Alzheimer's disease risk impacted by the liver, diet

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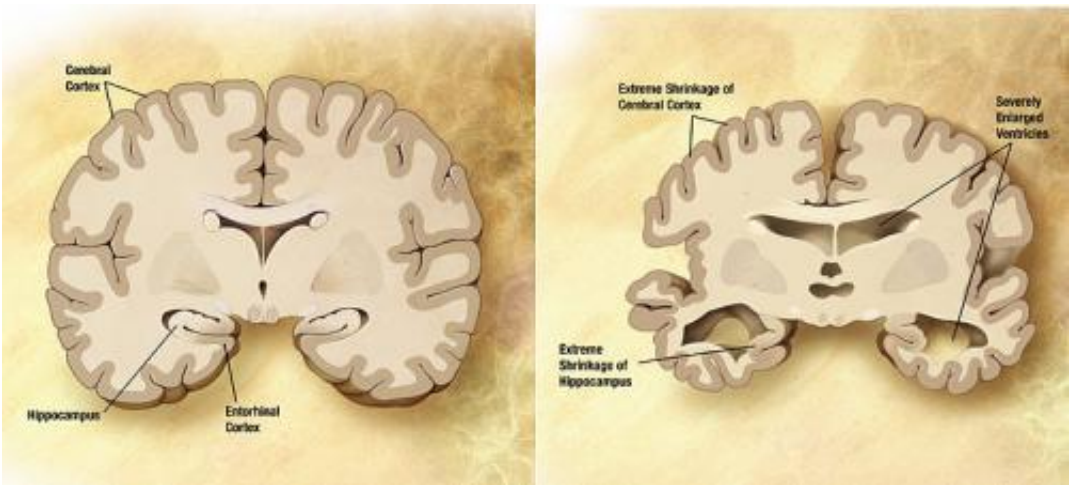

Diagram of the brain of a person with Alzheimer's Disease. Credit: Wikipedia/public domain.

CHICAGO -Reduced levels of plasmalogens—a class of lipids created in the liver that are integral to cell membranes in the brain—are associated with an increased risk of Alzheimer's Disease, according to new research presented this week at the Alzheimer's Association International Conference (AAIC) 2018 by Mitchel A. Kling, MD, an associate professor of Psychiatry in the Perelman School of Medicine at the University of Pennsylvania and the Veterans Affairs Medical Center.

Plasmalogens are created in the liver and are dispersed through the blood stream in the form of lipoproteins, which also transport cholesterol and

other lipids to and from cells and tissues throughout the body, including the brain. Kling, and the multi-institutional Alzheimer's Disease Metabolomics Consortium led by Rima F. Kaddurah-Daouk, Ph.D., at Duke University School of Medicine, developed three indices for measuring the amount of these lipids related to cognition, in order to identify whether reduced levels in the bloodstream are associated with an increased risk of Alzheimer's disease, mild cognitive impairment (MCI), overall cognitive function, and/or other biomarkers of neurodegeneration in Alzheimer's disease. The three indices measured: the ratios of plasmalogens to each other; the ratios of plasmalogens to their closely-related, more conventional lipid counterparts; and a combination of these two quantities.

They measured several plasmalogens including those containing omega-3 fatty acids docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), as well as an omega-6 fatty acid and closely-related non-plasmalogen lipids, in blood-based fluids collected from two groups: the first included 1,547 subjects that have Alzheimer's disease, MCI or significant memory concerns (SMC), and subjects who were cognitively normal (CN) and who are enrolled in the Alzheimer's Disease Neuroimaging Initiative; the second included 112 subjects from the Penn Memory Center, including those with Alzheimer's, MCI, and CN.

The team observed that lower values of these indices were associated with a higher likelihood of Alzheimer's disease. A similar pattern was seen with MCI and CN associations. Additionally, some of the decreased plasmalogen levels were correlated with increased levels of the tau protein in the brain, a marker of Alzheimer's disease.

"This research shows that an age-related deficiency of plasmalogens could lead to an increased risk of Alzheimer's disease, because the liver cannot make enough of them," said Kling, who is also a fellow of the Institute on Aging. "This research has a variety of interesting

implications. For example, it highlights a potential relationship between conditions such as obesity and diabetes and Alzheimer's—as the liver has to work harder to break down fatty acids over time. This could lead to the eventual destruction of the peroxisomes that create plasmalogens which thus, increases the risk of Alzheimer's."

The findings also provide a possible explanation for the observed lack of effect of fish oil or DHA administration on cognitive function or Alzheimer's disease, which has been shown in other studies. This is due to the defect in the liver that prevents these fatty acids from becoming incorporated into the plasmalogens that are critical for synaptic function in brain, which can affect cognition. Several of the genes associated with Alzheimer's are involved in lipid transport or metabolism, therefore ongoing research is looking to see how changes in the production or transport of lipids affect brain structure and function.

"Our findings provide renewed hope for the creation of new treatment and prevention approaches for Alzheimer's disease," Kling said. "Moving forward, we're examining the connections between plasmalogens, other lipids, and cognition, in addition to gene expression in the liver and the brain. While we're in the early stages of discovering how the liver, lipids, and diet are related to Alzheimer's disease and neurodegeneration, it's been promising."

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