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ALZHEIMER DISEASE

Alzheimer disease biomarkers in healthy individuals can predict cognitive decline several years later

Amyloid load in the brain and cerebrospinal fluid (CSF) levels of amyloid-β and tau could be useful for early identification of healthy individuals who are at increased risk of cognitive impairment and Alzheimer disease (AD), according to a recent study. "To our knowledge, no studies have directly compared the predictive value of these biomarkers," says Catherine Roe, lead author of the paper.

AD is characterized by brain deposition of amyloid plaques composed of amyloid-β, and of neurofibrillary tangles composed of hyperphosphorylated tau. Neuropathology is known to precede clinical AD by decades, suggesting the need for early-intervention strategies.

The current study involved longitudinal data on 201 participants at the Knight Alzheimer Disease Research Center in the USA. All participants were aged 45 years or more, were cognitively normal and had data available from PET amyloid imaging and CSF analysis for amyloid-β and tau species, conducted within 1 year of clinical assessment. All participants had also undergone at least one follow-up assessment.

> "...abnormal levels of any of the...biomarkers predicted time to cognitive impairment..."

Roe *et al.* found that abnormal levels of any of the tested biomarkers predicted time to cognitive impairment, which ranged from 0.96 to 7.53 years. Moreover, accuracy of predictions could be increased through use of a 'stepwise' statistical model that combined a given biomarker with other factors affecting risk of AD—namely, age, sex and ethnicity. Older men from ethnic minorities developed cognitive impairment more rapidly than did other groups in the cohort. As Roe notes, "this finding shows how advanced medical technology can be enhanced by including patient-specific information that is easy to measure and costs nothing."

Some individuals developed cognitive impairment in the absence of abnormal biomarker levels, whereas other participants with abnormal biomarker levels did not show cognitive deficits during the follow-up period. Future studies involving a broader range of biomarkers and longer follow-up should help to resolve these discrepancies.

"With ongoing efforts to develop disease-modifying AD treatments, we would like to be able to accurately predict which individuals are likely to develop AD, so that we can intervene before substantial brain damage occurs," says Roe.

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Original article Roe, C. *et al.* Amyloid imaging and CSF biomarkers in predicting cognitive impairment up to 7.5 years later. *Neurology* doi:10.1212/WNL.0b013e3182918ca6