Study of dietary intervention examines proteins in brain

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The lipidation states (or modifications) in certain proteins in the brain that are related to the development of Alzheimer disease appear to differ depending on genotype and cognitive diseases, and levels of these protein and peptides appear to be influenced by diet, according to a report published Online First by *JAMA Neurology*, a JAMA Network publication.

Sporadic Alzheimer disease (AD) is caused in part by the accumulation of β-amyloid (Aβ) peptides in the brain. These peptides can be bound to lipids or lipid carrier proteins, such as apolipoprotein E (ApoE), or be free in solution (lipid-depleted [LD] Aβ). Levels of LD Aβ are higher in the plasma of adults with AD, but less is known about these peptides in the cerebrospinal fluid (CSF), the authors write in the study background.

Angela J. Hanson, M.D., Veterans Affairs Puget Sound Health Care System and the University of Washington, Seattle, and colleagues studied 20 older adults with normal cognition (average age 69 years) and 27 older adults with amnestic mild cognitive impairment (average age 67 years).

The patients were randomized to a diet high in saturated fat content (45 percent energy from fat, greater than 25 percent saturated fat) with a high glycemic index or a diet low in saturated fat content (25 percent of energy from fat, less than 7 percent saturated fat) with a low glycemic index. The main outcomes the researchers measured were lipid depleted (LD) Aβ42 and Aβ40 and ApoE in cerebrospinal fluid.

Study results indicate that baseline levels of LD Aβ were greater for adults with mild cognitive impairment compared with adults with normal cognition. The authors also note that these findings were more apparent in adults with mild cognitive impairment and the Ɛ4 allele (a risk factor for AD), who had higher LD apolipoprotein E levels irrespective of cognitive diagnosis. Study results indicate that the diet low in saturated fat tended to decrease LD Aβ levels, whereas the diet high in saturated fat increased these fractions.

The authors note the data from their small pilot study need to be replicated in a larger sample before any firm conclusions can be drawn.

"Overall, these results suggest that the lipidation states of apolipoproteins and amyloid peptides might play a role in AD pathological processes and are influenced by APOE genotype and diet," the study concludes.

In an editorial, Deborah Blacker, M.D., Sc.D., of the Massachusetts General Hospital/Harvard Medical School, Boston, writes: "The article by Hanson and colleagues makes a serious effort to understand whether dietary factors can affect the biology of Alzheimer disease (AD)."

"Hanson et al argue that the changes observed after their two dietary interventions may underlie some of the epidemiologic findings regarding diabetes and other cardiovascular risk factors and risk for AD. The specifics of their model may not capture the real underlying biological effect of these diets, and it is unclear whether the observed changes in the intermediate outcomes would lead to beneficial changes in oligomers or plaque burden, much less to decreased brain atrophy or improved cognition," she continues.

"At some level, however, the details of the biological model are not critical; the important lesson from the study is that dietary intervention can change brain amyloid chemistry in largely consistent and apparently

meaningful ways – in a short period of time. Does this change clinical practice for those advising patients who want to avoid dementia? Probably not, but it adds another small piece to the growing evidence that taking good care of your heart is probably good for your brain too," Blacker concludes.

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