OMEGA-3 FATS MAY REDUCE RISK OF AGE-RELATED COGNITIVE DECLINE, DEMENTIA AND ALZHEIMER'S DISEASE

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Biological Mechanisms Addressing Neuroprotective Effects of Omega-3 Fats

Several recent studies have suggested that higher intake and blood levels of omega-3 fatty acids may help to reduce risk of age-related cognitive decline, dementia and Alzheimer's disease. (1-5). Three of four epidemiological studies have suggested a protective effect for omega-3 fatty acids, in this regard. (6) The major dietary sources of these fatty acids are fish and shellfish from both salt water and fresh water. EPA and DHA can also be synthesized from the elongation and desaturation of alpha-linolenic acid, which is present in some vegetable oils. (7) Flaxseed oil is an especially rich source of alpha-linolenic acid, an omega-3 fatty acid.

DHA is 22 carbons long and has six double bonds, with the first one occurring between carbon three and four from the omega end (the methyl end) of the fatty acid chain. It is the most prominent fatty acid in the brain, retina, and spermatozoa and is necessary for vision, cognition, and sperm motility. The neurons and synaptosomes of the cerebral cortex are especially rich in DHA, where it is incorporated into the membrane phospholipid structure. The brains of Alzheimer's patients have been shown to contain a lower content of DHA in the grey matter of the frontal lobe and the hypocampus than do the brains of patients without Alzheimer's disease. The brains of Alzheimer's patients also demonstrate a build-up of amyloid protein complex and an inflammatory component.(7)

The Framingham Heart Study showed that persons with plasma phosphatidylcholine DHA in the top quartile of values had a significantly (47%) lower risk of developing all-cause dementia than did those in the bottom quartile and significantly greater protection was obtained from consuming 2.9 fish meals per week than from consuming only 1.3 fish meals per week, on average. (7)

Several mechanisms have been proposed to explain how omega-3-fats can reduce nerve cell degeneration associated with these conditions.

Omega-3 fatty acids are known to provide anti-inflammatory effects due to their conversion to anti-inflammatory eicosanoids within the body. The eicosanoids formed from omega-3 fatty acids also improve blood flow by dilating vessels, and decreasing platelet stickiness (anti-thrombotic), and provide other benefits associated with cardiovascular health, such as improving endothelial function and lowering triglyceride blood levels. All of these effects are also associated with prevention of cognitive decline largely via preserved blood flow circulation to brain tissue (lower risk of cerebrovascular disease).

However, omega-3 fatty acids also play a direct role in nerve cell structure and function. Eicosapentaenoic acid (EPA) and docsahexaenoic acid (DHA) have been shown to improve the composition of nerve cell membranes, and stimulate the development, regeneration and function of nerve cells by stimulating synaptic plasticity and increasing neurotransmission, as well as increasing memory abilities. In short, long chain omega-3 fatty acids are structural components of neuronal and other cell membranes, affecting membrane fluidity, nerve transmission and nerve cell function in a positive way. They also modulate the production of eicosanoids and inflammatory cytokines and help preserve blood flow to the brain.

There is also the suggestion that oxidative stress (from oxygen and other free radicals), significantly contributes to neuronal damage seen in cases of cognitive impairment and Alzheimer's disease, by depleting the brain of vulnerable highly unsaturated fatty acids (e.g. EPA and DHA). Some researchers suggest that by replenishing brain cells with EPA and DHA via higher intake levels, individuals may help protect themselves against cognitive decline to a significant degree. (8-11)

Adding support to the epidemiological and experimental studies that suggest that omega-3 fatty acids can reduce risk of cognitive decline, the April 2007 issue of the *American Journal of Clinical Nutrition* contained the findings of two large prospective studies that evaluated intake of omega-3 fatty acids and subsequent risk of cognitive decline, dementia and Alzheimer's disease in older human subjects. Taken together, the findings of MA Beydoun et al (the *Atherosclerosis Risk in Communities Study*) and those of BM van Gelder et al (the *Zutphen Elderly Study*) indicate that a moderate intake of EPA and DHA were strongly associated with reduced risk of cognitive decline. (9, 10)

The ARIC Study

The *Atherosclerosis Risk in Communities Study* analyzed plasma fatty acids in cholesterol esters and phospholipids in whites residing in Minneapolis MN from 1987 through 1989. From 1990 through 1992 and from 1996 through 1998, 3 neurophysiological tests were administered. Effectively, this study assessed the association between plasma fatty acids and cognitive decline in adults aged 50-65 years of age at baseline and conducted a subgroup analysis. A striking finding among the 2251 study subjects was that higher levels of omega-3 fatty acids were associated with reduced risk of decline in verbal fluency, particularly in hypertensive and dyslipedemic subjects, whose tissues are exposed to greater oxidative stress from these conditions. In contrast, the risk of global cognitive decline increased with elevated palmitic acid (a saturated fat) and in subjects with higher levels of arachidonic acid (an omega-6 fatty acid found in meat and dairy products). (9) It should be noted that palmitic acid is a saturated fat that is highly associated with thrombosis and the elevation of LDL-cholesterol, both of which can lead to atherosclerosis obstruction, increasing the tendency to develop dementia (11)

The Zutphen Elderly Study

In the *Zuthen Elderly Study* data on fish consumption of 210 male participants, who were aged 70-89 years of age in 1990, and data on cognitive functioning collected in 1990 and 1995 were assessed. The intake of EPA and DHA was calculated for each participant. Results showed that fish consumers had significantly less 5-year subsequent cognitive decline than did non fish consumers and a linear trend (dose-dependent trend) was observed for the relation between the intake of EPA and DHA and cognitive decline. More specifically, the results showed that elderly men who consumed an average of approximately 400 mg per day of omega-3 fatty acids from EPA and DHA had significantly less cognitive decline over the five year period than did those consuming an average of approximately 20 mg per day of omega-3 fatty acids.

At present the American Heart Association recommends the consumption of fish (preferably fatty fish) at least twice per week, a recommendation that is compatible with the results of the Zutphen Elderly Study. To achieve 400 mg per day of EPA and DHA, one would have to consume 6 servings per week of lean fish (average serving size 140 gm or about 5 ounces) or one serving per week of fatty fish, such as mackerel or herring. (10) One can also achieve this level of intake by consuming a mere 20 gm of Chinook salmon (less than one ounce) or 100 gm of cod (a little more than 3.5 ounces). As such, two to three meals of fish per week would supply approximately 380 mg of EPA/DHA per day, on average. (7)

Summary

A number of epidemiological studies and experimental studies suggest that higher intake levels, brain levels and blood levels of EPA and DHA may help preserve cognitive function as we age, and reduce risk of dementia and Alzheimer's disease. A number of biological mechanisms have been proposed to explain the protective effects of EPA and DHA in regards to these neurodegenerative conditions. More recently, two prospective studies, involving older and elderly humans (the *ARIC* and *Zutphen Elderly* Studies) have shown a strong correlation between higher plasma and intake levels, respectively, of EPA and DHA, and subsequent decreased cognitive decline. The *Zutphen Elderly Study* highlighted the

fact that an average daily intake of 400 mg of EPA and DHA appears to be a significant threshold level at which a marked protective effect is observed. Some experts suggest that for people who are allergic to fish and/or shellfish and those who cannot or will not obtain sufficient intake of fish, that they consume 1000 mg per day of fish oil from supplementation (Connor WE, Connor SL, 2007). A supplement containing fish oil and flaxseed oil may also be a consideration providing the total amount of EPA and DHA reaches a minimum threshold intake value of 400 mg per day. Health practitioners should bear this information and these dosage levels in mind when making recommendations about specific essential fatty acid supplement products to their patients.

For more information on this or other related topics, visit Dr. Meschino's website at: http://www.renaisante.com/

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