Alzheimer's disease diagnosis: the end of the guessing game?

LGC scientists are collaborating on the development of a non-invasive diagnostic technique for early detection of Alzheimer's disease.

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The Requirement

There are currently around 800,000 people living with dementia in the UK, costing the economy £23 billion a year. By 2040 the number of people affected is expected to double and the costs are likely to treble.

Alzheimer's disease is the most common type of dementia, affecting 62% of those diagnosed. There is no known cure, with treatments limited to preserving cognitive function. Currently, there is no non-invasive method for diagnosing Alzheimer's disease with GP's relying on in depth cognitive tests, with clinical confidence in diagnosis typically at 70-80%.

If confident early diagnosis could be achieved through non-invasive techniques, treatment could be introduced earlier delaying the onset of memory impairment.

The solution

The development of plaques or tangles of certain proteins – β-amyloid and tau proteins – in the brain is a known feature in Alzheimer's disease. It is also known that abnormal accumulation of metals underlies several neurodegenerative diseases. Iron, in particular, is associated with the formation of neurofibrillary tangles in the β-amyloid plaques. The recent advances in the use of Magnetic Resonance Imaging (MRI) for the earlier detection of neurological diseases require validation to ensure the integrity of the images obtained is adequate for diagnostic purposes.

Researchers at LGC, in collaboration with partners, have been working to establish a link between novel MRI scans and quantitative elemental mapping of soft tissues. A method of mapping the levels of iron in sections of the brain using laser ablation (LA) coupled to Inductively Coupled Plasma Mass Spectrometry (ICP-MS) has been developed, along with a novel calibration strategy and standard to support quantitative tissue imaging. Correlation of the metal content associated with β-amyloid protein and MRI images will help diagnosis of AD at an early stage, where preventative therapy will have greater impact.

LGC has developed a novel calibration strategy for LA-ICP-MS that produced quantitative images for iron in whole mouse brain sections (provided through collaboration with Kings College London and the University of Warwick) and compared them with results from micro x-ray fluorescence (μ-XRF) (provided through collaboration with Ghent University and the University of Warwick). The data showed good agreement in total iron concentrations for a selection of areas within the mouse brain sections. This finding supports the proposed method as a quantitative approach; the calibration strategy has been published in the Journal of Analytical Atomic Spectrometry [1].

Impact

The development of this method for quantitative imaging of iron in the brain has the potential to lead to techniques for earlier diagnosis of Alzheimer's disease, enabling earlier intervention, therapies and treatment aimed at delaying the onset of symptoms.

Delaying the onset of neurodegenerative disorders, such as Alzheimer's disease, by five years could halve the number of deaths from the condition, saving 30,000 lives a year and billions of pounds in treatment costs. Reducing severe cognitive impairment in the elderly by 1% pa would cancel all estimated increases in long-term care costs due to our ageing population.

The methodology will also provide deeper understanding of the early development of Alzheimer's disease leading the way for new treatments aimed at preventing the disease.

Heidi Goenaga-Infante, Principal Scientist for inorganic analysis at LGC, commented:

> *"This cutting-edge research is already proving to be of significant benefit to the validation of non-invasive diagnostic tools for Alzheimer's disease. The potential for metal imaging mass spectrometry of other biological tissues to probe the reported links between metals and disease states is now a step closer."*

[1] J O'Reilly, D Douglas, J Braybrook, P.-W. So, E Vergucht, J Garrevoet, B Vekemans, L Vinczec and H Goenaga-Infante, "A novel calibration strategy for the quantitative imaging of iron in biological tissues by LA-ICP-MS using matrix-matched standards and internal standardisation", J Anal. At. Spectrom., 2014, 29, 1378-1384

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