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## New UC Davis study finds early Alzheimer's identification method

(SACRAMENTO, Calif.) — Abnormal brain images combined with examination of the composition of the fluid that surrounds the spine may offer the earliest signs identifying healthy older adults at risk of developing Alzheimer's disease, well before cognitive problems emerge, a study by researchers at UC Davis has found.

"Our findings indicate that a distinctive pattern of imaging and biomarker deviations from typical adults may be an early warning sign of neurobiological pathology and an early sign of Alzheimer's disease," said Laurel Beckett, a professor of public health sciences at UC Davis and the lead study author. "By the time people get diagnosed with Alzheimer's using cognitive tests, there's already a lot of brain damage. We hope that in the future methods that combine brain imaging and biomarker assessments can push the diagnosis back, while learning more about the mechanisms causing Alzheimer's disease, so we can develop better treatments."

Published in the journal *Neurobiology of Aging* in June, the study analysis picked out a subgroup of healthy adults who later would experience a decline in memory performance typical of early Alzheimer's disease long before other study participants.

For the study, Beckett and her team used data from the Alzheimer's Disease Neuroimaging Initiative, which provides researchers with access to brain scans, clinical data and other laboratory results from spinal fluid and blood tests from more than 800 older adults. Some study participants began with a clean slate of cognitive health, some with mild cognitive impairment — a condition that often presages Alzheimer's — and others with mild or moderate Alzheimer's disease.

The researchers analyzed data from 220 normal older adults who had undergone structural magnetic resonance imaging (MRI) and clinical examinations. About half also provided spinal fluid samples. Among the 96 participants, cluster analysis identified three distinct subgroups of individuals based solely on their baseline imaging and laboratory measures. During the next three years, few of these healthy

people showed any cognitive change. But cognitive tests for people in one of the subgroups — about 10 percent of the sample — declined at nearly five times the rate as healthy older adults. The researchers believe this group, which had the most extreme MRI and spinal fluid measurements, may represent the earliest stages of subclinical cognitive decline and Alzheimer's disease.

Beckett said that the finding is an important step toward discovering the constellation of imaging and fluid biomarkers that foreshadow cognitive decline, as well as a means of determining whether new treatments are effective.

"The problem with current clinical trials is that we don't know who is on the edge of experiencing dementia. And even if we did, how would we know if a treatment was working, since they haven't shown any clinical problems?" Beckett said. "This method could improve clinical trials for prevention and reduce the numbers of study participants necessary to speed drug discovery — and eventually change how the pharmaceutical industry and National Institutes of Health conduct Alzheimer's disease clinical trials."

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Other study authors include Jasmine Nettiksimmons, Danielle Harvey, Owen Carmichael and Charles DeCarli of UC Davis; James Brewer of UC San Diego; Clifford R. Jack Jr. and Ronald Petersen of the Mayo Clinic College of Medicine; and Leslie Shaw, John Trojanowski and Michael Weiner of UC San Francisco.

The study was funded by the Alzheimer's Disease Neuroimaging Initiative, the National Institutes of Health and the Dana Foundation.

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