Rethinking brain food

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If omega-3 (n–3) fatty acids are the functional food du jour, then that “jour” must first have been the fifth day of creation (according to Genesis 1:21), when the marine fish were created and exhorted to be fruitful and multiply. The exact time when these marine species became “brain food” for humans because of their high content of oils rich in n–3 polyunsaturated fatty acids (PUFAs) is clouded in the history of intelligent design. These flexible oils have had a distinguished history in the chemistry and nutrition science literature, which contain explanations ranging from how their presence in the diet has protected Eskimos from heart disease or sudden death to their use as antidotes for arthritis and chronic inflammatory conditions and hyperimmune states and for improving brain development and maintenance. Beneficial effects have been attributed to the presence of these n–3 PUFAs in cardiac myocyte membrane phospholipids and in brain membrane phospholipids (especially docosahexaenoic acid) as precursors of prostaglandins.

Another chapter in the history of the n–3 fatty acids as brain food is represented in this issue of the Journal in 2 articles (1, 2), which show associations between dietary n–3 fatty acid intakes and better performance or preservation of cognitive function in aging persons; this relation was tested in healthy persons rather than in persons with dementia or disease. The connection between the brain and n–3 fatty acid intake has been explored extensively, and a number of studies have reported that diets high in fish or marine oils are associated with a lower incidence of dementia (3–5). These recent reports are novel in that they address the association of n–3 fatty acid intake and cognitive function in nondemented individuals and, thus, present a shift in the attention to earlier stages of cognitive decline with the hope of preventing progression to states of dementia and disability before they become irreversible.

The notion of preventing age-associated dementia is a high stakes matter of global importance. In the United States, more than 5 million persons have some form of Alzheimer disease and possibly an equal number have vascular dementia. Forty percent of persons older than 85 y have some form of dementia, and the economic burden of Alzheimer disease alone is estimated at $80–100 billion. With the population aging in every country in the world, and dementia disabling increasing numbers of elderly in every country studied, the importance of preventing and slowing the progression of disabling dementia is a public health imperative.

Two studies in this issue of the Journal address the relation between n–3 fatty acid intake and cognitive function; one study was conducted in Norway (1) and the other in the Netherlands (2). Multiple tests of cognitive function were used to assess cross-sectional relations with fish intake in the Norwegian study, which showed a dose-response effect. The study conducted in Netherlands was prospective and showed that blood concentrations of n–3 PUFAs indicated a benefit of n–3 fatty acid intakes over 3 y of follow-up in an elderly Dutch population. However, these observational studies fall far short of showing a causal effect. The limited discrimination among different domains of cognitive function offer limited opportunities for hypotheses about how and where the putative beneficial effects of n–3 PUFAs are being exerted. We know that the n–3 fatty acid docosahexaenoic acid accounts for 40% of the membrane phospholipid fatty acids in the brain; certainly, this fatty acid must have an effect on membrane receptor function and even neurotransmitter generation.

More recent studies of nutritional factors in brain function, such as those conducted in Rotterdam (6), call attention to our increasing ability to identify anatomical and even functional locations in the brain that are associated with different domains of cognitive function. With the increasing use of magnetic resonance imaging and positron emission tomography we will be better able to associate patterns of function and dysfunction in cognitive domains with changes in brain volume and with specific brain locations, such as the hippocampus, frontal cortex, and amygdala.

Such studies will form an even stronger basis of support for hypotheses on the mechanism by which n–3 PUFAs affect brain function or potentially slow neurodegeneration and will also strengthen associations that should move us in the direction of public health and nutritional recommendations and interventions with sharper endpoints and outcomes.

The evidence-based orthodoxy today will quickly adjure us to present the results of randomized control trials not only for their elucidation of possible causal relations, but also as a basis for judging the usefulness of public health interventions or nutritional recommendations. Such trials are rare and have shown little benefit in patients with dementia (7); however, neither pharmacologic nor nutritional interventions conducted in patients with dementia have shown much benefit.

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We are well aware from previous work at Oxford (8) that the time frame over which dementia develops and brain volume shrinks can often be measured in decades. Therefore, these studies of nutritional associations with brain function during the elongated prodromal period of age-related neurodegeneration and decline offer an opportunity for early intervention to maintain brain function and slow progression to dementia, which is costly economically and in terms of quality of life.

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REFERENCES