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Blood test method may predict Alzheimer's protein deposits in brain

March 2, 2020 – NIH-funded study reports advance in blood-based detection of ptau181, a biomarker of Alzheimer's disease.

Researchers report an advance in the development of a blood test that could help detect pathological Alzheimer's disease in people who are showing signs of dementia. This approach could be less invasive and less costly than current brain imaging and spinal fluid tests. The blood test detects the abnormal accumulation of a form of tau protein known as

phosphorylated-tau-181 (ptau181), which is a biomarker that suggests brain changes from Alzheimer's. The study, funded by the National Institutes of Health, was published on March 2 in Nature Medicine.

Over the past 15 years, research advances in the development of biomarkers like tau protein have enabled investigators to more accurately diagnose Alzheimer's disease, select research participants, and measure response to investigational therapies. Tau and other biomarkers can be detected with PET scans of the brain and lab tests of spinal fluid. However, PET imaging is expensive and involves radioactive agents, and spinal fluid tests require spinal taps, which are invasive, complex and time-consuming. Simpler biomarker tests are still needed.

"The considerable time and resources required for screening research participants with PET scans and spinal taps slow the pace of enrollment for Alzheimer's disease treatment studies," said Richard J. Hodes, M.D., director of NIH's National Institute on Aging (NIA), which funded much of the study. "The development of a blood test would enable us to rapidly screen a much larger and more diverse group of volunteers who wish to enroll in studies."

An international team of researchers led by Adam Boxer, M.D., Ph.D., at the University of California, San Francisco, used the new test to measure the concentration of ptau181 in plasma, which is the liquid part of blood that carries the blood cells. The samples were collected from more than 400 participants from the University of California, San Francisco Memory and Aging Center, part of the NIA-funded Alzheimer's Disease Research Center; the NIH-supported Advancing Research and Treatment for Frontotemporal Lobar Degeneration (ARTFL) consortium; and a research study sponsored by Eli Lilly.

Their analysis demonstrated that the ptau181 in plasma could differentiate healthy participants from those with Alzheimer's pathology, and differentiate those with Alzheimer's pathology from a group of rare neurodegenerative diseases known collectively as frontotemporal lobar degeneration (FTLD).

“It has become clear that there are many possible biological pathways to dementia,” said Roderick Corriveau, Ph.D., program director at NIH’s National Institute of Neurological Disorders and Stroke (NINDS), which also supported the study. “Finding a blood test that specifically identifies the presence of Alzheimer’s pathology in the brain should greatly help researchers develop better treatments for the many who suffer from dementia.”

In addition, the results with the plasma ptau181 test mirrored results with two established biomarker tests for Alzheimer’s – a spinal fluid ptau181 test and a PET brain scan biomarker known as amyloid protein. The research team, which includes the NIH’s ARTFL–LEFFTDS Longitudinal Frontotemporal Lobar Degeneration (ALLFTD) research consortium that was announced last year, is now aiming to refine and improve the ptau181 blood test method.

“Because of NIH’s investments, we are poised to make dramatic advances in biomarker development for Alzheimer’s disease, FTLD, and related neurodegenerative disorders,” said Eliezer Masliah, M.D., director of NIA’s Division of Neuroscience

. In the future, improved biomarkers like ptau181 may help not just researchers but also physicians to detect and diagnose Alzheimer’s and related neurodegenerative disorders earlier, when interventions are more likely to be effective.

“This research is an example of how studies on rare diseases, in this case FTLD, may provide important insights into common disorders such as Alzheimer’s disease, which affects millions of people,” said Tiina Urv, Ph.D., program officer in the Office of Rare Diseases Research at the NIH’s National Center for Advancing Translational Sciences (NCATS), which also supported the study.

A different international team, this one led by Oskar Hansson, M.D., Ph.D., at Lund University in Sweden and supported in part by NIH, reported similar findings. Using the same plasma ptau181 test, these researchers were able to differentiate between Alzheimer’s and other neurodegenerative diseases nearly as well as they could with a spinal fluid ptau181 test and a PET brain scan for tau protein. In addition, they

followed participants for several years and observed that high levels of plasma ptau181 among those who were cognitively normal or had mild cognitive impairment may be used to predict later development of Alzheimer's dementia. These results were also published today in Nature Medicine.

The research led by Adam Boxer at the University of California, San Francisco was funded by multiple NIH grants, including LEFFTDS (U01AG045390) and the Frontotemporal Lobar Degeneration Clinical Research Consortium (U54NS092089). U54NS092089 is part of the Rare Diseases Clinical Research Network (RDCRN), an initiative of the NCATS Office of Rare Diseases Research (ORDR), and is funded through collaboration between NCATS and NINDS. Other grants include P01AG019724, U24AG21886, R01AG045611, P50AG023501, P50AG016574, R01AG045611, R01AG038791, K08AG052648 and K24AG053435. The research led by Oskar Hansson at Lund University was funded in part by NIH grants U24NS072026 and P30AG19610.

About the National Institute on Aging (NIA): NIA leads the U.S. federal government effort to conduct and support research on aging and the health and well-being of older people. Learn more about age-related cognitive change and neurodegenerative diseases via NIA's Alzheimer's and related Dementias Education and Referral (ADEAR) Center website. For information about a broad range of aging topics, visit the main NIA website and stay connected.

About the National Institute of Neurological Disorders and Stroke (NINDS): NINDS is the nation's leading funder of research on the brain and nervous system. The mission of NINDS is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease.

About the National Center for Advancing Translational Sciences (NCATS): NCATS conducts and supports research on the science and operation of translation – the process by which interventions to improve health are developed and implemented – to allow more treatments to get to more patients more quickly. For more information about how NCATS is improving health through smarter science, visit <https://ncats.nih.gov>.

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