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3 biomarkers in spinal fluid appear helpful to classify patients with Alzheimer's disease

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A "signature" consisting of three biomarkers in the cerebrospinal fluid was present in 90 percent of patients who had been diagnosed with Alzheimer's disease but also was found in more than one-third of cognitively normal older adults, according to a report in the August issue of *Archives of Neurology*, one of the JAMA/Archives journals.

"The initiation of the Alzheimer's disease pathogenic process is typically unobserved and has been thought to precede the first symptoms by 10 years or more," the authors write as background information in the article. "Therefore, demonstrating that Alzheimer's disease biomarkers, such as cerebrospinal fluid beta-amyloid protein 1-42 (CSF Aß1-42), total CSF tau protein and CSF phosphorylated tau181P (P-Tau181P) protein concentrations are true indicators of the pathogenic process at an early stage is a major challenge."

Geert De Meyer, Ph.D., of Ghent University, Ghent, Belgium, and colleagues in the Alzheimer's Disease Neuroimaging Initiative analyzed data from 114 older adults who were cognitively normal, 200 who had mild cognitive impairment and 102 who had Alzheimer's disease. They first modeled the data from all participants, without considering their cognitive status, to identify profiles that had different levels of three biomarkers: CSF Aß1-42, total CSF tau protein and P-Tau181P. One profile or signature was presumed to be associated with Alzheimer's disease while the other matched a "healthy" status.

When these profiles were applied to the data in the subgroups, the

Alzheimer's disease signature was found in 90 percent of those with Alzheimer's disease, 72 percent of those with mild cognitive impairment and 36 percent of those who were cognitively normal.

"Results were validated on two other data sets," the authors write. "In one study consisting of 68 autopsy-confirmed Alzheimer's disease cases, 64 of 68 patients (94 percent sensitivity) were correctly classified with the Alzheimer's disease feature. In another data set with patients (n=57) with mild cognitive impairment followed up for five years, the model showed a sensitivity of 100 percent in patients progressing to Alzheimer's disease."

The results suggest that this signature of biomarkers—developed independently of data on clinical diagnosis of Alzheimer's disease—can correctly classify patients with the condition. "The unexpected presence of the Alzheimer's disease signature in more than one-third of cognitively normal subjects suggests that Alzheimer's disease pathology is active and detectable earlier than has heretofore been envisioned," the authors conclude. "Thus, taken together, these data provide further support for the view that revision of current diagnostic criteria for Alzheimer's disease is needed, or at least as far as early-stage Alzheimer's disease is concerned."

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