

"Our technique is sensitive and specific towards iron. This is especially important in the study of Alzheimer's disease where investigating iron deposition may contribute towards our understanding of iron imbalances in disease pathology," says Ms Raven.

Changes in the chemical properties of brain iron were first observed more than 50 years ago, and disrupted iron metabolism appears to be a pathological hallmark in the Alzheimer's disease brain, say the researchers.

Proteins that regulate iron, such as ferritin and transferrin, appear to be dysfunctional and abnormally distributed in the Alzheimer's brain.

"In the Alzheimer's brain there is an infiltration of iron into the grey matter. The fact that Alzheimer's disrupts iron metabolism shows iron is involved in the early stages of the disease," says Dr Hare.

"But to understand how neurodegeneration happens, we need to know whether the iron build-up is a response to or a cause of Alzheimer's.

"Iron is a double-edged sword. It's very reactive and has many functions, but it's not sentient and reacts with anything around it.

"If you can stop the chemical reactions happening, you can decrease the toxicity of the iron."

Although this study was comparatively small in scope, says Dr Hare, its significance lies in proving the value of new imaging technologies that can probe the causes of disease at the fundamental chemical level.

More information: Dominic J. Hare et al. Laser ablation-inductively coupled plasma-mass spectrometry imaging of white and gray matter iron distribution in Alzheimer's disease frontal cortex, *NeuroImage* (2016). DOI: 10.1016/j.neuroimage.2016.05.057