Essential Fatty Acids and Human Brain

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Abstract- The human brain is nearly 60 percent fat. We've learned in recent years that fatty acids are among the most crucial molecules that determine your brain's integrity and ability to perform. Essential fatty acids (EFAs) are required for maintenance of optimal health but they can not synthesized by the body and must be obtained from dietary sources. Clinical observation studies has related imbalance dietary intake of fatty acids to impaired brain performance and diseases.

Most of the brain growth is completed by 5-6 years of age. The EFAs, particularly the omega-3 fatty acids, are important for brain development during both the fetal and postnatal period. Dietary decosahexaenoic acid (DHA) is needed for the optimum functional maturation of the retina and visual cortex, with visual acuity and mental development seemingly improved by extra DHA. Beyond their important role in building the brain structure, EFAs, as messengers, are involved in the synthesis and functions of brain neurotransmitters, and in the molecules of the immune system. Neuronal membranes contain phospholipid pools that are the reservoirs for the synthesis of specific lipid messengers on neuronal stimulation or injury. These messengers in turn participate in signaling cascades that can either promote neuronal injury or neuroprotection.

The goal of this review is to give a new understanding of how EFAs determine our brain's integrity and performance, and to recall the neuropsychiatric disorders that may be influenced by them. As we further unlock the mystery of how fatty acids affect the brain and better understand the brain's critical dependence on specific EFAs, correct intake of the appropriate diet or supplements becomes one of the tasks we undertake in pursuit of optimal wellness.

Key Words: Essential fatty acids, Human brain, Omega-3 fatty acids

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INTRODUCTION

The human brain is nearly 60 percent fat. Doctors probably ignored this fact because they thought dietary fat had little influence on the brain. Today we know differently. We've learned in recent years that fatty acids are among the most crucial molecules that determine your brain's integrity and ability to perform.

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Essential fatty acids (EFAs) are required for maintenance of optimal health but they can not synthesized by the body and must be obtained from dietary sources. They are also called polyunsaturated fatty acids (PUFAs). There are two classes of PUFAs--omega-6 and omega-3. The parent omega-6 fatty acid, linoleic acid (LA) is desaturated in the body to form arachidonic acid while parent omega-3 fatty acid alpha-linolenic acid (ALA) is desaturated by microsomal enzyme system through a series of metabolic steps to form eicosapentaenoic acid (EPA) and decosahexaenoic acid (DHA)[1]. Some of these long-chain metabolites form precursors to respective prostaglandins, thromboxanes, leukotrienes, and prostacyclin, which have a tremendous effect on the brain's blood flow, immune system and the neurotransmitter system[2] (Fig.).

Among the significant components of cell membranes are the phospholipids that contain fatty acids (FAs). The types of FAs in the diet determine the types of FAs that are available to the composition of the cell membranes. A phospholipid made from a saturated fat has a different structure and is less fluid than one that incorporates an EFA. In addition, LA and ALA per se have an effect on the neuronal membrane fluidity. They are able to decrease the cholesterol level in the neuronal membrane, which would otherwise decrease membrane fluidity, which in turn would make it difficult for the cell to carry out its normal functions and increase the cell's susceptibility to injury and death[3]. These consequences for cell function are not restricted to absolute levels of EFAs alone, rather it appears that the relative amounts of omega-3 FAs and omega-6 FAs in the cell membranes are responsible for affecting cellular function and subsequently promoting the pathogenesis of many chronic diseases, including cardiovascular disease, cancer, osteoporosis, and inflammatory and autoimmune diseases[4].

Very high levels of FAs and lipids can be found in two structural components: the neuronal membrane and the myelin sheath. About 50% of the neuronal membrane is composed of FAs, while in the myelin sheath lipids constitute about 70%. The lipid component has a relatively high turnover rate, in contrast to the protein component that is especially stable[5]. The integrity of the myelin is of utmost importance for the proper functions of axons in the nervous system. Breakage or lesions in the myelin can lead to disintegration of many of the nervous system functions. Recent studies emphasize the major role of dietary EFA to the normal functions of

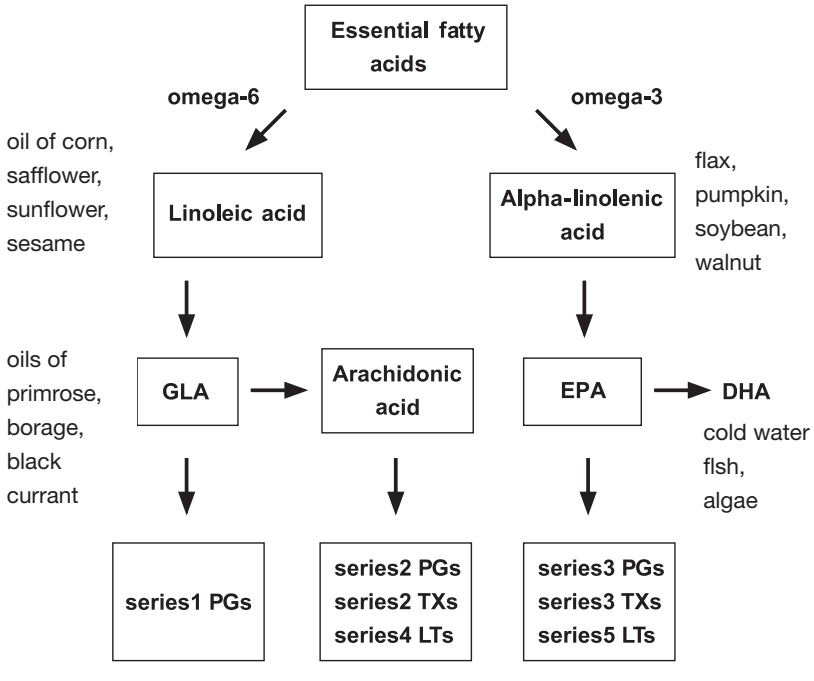

Figure. Metabolic pathway for essential fatty acids.
GLA: gamma linolenic acid; PGs: prostaglandins; TXs: thromboxanes; LTs: leukotrienes.

myelin. Moreover, the EFAs are important in the active phase of the myelin synthesis. If EFAs are not available in this phase or are metabolically blocked, amyelination, dysmyelination, or demyelanation may occur[6]. If EFA deficiency occurs during the postnatal period, a major delay in the myelination process will occur, accompanied by impaired learning, motor, vision, and auditory abnormalities[7]. The goal of this review is to give a new understanding of how EFAs determine our brain's integrity and performance, and to recall the clinical conditions of the brain that may be influenced by them.

DIETARY SOURCES OF EFAs

The main dietary sources of omega-6 FAs are vegetable oils like sunflower oil, safflower oil, sesame oil, and corn oil. The rich dietary sources of omega-3 FAs are vegetable oils like flaxseed or canola oil, peanut oil, walnut oil, green leafy vegetables, oily cold-water fish (mackerel, sardine, and salmon etc.) and fish oil. It is from these EFAs that our bodies make the vital brain-fats and the vital messengers that help regulate a vast array of body activity. Without the EFAs, our bodies run out of the building blocks our cells require to maintain peak function[8]. Returning to the dietary trends of humans, we'll recall that ancient diets contained a ratio of omega-6 to omega-3 FAs estimated to be roughly 1:1. Today the ratio is more on the order of 15:1-17:1[4] In addition, to such "acquired" dietary imbalances that lessen omega-3 intakes, the healthy human organism has limited capacity to elaborate the long chain DHA and EPA from shorter-chain precursors. Metabolic biochemists have calculated that five percent or less of dietary ALA is converted to EPA, and less than 0.5 percent of dietary ALA makes it to DHA[9]. This change ratio of FAs appears to have significant implications for brain function. When scientists studied the brain of people with multiple sclerosis, they found that the brain tissue was very low in important fatty acids such as DHA[10]. They also found low levels of omega-3 FAs in blood and almost no omega-3 FAs stored in fat tissues. Doctors in Australia who studied the blood of people with moderate to severe depression found the balance of EFAs was significantly altered; the level of the omega-3 FAs was too low[11]. Researchers of Purdue University found that individuals with symptoms of hyperactivity and attention deficit had lower levels of the omega-3 FA and DHA in their blood[12]. All these clinical observation studies related imbalance dietary intake of FAs to impaired brain performance and diseases in some genetic vulnerable individuals.

EFAs and brain development

Most of the brain growth is completed by 5-6 years of age. At birth brain weight is 70% of an adult, 15% brain growth occurs during infancy and remaining brain growth is completed during preschool years[13]. The EFAs, particularly the omega-3 FAs, are important for brain development during both the fetal and postnatal period. Both omega-3 and omega-6 FAs play important roles in neuronal growth, development of synaptic processing of neural cell interaction, and expression of genes regulating cell differentiation and growth. Dietary DHA is needed for the optimum functional maturation of the retina and visual cortex, with visual acuity and mental development seemingly improved by extra DHA[14]. In addition, the fetus and placenta are dependent on maternal EFA supply for their growth and development, with DHA-supplemented infants showing significantly greater mental and psychomotor development scores and breast-fed children do even better[15]. Reduced DHA is also associated with impairments in cognitive and behavioral performance, which are particularly important during brain development[16]. From above findings we may suggest that providing proper FA balance during the infant period increases the opportunity to ensure that any child can realize his or her peak potential. It also raises the possibility that a child suffering from learning, behavior, or other brain-related problems might be helped if FA balance is restored while he or she still a child. To achieve this we must be sure that nursing mothers have adequate ALA, and DHA in their diets.

THE ROLE OF EFAs IN BRAIN STRUCTURES AND FUNCTIONS

Because the brain is predominantly made of fat,

almost all of its structures and functions have a crucial dependency upon EFAs, which we get directly from our food.

In the brain, there is little LA or ALA. The brain prefers arachidonic acid (AA) and DHA. For the brain, these two fatty acids might be considered essential[17]. In a developing fetus, AA is taken from the mother to help develop the fetal brain. In infancy, AA is present in breast milk to further promote brain development. At about one year, a child is normally able to make enough of its own AA[18]. Thus, for the adult, dietary AA is no longer as important. Actually, when AA levels are too high in the lipids of cell membranes, there is a tendency toward formation of inflammatory substances such as prostaglandin E2, leukotrienes, and thromboxane A2. Over the past two decades we have learned that DHA is the critical long-chain omega-3 fatty acid found in the brain. Our bodies have the ability to make DHA from essential fatty acid ALA, but this process is often very inefficient[19]. Thus we seem to have a requirement for preformed DHA in the diet that cannot be met by other fatty acids. In this way, DHA may be a conditionally EFA and essential for the brain.

Beyond their important role in building the brain structure, EFAs have another crucial role – as messengers. EFAs are involved in the synthesis and functions of brain neurotransmitters, and in the molecules of the immune system[20]. It is noted that omega-3 deficiency reduces the dopamine vesicle density in the cortex and causes malfunction of the dopaminergic mesocorticolimbic pathway[21]. The role of EFAs in immune function is complicated since omega-3 and omega-6 have different effects on various immune components and is largely dependent on the omega-3 to omega-6 ratio. Several mechanisms have been proposed for EFAs to mediate their immunological functions in several disorders such as Alzheimer and schizophrenia. These include membrane fluidity (changes that might effect the capability of cytokines to bind to their respective receptors on the cell membrane); lipid peroxidation (decrease in free radical-induced tissue damage); prostaglandin production (an indirect mechanism whereby prostaglandins, which are derivatives of PUFA, modify cytokine activity); and regulation of gene expression (PUFA influences on the signal transduction pathways and modifies mRNA activity)[22].

FAs that form the structure of your cell membranes become messengers when a call to action is sent out. Neuronal membranes contain phospholipid pools that are the reservoirs for the synthesis of specific lipid messengers on neuronal stimulation or injury[23]. These messengers in turn participate in signaling cascades that can either promote neuronal injury or neuroprotection. Prostaglandins are synthesized as a result of cyclooxygenase activity. In the first step of the AA cascade, the short-lived precursor, prostaglandin H2, is synthesized. Additional steps in the cascade result in the synthesis of an array of prostaglandins, which participate in numerous physiological and neurological processes[24]. The prostaglandins derived from membrane EFAs include PGE1, PGE2, and PGE3. PGE1 is important in the nervous system as it affects the release of compounds from nerve cells that transmit nerve impulses. It tends to have anti-inflammatory properties and is immune enhancing. PGE2 is a highly inflammatory substance. It can cause swelling, increased pain sensitivity, and increased blood viscosity. Leukotrienes are related to PGE2 in that they are made from the fatty acid AA. PGE3 tends to be mildly anti-inflammatory and immune enhancing. It is thought to counter the effects of the powerful inflammatory PGE2. It prevents blood platelets from clumping and helps prevent blood vessel spasm. FAs important in PGE3 formation, like EPA and DHA, can also reduce AA in the cells. This reduces the chance of producing messengers from AA and is one way that these FAs can alter the production of highly inflammatory messengers. In another way, the membrane DHA might play a role of neuroprotection. It is the precursor of oxygenation products now known as the docosanoids, some of which are powerful counter-proinflammatory mediators. The mediator 10,17S-docosatriene (neuroprotectin D1, NPD1) counteracts leukocyte infiltration, NF-kappa activation, and proinflammatory gene expression in brain ischemia-reperfusion and is an apoptostatic mediator, potently counteracting oxidative stress-triggered apoptotic DNA damage in retinal pigment epithelial cells[23].

EFAs AND MENTAL PERFORMANCE

Given the fatty nature of the brain, it seems quite logical that the mental performance of some individuals with FA imbalance might be affected. Hibbeln et al.[25] recently have reported beneficial effects on child development with maternal seafood intakes of more than 340 g per week. They found that maternal seafood intake during pregnancy of less than 340 g per week was associated with increased risk of their children being in the lowest quartile for verbal intelligence quotient. In addition, low maternal seafood intake was also associated with increased risk of suboptimum outcomes for prosocial behaviour, fine motor, communication, and social development scores. In another study, Lucas A[26] also pointed to a beneficial effect of human milk on neurodevelopment. Children who had consumed mother's milk in the early weeks of life had a significantly higher IQ at 7.5-8 years than did those who received no maternal milk. There was a dose-response relation between the proportion of mother's milk in the diet and subsequent IQ. Furthermore, there is also evidence that healthy individuals can expect cognitive benefit from EFAs, mainly EPA and DHA. Fontani et al.[27] conducted a double-blind RCT on 33 healthy volunteers ages 22-51. For 35 days, subjects consumed either 4 g fish oil/day (800 mg DHA and 1,600 mg EPA) or 4 g olive oil as placebo. The DHA/EPA group improved significantly over placebo on several mood parameters: vigor, anger, anxiety, fatigue, depression, and confusion. Measures of attention and reaction time were also improved. Participants demonstrated marked improvement in sustained attention and a significant reduction in errors on the attention test.

Accelerated cognitive decline in middle age can make an individual more vulnerable to dementia in later life. Evidence is accumulating to suggest omega-3 FA deficiency contributes to accelerated cognitive decline. An epidemiology team led by Kalmijn tested 1,613 subjects, ages 45-70, for various cognitive functions at baseline and after five years and correlated the results with habitual food consumption reported on a self-administered food questionnaire[28]. Subjects exhibiting the most impaired cognitive function (lowest 10 percent of the group score) also had the lowest intake of DHA/EPA or fatty fish. Overall cognitive performance and psychomotor speed were positively correlated with DHA/EPA status. High intakes of cholesterol and saturated fat were both linked to increased cognitive impairment in this middle-aged population.

Recent studies have associated deficits in DHA abundance with cognitive decline during aging and in neurodegenerative disease[29]. The importance of DHA-derived NPD1 has been underscored in the homeostatic regulation of brain cell survival and repair involving neurotrophic, antiapoptotic and antiinflammatory signaling. Emerging evidence suggests that NPD1 synthesis is activated by growth factors and neurotrophins. It has important determinant and regulatory interactions with the molecular-genetic mechanisms affecting beta-amyloid precursor protein and amyloid beta peptide neurobiology.

EFAs AND NEUROPSYCHIATRIC DISORDERS

DHA/EPA in relation to dementia and mild cognitive impairment

In the past decade, epidemiological studies indicate relatively high DHA and EPA intake is linked to lower relative risk of dementia incidence or progression. In 1997, Kalmijn et al.[30] reported on a longitudinal cohort study, in which 5,386 participants ages 55 or older were screened for dementia. Dietary habits were evaluated using a semi-quantitative food frequency questionnaire and then re-evaluated after 2.1 years. Fish consumption was inversely related to dementia incidence (RR=0.4, 95% CI=0.2-0.9), and more specifically to the risk of developing Alzheimer's disease (RR=0.3, 95% CI=0.1-0.9). In a Chicago community study, 815 residents ages 65-94 were evaluated via a self-reported food questionnaire and tracked for an average 3.9 years[31]. A total of 131 participants developed Alzheimer's disease. Those who consumed a fish meal once weekly had a statistically significant 60-percent decreased risk of Alzheimer's disease, compared with those who rarely or never ate fish (RR=0.4, 95% CI=0.2-0.9). Total omega-3 and DHA intake, but not EPA intake alone, were significantly associated with this lessened Alzheimer risk. This suggests an intake of as little as 30 mg/day DHA/EPA

from fish might confer more protection against cognitive decline than eating no fish at all.

Longitudinal cohort studies can be more objective when blood or tissue is analyzed for specific nutrients. As part of the U.S. Framingham Heart Study, a cohort of 899 men and women (median age 76 years), who were free of dementia at baseline, were followed for a mean 9.1 years for development of all-cause dementia and Alzheimer's disease[32]. Ninety-nine new cases of dementia (including 71 of Alzheimer's disease) occurred. Baseline and follow-up blood samples were tested for fatty acids in the plasma phospholipid fraction. After controlling for other variables, subjects in the upper quartile of plasma phospholipid DHA levels had approximately half the relative risk of developing all-cause dementia (RR=0.53, 95% CI=0.29-0.97; $p \leq 0.04$) compared to subjects in the three lower quartiles. The upper quartile (n=488) had a mean DHA intake of 180 mg/day and a mean fish intake of 3.0 servings per week ($p<0.001$). In 2006, a team from Stockholm's Karolinska University Hospital published a double-blind RCT of DHA and EPA for 174 patients with mild-to-moderate Alzheimer's disease[33]. Patients received either 1.7 g DHA and 0.6 g EPA daily or a placebo for six months, after which all received the DHA/EPA supplements for six more months. After the first six months, decline in cognitive function did not differ between groups. However, in a subgroup with less severe cognitive dysfunction (Mini-Mental State Exam score >27 points), a significantly slower decline was observed in the DHA/EPA group. A similar slowing was observed in the placebo group after crossover to DHA/EPA for the second six months. These findings suggest patients with mild Alzheimer deterioration could benefit from taking a mixed dietary supplement formulation containing both DHA and EPA.

Mild cognitive impairment (MCI) is currently the condition most predictive for subsequent progression to dementia. MCI features severely impaired memory without substantial loss of other cognitive functions. Approximately 10-15 percent of MCI subjects progress to dementia within a year of diagnosis. Individuals cognitively impaired but not demented tend to have abnormally low blood levels of DHA and EPA[34].

In a recent systematic review[35], Issa AM et al. found a trend in favor of omega-3 FAs (fish and total omega-3 consumption) toward reducing risk of dementia and improving cognitive function. Although the available data are insufficient to draw strong conclusions about the effects of omega-3 FAs on cognitive function in normal aging or on the incidence or treatment of dementia they still suggest a possible association between omega-3 FAs and reduced risk of dementia.

EPA and Huntington disease

Huntington disease (HD) features abnormal multiplication of a specific DNA sequence on chromosome 4: cytosine-adenine-guanine (CAG). Healthy people have just one CAG sequence at this spot; people with HD can have several dozen CAG sequences. As a rule, the more CAGs the HD patient has, the more severe their disease[36]. On a suspicion that certain omega-3 responsive pathways could be involved, a team of British researchers have been using purified EPA in its ethyl ester form ("ethyl-EPA") as potential therapy for HD[37]. They conducted a small RCT with ethyl-EPA on seven in-patients with advanced (stage III) HD. After six months, the four patients who received ethyl-EPA demonstrated improvement on the orofacial component of the Unified Huntington Disease Rating Scale, while the three placebo patients had deteriorated ($p<0.03$). MRI brain scans revealed the placebo was associated with progressive cerebral atrophy and ethyl-EPA was associated with beneficial changes. Three years later, the group completed a multicenter, double-blind RCT[38]. A total of 135 Huntington patients received either 2 g/day ethyl-EPA or placebo. The primary endpoint was the score at 12 months on the Total Motor Score 4 (TMS-4) subscale. The ethyl-EPA group as a whole failed to show statistically significant improvement on TMS-4. Nevertheless, a subgroup including patients with fewer CAG showed significantly better TMS-4 improvement[39].

Omega-3 FAs and depression

If omega-3 FAs play a role in depressive disorders, then it would be expected that countries consuming greater amounts of these FAs (primarily through fish intake) would have a lower prevalence of depression.

Actually, in a research conducted by Joseph Hibbeln of the National Institutes of Health it was found that a significant negative correlation between worldwide fish consumption and prevalence of depression[40]. In another research involving a random sample within a nation, frequent fish consumption in the general population is associated with a decreased risk of depression[41].

Maternal postpartum depression (also called "perinatal depression") has been linked to omega-3 FA deficiency. As reviewed in Freeman[42], a survey of mother's milk in 23 countries determined that lower DHA content or lower seafood consumption was associated with higher rates of postpartum depression. Freeman noted that pilot trials of supplementation with DHA and EPA have produced mixed results and called for larger and better-designed trials to resolve this condition that endangers both mother and child.

Su and colleagues[43] recently reported a beneficial effect of omega-3 FAs in a 8 week duration double-blind placebo controlled trial of 22 patients with major depressive disorder using fish oil (daily dose of 2.2 g/day EPA and 1.1 g/day DHA) or an olive oil placebo. Of the patients completing the trial, the omega-3 FA group achieved a significantly greater reduction in depressive symptoms than the placebo group. In a recent meta-analytic review of double-blind, placebo-controlled trials of antidepressant efficacy of omega-3 FAs, Lin PY and his colleague[44] reviewed ten double-blind, placebo-controlled studies in patients with mood disorders receiving omega-3 FAs with the treatment period lasting 4 weeks or longer. They found a significant antidepressant effect of omega-3 FAs (effect size = 0.61, p= .003) and the dosage of EPA did not change the antidepressant efficacy significantly. However, significant heterogeneity among these studies and publication bias were noted. They therefore concluded that it is still premature to validate this finding due to publication bias and heterogeneity. More large-scale, well-controlled trials are needed to find out the favorable target subjects, therapeutic dose of EPA, and the composition of omega-3 FAs in treating depression.

Omega-3 FAs and bipolar disorder

Bipolar disorder (BD) with its complex spectrum of symptoms is likely associated with neural cell membrane dysfunction, most likely signal transduction abnormalities. The levels of seafood intake per capita in various countries of the world roughly correlate with the respective prevalence rates of BD in community samples[45]. The greater the seafood consumption per capita in a country, the lower the prevalence of bipolar spectrum disorders. Countries that consume a lot of fish on average (e.g., Iceland, Korea, and Taiwan) have relatively low incidence, while countries that consume very little fish (e.g., Germany, Switzerland, and Hungary) have up to seven times the incidence of countries with high fish intake. Noaghiul and Hibbeln estimated a "vulnerability threshold" for BD at seafood consumption below 50 pounds of seafood/person/year.

To date, four published double-blind trials on DHA/EPA for BD have been published. The first was a 1999 trial that found significantly longer remission of bipolar symptomology from a high-dose DHA and EPA mixture (9.6 g/day) compared to placebo[46]. Three more double-blind trials were published in 2006 with differing results. In the largest trial, Frangou et al found significant improvement using EPA only (ethyl-EPA) in 75 patients, with 1 g/day working just as well as 2 g/day[47]. Keck et al found no significant differences between placebo and 6 g/day EPA (no DHA) in 61 patients[48]. Marangell et al conducted a small study on 10 patients using only DHA and reported only that DHA was "well tolerated"[49]. In a recent Cochrane review Montgomery P et al.[50] found that only one study, involving 75 participants, provided data for analysis and showed positive effects of omega-3 as an adjunctive treatment for depressive but not manic symptoms in bipolar disorder from five studies. But they concluded that these findings must be regarded with caution owing to the limited data available.

Omega-3 FA and schizophrenia

FAs have also been the focus of intense study in the psychotic disorder schizophrenia[51]. A "phospholipid membrane hypothesis of schizophrenia", as reviewed in 2000 by Fenton and colleagues[52], encompasses abnormalities of long-chain omega-6 FAs such as AA, as well as DHA and EPA. Fenton et al. list multiple analyses of

RBC membranes (recognized markers for EFA status) that consistently document depletion of AA, DHA, and EPA. Also noted were studies documenting depletion in plasma, thrombocytes, and post-mortem brain tissue of schizophrenia patients[52].

Six double-blind RCTs with DHA/EPA have been conducted recently, involving 390 patients with schizophrenia or schizoaffective disorder[53-57]. Four of these documented clinical benefit from 2/g EPA daily for three months. One trial found high-EPA fish oil performed better than high-DHA fish oil or placebo[53]. Another dose-ranging trial of ethyl-EPA found 2 g/day worked better than 1 g or 4 g daily[54]. Two trials by the same group examined ethyl-EPA's effect on tardive dyskinesia associated with pharmaceutical management of schizophrenia. In a 2002 trial, Emsley et al found benefit at 3 g/day[55], but a later 2006 trial did not demonstrate benefit at the lower dose of 2 g/day[57]. Because all these clinical studies using omega 3 FA supplementation showed the inconsistent results in different doses of ethyl-EPA as compared with placebo a recent Cochrane review[58] concluded that the use of omega-3 FAs for schizophrenia still remains experimental and a large well designed, conducted studies is needed.

EPA supplementation in borderline personality disorder

Borderline personality disorder may also respond to omega-3 supplementation. In a double blind, placebo-controlled trial, 30 female subjects with moderately severe BPD received 1 g/day EPA only (as ethyl-EPA) or a placebo for two months. Those taking ethyl-EPA experienced significantly diminished aggression and less severe depression[59].

CORRECT INTAKE OF EFAs FOR BRAIN BENEFITS

As we better understand the brain's critical dependence on specific EFAs, correct intake of the appropriate diet or supplements becomes one of the appropriate tasks we undertake in pursuit of optimal wellness. In this review, we may have gathered the impression that omega-3 FAs are more important than omega-6 FAs. That's because most modern diets contain too much omega-6 and far too little omega-3. In reality, balance of EFAs is critical. We don't want to go overboard on any particular FA.

How does one know whether supplementation is necessary? Physical signs and symptoms of deficiency include excessive thirst, frequent urination, rough dry hair and skin, and follicular keratosis[60]. The current knowledge base on DHA/EPA for brain function does not generate a rational daily intake recommendation. Hibbeln, from his studies on national seafood intakes and affective disorder incidence, suggested pregnant women might want to consume a minimum 650 mg/day of DHA and EPA (with a minimum 300 mg/day of DHA) to prevent postpartum depression[40]. Although high doses of ALA can increase tissue EPA levels, ALA does not have the same effect on DHA levels[61], rendering supplementation necessary. For vegetarians cultivated microalgae are a good source of DHA.

CONCLUSIONS

Although the current clinical literature on EFAs for brain function is still relatively small compared to the literature on circulatory benefits, the weight of the current evidence strongly supports their utility for cognition, behavior, and mood, as well as for early brain development and overall mental performance. As we further unlock the mystery of how FAs affect the brain, we may be able to change the course of our individual lives and perhaps even society by making wise dietary changes.

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