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The Role of Dietary Docosahexaenoic Acid (DHA) for Cognitive Function

Nisma Hamda[1], Navaneetha R[2]
[1]Post graduate Student, [2]Associate Professor, Department of Food and Nutrition and Research Centre, Smt VHD Central Institution of Home Science, School of Home Science, Maharani Cluster University, Bengaluru, Karnataka, India.

Abstract: Docosahexaenoic acid (DHA) is a structural component of membranes in the Central Nervous System (CNS). Docosahexaenoic acid and eicosapentaenoic acid (EPA) are two long-chain polyunsaturated fatty acids known as "omega-3 fatty acids" and they have beneficial effects in a variety of organs and biological processes, including growth regulation and platelet activation. Brain structure and function rely on a constant and sufficient supply of EPA and DHA. It builds up in the fetal brain mostly during the third trimester of pregnancy and continues at high rates of accumulation until the end of the second year of life. At birth the proportion of brain weight to the body weight is 70% when compared to their proportions in adults, and 15% of brain growth occurs throughout the preschool years. The majority of brain development occurs between the age of 5 and 6 years. DHA is also essential for adults to maintain optimal brain function. The Google search engine, mdpi, kva, Cambridge, Elsevier, and karger were used to conduct a literature search on DHA. DHA is found in fatty fish such as salmon, mackerel, and tuna, as well as mother's milk. Meat and eggs contain low quantity of DHA. Long chain omega-3 fatty acids and DHA supplementation has shown to improve the brain cognitive performance in various studies.
Keywords: Docosahexaenoic acid, eicosapentaenoic acid, central nervous system, omega-3 fatty acid, cognitive function and development.

I. INTRODUCTION

Docosahexaenoic acid (DHA), a long chain omega-3 fatty acid, is a major lipid in the brain that is recognized as essential for normal brain function. DHA is essential for optimal visual and cognitive development in infants. DHA intake is typically low in toddlers and children, and some studies show improvements in cognition and behavior as a result of polyunsaturated fatty acid supplementation, including DHA. [1]

DHA is a critical nutritional n-3 PUFA (Polyunsaturated fatty acid) that must be obtained from the human diet. Due to its high fluidity, DHA is found in significant amounts in the retinal and neuronal cell membranes. DHA contributes to healthy ageing by preventing macular degeneration, Alzheimer's disease, and other brain disorders, as well as improving memory and strengthening neuro protection in general. DHA deficiency has been linked to cognitive decline as people age. [6]

Despite its importance in neurological development and health, mammals have a limited ability to synthesize DHA. DHA is most commonly obtained by humans by eating fish. [4] DHA is primarily found in fatty, cold-water fish, and a couple of meals per week of low mercury fish appear to provide adequate amounts of DHA during pregnancy. Salmon, sardines, trout, herring, anchovies, and mackerel are examples of fish that are low in methyl mercury but high in DHA (not King mackerel). [10]

Along with the benefits for brain and visual development that make DHA an essential fatty acid during pregnancy, several studies have recently shown that the fatty acid has a neuroprotective role, particularly during ageing and in neurodegenerative diseases of the brain. [7]

II. DIETARY SOURCES OF DHA

DHA, like EPA and n-3 DPA, is found in relatively high amounts in seafood and seafood-derived products. There is clearly a 10-fold difference in DHA content per portion (i.e. per serving) of seafood, with fatty fish being able to provide as much as 1–1.75 g of DHA per portion. Fatty fish include mackerel, salmon, trout, herring, tuna, and sardines. Lean fish such as cod, haddock, and plaice, on the other hand, typically provide about 0.1–0.2 g of DHA per portion. Although tuna is a fatty fish, the oil has been removed during processing, making canned tuna low in n-3 fatty acids, including DHA. Similarly, some organ meats, such as brain, are high in DHA but are rarely consumed by most people. DHA can be found in small amounts in animal-derived foods such as eggs and meat. DHA is found in human breast milk and other mammalian milks [9] . DHA is also found in fish body , fish liver, algal and krill oils, concentrated supplements, and pharmaceutical grade preparations used to control blood triglyceride levels. Infant formulas contain DHA-rich oils derived from algae or tuna. [9]

Sea mammals' meat and blubber, such as seals and whales, are also high in n-3 fatty acids, including DHA, though most humans do not consume them. DHA can be found in small amounts in animal-derived foods such as eggs and meat.
Fish oil is another option for getting DHA and EPA. These highly refined oils can be consumed as capsules, micro-encapsulated, and, more recently, nano-encapsulated, allowing them to be incorporated into a wide range of food matrices (milk, juices, cereals, etc.). DHA is found in both lean and oily fish flesh, with much higher concentrations in the latter, as well as in the liver of some lean fish species, such as cod. There is also fish oil made from these DHA-rich raw materials. [6]

III. NEURO DEVELOPMENT AND DIETARY DHA

DHA is found in high concentrations within the lipid bilayer of neurons, where it plays a functional role in membrane fluidity/flexibility, influencing neuronal transmission. [8] DHA is a critical fatty acid for not only neuronal structure but also neuronal signaling. This fatty acid was recently discovered to be a neuroprotective agent against cerebral ageing, neurodegenerative diseases, and cerebrovascular diseases, particularly in the injury caused by ischemia-reperfusion episodes. [7] Lipid, particularly structural lipid, accounts for more than half of the dry weight of the human brain (i.e. phospholipids). DHA, arachidonic acid, and adrenic acid are the most abundant fatty acids in the brain. In comparison to other tissues, the human brain and retina have a particularly high proportion of DHA and very little EPA. DHA, for example, has been reported to contribute an average of 18 percent of fatty acids to adult human brain grey matter, while human infant cerebral cortex and retina have average DHA contents of about 8 and 12 percent of the fatty acids [9]

A. *Dietary DHA and development of foetus*

DHA is required for the development of the foetal central nervous system and the retina. DHA may be beneficial in terms of birth weight and gestational length, as well as maternal depression. [10]
Half of the DHA in the brain is produced during pregnancy, when the developing infant brain requires five times the amount of lipid per day when compared to what an adult brain requires. Because the foetal and placental production of DHA is insufficient to meet the need of rapidly developing neural tissues, maternal DHA, which is dependent on the mother's food intake, becomes a critical element in foetal brain development. [11]
The human brain experiences a growth spurt between the beginning of the third trimester of pregnancy and till 18 months after birth. During the brain growth spurt, the amount of DHA in the brain increases dramatically. Human brain weight increases from approximately 100 g at 30 weeks of gestation to approximately 1,100 g at 18 months of age. During this time, the DHA content of the brain rises from 900 g/g (90 mg total) to 3,000 g/g (3,300 mg total). [9]
The accumulation of DHA in the brain occurs during the intrauterine and neonatal period up to two years of age, and the high levels of DHA in the brains are maintained throughout life. Maternal transfer of PUFA through breast milk supports postnatal accumulation of LC-PUFA (Long chain PUFA) in infant tissues, and blood levels of LC-PUFA in breast-fed infants remain higher than maternal levels for some time postnatally. Furthermore, brain autopsies from human infants revealed a roughly 25% higher mean FA percent (percent of the fatty acids) of DHA in cortical phospholipids of breast-fed (9.7 percent) infants when compared to age-matched formula-fed infants (7.6 percent). [2]
DHA is transferred across the placenta in a selective and preferential manner. [10] In the last trimester of pregnancy, the estimated rate of DHA accretion into the human brain is 15–22 mg/week. This is also the busiest time for brain cell division. As a result, it is believed that a sufficient supply of DHA during this period is required for normal growth, neurological and visual development and function, and learning behavior. [9] DHA must be mobilized from maternal stores, or adequate amounts of preformed DHA must be included in the prenatal diet. [10]

B. *Dietary DHA and Postnatal Development*

It is critical to maintain a supply of preformed DHA after a baby is born. Maternal supplementation with fish oil can increase the DHA content of breast milk. DHA-rich oil, n-3 LCPUFA-rich eggs, or increased maternal fatty fish consumption are all options. [9]
DHA is obtained during development via gestational placental transfer and through mother's milk during infancy. Depending on the mother's diet and number of pregnancies, DHA levels in mother's milk can reach 1.4 percent of total fatty acids, compared to a worldwide average of 0.32 percent of total fatty acids. However, when pregnant mothers were given 4 g of fish oil daily for a shorter period of time (only during late gestation), no effects on overall mental or psychomotor development were observed at 10 months of age, but it did improve hand and eye coordination at 2.5 years. [3]

During pregnancy and lactation, an average daily intake of 200 mg DHA is currently recommended. DHA and ARA are the primary omega-3 and omega-6 long-chain polyunsaturated fatty acids (LCPUFAs) of neural tissues, respectively, and DHA is the primary fatty acid of retinal photoreceptor membranes. Some research suggests that DHA and ARA supplementation improves visual acuity and psychomotor development, particularly in premature infants. [10]

C. *Neuro Behavioral Outcomes in Older Children*

DHA accretion in the brain continues into childhood, and while the rate of accretion decreases, DHA incorporation remains high at least during the preschool years. A study that pooled data from three trials that randomized to LC-PUFA formulas immediately after birth or after breastfeeding for 6 weeks or 4–6 months, respectively, and continued supplementation throughout the first year of life found that only the two studies that started intervention early had significant beneficial effects on problem solving at 9 months of age. However, one study that looked at the effects of DHA-enriched baby food discovered an improvement in cognitive outcomes. Furthermore, a trial that gave children aged 9 to 12 months a teaspoon of cod liver oil (free of Vitamin A and D) found an increase in voluntary attention in a free play test after the intervention, especially in boys, when compared to un-supplemented children. [2]

D. *Neuro Behavioral Outcomes Beyond Childhood*

During middle adulthood, cognitive Function peaks. DHA supplementation improved memory in healthy, young adults whose diets were low in DHA, and the response was still modulated by sex, implying consistency with the effects observed in late infancy with the achievement of gross motor milestones [3] . An observational study of 6158 people over the age of 65 discovered that high fish consumption, but not dietary n-3 LC-PUFA intake, had a protective effect on cognitive decline. [2]

DHA may also have cardiovascular benefits in adulthood, resulting in improved brain perfusion. These advantages include reduced blood pressure, increased vasoreactivity, reduced hepatic triglyceride synthesis, and decreased platelet aggregation. The brain is the most perfused organ in the human body, and cardiovascular diseases (which are common with ageing) increase the risk of developing dementia. [3]

E. *DHA and its role in Cognitive Ageing*

Cognitive abilities can deteriorate in a variety of ways and to varying degrees, and it can affect people of all ages, not just the elderly. [6] DHA plays an important role in promoting healthy ageing by possibly preventing macular degeneration, Parkinson's disease, and other brain disorders, as well as improving memory and neuroprotection in general. Reduced DHA levels in the blood have been linked to cognitive decline as people age. [6]

IV. BRAIN UPTAKE OF DHA

The brain is the most energy-demanding organ in the human body, accounting for 2.3 percent of total body weight but 23 percent of body energy utilization in adults and 74% of energy utilization in newborn term infants. The brain is the second most lipid-dense organ after adipose tissue. Brain lipids are far more complex in terms of structure and function. Indeed, phospholipids account for 60% of the dry weight of the brain. The ethanolamine (PE) and serine (PS) glycerophospholipids have the highest DHA content in the brain (phosphoglycerines). [5]

Grey matter is mostly neurons and contains 40% lipids, whereas white matter contains myelin and contains 50–70% lipids. The distribution of unsaturated fatty acids in brain glycerophospholipids differs by tissue, with white matter having more monounsaturated fatty acids and grey matter having more polyunsaturated fatty acids.

DHA is the most abundant omega-3 fatty acid in the brain, while Arachidonic Acid (AA) is the most abundant omega-6 fatty acid. DHA predominates over AA in grey matter, but the opposite is true in white matter. [5]

V. GUIDELINES FOR DIETARY SUPPLEMENTATION OF DHA

Omega-3 fatty acids are generally more unsaturated than omega-6 fatty acids. Linoleic acid (LA or 18:2 n-6) is found in a variety of vegetable seed oils, including sunflower seed oil, and has 18C and two double bonds. Alpha-linolenic acid (ALA or 18:3 n-3) rich in flaxseed oil and green leafy vegetables, has 18C with three double-bonds. 18C fatty acids serve as precursors for longer-chain fatty acids. They are omega-6 arachidonic acid (AA or 20:4n-6) and omega-3 eicosapentaenoic acid (EPA or 20:5n-3) and docosahexaenoic acid (DHA) (DHA or 22:6n-3). In most Western countries, health bodies currently recommend 500 mg of EPA + DHA per day for the prevention of coronary heart disease, which is the equivalent of two oily fish meals per week.

When nutrients are consumed, either as fortified food or supplements, for the purpose of disease prevention and/or treatment, they are referred to as nutraceuticals. Some studies recommend 200 mg DHA per day during pregnancy, while DHA intakes of up to 3 g per day have been shown to be safe. [5]
DHA content differentiates three main classes of fish products: relatively poor DHA sources (black scabbard fish, catfish, hake, megrim, tilapia); moderately rich DHA sources (halibut, Pollock); and very rich DHA sources (herring, mackerel, salmon, sardine), with approximate ranges of 300, 300–500, and >500 mg/100 g, respectively. [6]
Another dietary source of DHA is hen egg yolk, the DHA content of which is determined by the diet of the hen. Given that eating eggs is less expensive than eating fish, hen egg yolk enriched in DHA phospholipids may be a good option for increasing DHA consumption in the general population. [7]

VI. ABBREVIATIONS

1) AA: Arachidonic acid.
2) ALA: Alpha linolenic acid.
3) DHA: Docosahexaenoic acid.
4) EPA: Eicosapentaenoic acid.
5) FA%: Percentage of the fatty acids.
6) LA: Linoleic acid.
7) LC-PUFA: Long chain PUFA.
8) PUFA: Polyunsaturated fatty acid.
9) RBC: Erythrocyte.
10) EFA: Essential fatty acids.
11) ARA: Arachidonic acid.
12) ω- 3: Omega-3 fatty acids.
13) ω- 6: Omega-6 fatty acid.
14) PL: Phospholipids
15) PE : Ethanolamine
16) PS: Glycerophospholipids

VII. CONCLUSION

DHA is a type of n-3 fatty acid that has a long chain and is highly unsaturated. It has a structure that allows it to have distinct physical and functional properties. DHA is metabolically related to other n-3 fatty acids in that it can be synthesized from the plant essential fatty acid ALA through EPA. Ample evidence indicates that adequate amounts of DHA in the diet result in health benefits for humans, particularly for foetal and infant neurodevelopment. DHA concentration must be maintained throughout life, but pregnancy, lactation, and infancy are vulnerable times when insufficient DHA supply can impair mental and visual development and performance. Childhood and adolescence are periods of rapid neuronal maturation, synaptogenesis, and grey matter expansion, all of which are associated with DHA accumulation in the brain. Because DHA synthesis from its fatty acid precursors is known to be inefficient, dietary sources of preformed DHA are essential.
DHA is found in breast milk. DHA is esterified into complex lipids in the bloodstream, adipose tissue, and cell membranes. Its concentration varies greatly between compartments. When compared to other organs, the brain and eye have high DHA contents. DHA is abundant in the grey matter of the brain and the rods of the retina. DHA is involved in neuronal signaling in the brain, as well as visual quality in the eye. DHA builds up in the brain and eyes late in pregnancy and early infancy. As a result, pregnant and lactating women, as well as infants, must consume adequate preformed DHA to support brain and eye development and function. Increased DHA intake by pregnant women and infants results in higher DHA concentrations in the majority of body compartments. Dietary DHA intake by the lactating mother has a strong influence on the DHA concentration in breast milk.
DHA is primarily found in seafood, with marine fish and shellfish being particularly high in DHA content. Oily fish, such as herring, salmon, sardine, and tuna, contain the most DHA per meal. DHA, in particular, plays an important role in the nervous system. Supplemental DHA from fish oil or vegetarian (algal oil) sources is ideal for those who are unable to obtain adequate amounts of DHA through diet. Millions of people worldwide take DHA supplements on a daily basis, and they have been shown to be safe and well tolerated even at relatively high doses.

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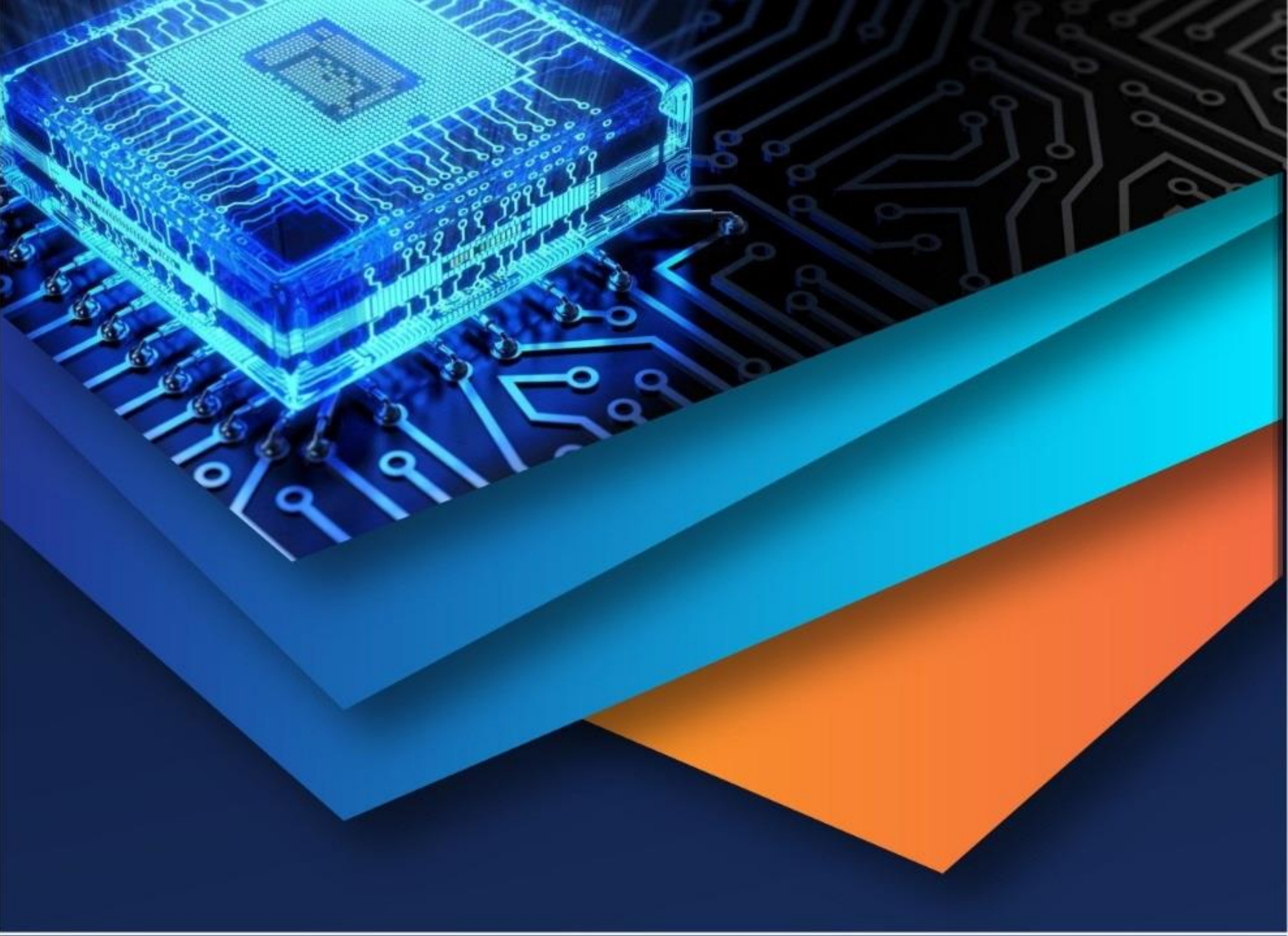

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