Spinal fluid biomarkers detect neurodegeneration, Alzheimer's disease in living patients

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Alzheimer's disease and related diseases can still only be confirmed in deceased patients' brains via autopsy. Even so, the development of

biomarkers can give patients and their families answers during life: Alzheimer's disease can be accurately detected via peptides and proteins in a patient's cerebrospinal fluids (CSF), which can be collected through a lumbar puncture and tested while the patient is alive. In 2018, a new framework suggested combining three Alzheimer's disease biomarkers in CSF—pathologic amyloid plaques (A), tangles (T), and neurodegeneration (N), collectively called ATN. According to recent research from the Perelman School of Medicine at the University of Pennsylvania, the ATN framework can be extended to detect another neurodegenerative condition: frontotemporal degeneration.

Patients with frontotemporal degeneration can experience a range of symptoms, including behavioral changes, executive dysfunction, and language impairments. Distinguishing frontotemporal degeneration from Alzheimer's disease can be a challenge for clinicians: the symptoms of frontotemporal degeneration can sometimes overlap with Alzheimer's disease, and a subset of patients can even have both pathologies. Biomarkers can fill the gap by providing evidence of whether Alzheimer's pathology underlies a patient's symptoms.

"CSF biomarkers work similarly to a pregnancy test, offering a simple positive or negative result when enough of a substance is detected. But like a pregnancy test, biomarkers for Alzheimer's disease can provide false negatives or positives," said lead investigator Katheryn A.Q. Cousins, Ph.D., a research associate in the Frontotemporal Degeneration Center in the Department of Neurology at Penn Medicine. "Alzheimer's is a diverse disease, and it is common for other conditions to also be present in the brain. The ATN framework may provide a more complete look at a person's diagnosis and give us a much richer understanding of not only Alzheimer's disease, but other co-occurring neurodegenerative conditions. However, to accomplish this, additional biomarkers that can detect other neurodegenerative conditions are critically needed."

The findings, published in *Alzheimer's and Dementia: The Journal of the Alzheimer's Association*, show that ATN incorporating neurofilament light chain (NfL) may provide a more accurate and precise diagnosis for patients with frontotemporal degeneration. NfL is a protein abundant in the brain, whose levels increase as degeneration progresses. Cousins' work shows that CSF NfL may be a more accurate marker of neurodegeneration for patients with frontotemporal degeneration, including for Alzheimer's disease.

"While the ATN framework is very exciting and offers much opportunity for patients with Alzheimer's disease, these biomarkers don't capture every case of the disease. We want to be able to detect and treat every patient with neurodegenerative disease as early as possible, and more research is needed to fully understand how biofluids track with the disease process," said Cousins. "I am eager to conduct additional research into which patients might be missed by these markers, what they have in common, and what causes the pathological and clinical differences in the disease."

More information: Katheryn A Q Cousins et al, ATN incorporating cerebrospinal fluid neurofilament light chain detects frontotemporal lobar degeneration, *Alzheimer's and Dementia: The Journal of the Alzheimer's Association* (2021). DOI: 10.1002/alz.12233

Provided by Perelman School of Medicine at the University of Pennsylvania

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