ΕΛΛΗΝΙΚΗ ΕΠΙΘΕΩΡΗΣΗ ΔΙΑΙΤΟΛΟΓΙΑΣ-ΔΙΑΤΡΟΦΗΣ 2010, 1(2), 71–72

Editorial

The Omega-6/Omega-3 fatty acid ratio in neurodevelopment
Η αναλογία Ωμέγα-6/Ωμέγα-3 λιπαρών οξέων στην ανάπτυξη του νευρικού συστήματος

A.P. Simopoulos
M.D.The Center for Genetics, Nutrition and Health

Studies on the evolutionary aspects of diet indicate that major changes have taken place in our diet, particularly in the type and amount of essential fatty acids (EFA) and in the antioxidant content of foods.[1,2] An absolute and relative change of omega-6 and omega-3 fatty acids in the food supply of Western societies has occurred over the last 150 years. A balance existed between omega-6 and omega-3 fatty acids for millions of years during the long evolutionary history of the genus Homo, and genetic changes occurred partly in response to these dietary influences. During eons of evolution, omega-3 fatty acids were present in all foods consumed: meat, wild plants, eggs, fish, nuts, and berries.[3,4] However, rapid dietary changes over short periods of time as they have occurred over the past 100–150 years, is a totally new phenomenon in human evolution. These dietary changes are the result of agribusiness and modern agriculture that led to animal feeds consisting primarily of grains, instead of the animals grazing, and to the production of vegetable oils from seeds such as corn, sunflower, safflower, cottonseed, and soybean that are high in omega-6 fatty acids and poor in omega-3s.

Today, industrialized societies are characterized by (1) an increase in energy intake and decrease in energy expenditure; (2) an increase in saturated fat, omega-6 fatty acids and trans fatty acids, and a decrease in omega-3 fatty acid intake; (3) a decrease in complex carbohydrates and fiber; (4) an increase in cereal grains and a decrease in fruits and vegetables; and (5) a decrease in protein, antioxidants, vitamins especially C, E and D, trace elements and calcium intake. The increase in trans fatty acids is detrimental to health. In addition, trans fatty acids interfere with the desaturation and elongation of both omega-6 and omega-3 fatty acids, thus further decreasing the amount of arachidonic acid, eicosapentaenoic acid, and docosahexaenoic acid availability for human metabolism.

☞ **Address for correspondence:**
Artemis P. Simopoulos
The Center for Genetics, Nutrition and Health
2001 S Street, NW, Suite 530
Washington DC 20009, USA
Phone: (202) 462-5062
Fax: (202) 462-5241
E-mail: cgnh@bellatlantic.net

Whereas major changes have taken place in our diet over the past 10,000 years since the beginning of the agricultural revolution, our genes have not changed. The spontaneous mutation rate for nuclear DNA is estimated at 0.5% per million years. Therefore, over the past 10,000 years, there has been time for very little change in our genes, perhaps 0.005%. In fact, our genes today are very similar to the genes of our ancestors during the Paleolithic period 40,000 years ago, at which time our genetic profile was established. Humans today live in a nutritional environment that differs from that for which our genetic constitution was selected. It is the interaction of genes with various environmental factors that determines the phenotype throughout development. Nutrition is an environmental factor of major importance.

Studies in rodents, chickens, primates, and visual and cognitive trials in human infants have shown that both AA and DHA are essential for brain development and function. AA and DHA have been shown to be independent determinants of brain growth and evolution.[6] Moreover, the competition that exists between omega- 6 and omega-3 fatty acids applies to their balance being critical for brain development and structural integrity. DHA is essential for vision, brain neurons, and cell signaling. While DHA is clearly concentrated in the signaling systems of the brain, EPA is more likely to be involved in vascular blood flow and eicosanoid production where it can down-regulate the AA metabolites to maintain homeostasis.

The brain contains little parent EFA (LA and ALA) and typically has AA, docosatetraenoic acid, and DHA as the principal long-chain fatty acids. Although the size of the brain differs between mammalian species, the profile of AA and DHA does not vary suggesting a high degree of evolutionary conservation of the neural lipid profile. DHA is rapidly and selectively incorporated in the (sn)-2 position of neural phospholipid membranes, and is concentrated in the photoreceptor and selectively at synaptic signaling sites. It is the most unsaturated of the cell membrane fatty acids in the brain. The proportions of omega-6 and omega-3 in the diet are a determinant of biochemical efficiency, which is important in providing the optimal conditions for neurodevelopment. Therefore, approaching the ideal ratio of 2:1 or 1:1 could be of relevance to both neurodevelopment and the prevention of early neurodegeneration.[6] Because the enzymes involved in the metabolism of the LA and ALA are shared, there is competition between them and the omega-6 and omega-3 fatty acids also regulate each other. The balance between LA and ALA and their polyunsaturated fatty acid (PUFA) metabolites in the diet is vital. In humans, the brain is the most outstanding organ in biological development: it follows that the priority is brain growth and development, and in the brain, the balance between omega-6 and omega-3 PUFA metabolites is close to 1:1. This ratio (between 2:1 and 1:1) should be the target for human nutrition. In Western diets, the omega-6/omega-3 ratio has increased to between 10:1 and 20:1. This high omega-6 proportion is largely made up by LA, is far from optimal, and is highly inappropriate for normal growth and development and increases the risk of obesity.[7] A most recent meta-analysis indicates that LA increases the risk for coronary heart disease (CHD).[8,9] Furthermore a high omega-6:omega-3 fatty acid ratio increases the expression of genes that lead to inflammation which is at the base of CHD, Obesity, Diabetes, Cancer and other chronic diseases.[10,11]

Diets must be balanced in the omega-6 and omega-3 fatty acids to be consistent with the evolutionary understanding of the human diet. This balance can best be accomplished by decreasing the intake of oils rich in omega-6 fatty acids (corn oil, sunflower, safflower, cottonseed, and soybean) and increasing the intake of oils rich in omega-3s (canola, flaxseed, perilla, and chia) and olive oil which is particularly low in omega-6 fatty acids.

References

1. Eaton SB, Konner M. Paleolithic nutrition. A consideration of its nature and current implications. *New Engl J Med* 1985, 312:283–289
2. Simopoulos AP. Omega-3 fatty acids in health and disease and in growth and development. *Am J Clin Nutr* 1991, 54:438–463
3. Crawford MA. Fatty acid ratios in free-living and domestic animals. *Lancet* 1968, i:1329–1333
4. Simopoulos AP. Omega-3 fatty acids in wild plants, seeds and nuts. *Asian Pacific J Clin Nutr* 2002, 11:163–173
5. Simopoulos AP, Bazan NG. Omega-3 Fatty Acids, the Brain and Retina. *World Rev Nutr Dietetics* 2009, 99:1–5
6. Lukiw WJ, Bazan NG. Docosahexaenoic acid and the aging brain. *J Nutr* 2008, 138:2510–2514
7. Massiera F, Barbry P, Guesnet P et al. A Western-like fat diet is sufficient to induce a gradual enhancement in fat mass over generations. *J Lipid Res* 2010, 51:2352–2361
8. Ramsden CE, Hibbeln JR, Majchrzak SF et al. n-6 fatty acid-specific and mixed polyunsaturate dietary interventions have different effects on CHD risk: a meta-analysis of randomized controlled trials. *Br J Nutr* 2010, 104:1586–1600
9. Calder PC. The American Heart Association advisory on n-6 fatty acids: evidence based or biased evidence? *Br J Nutr* 2010, 104:1575–1576
10. Simopoulos AP. The importance of the omega-6/omega-3 Fatty Acid ratio in cardiovascular disease and other chronic diseases. *Exp Biol Med* (Maywood) 2008, 233:674–688
11. Simopoulos AP. Genetic variants in the metabolism of omega-6 and omega-3fatty acids: their role in the determination of nutritional requirements and chronic disease risk. *Exp Biol Med* 2010, 235:785–795