A window into the aging mind: MRI imaging of Alzheimer's disease

A problematic obstacle in the study and treatment of Alzheimer's disease lies in the inability to definitively diagnose a patient. Taking brain samples from living patients in search of the pathological features of the disease is impossible and non-invasive techniques are not yet available. However, Dr. Takaomi C. Saido and his team of researchers in the Laboratory for Proteolytic Neuroscience at RIKEN Brain Science Institute may have found a way around this obstacle. In the March 2005 issue of *Nature Neuroscience*, they reported using magnetic resonance imaging (MRI) to identify one of the biological artefacts of Alzheimer's disease, non-invasively, in the brains of living animal models. If this method can be developed for use on humans, it will provide a low-cost, efficient diagnostic method for this devastating disease.

Alzheimer's disease currently affects more than 18 million people worldwide. Experts predict that this number will significantly rise, especially in developing nations as more people in those nations live longer. Alzheimer's disease is characterised by the appearance of plaques around and tangles in neurons. As these abnormal protein clusters accumulate in the brain, neurons are isolated, damaged and killed resulting in memory loss and cognitive decline. The slow progression of this disease is costly and devastating as it robs individuals of mental, and later physical, functions. The physical, mental, and economic costs on care providers, as the disease progresses are also extreme. Estimates place the cost of care for these patients around 100 billion dollar just in the United States alone .

Treatment might offset some of those costs, but it often starts too late because no reliable method to diagnose Alzheimer's disease exists. The biological products of the disease would need to be made visible, reliably and without harming the patient, well before the first signs of dementia appear for any treatment to have real benefits. Saido's team developed FSB as a biological marker for β-amyloid, the protein fragment found in

the extra-cellular plaques. This non-endogenous marker has a high affinity for β-amyloid that effectively reduces the amount of non-β-amyloid readings detected in the functional MRI. Highly reliable readings are produced.

FSB's effectiveness was tested in normal and APP-transgenic mice, a model for Alzheimer's disease that develops β-amyloid plaques. Even in low doses, the probe effectively indicated the presence of plaques in key areas of the animals' brains without harming them. After repeatedly scanning APP mice in one-hour intervals, they found images of clustered plaques in the hippocampus and entorhinal cortex. Tissue sample analysis confirmed that the images were indeed β-amyloid plaques. This method may also detect tangles, another characteristic of Alzheimer's disease.

Before this method can become a useful tool for research and for clinical applications, it needs refinement. Reducing the amount of time in the MRI will also be required. At the same time, the laboratory will continue to explore the full potential of this method in identifying other pathological symptoms associated with AD and other neurodegenerative diseases. When these combined developments have advanced, better research and less invasive clinical practice will be possible with this cost-effective diagnostic tool. An important point as the rising number of Alzheimer's disease cases puts more strain on available care resources.

1. According to Alzheimer's Disease International
2. Alzheimer's Association Fact Sheet on AD,
   http://www.alz.org/Resources/TopicIndex/BasicFacts.asp#statistics

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