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Imaging procedure can identify biomarker associated with Alzheimer's disease

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Preliminary research suggests that use of a type of molecular imaging procedure may have the ability to detect the presence of beta-amyloid in the brains of individuals during life, a biomarker that is identified during autopsy to confirm a diagnosis of Alzheimer disease, according to a study in the January 19 issue of *JAMA*.

"Both diagnosis and treatment of Alzheimer disease (AD) are hampered by the lack of noninvasive biomarkers of the underlying pathology. Between 10 percent and 20 percent of patients clinically diagnosed with AD lack AD pathology at autopsy, and community physicians may not diagnose AD in 33 percent of patients with mild signs and symptoms," according to background information in the article. "The ability to identify and quantify brain beta-amyloid could increase the accuracy of a clinical diagnosis of Alzheimer disease." Several types of positron emission tomographic (PET) imaging tests are under study, with florbetapir F 18 (a diagnostic chemical that binds with beta-amyloid) PET showing promise. "However, the definitive relationship between the florbetapir-PET image and beta-amyloid deposition has not been established."

Christopher M. Clark, M.D., of Avid Radiopharmaceuticals, Philadelphia, and colleagues conducted a study to determine if florbetapir F 18 PET imaging performed during life accurately predicts the presence of beta-amyloid in the brain at autopsy. Florbetapir-PET imaging was performed on 35 patients from hospice, long-term care, and community health care facilities near the end of their lives (6 patients to

establish the protocol and 29 to validate), which was compared with measures of brain beta-amyloid that was determined by autopsy after their death. PET images were also obtained in 74 young individuals (18-50 years) presumed free of brain amyloid to better understand the frequency of a false-positive interpretation of a florbetapir-PET image.

Florbetapir-PET imaging was performed an average of 99 days before death for the 29 individuals in the primary analysis group. Fifteen of the 29 individuals (51.7 percent) met pathological criteria for AD. Analysis of images and other data indicated a correlation between florbetapir-PET images and presence and quantity of beta-amyloid pathology at autopsy. "Florbetapir-PET images and postmortem results rated as positive or negative for beta-amyloid agreed in 96 percent of the 29 individuals in the primary analysis cohort. The florbetapir-PET image was rated as amyloid negative in the 74 younger individuals in the nonautopsy cohort," the researchers write.

They add that while amyloid pathology is an essential element for an AD diagnosis, "clinically impaired function may depend, in part, on the ability of the individual's brain to tolerate aggregated amyloid. Genetic risk factors, lifestyle choices, environmental factors, and neuropathological comorbidities may alter the threshold for the onset of cognitive impairment associated with beta-amyloid aggregation."

"This prospective imaging to autopsy study provides evidence that a molecular imaging procedure can identify beta-amyloid pathology in the brains of individuals during life. Understanding the appropriate use of florbetapir-PET imaging in the clinical diagnosis of AD or in the prediction of progression to dementia will require additional studies," the authors conclude.

More information: JAMA. 2011;305[3]:275-283.

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