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New study identifies link between Alzheimer's disease biomarkers in healthy adults

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A study published in the November issue of the *Journal of Alzheimer's Disease* provides an insight into normal, physiological levels and association between proteins involved in development of Alzheimer's disease. A group of scientists and physicians from the University of Washington and Puget Sound Veterans' Affairs Health Care System in Seattle, in collaboration with groups from the University of Pennsylvania and the University of California San Diego, performed a study in cognitively normal and generally healthy adults, from young to old (age range 21-88 years), of both genders, measuring levels of different brain-derived molecules associated with Alzheimer's disease.

Investigators determined that cerebrospinal fluid (CSF) levels of apolipoprotein E (apoE), one of the most important proteins involved in transfer of fatty substances between different brain cells, are highly correlated with the levels of proteins known to be involved in development of Alzheimer's disease, amyloid precursor protein (APP) and tau. While many studies have previously shown that apoE gene is very important for Alzheimer's disease development, the connection between apoE protein and other relevant CSF markers in healthy adults was not known.

Although this type of study cannot establish causal associations, the results strongly suggest that the CSF levels of apoE may explain a significant proportion of the levels of APP- and tau-related biological

markers in the healthy human brain, indicating a strong physiological link between apoE, APP and tau. In other words, the study points to a possibility that modulation of the levels of apoE may affect the levels of APP and tau in the brain.

Furthermore, the study has shown that people who have a "beneficial" genetic form of apoE (so-called APOE2), which is associated with lower risk of Alzheimer's disease, have lower CSF levels of beta-amyloid peptide 42, a molecule implicated in development of Alzheimer's disease plaques. This finding may explain some of the basis for the known protective effects of the APOE2 observed in large population studies.

Dr. Simona Vuletic, Northwest Lipid Metabolism and Diabetes Research Laboratories, University of Washington School of Medicine, Seattle, commented, "Understanding the associations between these important molecules in the brain of cognitively normal, healthy people will help us develop better strategies not only for diagnosis, but possibly also better prevention and treatment for Alzheimer's disease. This study also provides baseline data and an opportunity to understand how these normal relationships change, leading to the disease."

The article is "Apolipoprotein E Highly Correlates with AâPP- and Tau-Related Markers in Human Cerebrospinal Fluid" by Simona Vuletic, Ge Li, Elaine R. Peskind, Hal Kennedy, Santica M. Marcovina, James B. Leverenz, Eric C. Petrie, Virginia M-Y. Lee, Douglas Galasko, Gerard D. Schellenberg, John J. Albers. It is published in the Journal of Alzheimer's Disease 15:3 (November 2008).

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