Study finds the timing of CSF biomarker divergence for Alzheimer disease, normal cognition varies

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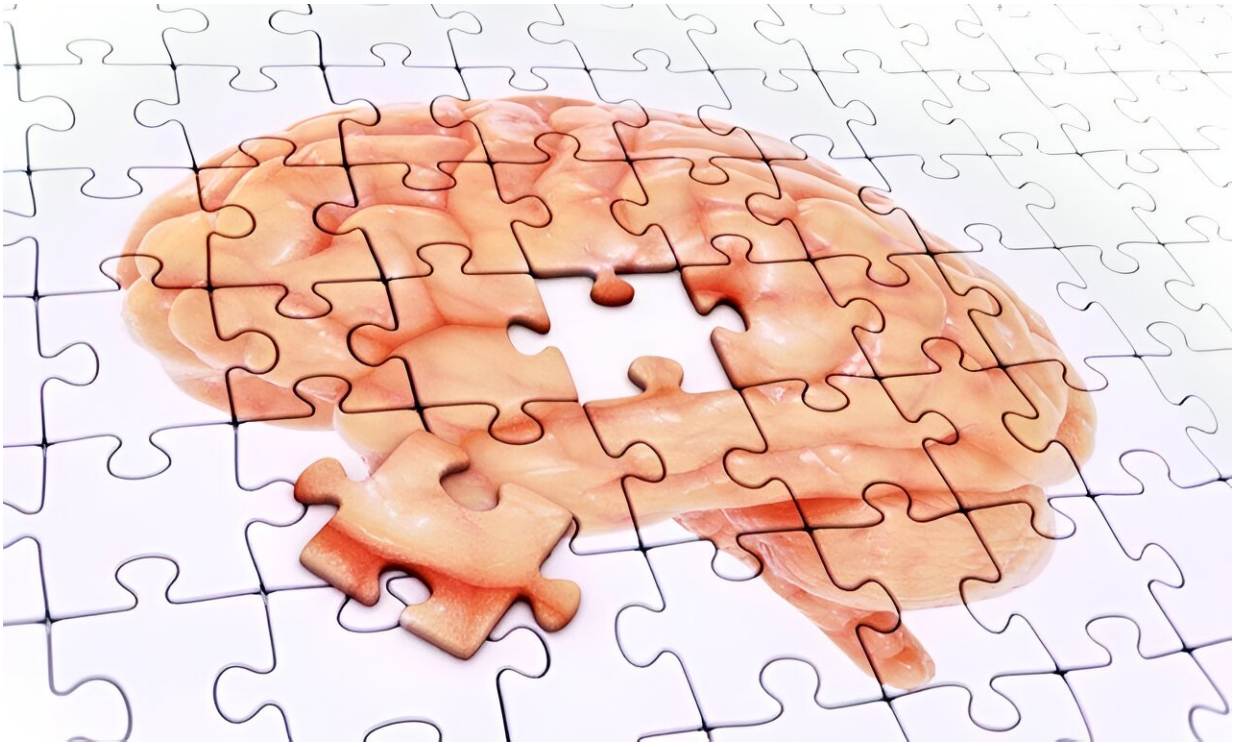

Cerebrospinal fluid (CSF) and other biomarkers differ for individuals with Alzheimer disease and cognitively normal controls, with the estimated times of divergence varying from 18 to six years before

diagnosis, according to a study published in the Feb. 22 issue of the *New England Journal of Medicine*.

Jianping Jia, M.D., Ph.D., from Xuanwu Hospital in Beijing, and colleagues conducted a multicenter, nested case-control study of Alzheimer disease biomarkers in cognitively normal individuals. At two- to three-year intervals, a subgroup of these participants underwent CSF testing, cognitive assessments, and brain imaging. A total of 648 participants in whom Alzheimer disease developed were matched with 648 participants with normal cognition.

Participants were followed for a median of 19.9 years. The researchers found that CSF and imaging biomarkers in the Alzheimer disease group diverged from those in the cognitively normal group a number of years before diagnosis: amyloid-beta $(A\beta)_{42}$ at 18 years; ratio of $A\beta_{42}$ to $A\beta_{40}$ at 14 years; phosphorylated tau 181 at 11 years; total tau at 10 years; neurofilament light chain at nine years; hippocampal volume at eight years; and cognitive decline at six years.

The changes in CSF biomarker levels in the Alzheimer disease group initially accelerated and then slowed as cognitive impairment progressed.

"The importance of the work by Jia et al. cannot be overstated," Richard Mayeux, M.D., from Columbia University in New York City, writes in an accompanying editorial. "Knowledge of the timing of these physiological events is critical to provide clinicians with useful starting points for prevention and therapeutic strategies."

More information: Jianping Jia et al, Biomarker Changes during 20 Years Preceding Alzheimer's Disease, *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMoa2310168

Richard Mayeux, Alzheimer's Disease Biomarkers—Timing Is

Everything, *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMe2400102