K Int J Health Sci. April 2022;Vol 5(1): 35-47

REVIEW ARTICLE

Effects of Omega-3 Fatty Acids on Cognitive Performance

Feyzanur Turgay[1*], Ayşe Güneş Bayır[2]

1Dietitien, Istanbul, Turkey

2Department of Nutrition and Dietetics, Faculty of Health Sciences, Bezmialem Vakıf University, Istanbul, Turkey

Corresponding author: Feyzanur Turgay e-mail: *feyzanurtrgy@gmail.com, Istanbul, Turkey*

***Ethical approval**: No need*

***Conflict of interest:** No conflict of interest with any person or organization*

***Received:** 12.03.2022, **Accepted:** 15.04.2022*

ABSTRACT

***BACKGROUND**: Omega-3 polyunsaturated fatty acids (n-3 PUFA) are composed of ALA (alpha-linolenic acid), EPA (eicosa-pentaenoic acid), DHA (docosa-hexaenoic acid), SDA (stearidonic acid) and DPA (docosa-pentaenoic acid). Omega-3 polyunsaturated fatty acids are essential components of neural membrane phospholipids and may improve cognition by supporting different aspects of neuronal function. DHA is more important than other n-3 PUFAs in terms of brain functions. It affects various neurologic pathways and processes. The brain and eye have higher DHA content than other organs. EPA and DHA help the cells in the human brain to regenerate and ensure the proliferation of brain and retinal cells. EPA and DHA could be synthesized by humans in small amounts from the essential fatty acid precursor ALA. Dietary intake of DHA and EPA is important because of the limited transformation in the human body. Therefore, foods containing omega-3 PUFA should be included in the diet. Brain development is very rapid in the last trimester of gestation and up to the age of two. During this period, DHA is constantly accumulating in the brain. Breast milk contains n-3 PUFAs, especially DHA. The DHA content of breast milk is greatly affected by dietary DHA intake. Low DHA intake is linked to impaired cognitive development and visual function. Therefore, it is important for pregnant women, breastfeeding women and infants to consume enough DHA to support the development and function of the brain and eye. Moreover, consumption of oily fish may be associated with better cognitive performance, normal aging processes, and a reduction in dementia progression due to its n-3 PUFA content. In the aging process, there is a decrease in brain functions. In this process, n-3 fatty acid supplements could help support the brain. Nutrition plays a role in preventing cognitive decline; however, nutrition alone may not be as effective as a multi-site intervention. This study aims to present the current findings on the effect of omega-3 fatty acids on cognitive performance and cognitive development in the light of current literature.*

***KEYWORDS:** Omega-3 fatty acids; Cognitive performance; Pregnancy; Lactation period; Childhood; Aging*

INTRODUCTION

Today, the importance of adequate and balanced nutrition for a healthy life is known by many people (1). Adequate and balanced nutrition is adequate intake and use of energy and nutrients required for the growth, renewal and functioning of the body (2). Adequate and balanced nutrition is the basis

for the protection and development of health and the prevention of diseases (2,3). Fats are macronutrients that are very important for maintaining a healthy life (4). Fats, which are one of the basic food groups in human nutrition, not only provide a high energy source but are also very important because they contain functional compounds such as omega-3 fatty acids (1). Studies conducted in recent years have shown that the types and amounts of fatty acids in oils are important for the protection and maintenance of health (5). The Western pattern diet habits, which have increased frequency in our country in recent years, are generally characterized by low intake of n-3 PUFA and high intake of n-6 PUFA (6). While the ratio of n-6/n-3 is expected to be 1/1, this ratio rises to 10-20/1 in the western type of nutrition approach (3,5,6). In Turkey, the n-6/n-3 ratio is approximately 16/1 for women and 15-16/1 for men (7). This ratio is not convenient for normal growth and development. The balance between omega-6 and omega-3 fatty acids is an important determinant of homeostasis, cognitive development, normal growth and maintenance of mental health throughout the life cycle (5). According to the DRI (Dietary Reference Intake), the daily intake of omega-3 fatty acids is 1.1 grams for women, 1.6 grams for men and 0.5 grams for infants (8). According to the TBSA 2019 report, the daily intake of omega-3 fatty acids in our country is 1.3-1.6 grams in men and 1.1-1.3 grams in women (7). Total EPA and DHA consumption are between 0.2 grams/day for women and 0.2-0.3 grams/day for men. Seafood, especially oily fish, is rich in n-3 PUFAs content (9). Average weekly fish consumption in Turkey is reported as 250 grams (3). According to Turkey Nutrition Guidelines, fish consumption should be at least 2-3 servings per week (approximately 300-500 grams) (4). In a review study, it is seen that the current fish consumption in Turkey is not sufficient to meet the omega-3 requirement (3). This situation reveals the importance of the Mediterranean diet, which emphasizes the consumption of fish and seafood, contrary to the western type of eating habits (10). Fish consumption is recommended at least twice a week in the Mediterranean diet. At the same time, studies are showing that accommodating the Mediterranean diet positively affects cognitive performance (11,12). The effect of omega-3 fatty acids on cognitive performance and cognitive development is still being investigated today (13). Therefore, this study aimed to present the current findings on the effect of omega-3 fatty acids on cognitive performance and cognitive development of human according to current literatures. Omega-3 fatty acids consist of unsaturated fatty acids with double bonds (9). Omega-3 fatty acids (n-3 PUFA); ALA (alpha-linolenic acid, 18:3 n-3), EPA (eicosapentaenoic acid, 20:5 n-3), DHA (dokosahexaenoic acid, 22:6 n-3), SDA (stearidonic acid, 18:4 n-3) and DPA (dokosapentaenoic acid, 22:5 n-3). ALA and SDA are short-chain; DHA, EPA, and DPA are long-chain omega-3 fatty acids (14).

METABOLIC AND PHYSIOLOGICAL FUNCTIONS OF OMEGA-3 FATTY ACIDS

Effects on the Central Nervous System

Omega-3 fatty acids are essential for brain development (5). The fatty acid composition of the brain consists of high levels of palmitate (16:0), omega-6 PUFA arachidonic acid (AA, 20:4 n-6) and DHA (14). It also contains low levels of other omega-3 PUFAs, especially EPA (6). The amount of EPA in the brain is about 250-300 times less than DHA. Therefore, DHA is more important to the brain than other omega-3 PUFAs (14). DHA accumulates in areas of the brain involved in memory and attention, such as the cerebral cortex and hippocampus (15). The most important omega-3 fatty acid in the brain is quantitatively considered DHA (16). However, the evidence that other omega-3 fatty acids, including EPA and DPA, also have neuroprotective properties has been increasing with studies in recent years. DHA, which is the most abundant omega-3 LCPUFA in the central nervous system of mammals, is present in the human brain

approximately 5 grams and constitutes 15-20 % of the total fatty acids in the brain (6). Any deviation in the physiological levels of DHA in the brain can cause cognitive disorders and some developmental disorders such as attention deficit, autism, and motor problems (17). All these disorders could affect learning performance. In the brain, DHA and DPA are predominantly found in phosphatidyl-ethanolamine (PE) and phosphatidyl-serine (PS) structures, while EPA is in esterified form (14). EPA and DHA have effects on membrane receptor function, neuro-transmitter production and metabolism (5). EPA and DHA, which make up 50% of the neuronal membrane and 70% of myelin composed of lipids, have very important functions in the central nervous system (18). In addition, EPA and DHA help regenerate cells in the brain and ensure the proliferation of brain and retinal cells (1). DHA, as a component of lipoproteins, can be transported in the blood and stored in adipose tissues. Compared to other body tissues, the brain and eye have high concentrations of DHA (19). DHA is particularly concentrated in the gray matter of the brain and the outer rods of the retina. DHA is involved in neuronal signaling in the brain. It also plays a role in the quality of vision of the eye. The deficiency of omega-3 fatty acids causes a significant reduction in catecholamines that affect glucose transport and utilization in the brain (17). Animal studies are shown that DHA deficiency has critical effects on neuronal development and behavioral changes such as learning, memory, auditory changes, and smell in the brain (15).

Neuroprotective Effects

A healthy brain is rich in omega-3 fatty acids, especially DHA (14). There are many mechanisms in the brain related to the cognitive benefit of omega-3 fatty acids. These include mechanisms involving neuroprotective actions such as neurogenesis, neuroplasticity, synaptogenesis, anti-inflammatory, antithrombotic and vasodilator effects (20). Omega-3 fatty acids are thought to have trophic neural effects. High consumption of fatty acids is expected to increase gray matter volume in regions of the brain such as the amygdala, hippocampus, and anterior cingulate cortex (21).The level of plasma omega-3 fatty acids in humans is dependent on dietary intake and conversion by de novo synthesis from alpha-linolenic acid, the precursor of omega-3 fatty acids (5). In humans, the conversion of PUFAs via ALA is catalyzed by β-oxidation, desaturation (increasing the number of double bonds) and elongation (extension of the carbon chain) (2,5,13). Omega-3 PUFAs are synthesized from ALA by some enzymes such as elongaz, delta-5 saturase, and delta-6 saturase (9). Delta-5 and delta-6 desaturases in this pathway are rate-limiting enzymes. Therefore, the desaturation and elongation capacity of n-3 PUFAs is limited (5). Since the biological conversion of ALA to EPA and DHA is limited in the human body, consumption through diet is important (9).

Oily fish contain high levels of EPA and DHA and lesser amounts of DPA (9). Examples of oily fish are bonito, horse mackerel, anchovy, garfish, bluefish, red mullet, sardine, trout, salmon, mackerel, swordfish, and tuna (22). Coldwater fish contain higher amounts of n-3 LCPUFA than warm water fish due to the excess amount of adipose tissue that helps them adapt to the cold environment (6). Oily fish are rich in n-3 LCPUFA. However, it should be noted that oily fish contain higher levels of pollutants such as methylmercury (MeHg), digoxin, polychlorinated biphenyls (PBC) than white fish (non-oily) (23). Studies are shown that mercury in oily fish does not adversely affect the neurodevelopmental processes of infants and children (24,25). However, some studies support the neurotoxic risk of MeHg for the fetus and newborn (23). For this reason, it is useful to limit the consumption of fish with high mercury content, especially for women who are pregnant and of childbearing age (26). Wild (marine) fish contain a higher amount of n-3 PUFA than culture (pool) fish (6). Because most marine fish are fed with phytoplankton and zooplankton containing n-3 PUFAs in abundance, while culture fish are fed mostly with feeds consisting of grains

and vegetable oils. SDA is found in fish oils, genetically modified soybean oil, blackcurrant seed oil, and hemp oil (22). ALA is mostly found in plant-based foods. It is concentrated in nuts, some seeds and some vegetable oils. Linseed and linseed oil, perilla oil, canola oil, soybean oil, chia seeds, walnuts are known as good sources of ALA (9,22).

Effect of Omega-3 Fatty Acids on Cognitive Performance

The requirement for omega-3 fatty acids in human life begins in the mother's womb (16). It continues through childhood, adolescence, adulthood and old age. During all these periods, studies on the effects of omega-3 fatty acids on cognitive development, cognitive performance and cognitive decline are ongoing. The requierement dose for omega-3 fatty acids throughout human life varies with age and could affect cognitive performance differently in different age groups (18).

Pregnancy and Lactation Periods

The gestation period is a sensitive period for maternal and fetal health (19). Food consumption of the mother directly affects the growth and development of the fetus (23). Omega-3 fatty acids are essential for fetal development (27). Omega-3 fatty acids, especially DHA, have an important role in the development of the brain, retina and nervous system of the fetus (1). Maternal plasma phospholipids are an important source of DHA for the fetus (19). DHA accumulates in the central nervous system before birth and is involved in early developmental processes such as gene expression and neurite outgrowth (28,29). DHA is concentrated in the circulatory system and tissues of the fetus during the biomagnification process (19). Adequate dietary DHA consumption by pregnant women plays a key role in optimum fetal development (19). Because the main source of DHA is seafood, the mother needs to pay attention to fish consumption during gestation (23). MeHg, especially found in oily fish, is the most harmful form of mercury to humans. Since MeHg is fat-soluble, it can easily cross the placenta and pose a risk to the fetus. The United States Food and Drug Administration (FDA) recommends that women of pregnancy and childbearing age limit their consumption of fish that contain particularly high levels of mercury (26). The recommended fish species and consumption frequency according to FDA recommendations are given in Table1.

Table 1. Fish Consumption Recommendations for Pregnant and Breastfeeding by FDA (26)

Some types of fish recommended consuming 2-3 servings* per week	Anchovy, Atlantic mackerel, Black sea bass, Butterfish, Cod, Flounder, Haddock, Hake, Herring, Mullet, Perch (freshwater and ocean), Pickerel, Salmon, Sardine, Shad, Shrimp, Sole, Trout (freshwater)
Some types of fish recommended consuming 1 serving* per week	Bluefish, Buffalofish, Carp, Grouper, Halibut, Mahi Mahi, Monkfish, Rockfish, Sablefish, Stripped bass (ocean), Tuna
Fish species with very high mercury content and not recommended for consumption	King mackerel, Marlin, Orange roughy, Shark, Swordfish, Tilefish (Gulf and Mexico), Tuna (bigeye)

* 1 serving is stated as approximately 114 grams.

Nutrition is very important for brain development (13). Breast milk, which is the first food of a newborn baby, contains essential nutrients for babies who are 0-6 months old (30). However, breast milk also contains enough omega-3 fatty acids for the baby's growth and development (31). Omega-3 fatty acids, especially DHA, are found in high amounts in breast milk. At the same time, it supports cognitive development and increases the visual functions of the baby. During the last trimester of gestation and the first two years of life, brain development is quite rapid and DHA is constantly accumulating in the brain during this period (28). The nutritional composition of breast milk during lactation is affected by the mother's food consumption habits (23,27). The DHA content of breast milk is greatly affected by dietary DHA intake (19,31). Exclusive breastfeeding is recommended for the first 6 months of life, and the brain weight of infants nearly doubles during this period. (27). Babies 0-6 months have a higher brain/body weight ratio than adults, which means that the infant may be at higher risk for nutritional and energy deficiencies. It is stated that for the optimum growth and development of the newborn, 1-2 servings/week of oily fish consumption by the mother will be sufficient in terms of EPA and DHA (23). However, many women consume less fish than recommended. In this case, it is recommended that pregnant and lactating women take at least 200 mg/day DHA supplement to ensure optimal growth and development of the baby (23,27). Consumption of fish with high mercury content should be limited in the diet of the nursing mother, as in the gestation period. (23). Gestation and lactation are sensitive periods when insufficient DHA intake can affect mental and visual development and performance (19). In a study, 125 pregnant women were studied. DHA consumption levels were measured in the 2nd and 3rd trimesters of pregnancy and were grouped as low, medium and high (32). Infants were assessed at 4.5 and 9 months using specific tests of visual acuity, visual attention and habitation. As a result of the 9 month visual acuity test, it was reported infants whose mothers were in the medium DHA group performed significantly better than those with low or high DHA consumption. This study supports that high DHA consumption levels do not have a positive effect on cognitive development. Another study studied a total of 1904 Mexican women to investigate the long-term effects of increasing DHA intake during pregnancy from infancy to childhood (33). Participants were randomly assigned to receive either a 400 mg/day DHA supplement or placebo from week 18-22 of gestation until delivery. Measures of cognition, behavior, and attention were tested when children reached age 5 (n = 797). The findings show no significant difference between the placebo group and the supplement group. The results of a systematic review study show that supplementation with omega-3 fatty acids during gestation and lactation has no evidence of an effect on children's skills and cognitive development (34). A meta-analysis study was conducted to investigate the role of omega-3 PUFA supplementation on cognitive development, cognitive function, and cognitive decline (30). Compared with the placebo group, the use of supplements has been shown to support infants' mental, psychomotor, and cognitive development. As a result of the study, they found that n-3 PUFA supplements could significantly improve cognitive development in infants, but were not effective in improving cognitive performance in children, adults, and the elderly. Consumption of omega-3 PUFA supplements, especially DHA, may benefit cognitive development in infancy. In a study conducted to investigate the effect of maternal DHA supplementation on the development of the baby during pregnancy, 400 mg/day DHA supplementation was given to pregnant women from the 16th week of pregnancy until delivery (29). The infants were followed for 14 to 18 months after birth. Omega-3 supplementation has been reported to be associated with a reduced risk of poor language development compared to

placebo. In another study conducted in the USA, DHA supplementation was given to lactating women (n=89) (27). The effects of DHA on the fatty acid composition of breast milk and plasma concentrations of breastfeeding mothers and infants were investigated. Participants were given 200 mg DHA, 400 mg DHA, and a placebo for 6 weeks 4-6 weeks postpartum. Breast milk fatty acid composition and maternal plasma and infant plasma DHA were significantly higher in the supplemented groups compared to placebo.

Childhood and Adolescence

Many studies have been conducted on how the consumption of omega-3 fatty acids in childhood and adolescence affects cognitive performance (34-39). According to TUBER, fish consumption portion recommendations for children and adolescents are given in Table 2.

Table 2. Fish Consumption Portion Recommendations for Children and Adolescents (4).

Age Range	Portion/Week
2-3 years	2/3 – 1
4-6 years	1 – 1,5
7-10 years	1,5 – 2
11-14 years	2
15-18 years	2

It was investigated how increasing salmon consumption in preschool children's diet would affect cognitive performance compared to a meat-based diet. (35). Children (n=205, age 4-6 years) were randomly assigned to eat meals containing Atlantic salmon or meat 3 times a week for 16 weeks. Cognitive tests, fine motor coordination tests, and biochemical tests were performed before and after the intervention. It was concluded that increasing salmon consumption did not indicate an effect on general IQ, but had a positive effect on some subtests such as image comprehension and symbol search. Another study studied 197 children aged 8 and 9 years to reveal the effect of oily fish consumption on cognitive performance and socio-emotional functions in children (36). Children were randomly allocated to receive 300 grams of oily fish or poultry. The findings support a dose-dependent beneficial effect of oily fish consumption on cognitive performance in healthy children. A meta-analysis study was conducted to expand the existing findings on the effects of omega-3 supplements on cognitive test performance in youth (37). It was concluded that omega-3 supplements did not have a main effect on domain-specific cognitive test performance in youths. Subgroup analyses identified beneficial effects of EPA rich formulations in the domains of long-term memory, working memory and problem solving and a tendency towards beneficial effects in clinical populations. Another study concluded that there is insufficient evidence for the beneficial effects of omega-3 supplementation for improving cognitive function in attention deficit or hyperactivity disorder in childhood and adolescence (34). In a study conducted in England, the effect of dietary omega-3 PUFA supplementation in children with attention deficit hyperactivity disorder, behavior/learning disorder, or low blood omega-3 PUFA levels was investigated (38). 493 school children aged 7-9 were included in the study. As a result of the study, lower DHA concentrations were associated with poorer reading ability and working memory performance. Lower DHA was also associated with higher levels of

parent rated oppositional behavior and emotional lability. In another study conducted in Sweden, children aged 9-10 were given omega 3/6 capsules (558 mg/day EPA, 174 mg/day DHA, and 60 mg/day gamma-linoleic acid) twice daily for 3 months (39). The result of the study reported improvements in the reading skills of the children who received the supplement. Clinically, 'phonological decoding time' and 'visual analysis time' showed significant improvements compared to placebo, especially in children with attention problems. To investigate the effect of omega-3 supplementation on neuropsychological functions in malnourished children, 55 Mexican children aged 8-12 years with mild to moderate malnutrition were included in a study (17). Neuropsychological performance was measured at baseline and three months later. For the duration of the intervention, children were given omega-3 fatty acid capsules (60 mg DHA and 90 mg EPA) three times daily. The results report that children in the treatment group showed improvements in 11 of 18 neuropsychological variables. More than 70% of the omega-3 supplemented children showed improvement in visual-motor coordination, processing speed, perceptual integration, attention, and executive functions.

Adulthood

Maintaining optimal brain functions during adulthood is the main goal. Although brain development is stable during this period, neuroplasticity continues (15). Studies show that omega-3 PUFA consumption supports brain health and cognitive performance (16,40). Omega-3 fatty acids, especially DHA, have an effect on the branching of neuron dendrites in memory formation and the regeneration of axons and dendrites in neuronal wounds (28). Some studies report that n-3 PUFA supplementation has no significant effect on cognitive performance in adults (18,41,42). Therefore, the evidence for the use of omega-3 supplements to support cognitive performance in adults is conflicting and insufficient (41). One study investigated the effect of omega-3 supplementation in healthy young adults on mood, cognition, and physiological stress markers (43). Participants (n=72) were given 2800 mg/day fish oil (1680 mg EPA and 1120 mg DHA) for 35 days. According to the results of the study, the effect of Omega-3 PUFA supplementation on mood and cognition in adults is minimal. In a study conducted on healthy adults aged 18-45 years with low DHA intake, the effect of using DHA supplements on cognitive performance was investigated (15). In this study, it was stated that DHA supplementation significantly benefits episodic memory in women and working memory in men. It has been concluded that using supplements improves memory in individuals with low DHA intake. In a study conducted in Australia, 299 Australian young women aged 18-35 were studied to examine the relationship between omega-3 levels and cognitive function (41). Omega-3 levels were determined by taking blood tests from the participants and they were classified as low, medium and high. Participants completed a computer-based cognition testing battery evaluating the domains of impulsivity, attention, information processing, memory and executive function. A significant correlation was found between low omega-3 levels and low attention cognitive scores. However, no significant relationship was found in other cognitive domains. In another study, it was aimed to investigate the effect of omega-3 supplements rich in EPA and DHA on cognitive performance and functional brain activation in young adults (44). Participants were given EPA-rich (590 mg EPA and 137 mg DHA) and DHA-rich (159 mg EPA and 417 mg DHA) supplements. Biochemical parameters, brain activation (fMRI), and behavioral outcomes were evaluated. It has been stated that EPA-rich supplements showed better cognitive performance on participants and were more effective at improving neurocognitive function than DHA-rich supplements. In a study were assessed the cognitive effects of fish oil supplementation at college-age and were

hypothesized benefits on effect, executive control, inhibition, and verbal learning and memory (18). College-aged participants were assigned to active or placebo treatments, receiving fish oil (480 mg DHA/720 mg EPA) or coconut oil, respectively. As a result of the study, it was reported that fish oil did not have a significant cognitive effect compared to placebo.

Old Age

Life expectancy is getting longer with the advancement of technology and the development of the healthcare system, and the number of elderly people is increasing worldwide (45). Age-related cognitive decline is seen as an important health problem for the elderly population. Omega-3 fatty acids have a fundamental role in the development, functioning and aging of the brain, as they have various physiological functions related to neurogenesis, neurotransmission and neuroinflammation (13). Insufficient dietary omega-3 and omega-6 intakes may be associated with lower cognitive performance in the elderly (45). Likewise, long-chain omega-3 polyunsaturated fatty acids, especially EPA and DHA, may have beneficial effects on the aging brain (46). In particular, DHA may be a useful therapeutic agent to prevent or delay cognitive impairment in individuals with mild Alzheimer's disease (21). Some studies are shown that a Mediterranean based diet that emphasizes fish consumption can prevent age-related cognitive decline (11,12). Increasing fish consumption may be beneficial because they contain high levels of omega-3 fatty acids (9). However, clinical trials with omega-3 PUFAs in older adults mostly used different ratios of EPA and DHA supplements (14). Some studies are shown that high n-3 LCPUFA supplement consumption is associated with a reduced risk of cognitive decline (20,47-50). In a study conducted to investigate the effect of high intake n-3 LCPUFA supplement use on cognitive performance in the elderly, 65 healthy individuals aged 50-75 years were studied (46). Participants received either 2.2 g/day (1320 mg EPA and 880 mg DHA) fish oil or placebo for 26 weeks. Cognitive performance, structural neuroimaging (MRI), vascular markers, and blood parameters were measured before and after the intervention. As a result of the study, a significant (P=0.023) increase was detected in the cognitive functions of the supplement group compared to the placebo group. In a systematic review and meta-analysis study was conducted to determine the changes in cognitive function after intervention with n-3 LCPUFA supplementation in non-demented adults, including those with mild cognitive impairment (47). It was aimed to identify changes in cognitive function after intervention with omega-3 supplementation. It was concluded that omega-3 supplementation may have mild benefits in improving memory function in older adults. Another systematic review study concluded that omega-3 supplements may have a positive effect on cognition (48). It has been stated that omega-3 supplements can be used as a therapeutic tool for cognitive decline in older and older adults. A meta-analysis study from clinical and observational studies reported that >1 g/day DHA/EPA supplementation significantly improved episodic memory in older adults with mild memory complaints (49). Another study studied 44 cognitively healthy female participants aged 50-75 years (20). Participants were given 2.2 g (4 capsules) of omega-3 supplements daily. It was observed that there was a significant increase in memory functions such as learning and remembering in the supplement group compared to the placebo. There are also some studies that concluded that there was no significant association between the use of omega-3 supplements for cognitive decline in the elderly (50,51). A meta-analysis study investigated the neuropsychological impact of high omega-3 fatty acid supplement consumption in AD, mild form of cognitive impairment, or healthy individuals (50). The results suggest that the use of n-3 LCPUFA supplements significantly improved the attention and processing speed tests of

participants with mild forms of cognitive impairment. However, no significant benefit was found in participants with Alzheimer's disease and healthy individuals. The results of the study support that the use of omega-3 supplements in patients with a mild form of cognitive impairment shows benefits in certain cognitive areas. A study conducted in Australia investigated omega-3 supplement consumption and its relationship with age-related cognitive decline (51). Individuals aged 65 and over in Australia use higher levels of supplementation compared to those aged 19-64. However, it has been stated that this high consumption does not slow down cognitive decline. It was also mentioned that a diet characterized by fish consumption, such as the Mediterranean diet, may provide cognitive benefits and be associated with a lower risk of dementia. The study supports that it is more beneficial to increase fish consumption than to use supplements. The World Health Organization does not recommend using omega-3 PUFA supplementation to reduce the risk of cognitive decline or dementia, as the evidence is conflicting and insufficient (52). Omega-3 PUFAs can be used as potential nutrients in the prevention of different negative consequences of aging. However, the current data suggest that more studies are needed to use high consumption of omega-3 PUFAs through diet or certain supplements to prevent aging-related loss of function (53).

CONCLUSION AND RECOMMENDATIONS

Omega-3 polyunsaturated fatty acids are essential for the growth, development, and maintenance of health. They are mostly found in seafood, especially oily fish. For this reason, it is recommended to consume fish at least 2 times a week. Consumption of n-3 PUFA supplements by individuals with omega-3 PUFA deficiency may positively affect cognitive performance.

Supplementation is recommended in case of deficiency, especially in pregnant women, lactating women, and infants. However, more studies are needed to prove its beneficial effect in the general population and those with neurodevelopmental disorders. There are current studies that suggest that it may be more beneficial to increase the consumption of oily fish rather than taking omega-3 PUFAs as supplements. However, women in the gestational and lactation period should limit the consumption of fish with high mercury content in their diets. There are conflicting findings in the literature regarding the effects of omega-3 PUFAs on cognitive decline. More studies are needed to prove its beneficial effect on cognitive activities.

REFERENCES

1.Çelebi Ş, Kaya H, Kaya A. Omega-3 Yağ Asitlerinin İnsan Sağlığı Üzerine Etkileri. Alinteri Journal of Agriculture Sciences. 2017;32(2):105-112.

2.T.C. Sağlık Bakanlığı. Türkiye'ye Özgü Besin ve Beslenme Rehberi [Internet]. Ankara (TR): T.C. Sağlık Bakanlığı; c1520 [cited 15 December 2020].https://www.foodelphi.com/turkiyeye-ozgu-besin-ve-beslenme-rehberi-hacettepe-universitesi/

3.Erkan N. Türkiye'de Tüketilen Su Ürünlerinin Omega-3 (ω-3) Yağ Asidi Profilinin Değerlendirilmesi. Journal of Fisher Sciences. 2013;7(2):194-208.

4.T.C. Sağlık Bakanlığı. Türkiye Beslenme Rehberi [Internet]. Ankara (TR): T.C. Sağlık Bakanlığı; c1520 [cited 15 A December 2020]. https://dosyasb.saglik.gov.tr/Eklenti/10915,tuber-turkiye-beslenme-rehberi.pdf.

5.Simopoulos AP. Evolutionary aspects of diet: the omega-6 / omega-3 ratio and the brain. Molecular Neuro-biology. 2011; 44(2): 203–215.

6.Saini RK, Keum Y. Omega-3 and omega-6 polyunsaturated fatty acids: dietary sources, metabolism, and significance – A review. Life Science. 2018;15(203):255-267.

7.T.C. Sağlık Bakanlığı. Türkiye Beslenme ve Sağlık Araştırması [Internet]. Ankara (TR): T.C. Sağlık Bakanlığı; c1520 [cited 15 December 2020].

8.https://hsgm.saglik.gov.tr/depo/birimler/saglikli-beslenme-hareketli-hayat-

db/Yayinlar/kitaplar/TBSA_RAPOR_KITAP_20.08.pdf

9.Institute Of Medicine The National Academic Press. Dietary Reference Intakes: The Essential Guide to Nutrient Requirements [Internet]. Washington, DC: Institute Of Medicine; c1520 [cited 15 December 2020].Availablefrom: https://www.nal.usda.gov/sites/default/files/fnic_uploads/DRIEssentialGuideNutReq.pdf

10.Shahidi F, Ambigaipalan P. Omega-3 polyunsaturated fatty acids and their health benefits. Annual Review of Food Science and Technology. 2018;25(9):345-381. 11.Davis C, Bryan J, Hodgson J, Murphy K. Definition of the Mediterranean diet; a literature review. Nutrients. 2015; 7(11): 9139-9153.

12.Wengreen H, Munger RG, Cutler A, Quach A, Bowles A, Corcoran C, et al. Prospective study of Dietary Approaches to Stop Hypertension- and Mediterranean-style dietary patterns and age-related cognitive change: the Cache County Study on Memory, Health and Aging. The American Journal of Clinical Nutrition. 2013;98(5):1263–1271.

13.Tangney CC, Kwasny MJ, Li H, Wilson RS, Evans DA, Morris MC. Adherence to a Mediterranean-type dietary pattern and cognitive decline in a community population. The American Journal of Clinical Nutrition. 2011;93(3):601–607.

14.Lange KW. Omega-3 fatty acid and mental health. Global Health Journal. 2020;4(1):18-30.

15.Dyall CD. Long-chain omega-3 fatty acids and the brain: a review of the ındependent and shared effects of EPA, DPA and DHA. Frontiers in Aging Neuroscience. 2015;21(7):52.

16.Stonehouse W. Does consumption of LC omega-3 PUFA enhance cognitive performance in healthy school-aged children and throughout adulthood? Evidence from clinical trials. Nutrients. 2014;6(7):2730–2758.

17.Derbyshire E. Brain health across the lifespan: a systematic review on the role of omega-3 fatty acid supplements.Nutrients. 2018;10(8):1094.

18.Portillo-Reyes V, Pérez-García M, Loya-Méndez Y, Puente AE. Clinical significance of neuropsychological improvement after supplementation with omega-3 in 8-12 years old malnourished Mexican children: a randomized, double-blind, placebo and treatment clinical trial. Research in Developmental Disabilities. 2014;35(4):861–870.

19.Karr JE, Grindstaff TR, Alexander JE. Omega-3 polyunsaturated fatty acids and cognition in a college aged population. Experimental and Clinical Psychopharmacology. 2012; 20(3): 236–242.

20.Calder PC. Docosahexaenoic acid. Annals of Nutrition and Metabolism. 2016;69(1):8-21.

21.Külzow N, Witte AV, Kerti L, Grittner U, Schuchardt JP, Hanhn A, et al. Impact of omega-3 fatty acid suplementation on memory functions in healthy older adults. Journal of Alzheimer'd Disease. 2016; 51(3): 713-725.

22.Hashimoto M, Hossain S. Neuroprotective and ameliorative actions of polyunsaturated fatty acids against neuronal diseases: beneficial effect of docosahexaenoic acid on cognitive decline in alzheimer's disease. Journal of Pharmacological Sciences. 2011;116(2):150-62.

23.Food and Agriculture Organization of the United Nations. Fats and fatty acids in human nutrition: report of an expert consultation [Internet]. Rome, IT: Food and Agriculture Organization of the United Nations; c1520 2020. https://www.fao.org/3/i1953e/I1953E.pdf

24.Öksüz A, Alkan B Ş, Taşkın H, Ayrancı M. Yaşam Boyu Sağlıklı ve Dengeli Beslenme İçin Balık Tüketiminin Önemi. Food and Health. 2018;4(1):43-62.

25.Kvestad I, Vabø S, Kjellevold M, Nøstbakken OJ, Midtbø LK, Hysing M,et al. Fatty fish, hair mercury and cognitive function in Norwegian preschool children: Results from the randomized controlled trial FINS-KIDS. Environment International. 2018;121(Pt 2):1098–1105.

26.Cressey P, Miles G, Saunders D, Pearson AJ. Mercury, methylmercury and long-chain polyunsaturated fatty acids in selected fish species and comparison of approaches to risk-benefit analysis. Food and Chemical Toxicology. 2020;146:111788.

27.U.S. Food and Drug Administration. Advice About Eating Fish What Pregnant Women & Parents Should Know [Internet]. Viginia, USA: U.S. Food and Drug Administration; c1220 2020. https://www.fda.gov/food/consumers/advice-about-eating-fish

28.Sherry CL, Oliver JS, Marriage BJ. Docosahexaenoic acid supplementation in lactating women increases breast milk and plasma docosahexaenoic acid concentrations and alters infant omega 6:3 fatty acid ratio. Prostaglandins, Leukotrienes and Essential Fatty Acids. 2015; 95: 63–69.

29.Gezer C, Samur G. Omega-3 Yağ Asitlerinin Bilişsel Gelişimdeki Rolü. Beslenme ve Diyet Dergisi. 2012; 40(1): 43-49.

30.Mulder KA, King DJ, Innis SM. Omega-3 fatty acid deficiency in infants before birth identified using a randomized trial of maternal DHA supplementation in pregnancy. PloS one 2014;9(1):e83764.

31.Jiao J, Li Q, Chu J, Zeng W, Yang M, Zhu S. Effect of n-3 pufa supplementation on cognitive function throughout the life span from infancy to old age: a systematic review and meta-analysis of randomized controlled trials. The American Journal of Clinical Nutrition. 2014;100(6):1422–1436.

32.Quinn EA, Kuzawa CW. A dose-response relationship between fish consumption and human milk dha content among filipino women in cebu city, philippines. Acta Paediatrica. 2012;101(10):439- 445.

33.Rees A, Sirois S, Wearden A. Prenatal maternal docosahexaenoic acid intake and infant information processing at 4.5mo and 9mo: a longitudinal study. Public Library of Science. 2019;14(2):e0210984.

34.Ramakrishnan U, Gonzalez Casanova I, Schnaas L, DiGirolamo A, Quezada AD, Pallo BC, et al. Prenatal supplementation with DHA improves attention at 5 y of age: a randomized controlled trial. The American Journal of Clinical Nutrition. 2016;104(4):1075–1082.

35.Rangel-Huerta OD, Gil A. Effect of omega-3 fatty acids on cognition: an updated systematic review of randomized clinical trials. Nutrition Reviews. 2018;76(1):1–20.

36.Demmelmair H, Øyen J, Pickert T, Rauh-Pfeiffer A, Stormark KM, Graff IE,et al. The effect of Atlantic salmon consumption on the cognitive performance of preschool children- A randomized controlled trial. Clinical nutrition. 2019;38(6):2558–2568.

37.Teisen MN, Vuholm S, Niclasen J, Aristizabal-Henao JJ, Stark KD, Geertsen SS, et al. Effects of oily fish intake on cognitive and socio emotional function in healthy 8-9-year-old children: the FiSK Junior randomized trial. The American Journal of Clinical Nutrition. 2020;112(1):74–83.

38.Emery S, Häberling I, Berger G, Walitza S, Schmeck K, Albert T, Baumgartner N, Strumberger M, Albermann M, Drechsler R. Omega-3 and its domain-specific effects on cognitive test performance in youths: A meta-analysis. Neuroscience and Biobehavioral Reviews. 2020; 112: 420–436.

39.Montgomery P, Burton JR, Sewell RP, Spreckelsen TF, Richardson AJ. Low blood long chain omega-3 fatty acids in UK children are associated with poor cognitive performance and behavior: a cross-sectional analysis from the DOLAB study. Public Library of Science. 2013;24(8):6.

40.Johnson M, Fransson G, Östlund S, Areskoug B, Gillberg C. Omega 3/6 fatty acids for reading in children: a randomized, double-blind, placebo-controlled trial in 9 year old mainstream school children in Sweden. Journal of Child Psychology, Psychiatry and Allied Disciplines. 2017; 58(1): 83–93.

41.Luchtman DW, Song C. Cognitive enhancement by omega-3 fatty acids from child-hood to old age: findings from animal and clinical studies. Neuropharmacology. 2013; 64: 550–65.

42.Cook RL, Parker HM, Donges CE, O'Dwyer NJ, Cheng HL, Steinbeck KS, et al. Omega-3 polyunsaturated fatty acids status and cognitive function in young women. Lipids in Health and Disease. 2019; 18(1): 194.

43.Jackson PA, Reay JL, Scholey AB, Kennedy DO. Docosahexaenoic acid-rich fish oil modulates the cerebral hemodynamic response to cognitive tasks in healthy young adults. Biological Psychology. 2012; 89(1): 183–190.

44.Giles GE, Mahoney CR, Urry HL, Brunyé TT, Taylor HA, Kanarek RB. Omega-3 fatty acids and stress-induced changes to mood and cognition in healthy individuals. Pharmacology Biochemistry and Behaivor. 2015; 132: 10-19.

45.Bauer I, Hughes M, Rowsell R, Cockerell R, Pipingas A, Crewther S, et al. Omega-3 supplementation improves cognition and modifies brain activation in young adults. Human Psycho pharmacology. 2014;29(2):133–144.

46.Dong X, Li S, Chen J, Li Y, Wu Y, Zhang D. Association of dietary ω-3 and ω-6 fatty acids intake with cognitive performance in older adults: National Health and nutrition examination Survey (NHANES) 2011–2014. Nutrition Journal. 2020; 28(19): 25.

47.Witte AV, Kerti L, Hermannstädter HM, Fiebach JB, Schreiber SJ, Schuchardt JP, Hahn A, Flöel A. Long-chain omega-3 fatty acids improve brain function and structure in older adults. Cerebral Cortex. 2014;24(11):3059–3068.

48.Alex A, Abbott KA, McEvoy M, Schofield PW, Garg ML. Long-chain omega-3 polyunsaturated fatty acids and cognitive decline in non-demented adults: a systematic review and meta-analysis. Nutrition Reviews. 2020;78(7): 563–578.

49.Martí Del Moral A, Fortique F. Omega-3 fatty acids and cognitive decline: a systematic review. Omega-3 y deterioro cognitivo: una revisión sistemática. Nutricion Hospitalaria. 2019; 36(4): 939–949.

50.Yurko-Mauro K, Alexander DD, Van Elswyk ME. Docosahexaenoic acid and adult memory: a systematic review and meta-analysis. PloS One. 2015;10(3):e0120391.

51.Mazereeuw G, Lanctôt KL, Chau SA, Swardfager W, Herrmann N. Effects of ω-3 fatty acids on cognitive performance: a meta-analysis. Neuro biology of Aging. 2012; 33 (7): 1482.e17-1482.e1.482E29.

52.Wade AT, Tregoweth E, Greaves D, Olds TS, Buckley JD, Keage HAD, Coates AM, Smith AE. Long-Chain Omega-3 Fatty Acid Intake Is Associated with Age but not Cognitive Performance in an Older Australian Sample. The Journal of Nutrition, Health & Aging. 2020; 24(8): 857–864.

53.World Health Organization. Risk reduction of cognitive decline and dementia: WHO guidelines [Internet]. Geneva, CH: World Health Organization; c1220 [cited 12 December 2020]. https://www.who.int/publications/i/item/9789241550543

54.Molfino A, Gioia G, Rossi Fanelli F, Muscaritoli M. The role for dietary omega-3 fatty acids supplementation in older adults. Nutrients. 2014; 6(10):4058–4073.