Imaging May Offer Alzheimer’s Diagnosis Tool

BY MICHÈLE G. SULLIVAN
FROM JAMA

Positron-emission tomography in combination with the radiolabeled compound florbetapir F-18 detected beta-amyloid plaques with 93% sensitivity and 100% specificity in the brains of 35 elderly patients, most of whom had some form of dementia.

Lead investigator Dr. Christopher Clark and his colleagues wrote that florbetapir-PET imaging could be an important diagnostic tool for Alzheimer’s disease—perhaps with the ability to detect brain plaques early in a prodromal stage of the disease—and to measure plaque changes in relation to therapeutic response in future drug studies, according to Dr. Clark, medical director of Avid Radiopharmaceuticals, the company testing the compound (JAMA 2011;305:275-83).

The study also represents the first time an amyloid imaging agent has been tested against autopsy results, said investigator Dr. Marwan N. Sabbagh, founding director of the Cleo Roberts Center for Clinical Research in Sun City, Ariz. “It’s really exciting to be able to correlate imaging so strongly with autopsy findings,” Dr. Sabbagh said.

But Dr. Clark and his coinvestigators cautioned that the study does not make it clear what specific clinical applications the imaging procedure could have, be it the clinical diagnosis of Alzheimer’s disease or the prediction of progression to dementia.

The Food and Drug Administration’s Peripherial and Central Nervous System Drugs Advisory Committee will meet on Jan. 20 to discuss the compound and the study’s findings.

Like Pittsburgh imaging compound B (PiB), florbetapir binds to beta-amyloid plaques in the living brain. PiB’s use, however, has been limited by its short half-life of 20 minutes.

Florbetapir achieves maximum uptake at 30 minutes and remains unchanged for the next 60 minutes, “providing a wide time window to obtain a 10-minute image,” the authors noted.

The prospective study involved 35 patients in hospice or long-term care facilities, and a control group of 74 young, healthy volunteers.

Disclosures: The study was funded primarily by Avid Radiopharmaceuticals. Dr. Clark and eight of the coauthors are stockholders and/or employees of the company. All of the other coauthors received research grants, and most are educators, paid investigators, or members of the speakers bureau for Avid or for Eli Lilly, which acquired the company last November.

Major Finding: PET brain imaging with florbetapir was 93% sensitive and 100% specific for detecting beta-amyloid plaques in 35 elderly patients, most of whom had a clinical diagnosis of some form of dementia.

Data Source: A prospective study of 35 elderly patients in hospice or long-term care facilities, and a control group of 74 young, healthy volunteers.

Low Plasma Beta-Amyloid Ratio Linked to Cognitive Decline

BY MARY ANN MOON
FROM JAMA

Older adults without dementia who had a low ratio of beta-amyloid 42:40 in plasma showed faster cognitive decline in a 9-year study than did those with a higher ratio of the two beta-amyloid peptides, according to a report in JAMA.

This cognitive decline was more marked in subjects who had less cognitive reserve, as estimated by their lower educational attainment and lower literacy.

“These results are important, as the prevalence of cognitive impairment is increasing exponentially and prevention will be crucial. To identify those at risk of dementia, biomarkers like plasma beta-amyloid level that are relatively easy to obtain and minimally invasive could be useful,” wrote Dr. Kristine Yaffe of the University of California, San Francisco, and her associates.

The investigators assessed the relationship between beta-amyloid levels and cognitive decline using a cohort of 3,075 community-dwelling residents of Memphis and Pittsburgh who had been enrolled in an aging study in 1997-1998 when they were 70-79 years old. They studied 997 of the individuals who had undergone repeated cognitive assessments during follow-up through 2007.

The mean age at baseline was 74 years. Approximately 55% of the study subjects were women, and 54% were African American.

A low beta-amyloid 42:40 ratio at baseline was significantly associated with greater cognitive decline on the Modified Mini-Mental State Examination, which has a maximum score of 100. Mean scores on the Modified Mini-Mental State Examination after 9 years of follow-up declined 6.59 points among people in the lowest tertile of plasma beta-amyloid 42:40 ratio, 6.16 points among those in the middle tertile, and 3.60 points among those in the highest tertile.

The investigators also detected a significant, but less robust, association between tertiles of plasma beta-amyloid 42 levels and cognitive decline.

Both associations remained significant when the data were adjusted to account for subject age, race, education level, smoking status, diabetes status, and apolipoprotein E E4 status, according to Dr. Yaffe and her colleagues (JAMA 2011;305:261-6).

Moreover, the association between plasma beta-amyloid 42:40 ratio and cognitive decline was strongest among people with a low cognitive reserve (as measured by less than a high school diploma or 6th grade literacy) and weakest among people with higher cognitive reserve.

People who carried the apolipoprotein E E4 allele also showed a stronger association between plasma beta-amyloid 42:40 ratio and cognitive decline.

“Our results suggest that the plasma beta-amyloid 42:40 ratio appears to be a biomarker of cognitive decline,” the researchers noted.

The modifing effect of cognitive reserve on the association between cognitive decline and plasma beta-amyloid 42:40 ratio “suggests possible pathways such as cognitive activity or ongoing education, for mitigating or preventing beta-amyloid effects on cognition,” they added.

The investigators did not measure cerebrospinal fluid levels of beta-amyloid 42 and 40 and so could not correlate them with plasma levels of the peptides, Dr. Yaffe and her associates said.