Study finds some motor neuron disease and dementia patients share genetic defects

May 9 2023

Gene breakthrough: Researchers have found some people with motor neuron disease and dementia carry the same genetic defects. Credit: Macquarie University

New research has discovered that some patients with motor neuron disease (MND) and frontotemporal dementia (FTD) carry the same rare

genetic defects that cause other neurodegenerative diseases.

Researchers from the Macquarie University MND Research Center and The Walter and Eliza Hall Institute of Medical Research have identified the defects in the genomes of some people with non-inherited, or sporadic, MND and FTD.

MND results in the death of the neurons, or motor nerves, connecting the brain and spinal cord to the muscles. These are the cells that control our ability to move, breathe and swallow. The disease is progressive and eventually fatal.

FTD also causes the death of neurons in part of the brain, resulting in a range of progressive symptoms such as memory loss, unusual behavior, personality changes and communication problems. It is the same form of dementia with which actor Bruce Willis was recently diagnosed, and unlike older-onset dementia, it tends to affect people under 65.

The majority of cases in both diseases—about 90% in the case of MND and 60%–70% in FTD—are sporadic, with the rest occurring in families.

These gene defects, known as short tandem repeat expansions, are the cause of more than 20 neurodegenerative diseases including spinocerebellar ataxias and myotonic dystrophy. This Australian study has been the most comprehensive assessment of these gene defects in MND and FTD patients worldwide.

Macquarie University Postdoctoral Research Fellow Dr. Lyndal Henden says the findings were a surprise.

"We found almost 18% of sporadic MND and FTD patients carried a DNA repeat expansion thought to be involved in other degenerative diseases," she says.

"Finding this genetic connection between MND and FTD offers a fresh opportunity to uncover common risk factors for neuron death, and it will have implications for understanding both diseases."

Macquarie University Associate Professor Kelly Williams directed the study, and says the team suspected there could be some overlap with other diseases, but not to such an extent.

"This suggests shared risk factors among these diseases, shared mechanisms that cause nerves to die—and perhaps shared therapeutic strategies in the future," she says.

"While the causes of sporadic MND and FTD remain unknown, this is an important step in a long-term effort to identify the risk factors for developing one of these diseases."

Work can now begin to understand how these shared repeat expansions contribute to neuron death.

The study, published in the latest edition of the journal *Science Advances*, is the culmination of 10 years of research that could not have been possible without the cooperation of patients with MND and FTD, who have donated biological samples for DNA at both Macquarie University and the University of Sydney.

More information: Lyndal Henden et al, Short tandem repeat expansions in sporadic amyotrophic lateral sclerosis and frontotemporal dementia, *Science Advances* (2023). DOI: 10.1126/sciadv.ade2044

Provided by Macquarie University