



Short Term Effect of Omega Fatty Acid on Hippocampus – A Brief Review

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ABSTRACT

Omega fatty acids are polyunsaturated fatty acids with a double bond. The fatty acids have two ends, the carboxylic acid (-COOH) end and methyl end. Omega fatty acids are vital for normal metabolism. Omega fatty acid is considered essential fatty acids, meaning that they cannot be synthesized by the human body -except that mammals have some abilities. We need them for our body to work normally. Omega fatty acids inhibit the development of premalignant and malignant lesions in a rat model of bladder cancer, which might be due to anti-inflammatory, antioxidant, anti-proliferative, and anti-angiogenic properties. The new findings indicate that ADHD has a biological component and that the intake of omega may influence ADHD symptoms. Omega fatty acids are important for several neuronal and cognitive functions. Altered omega fatty acid status has been implicated in reduced resistance to stress and mood disorders. Rats chronically lacking omega fatty acid exhibited an increased startle response, a stress-induced decrease in loco motor activity and exaggerated grooming. Feeding enriched omega fatty acid beef to rats increases omega fatty acid content of heart and liver membranes and decreases serum vascular cell adhesion and cholesterol levels. Agriculture practice of feeding a high omega fatty acid diet to cattle can produce positive health benefits to the consumer. A combination of antioxidants and omega fatty acids may represent potential protection against oxidative stress.

Keywords: Cerebrospinal fluid, Cognitive, Endogenously, Mortality, Omega fatty acid, Polyunsaturated fatty acid.

INTRODUCTION

Omega fatty acids are long-chain polyunsaturated fatty acids found in various plant and marine life.¹ The marine-based omega fatty acids primarily consist of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). In contrast, those from plants (flaxseed, walnuts, and canola oil) are usually in the form of the parent omega fatty acid, alpha- linolenic acid. The dietary alpha-linolenic acid can be endogenously converted to EPA and DHA. Fish provide varying amounts of omega fatty acids in the form of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA).² Several studies of omega fatty acids have been performed in behavioural disorders and have found few side effects in both humans and animals.³ There is evidence suggesting that omega fatty acid has an effect on human cerebrospinal fluid, serotonin metabolites.⁴ A report that separately analyzed data for men and women found a trend of decreased stroke with increasing fish consumption for women between ages 45 and 74, but not for men.⁵ Omega fatty acids have potentially favourable effects that may protect against cardiovascular disease and reduce mortality in non-transplanted patient.⁶ These essential fatty acids are highly concentrated in the brain and appear to be particularly important for cognitive (brain memory and performance) and behavioural function.⁷ Docosahexaenoic acid, one of the major polyunsaturated fatty acids in the brain, is essential for normal neurological development, maintenance of learning and memory, and neuronal plasticity.⁸

ANATOMY OF HIPPOCAMPUS

The hippocampus is one of the brain structures making up the limbic system. The hippocampus is composed of only three layers. The hippocampus is so named since early on its appearance was likened to a "seahorse". The hippocampal formation is a bi-lateral limbic structure". Although the hippocampus lies beneath the cerebral cortex it is not truly a sub cortical structure in that it is really a cortical infolding itself, albeit much older and more primitive than the surrounding neocortex. Hence, it is also referred to as archicortex, or paleocortex (Figure 1).

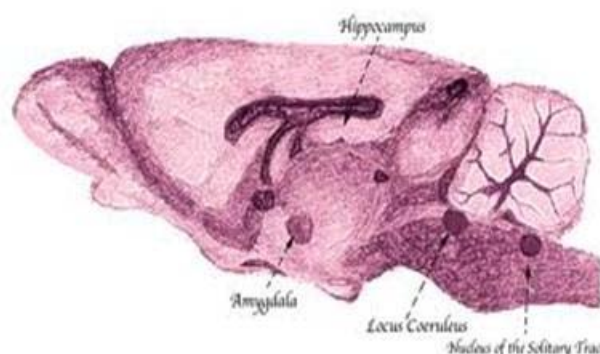


Figure 1

Composition of omega fatty acid

Omega fatty acids are a family of unsaturated fatty acids that have in common a final carbon-carbon double bond in the n-3 position; that is, the third bond from the

methly end of the fatty acid. These are also known as polyunsaturated fatty acids.⁷ There are three major types of omega 3 fatty acids that are ingested in foods and used by the body: alphalinolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). Once eaten, the body converts ALA to EPA and DHA, the two types of omega-3 fatty acids more readily used by the body. These three polyunsaturates have 3, 5 or 6 double bonds in a carbon chain of 18, 20 or 22 carbon atoms, respectively. All double bonds are in the cis configuration, i.e. the two hydrogen atoms are on the same side of the double bond.^{7,9} The human body cannot synthesize *n*-3 fatty acids de novo, but it can form 20-carbon unsaturated *n*-3 fatty acids (like EPA) and 22-carbon unsaturated *n*-3 fatty acids (like DHA) from the eighteen-carbon *n*-3 fatty acid α -linolenic acid.^{9,10} The balance of omega fatty acids is important to consider. The so-called omega-3: omega-6 ratio has become a model for gauging the proper balance of these fats in oils and the diet. Diets with greater than a 1:10 ratio of omega-3 to omega-6 are not recommended, whereas a 1:1 ratio is considered perfect. Very unhealthy ratios of 1:25 and 1:50 are common, especially with regular consumption of 'fast-food', high amounts of fried food, and low intake of fresh whole foods. Thus, 'Eating to live and not living to eat' becomes an important consideration with increases in modern, convenient, non-functional food choices.¹¹

DIETARY SOURCES OF OMEGA FATTY ACID

Although fish is a one of the main dietary source of omega fatty acids, they do not synthesize these fatty acids they obtain it from the algae or plankton through their diet. The most widely available source of EPA and DHA is cold water oily fish such as salmon, herring, mackerel, anchovies and sardines. Oils from these fish have a profile of around seven times as much *n*-3 as *n*-6. Other oily fish such as tuna also contain omega fatty acid but it is lesser in amounts.¹⁰ Flax Seeds produce linseed oil, which has very high amount of omega fatty acid content which is about six times richer than that of fish oils. The microalgae *Cryptocodinium cohnii* and *Schizochytrium* are rich sources of DHA. Egg has a high content of omega fatty acid mostly ALA. Some vegetables also have high amount of omega fatty acid like strawberries and broccoli. Linoleic acid (LA) is the main omega-6 'precursor' in plant/vegetable oils. The omega fatty acid (AA) is bioactive and found in red meat.¹² Most marine EPA and DHA do not originate in fish, but accumulate in the marine food chain from sources like microalgae. Certain non-toxic algal phyla contain high levels of EPA compared to DHA. *Thraustochytrids* is one of the food sources for shellfish, which form a significant part of the human diet in coastal regions around the world. *Schizochytrium* DHA-rich oil has no unpleasant flavor, no detectable environmental pollutants, and may be supplied as oil or in starch powder formulations for various purposes like cooking, encapsulation, infant milk formula, rice powder, and as additives to cereal and other products.

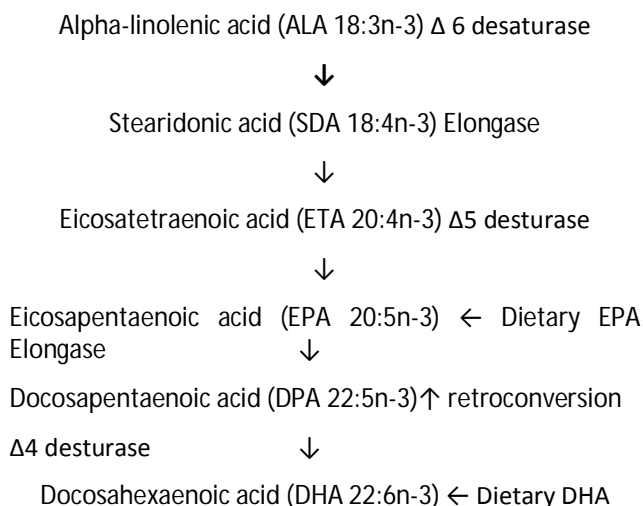
Functions of Omega Fatty Acid

Omega fatty acids are helpful in treating a variety of health conditions. The biological effects of the omega fatty acid are largely mediated by their interactions with the *n*-6 fatty acids. A small amount of omega fatty acid in the diet (~1% of total calories) enable normal growth. Omega fats also play an important role in the production of powerful hormone like called prostaglandins. Prostaglandins help to regulate many important physiological functions including blood pressure, blood clotting, nerve transmission, the inflammatory and allergic responses and also the functions of the kidneys and gastrointestinal tract, and the production of other hormones.^{13,14} Omega-3 fatty acids are important for a number of bodily functions, including muscle activity, blood clotting, digestion, fertility, and cell division and growth. DHA is important for brain development and function. ALA is an "essential" fatty acid, meaning that people must obtain it from food or supplements because the human body cannot manufacture it. The dietary essential v-3 fatty acid (FA), a linolenic (ALA; 18 : 3n-3) is the precursor of LCPUFA, eicosapentaenoic (EPA; 20 : 5n-3) and docosahexaenoic acid (DHA; 22 : 6n-3), which are important structural elements of cell membranes which are needed for the normal development of the central nervous system and retina.^{15,16} The women of reproductive age appear to have a greater capacity than men to convert the essential n-3 FA ALA (obtained predominantly from unsaturated vegetable oils) to EPA and DHA.¹⁷ The low incidence of atherosclerotic and chronic inflammatory diseases in Eskimos of Greenland is due to their traditional diet consisting mostly of marine food, rich in the eicosapentaenoic acid (EPA)' and docosahexaenoic acid.^{18,19} Many clinicians believe that flaxseed (which contains omega-3 fatty acids) is helpful for treating acne. Omega-3 exerts neuroprotective action in Parkinson's disease and exhibit a protective effect (much like it did for Alzheimer's disease as well). The scientists found that high doses of omega-3 completely prevent the neurotoxin-induced decrease of dopamine that ordinarily occurs. EPA had a statistically significant decrease in the thickness of the carotid arteries along with improvement in blood flow. Purified EPA improves the thickness of carotid arteries along with improving blood flow in patients with unhealthy blood sugar levels. Daily omega-3 fatty acid supplements dramatically reduce the risk of death, subsequent heart attacks, and stroke. Similarly, people who eat an ALA-rich diet are less likely to suffer a fatal heart attack.²⁰ There is some evidence that omega-3s of the types found in seafood and fish oil may be modestly helpful in relieving symptoms in rheumatoid arthritis. Omega supplements (primarily fish oil supplements) also have been studied for preventing or treating a variety of other conditions such as allergies, asthma, cachexia (severe weight loss) associated with advanced cancer, Crohn's disease, cystic fibrosis, diabetes, kidney disease, lupus, menstrual cramps, obesity, osteoporosis, and ulcerative colitis, as well as



organ transplantation. Recent NCCAM-sponsored studies have been investigating the effects of omega-3s/fish oil on conditions including: Adolescent depression, Autism spectrum disorders, Brain injury, and Complications of HIV infection, including bone loss, Depression during pregnancy and postpartum depression, Treatment-resistant epilepsy.

Metabolic Pathway of Dietary Omega Fatty Acid



[Possible mechanism and therapeutic value in major depression by Alan c. Logan, ND, FRSH, MS (cand.)]

EFFECT OF OMEGA FATTY ACID ON HIPPOCAMPUS

The hippocampus is one of the major components of the brains of humans and other vertebrates. It plays important roles in the consolidation of information from short-term memory to long-term memory and spatial navigation. Humans and other mammals have two hippocampi, one in each side of the brain. The hippocampus is located under the cerebral cortex.²¹ In rodents, the hippocampus has been studied as part of a brain system responsible for spatial memory and navigation. Many neurons in the rat and mouse hippocampus respond as place cells which means, they fire bursts of action potentials when the animal passes through a specific part of its environment. If damage to the hippocampus occurs in only one hemisphere, the brain can retain near-normal memory functioning. Severe damage to the hippocampi in both hemispheres results in profound difficulties in forming new memories (anterograde amnesia) and often also affects memories formed before the damage occurred (retrograde amnesia)²² Mild TBI (Traumatic brain injury) reduces the expression of Sir2 α (silent information regulatory α) in the hippocampus, in proportion to increased levels of protein oxidation. In addition, we show that dietary supplementation of omega-3 fatty acids that ameliorates protein oxidation which is very effective that it reverse the reduction of Sir2 α level in injured rats. Hippocampal levels of total and phosphorylated AMPK were reduced after TBI and levels were normalized by omega-3 fatty acts supplements. According to recent studies, Sir2 may play an important role in mechanisms that provide

neuroprotection in mammals. Deletion of Sir2 gene has been reported to cause developmental disorders of brain, heart, and retina in mice.²³ A fish oil which is rich in omega-3 fatty acids has been shown to protect the brain against the effects of TBI. The research on rats that were stressed by exposure to cold (hypothermia) and low oxygen levels (hypoxia). When they had been pre-treated with omega fatty acid, these rats produced less than the expected amount of a type of protective protein in certain brain areas, notably the hippocampus and cerebral cortex. Omega fatty acid had apparently made those brain areas less susceptible to hypothermic and hypoxic stress by increasing the brain's available store of protective enzymes. Omega fatty acid somehow made those regions of the brain less susceptible to stress them in a relatively non stressed state even in the presence of stress.

CONCLUSION

The importance of omega 3 fatty acids in health promotion and disease prevention has received awareness. It should be noted that administration of omega fatty acids, most often via high doses of flaxseed oil, may induce hypomania, mania, or other behavioural changes in a small percentage (less than 3%) of individuals.^{24,25} Omega fatty acid posses certain antioxidative and neuroprotective properties ,which is used for treatment of neurodegenerative disorders and neuron degenerations.

REFERENCES

1. Leaf A, Weber PC: A new era for the science of nutrition, *Am J Clin Nutr*, 45, 1987, 1048–1053.
2. Holub BJ, Clinical Nutrition: 4. Omega-3 fatty acids in cardiovascular care, *CMAJ*, 166, 2002, 608-615.
3. Hamazaki T, Sawazaki S, Itomura M, Asoka E, Nagao Y, Nishimura N, Yazawa K, Kuwamori T, Kobayashi M: The effect of docosahexaenoic acid on aggression in young adults: a placebo-controlled double-blind study, *J Clin Invest*, 97, 1996, 1129–1133.
4. Hibbeln JR, Umhau JC, Linnoila M, George DT, Ragan PW, Shoaf SE, Vaughan MR, Rawlings R, Salem N Jr: A replication study of violent and nonviolent subjects: cerebrospinal fluid metabolites of serotonin and dopamine are predicted by plasma essential fatty acids, *Biol Psychiatry*, 44, 1998, 243–249.
5. Gillum RF, Mussolino ME, Madans JH, The relationship between fish consumption and stroke incidence, *The NHANES I Epidemiologic Follow-up Study (National Health and Nutrition Examination Survey)*, *Arch Intern Med*, 156(5), 1996, 537-542.
6. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico, *Lancet*, 354, 1999, 447–455.
7. JL McGuire, "Pharmaceutical classes, Therapeutic Agents, Area of application." Vol-IV, (Miscellaneous drug Related Technology) 344, 2046.



8. Green P, Yavin E, Mechanisms of docosahexaenoic acid accretion in the fetal brain, *J. Neurosci. Res.*, 52, 1998, 129-136.
9. Dr AC Deb, "Fundamental of biochemistry", Sixth Edition 1996, 39-40.
10. Vinod. D. Rangari, "Pharmacognosy & phytochemistry", Career Publication, First Edition, PartII, 6, 77.
11. Harris WS, The omega-6/omega-3 ratio and cardiovascular disease risk: uses and abuses, *Curr Atheroscler Rep*, 8(6), 2006, 453-459.
12. Harris WS, The omega-6/omega-3 ratio and cardiovascular disease risk: uses and abuses, *Curr Atheroscler Rep*, 8(6), 2006, 453-459.
13. http://en.wikipedia.org/wiki/Omega-3_fatty_acid,
14. [http://www.whfoods.com/genpage.php?name=nutrient & dbid=84](http://www.whfoods.com/genpage.php?name=nutrient&dbid=84)
15. Crawford MA, Hassam AG, Williams G, Essential fatty acids and fetal growth, *Lancet*, 1, 1976, 452-453.
16. Demmelmair H, Larque E, Koletzko B, Perinatal long chain polyunsaturated fatty acid supply: are there long-term consequences, *Oleagineux Corps gras Lipides (John Libbey Eurotext)* 14, 2007, 155-158.
17. Bakewell L, Burdge GC, Calder PC, Polyunsaturated fatty acid concentrations in young men and women consuming their habitual diets, *Br J Nutr*, 96, 2006, 93-99.
18. Kromann N, A Green, Epidemiological studies in the Upernavik district, Greenland, *Acta. Med. Scand.*, 208, 1980, 401-406.
19. Bang HO, J Dyerberg, A Nielsen, Plasma lipid and lipoprotein pattern in Greenlandic west coast Eskimos, *Lancet*, 1, 1971, 1143-1145.
20. Iso H, Rexrode KM, Stampfer MJ, Manson JE, olditz GA, Speizer, Intake of fish and omega-3 fatty acids and risk of stroke in women, *JAMA*, 285(3), 2001, 304-312. Ed molecular degeneration, *Arch Ophthalmol.*, 119(8), 2001, 1191-1199.
21. Pearce J, The effects of telencephalic pallial lesions on spatial, temporal, and emotional learning in goldfish, *J Neurol Neurosurg Psychiatry*, 71(3), 2001, 351. doi:10.1136/jnnp.71.3.351. PMC 1737533. PMID 1151170.
22. Di Gennaro G, Grammaldo LG, Quarato PP, Esposito V, Mascia A, Sparano A, Meldolesi GN, Picardi A, "Severe amnesia following bilateral medial temporal lobe damage occurring on two distinct occasions", *Neurological Sciences*, 27(2), 2006, 129-33. doi:10.1007/s10072-006-0614-y. PMID 16816912.
23. Cheng HL, Mostoslavsky R, Saito S, Manis JP, Gu Y, Patel P, Bronson R, Appella E, Alt FW, Chua KF, Developmental defects and p53 hyperacetylation in Sir2 homolog (SIRT1)-deficient mice. *Proc. Natl Acad. Sci. USA*, 100, 2003, 10794-10799. Sakamoto J, Miura T, Shimamoto K, Horio, Y, Predominant expression of Sir2alpha, an NAD-dependent histone deacetylase, in the embryonic mouse heart and brain, *FEBS Lett*, 556, 2004, 281-286.
24. Rudin DO, The major psychoses and neuroses as omega-3 essential fatty acid deficiency syndrome: Substrate pellagra, *Biol Psychiatry*, 16, 1981, 837-850.
25. Kinrys G, Hypomania associated with omega3 fatty acids, *Arch Gen Psychiatry*, 57, 2000, 715-715.

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