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TAU IN THE BRAIN: A BETTER PREDICTOR OF ALZHEIMER'S DISEASE PROGRESSION?

SAN DIEGO, CALIFORNIA, November 14, 2013. Researchers from around the world continue to report progress in efforts to image the progression of Alzheimer's disease (AD) and other dementias using a class of agents called tau tracers. These agents are used in conjunction with positron emission tomography (PET) scans to visualize pathology in the brain. At the Clinical Trials in Alzheimer's Disease (CTAD) meeting in San Diego, three groups presented their most recent data, which show that these tracers bind to tau protein aggregates in the brain and that the amount of binding correlates with the level of cognitive impairment.

Tau is a protein that forms fibrillary tangles, which accumulate in the brains of people with AD leading to degeneration of neurons. Tau is also found in the brains of people with other dementing diseases such as progressive supranuclear palsy (PSP) and chronic traumatic encephalopathy (CTE), which has been seen in football players, soldiers, and others who have sustained a head injury. Since tangle formation identified at autopsy is associated with the severity of dementia, researchers have been searching for a way to see when and where tau accumulates.

From Tohoku University School of Medicine in Sendai, Japan, Nobuyuki Okamura, MD, PhD, and colleagues reported results from 14 individuals who underwent PET scans using a tau tracer called THK5117. These individuals included 6 healthy controls and 8 patients with mild to severe AD. Subjects also had PET scans with an agent that visualizes deposition of amyloid, the other protein that aggregates in the AD brain. The results showed that THK5117 retention followed a similar regional pattern to the neurofibrillary tangles seen in the postmortem AD brain. The distribution seen in the scans suggest that tau pathology spreads throughout the brain as the disease progresses. The amount of THK5117 retention was also closely associated with dementia severity. Dr. Okamura concluded that non-invasive imaging of tau pathology with this agent could help predict the progression of cognitive decline in the near future and may also be useful in evaluating the efficacy of anti-tau drugs in clinical trials.

Two other research groups presented data using a different tau imaging agent called T807. Mark Mintun, MD, from Avid Radiopharmaceuticals, a wholly owned subsidiary of Eli Lilly, reported the latest findings from studies in cognitively normal and cognitively impaired subjects. As was previously reported, the uptake of T807 correlated with the extent of cognitive impairment. According to Dr. Mintun, tau imaging provides different information from that obtained with amyloid imaging. "While both beta-amyloid and tau deposits are part of Alzheimer's disease pathology, the different types of deposits are thought to represent different types of dysfunction.

While amyloid may tell us about the progression of the disease in its early stages, the amount of tau deposits may help us understand the progress of disease in later, symptomatic stages," he said.

Indeed, Keith Johnson, M.D., and colleagues presented data from a group of older clinically normal individuals who underwent both tau and amyloid PET imaging, as well as tests of cognitive performance. Dr. Johnson reported that greater uptake of T807 was found in certain areas of the brain and was associated with worse memory performance but not with worse performance on tests of executive function or word retrieval. These results suggest that tau imaging may help elucidate the neural basis of memory impairment in the preclinical stages of AD.

While experience with tau tracers is still limited to only a few dozen subjects, researchers and clinicians have greeted these studies with enthusiasm. "We are entering an exciting new era when we can expect tau PET imaging to complement other imaging technologies, along with CSF and other biomarkers," said John Trojanowski, MD, PhD, co-director of the Center for Neurodegenerative Disease Research (CNDR) at the University of Pennsylvania. "These tools will enable us to more precisely map the onset and progression of pathology as it emerges in cognitively normal individuals and then increases as subjects develop the clinical features of AD. Importantly, they will also improve the accuracy and efficiency of clinical trials, which hopefully will accelerate efforts to identify effective treatments for AD and related tauopathies."