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THE RELATIONSHIP WITH BRAIN AND FATTY ACIDS

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ABSTRACT

Fatty acids, which are the content of fats, have functions in many syntheses in organs in the body, as well as in synthesis in the brain. These functions are not only high energy sources. It has very important roles in the process of health formation, protection and treatment of discomforts depending on the properties of fatty acids. Briefly, adjuvant and neoadjuvant effects are clearly known. The aim is to emphasize its importance in the light of recent studies on the effects of fatty acids on brain and health.

KEYWORDS: Fatty Acids, Essential Fatty Acids, Brain, MUFA, PUFA.

INTRODUCTION

The clinical importance of essential fatty acids (EFA) from the first years they were discovered to the present has been attracting attention in every aspect for the last few years. Its wide possibilities, chemical structure and role in physiological importance are a must in therapeutic use,[1] In neuronal membranes, it is known how EFAs, which are specific lipids, form the integrity of our brain and affect the performance of the brain. The brain is a lipid-rich organ, the majority of which contain complex polar phospholipids, sphingolipids, gangliosides and cholesterol. These lipids play a role in the structure and function of cell membranes in the brain. The glycerophospholipids in the brain contain EFA, linoleic acid (LA) and highly polyunsaturated fatty acids (PUFA), derived from alpha-linolenic acid (ALA). PUFA in the brain is omega 3 fatty acid, docosahexaenoic acid (DHA) derived from ALA and arachidonic acid (AA). In the last 10 years, interest in adjuvant treatment of neuropsychological disorders with omega 3 polyunsaturated fatty acids has increased.[2] The appropriate fatty acid composition of brain lipids is critical to the functioning of this organ. Brain fatty acids deficiencies can lead to neurological and neurodegenerative diseases.[3] Almost 60 percent of the human brain is fat, and fatty acids are among the important molecules that reveal the integrity, performance and functionality of the brain. Clearly, EFAs are effective in maintaining optimal health. However, they cannot be synthesized by the body and are taken into the body by diet. Clinical observation studies link the fatty acids together with the diet to an imbalance, resulting in impaired brain performance and diseases.

Saturated and monounsaturated fatty acids are mainly synthesized in the brain. In contrast, polyunsaturated fatty acids are derived from dietary linoleic and linolenic acid. Saturated fatty acid biosynthesis takes place in mammalian cells in three main ways. One of them is de novo synthesis of fatty acids from acetyl-CoA via malonil-CoA. In vivo studies in the brain are synthesized with very long chain fatty acids elongation. A decrease in the acids of the linolenic series within the membranes results in a 40% reduction in the nerve terminals of Na-K-ATPase and a 20% reduction in the 5'-nucleotidase in the whole brain homogenate. A diet low in linolenic acid leads to abnormalities. Learning, memory affects attention tasks seriously. The presence of linolenic acid in the diet provides greater resistance to some neurotoxic agents.[4]

When the effect of PUFA's deficiency is investigated extensively; It has been determined that long-term deficiency causes death in animals. It was observed that in animals fed with fats with low alpha-linolenic content, the rate of recovery in organs slowed down the mechanism in brain cells, organelles and microvascular vessels, in contrast to other organs. A decrease in alpha-linolenic acids in the membranes, a 40% reduction in the Na-K-ATPase of nerve terminals and a 20% reduction in 5'-nucleotidase were observed.[5]

Many functional properties of Na, K-ATPaz strongly depend on the membrane fatty acid composition. In the study, the sciatic nerve and red blood cells were enriched with omega-3 polyunsaturated fatty acids. A standard diet of 30 or 60 mg/kg/day DHA supplemented/ unsupported was given for eight weeks. It was observed that variations in Na, K-ATPase activity were positively

and significantly associated with changes in the omega6/omega3 ratio in SN and RBC. Based on these data, it was emphasized for the first time that the diet clearly demonstrated to report that it can modulate Na, K-ATPase activity through the omega6/omega3 ratio in the membranes.[6]

Fatty acids are part of phospholipids and, consequently, all biological membranes. Polyunsaturated fatty acids are made from a hydrocarbon chain of variable length with double bonds. Its functioning depends on the membrane fluidity, lipid components. Phospholipids synthesized from these fatty acids increase membrane fluidity. This event increases cholesterol membrane viscosity.[5] The main components of the membrane double layer interact with membrane proteins and perform the communication and homeostatic processes required for normal cell function. The role of dietary fats in regulating physiological function and its membrane potential is known.[7] The brain is the organ with the second largest lipid concentration. In brain development, it is necessary to ensure that the amount of lipids is taken with the necessary foods in genetic coding and differentiation and proliferation of nerve cells.[5]

The molecules of lipids are EFAs and their derivatives are part of the structure of DHA and AA brain tissue. EFAs are necessary for biological processes, but they cannot be synthesized in the body, they are taken with nutrients.[8] EFAs play an important role in the synthesis of prostaglandins, thromboxanes, prostacyclines and leukotrienes. The order of enzymatic reactions to which the biosynthesis of these substances depends varies in some human pathologies.[9]

In case of any dietary deficiency of EFA fatty acids, it creates changes in cerebral development and activity of cerebral membrane enzymes.[10] One study reported the effect of impaired brain function due to EPA reduction in mice fed a high fat diet for 19 weeks.[3]

The neural system creates complex neural circuits in the brain. It then produces neuron and glial cells. These neurons function in a variety of brain functions, such as olfactory functions, learning and memory, pattern separation, and mood control. The neural system is regulated by various internal and external factors. Diet is one of the important external factors and lipids are important because they form the cell membrane, are a source of energy and function as signal molecules. Lipids are important regulators of the neural system[11]. PUFA and antioxidants are important mediators in the central nervous system. It has been observed that it protects against acute and chronic oxidative stress.[12]

Among the various organs, in the brain, the most commonly studied fatty acids are omega-3 fatty acids. The deficiency of this fatty acid changes the structure and function of the membranes. They are known to induce small cerebral dysfunctions in the animal model.[13] The brain contains two main PUFAs, AA and DHA. Free AA is formed eicosanoids, sleep induction (PGD2), long-term strengthening, spatial learning and synaptic plasticity (PGE2), anti-inflammatory. Neuroprotective bioactivity consists of DHA. In neural trauma and neurodegenerative diseases, eicosanoids are very important for the normal functioning of the brain, PUFA itself is also important for its membrane structure and function.[14] Considering that brain development is generally completed at the age of 5-6, EFAs, especially omega-3 fatty acids, are important for brain development in both the fetal and postnatal period.[15]

Eicosapentaenoic acid (EPA) and DHA play a critical role in maintaining the structural and functional integrity of the central nervous system and retina. DHA is the dominant structural fatty acid in the central nervous system and retina and is essential for brain development. It is also important for brain development, learning ability and visual acuity.[16]

Brain development is usually completed at the age of 5-6. Considering this, EFAs, especially omega-3 fatty acids, are important for brain development in both the fetal and postnatal period. In order for the visual cortex and retina to gain optimum functionality, DHA in the diet improves visual acuity and mental development , increased vision, brain synthesis and functions of brain neurotransmitters, and Its role in the immune system is important.[15,17,16] ALA also takes part in the synthesis of EPA and DHA.[18] DHA is an important component of the brain and retina. EPA and DHA also replenish the cells in the human brain, as well as the growth of the retinal cells with the brain.[16] EFA and DHA-supplemented mothers' babies are known to have higher mental processing scores, psychomotor development, eye hand coordination and stereo acuity at the age of 4. EFA and DHA intake may also play a useful role in preventing attention deficit hyperactivity disorder (ADHD) and increasing learning capacity and academic performance.[8] In EFA brain development and the functioning of the brain, members of the omega-3 series DHA and EPA provide fluidity to the cell membrane and facilitate certain processes such as neurotransmission and ion channel flow.[19] While DHA plays an important role in childhood neuro development during pregnancy, breastfeeding or childhood, arachidonic acid (ARA) is also important for infant growth and development. DHA levels in the blood show improvement in cognitive and visual function tests in children[20]

EFA and its metabolites have been shown to kill tumor cells in vitro, and this effect was thought to be the end of the increase in the formation of free radicals in the tumor cell. As a result of the study, it was determined that tumor cells can be killed by EPA both in vitro and in vivo. In addition, it has been reported that the cytotoxic effect of fatty acids can prevent the cytotoxic effects together with the protein content in the environment.[21]

OA-519, defined as fatty acid synthase, is a prognostic molecule found in tumor cells of cancer patients. Tumor fatty acid synthase is synthesized fatty acids consisting of 80% palmitate, 10% myristate and 10% stearate. Fatty acid synthase was observed to inhibit acylglycerol synthesis and cause growth inhibition in tumor cells and fibroblast controls. Its significant inversion of growth inhibition shows that the role in growth inhibition is due to fatty acid synthase.[22] Considering its effect on enzyme, fatty acid synthase (FAS) tumor progression and prognosis, which catalyze the synthesis of fatty acids, FAS is thought to represent the therapeutic target.[23] In the experimental study conducted; It was investigated whether there is a relationship between glial tumor grade and free fatty acid level of tumor tissue. Low-grade tumors had high levels of oleic acid, LA, EPA, AA and DHA acid in the tumor tissue. Myristic acid, palmitic acid, stearic acid, ALA, DHA levels were high in tumor tissue of high-grade glial tumors. However, although these values were high, none were statistically significant. High behenic acid values, which are a saturated fatty acid, were found statistically significant.[24] It is thought to be an important result in brain tumor studies. A dietary increase of PUFA has been shown to strongly reduce tumor necrosis factor alpha production.[11]

The decrease in the level of DHA in brain cells is the cause of depression, memory loss, alzheimer's, schizophrenia and visual impairments. Omega-3 fatty acids are effective in biochemical and physiological activities in the body and regulate the concentration of fat in the brain, brain functions and blood in the human body.[16] It is important in the treatment of immune system disorders of omega-3 fatty acids.[25] The ratio of omega-6 and omega-3 fatty acids to each other (n6/n-3) is very important.[17] It is immune-enhancing and anticancer and has beneficial effects on human health.[26,27,28]

It is observed that there is a possible link between epidemiological, biomarker and treatment studies and neuroscientific theories, omega-3 fatty acids and perinatal depression (PND). More research is needed in this area.[29] There is evidence that low n-3 polyunsaturated fatty acids play a role in the pathophysiology of a number of psychiatric disorders.[30]

Fatty acids are also used for therapeutic purposes. In a double-blind placebo-controlled study on 30 patients with bipolar disorder, the addition of polyunsaturated omega 3 fatty acids was associated with a longer remission period. In addition, all prognosis measures were better in the omega 3 group. Recently, a controlled study showed the benefits of adding an omega 3 fatty acid, EPA among depressed patients. It was emphasized that omega-3 fatty acids, which are reported to be effective in the treatment of various psychiatric disorders, may have a mildly beneficial effect on depressive symptoms when added to an existing psychopharmacological maintenance treatment for bipolar disorder.[31]

It causes weakening in learning and memory due to omega 3 deficiency. The increase in depression has been ongoing for centuries. According to some epidemiological data, low depression and/or suicide rates support the hypothesis relationship due to high fish consumption. In all depressions, a significant reduction was observed as a result of supplementation of polyunsaturated omega 3 fatty acids. It is derived from polyunsaturated fatty acids in cytokines. It has opposite physiological functions compared to the omega 3 or omega 6 precursor. Diets with a high source of LA significantly increased the production of pro-inflammatory cytokines such as TNF-alpha. Some epidemiological, experimental and clinical data support the hypothesis that polyunsaturated fatty acids may play a role in the pathogenesis and/or treatment of depression.[10] Depressive disorders such as omega-3 fatty acids and their derivatives regulate the inflammatory effect.[32] Depression is one of the most important health problems worldwide. The results that report their effects on depressive and cognitive disorders in women are diffuse and heterogeneous.[33]

A long-term effect of omega-3 deficiency at various levels was determined in the fetal and postnatal period, and a positive relationship was observed between mood disorders[32] The increase in mood disorders in children is remarkable. In the study of omega-3 fatty acids from pediatric patients in depressive disorder, a randomized and double-blind controlled study was performed. Significant reductions in only the omega-3 group were reported after 12 weeks of treatment in 35 patients. It is thought that adjuvant supplements may be used in the treatment of depressive disorders in children.[10] Rapidly increasing observational and epidemiological studies show that mental illness, especially mood disorders, is associated with reduced dietary intake or an abundance of omega-3 polyunsaturated fatty acids. In the analysis of studies involving patients with major depressive disorder and bipolar disorder, evidence was provided that omega-3 polyunsaturated fatty acids reduce symptoms of depression. However, meta-regression analysis was reported from DHA to be more useful for mood disorders than EPA. Omega-3 polyunsaturated fatty acid was found to have positive results, especially with attention, anxiety and mood disorders.[34]

Omega-3 polyunsaturated fatty acids may also be beneficial in patients with schizophrenia. In the study conducted to determine whether it reduces the progression rate to the first episode psychotic disorder in adolescents between 13-25 years old and young adults with sub-threshold psychosis, the risk of progression to psychotic disorder was determined.[35]

Current studies of patients with major depressive disorder (MDD), treatment of mood disorders, and on

omega-3 fatty acids in depression show that it is effective as a reasonable strengthening strategy for the treatment of these diseases.[36] MDD has an important role for metabolism on the pathophysiology of psychiatric disorders such as post-traumatic stress disorder (PTSD) and schizophrenia. Epidemiological evidence in the historical process links fatty acid intake directly to the prevalence of psychiatric disorders with altered concentrations of fatty acids measured in psychiatric patients. These fatty acid changes are linked to biological stress (hypothalamic-pituitary-adrenal and oxidative stress), inflammation and other accompanying pathophysiological mechanisms, including the structure and function of the brain network. It is an additional EPA given clinically, especially in depressed patients with signs of inflammation. Subsequently, it is emphasized that fatty acid changes prevent treatment response or recurrence of depression in new clinical applications for new neurometabolic insights.[37] It is thought that fatty acids should be evaluated more as biomarkers in psychosis group diseases such as psychotic symptoms, depressive symptoms and mania symptoms.[38]

In researches, DHA played a fundamental role in brain structure and function, as well as determined its role in the etiology of depression. In the last decade, as a result of intervention for 4 to 16 weeks, using various long-chain PUFA preparations in unipolar and bipolar depression; It was reported that positive results were observed in depressed individuals and bipolar patients.[39]

In degenerative diseases such as alzheimer's and parkinson's, the role of young people and the elderly during brain aging due to metabolic disorders, chronic inflammation and oxidative stress was investigated. The role of lubrication, fatty acids, antioxidants and physical inactivity in the pathophysiology of the brain and the molecular mechanisms of aging were determined. Preservation of his condition and control of neuroglial signaling under stress were observed. Omega-3 and -6 fatty acids act competitively to form the tool for energy metabolism, and nutritional behavior in the aging process affects neural plasticity and memory. In this case, a decrease in neurodegenerative emotions was detected.[40]

In some neuropsychiatric disorders, it plays a role in dementia as well as in depression, especially in alzheimer's disease. The frontal cortex and pituitary gland are more severely affected. It is clear that it causes obvious abnormalities in some cerebral structures. It was observed that these selective symptoms followed by behavioral disorders accompanied by negative habits and compatibility with new conditions. Deficiency decreases the perception of pleasure by affecting the cerebral structures in the sensory organs. It resulted in a deficiency in age related hearing, vision and odor impairment, both in the reduced effectiveness of the parts of the relevant brain, and especially in the sensory receptor disorders of the inner ear or retina. To reverse the consequences of this deficiency, it is inevitable to state that egg and plant phospholipids, that is, natural oils, are quite effective.[41]

In 31 patients with Parkinson's and major depression, an improvement in the depressive symptoms of Parkinson's patients was observed when comparing two groups with or without antidepressants (fish oil). It shows that omega-3 intake can be used as an adjuvant therapy with an antidepressant effect. It is the first pilot study performed with omega-3 supplementation in Parkinson's patients, with very important results reported.[42]

The aim of increasing brain glucose metabolism and neuronal metabolism in the early stages of Alzheimer's disease is remarkable. As a hypothesis showing that alternative energy sources can protect neurons, it is of clinical importance to report that medium chain fatty acids (MCT) are an alternative energy source for neurons. MCT has been shown to improve cognitive characteristics in mild to moderate alzheimer's patients.[43] Brain glucose is important in patients with hypometabolism alzheimer's. It has been determined that the ketones produced with ketogenic diet or MCT supplement are an alternative energy source in alzheimer's patients and their positive effects on cognitive properties.[44] In the study in the elderly, when the relationship between dietary fat intake and the risk of cognitive impairment was examined, it was found to be inversely related to cognitive impairment.[45]

While ghrelin requires modification with MCT to show its physiological effects, it is important in anorexia nervosa.[46,47] It is also thought to be good for the treatment of many diseases.[48,49]

The ketogenic diet blocks sodium calcium sensitive channels by increasing polyunsaturated fatty acids in the brain.[50] In many studies in the last decade, ketogenic diet has been used more frequently as an important treatment option for children with epilepsy. As with autism and brain tumors, an increase in the use of this diet is observed in epilepsy and neurological disorders other than the brain.[51] In a study with 50 children diagnosed with resistant epilepsy, it was observed that the diet containing MCT provided complete control of epileptic seizures in eight patients, and 50-90% less seizures occurred in four patients with the addition of anticonvulsant to the MCT diet. It was determined that the extra MCT supplement before bedtime had a positive effect on the control of night attacks.[52] In this way, it inhibits the stabilization of neuronal membranes and excessive electrical discharge of neurons. The ketone bodies formed in the brain increase the gamma amino butyric acid (GABA) receptor count and glutamate. It has been determined that glutamate has an anticonvulsant role and that the GABA formed has antiepileptic properties.[50] When the ketogenic diet antiepileptic drugs were given in children with epilepsy and when the treatment was not possible, compared with the drugs and the diet containing MCT, the result was less sedation

(deep sleep) and more neuroprotective effects. It has been reported that the effect of MCT-containing ketogenic diet on seizure control is stronger than ketogenic drugs.[52]

In the research that schizophrenic symptoms may be a result of changing neuronal membrane structure and metabolism, it suggests that the effects of fatty acids on schizophrenic patients may have some antipsychotic properties compared to placebo.[53] While there are very few studies that have a clinically meaningful effect for schizophrenia and borderline personality disorder, in many studies, benefits are observed compared to placebo when attention deficit hyperactivity disorder and related disorders are concerned.[54]

In an experimental study to investigate the relationship between decreased symptoms and severe behaviors in patients with schizophrenia, severity decreased in patients with severe schizophrenia treated with fish oil, however, the effect of healing positive and negative symptoms was very low.[55]

Anxiety disorders are a common group of psychiatric illnesses with personal, family and social costs. Anxiety disorders may show significant similarities with mood disorders. Given that the omega-3 rich supplement may be effective in the treatment of major depressive disorder, it is suggested that they may have anxiolytic properties.[56] It is clear that omega-3 reduces anxiety behavior, however, there is a lack of information about its effects on anxiety in humans.[59] Anxiety and dietary fat quality (DFQ), in a study with 300 women aged 18-49, while SFA intake was positively associated with anxiety disorder, monounsaturated fatty acids were negatively related to oleic acid anxiety.[58] Recent studies have little evidence of stress and anxiety, as well as the relationship between fatty acid profile and psychological disorders. In the relationship between stress and anxiety and erythrocyte fatty acid (FA) profile, the amount of linoleate and DHA was inversely proportional to stress and anxiety scores.[59]

A new area of research highlights the presence of interactions between metabolic syndrome (MS) and cognitive function in patients with schizophrenia. A diet of 7 days was applied to 30 patients from 87 diagnosed with schizophrenia and from 83 patients diagnosed with metabolic syndrome. As a result, it was observed that changing eating habits could be an important element of a holistic approach to the problems of schizophrenia treatment.[60]

It was reported that substance addicts had poor eating habits and that there was a strong relationship between anxiety disorders and substance use disorders. In the study of omega 3 supplements, it was observed that a group of drug addicts might have an anxiety level reduction.[57] Omega-3 supplements, which have been used for a long time in the etiopathogenesis of mental illnesses and disorders characterized by impulsivity, are very important. The relationship between plasma and erythrocyte membrane basal PUFA composition and impulsivity was investigated in people with gambling disorder. EPH was found in the erythrocyte membrane of impulsive gamblers more than fifty five men with gambling disorder than non-impulsive gamblers. It was observed to have a lower AA/EPA and AA /DHA ratio. With this result, it is thought that in disorders characterized by high impulsivity, it determines the relationship between EFA and disorders characterized by high impulsivity.[61]

In traumatic brain injury, octanoic and decanoic acids, one of the MCT fatty acids, are thought to play an important role in the crisis of mitochondrial injuries due to energy needs.[62] In another study, omega-3 caused great reductions in aggressive, antisocial and violent behavior in young people. It is considered that high levels of unsaturated fats in omega-3 can have negative effects on brain development and neurodevelopmental outcomes.[63]

CONCLUSION

Neuronal membranes are also emphasizing how specific lipids, fatty acids, EFAs, in forming our brain's integrity and how it affects brain performance, providing a new understanding and highlighting effects on neuropsychiatric disorders that may be affected by them. It is our aim to draw attention to the fact that how fatty acids affect the brain and the dependence of the brain on certain EFAs should be better understood, the proper diet should be taken with the right diet and natural foods, especially in terms of protecting health and treating diseases, and it is our aim to draw attention to the need for studies. PUFA's deficiencies are thought to be effective in the pathophysiological processes of psychotic disorders. It is also thought that fatty acids can be used as adjuvants to reduce recurrence in cancer after main treatment and in neoadjuvant treatment before main treatment, i.e., to shrink the tumor and facilitate surgery in cancer.

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