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Molecular imaging detects signs of Alzheimer's in healthy patients

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An arsenal of Alzheimer's research revealed at the Society of Nuclear Medicine's 59th Annual Meeting indicates that beta-amyloid plaque in the brain not only is involved in the pathology of Alzheimer's disease but may also precede even mild cognitive decline. These and other studies advance molecular imaging for the early detection of beta-amyloid, for which one product is now approved in the United States , as a major push forward in the race for better treatments.

"Diagnosis of Alzheimer's disease can now be made when the patient first presents symptoms and still has largely preserved mental function," says Christopher Rowe, M.D., a lead investigator for the Australian Imaging, Biomarkers and Lifestyle study of aging (AIBL) and professor of nuclear medicine at Austin Hospital in Melbourne, Australia. "Previously there was an average delay of three years between consulting a doctor over memory concerns and the diagnosis of Alzheimer's, as the diagnosis required the presence of dementia. When used as an adjunct to other diagnostic measures, molecular imaging can help lead to earlier diagnosis. This may give the patient several years to prepare for dementia while they still have control over their destiny."

According to the World Health Organization, Alzheimer's disease affects an estimated 18 million people worldwide, and incidence of the disease is expected to double by the year 2025 to 34 million. The National Institute on Aging estimates that as many as 50 percent of Americans aged 85 or older are affected.

Alzheimer's disease is a chronic and currently incurable neurodegenerative disease. Beta-amyloid burden can begin to build in the brain several years, if not more than a decade, before an individual shows any sign of dementia. Those who go on to develop Alzheimer's disease not only lose their ability to remember their loved ones but also have difficulty with essential bodily functions such as breathing and swallowing in the late stages of disease.

In one study, researchers used a molecular imaging technique called positron emission tomography (PET), which images physiological patterns in the body. PET was combined with an imaging agent called F-18 florbetaben, which binds to amyloid in the brain. This and other PET agents are drawn to targets in the body and emit a positron signal that is picked up by a scanner. Here molecular imaging was performed in conjunction with clinical and neuropsychological testing in order to better understand the long-term effects of beta amyloid plaques in the brains of older individuals with mild cognitive impairment. Those of the 45 subjects in the study who showed high levels of imaging agent binding during imaging and atrophy of the hippocampus, the memory center, had an 80 percent chance of developing Alzheimer's disease within two years, researchers said.

"Molecular imaging is proving to be an essential part of Alzheimer's disease detection," says Rowe. "This and other amyloid imaging techniques will have an increasing role in the earlier and more accurate diagnosis of neurodegenerative conditions such as Alzheimer's disease due to their ability to measure the actual underlying disease process."

Another AIBL study included 194 healthy participants, 92 people with mild cognitive impairment and 70 subjects with Alzheimer's disease, and used another imaging agent called C-11 PiB (Pittsburgh compound B) with PET to gauge amyloid burden in the brain. Researchers showed that, in this study group, widespread amyloid plaque build-up preceded

cognitive impairment, and those with extensive amyloid burden were at higher risk of cognitive decline.

This and another study mark two of the first studies of their kind focusing on beta amyloid in healthy subjects. In the other study, 137 adults with normal cognitive function aged 30 to 89 years were imaged using PET with F-18 florbetapir, now FDA-approved for the detection of beta amyloid plaques, as well as functional magnetic resonance imaging in order to explore how amyloid build-up affects connections in specific areas of the brain involved in cognition, namely the default mode and salience networks, which are responsible for different states of wakeful rest and alertness. Those with increased amyloid burden in these neural networks were prone to impaired cognitive performance.

"The effect of beta amyloid in healthy aging is of great interest since this protein is strongly associated with Alzheimer's disease and may be predictive of the transition from mild cognitive impairment to Alzheimer's disease," says Michael Devous, Sr., Ph.D., director of neuroimaging at the Alzheimer's Disease Center at UT Southwestern Medical Center in Dallas, Texas. "Less is known about its impact on cognition in otherwise healthy aging individuals. In addition, brain connectivity in these areas is thought to be sensitive to early changes in brain function caused both by aging itself and by disease processes such as Alzheimer's disease."

Another study assessed the PET imaging agent C-11 PiB for its ability to detect amyloid plaque in comparison to another imaging agent, 18-F fluorodeoxyglucose (F-18 FDG). The latter acts like glucose, the brain's primary energy source, to map out the metabolic functioning of the brain. Results of the study showed C-11 PiB amyloid imaging to be a better means of evaluating amyloid patterns in the brain than F-18 FDG imaging. In addition, of the 100 healthy participants, 15 percent were shown to have some amyloid build-up when molecular imaging was

performed.

"We are using state-of-the-art, noninvasive PET and MRI technologies to look at some of the earliest developments of Alzheimer's disease onset in the brains of normal middle-aged people," says Guofan Xu, M.D., Ph.D., lead author of the study and research scientist at the department of nuclear medicine and radiology at the University of Wisconsin located in Madison. "With this we can evaluate whether pathological changes associated with Alzheimer's disease are happening many years before onset of significant clinical symptoms."

No treatments are currently available to cure or prevent Alzheimer's disease. With advances in molecular imaging to detect beta amyloid plaques, researchers have an important new tool that may bring the medical community one step closer to making therapies and vaccines a reality for the disease.

Provided by Society of Nuclear Medicine

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