The importance of fish and docosahexaenoic acid in Alzheimer disease1,2

William E Connor and Sonja L Connor

Alzheimer disease is devastating both to the afflicted person and to that person’s family. Capable persons become helpless and must be cared for by the family and by the community. This common problem of aging will expand in the near future because people are living longer. It is estimated that 20–40% of the population now over the age of 85 y may have Alzheimer disease (1). A further daunting statistic is that, once Alzheimer disease is identified as the cause of cognitive decline, the patient may live for many years with a high yearly cost of care. Are there potential and safe measures that would prevent this slide into cognitive failure? Fish and fish oil contain 2 fatty acids, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), that may have promise. The major dietary sources of these 2 fatty acids are fish and shellfish, from both salt water and fresh water. DHA can also be synthesized in the body from the n−3 fatty acid α-linolenic acid (18:3), which is present in some vegetable oils and some nuts and seeds. However, this synthetic step is relatively inefficient. DHA is 22 carbons long and has 6 double bonds with the n−3 configuration. It is the most prominent fatty acid in the brain, retina, and spermatozoa (2) and is necessary for vision, cognition, and sperm motility. DHA is especially rich in the neurons and synaptosomes of the cerebral cortex, where it occupies the no. 2 position of membrane phospholipids. In premature infants whose formula contained DHA balanced with n−3 fatty acids fish and shellfish, from both salt water and fresh water. In contrast, the risk of cognitive decline was associated with lower plasma n−6 fatty acid arachidonic acid (20:4n−6) in both cholesterol esters and phospholipids. In contrast, the risk of cognitive decline was lower with a higher concentration of linoleic acid (18:2n−6). Cognitive decline was associated with lower plasma n−3 fatty acids (DHA+EPA) in the subgroup of subjects with hypertension and dyslipidemia, but this association was not found for the entire group.

In each of these studies, the n−3 fatty acids retarded the decline in cognition over time. One mechanism for the positive

1 From the Division of Endocrinology, Diabetes and Clinical Nutrition, Department of Medicine, Oregon Health & Science University, Portland, OR.
2 Reprints not available. Address correspondence to WE Connor, Division of Endocrinology, Diabetes and Clinical Nutrition, Department of Medicine, L645, Oregon Health & Science University, Portland, OR 97239-3098. E-mail: connorw@ohsu.edu.

effect could be the antithrombotic and antiinflammatory properties of EPA (9). Moreover, the entrance of DHA into the brain could correct DHA deficiency in membrane phospholipids in the cerebral cortex in patients with Alzheimer disease (5), and EPA would counter the proinflammatory action of arachidonic acid, which is a precursor of cytokine and proinflammatory eicosanoids that may be associated with greater cognitive decline. The association of palmitic acid in the plasma cholesterol esters and phospholipids is of interest. This 16-carbon saturate is associated with thrombosis and the elevation of plasma LDL cholesterol that can lead to atherosclerotic obstruction. Both of these conditions could increase the tendency to develop dementia.

Along with numerous previous studies, the Zutphen and Minneapolis studies provide the rationale for a future clinical trial of fish, fish oil, or both in elderly patients prone to the development of Alzheimer disease. Such a trial would involve blood measurements of fatty acids in the plasma and in the red blood cells (red blood cells are more representative of tissue fatty acid composition than is plasma) and tests of cognition at baseline and at a future time, perhaps after 5 y. Because there may be a vascular component to Alzheimer disease, the background diet of any fish-oil trial also should be low in saturated fat and cholesterol (10). Alzheimer disease is so prevalent and so disastrous that definitive clinical trials to delay or prevent it must be carried out. In the meantime, because evidence exists that n−3 fatty acids prevent episodes of sudden death, the American Heart Association has already recommended that all adults consume 2 fish meals per week (11). For people who are allergic to fish or who cannot obtain fish, we suggest the consumption of one fish-oil capsule (1000 mg) per day. The possibility that the fatty acids DHA and EPA in fish and fish oil may delay the ravages of Alzheimer disease is of great interest.

Neither author had a personal or financial conflict of interest with the 2 studies discussed or with the authors of those studies.

REFERENCES