Research project by
Dr Pratishtha Chatterjee

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Dementia Australia Research Foundation

Diagnose

Pioneering new pathway for Lewy body dementia detection and treatment

What is the focus of the research?

Investigating a pain-free method of detecting abnormal protein clumps found in dementia with Lewy bodies, and whether those clumps can be prevented with already-existing drug treatments.

Why is this important?

Dementia with Lewy bodies is a devastating form of dementia. People may experience delirium, visual hallucinations, paranoia, disorganised thought and speech, sleep difficulties, and impaired movement. Memory isn't generally affected, but the ability to process information slows down. The loss of motivation to initiate tasks or perform daily routines leads to apathy.

People who have dementia with Lewy bodies have abnormal clumps of the protein alpha-synuclein in their brain cells, which disrupts messaging signals.

What is alpha-synuclein?

A protein in neurons that helps important chemical signals move around the brain. These signals allow us to move well and control automatic bodily functions like blood pressure, heart rate and temperature.

In dementia with Lewy bodies and some forms of Alzheimer's disease, alpha-synuclein becomes toxic. Neurons can't repair it, so it starts to clump and stop those chemical signals from moving between neurons. This clumping also occurs in Parkinson's disease and causes many of the same physical symptoms.

This clumping is also present in some people living with Alzheimer's disease and accelerates their cognitive decline.

Unfortunately, these clumps can only be detected with a lumbar puncture, where spinal fluid is removed with a needle. Dr Chatterjee is hoping to eliminate the need for this painful procedure by detecting alpha-synuclein in blood. She'll do this using a technique called proteomics, which analyses blood-based proteins to identify unique patterns that represent abnormal alpha-synuclein in brain cells.

Dr Chatterjee will also aim to discover if drugs used to treat other conditions can be repurposed to prevent or reduce alpha-synuclein clumping. If successful, this project may lead to earlier and less invasive diagnosis of dementia with Lewy bodies and move us closer to identifying treatments that can stop disease progression.

How will this happen?

Stage 1: study already-existing spinal fluid and blood samples of people living with dementia with Lewy bodies and Alzheimer's disease to identify the unique patterns that indicate alpha-synuclein clumping.

Stage 2: use a specialised medical database screening method to identify pre-existing drug treatments that contain compounds which may prevent alpha-synuclein clumping. Test those drugs on the diseased spinal fluid samples and monitor their impact.

What could it mean for dementia research?

- Earlier and less invasive diagnosis.
- Potential for prevention or slowing of disease with drug treatments that are already available.

Who's undertaking the research?

Dr Pratishtha Chatterjee, The University of Melbourne

Dr Chatterjee is a senior research fellow in the Centre of Research Excellence for Enhanced Dementia Diagnosis at the Florey Institute of Neuroscience and Mental Health, The University of Melbourne. She has a proven track-record of conceptualising, designing and leading projects on blood-biomarkers reflecting Alzheimer's disease-related pathologies for diagnosis, prognosis, and longitudinal monitoring of the disease.

The title of Dr Chatterjee's project is *Determining and targeting alpha-synuclein pathology in dementia with Lewy bodies and Alzheimer's disease.*

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