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A Recent Review On: Effect of Nutrients On Brain Function and Development

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ABSTRACT

Recent studies have demonstrated the important role that nutrition plays in maintaining cognitive health by highlighting the substantial effects of different nutrients on brain growth and function. Research articles from Google scholar, scihub, PUBMED was searched for food and nutrients for brain development and function. Important nutrients that are connected to neurodevelopment, synaptic plasticity, and general cognitive function include omega-3 fatty acids, B vitamins, antioxidants, and vital minerals. The structure and function of the brain depend on omega-3 fatty acids, especially DHA, and neurotransmitter production and cognitive resilience are supported by B vitamins. Vitamins E and C are examples of antioxidants that reduce oxidative stress and support the health of neurons. Cognitive deficits are linked to mineral shortages, especially those involving iron and zinc. This review summarizes research on the relationship between long-term cognitive problems and nutritional deficiencies, particularly during important developmental stages. Additionally, diets high in particular nutrients are linked to better mental health outcomes and lowers risks of various illnesses caused by neurodegeneration. Overall, this review highlights how crucial a balanced diet is for promoting brain health throughout life.

INTRODUCTION

Brain development is a carefully controlled process involving cell division, differentiation, migration, and connectivity that depend on overlapping stages. Any disruption to this process can affect brain function (1). Adequate nutrition is important during pregnancy (2) and the first few years of life, because it is during the prenatal and early postnatal period that the brain undergoes rapid growth and development, laying the foundation for cognitive, motor, and socioemotional skills (3). All nutrients are important for all cells to function (4). However, certain nutrients are essential for the anatomical and functional growth and development of the brain, and they are especially crucial for the metabolism of fat, protein, and carbohydrates for energy. long-chain polyunsaturated fatty acids (LC-PUFAs) particularly docosahexaenoic acid (DHA) and Alpha Linoleic Acid (ALA) are crucial for brain development (5). vitamin B complex vitamin C, Vitamin E support neurotransmitter synthesis and oxidate stress for neuronal health. Minerals specially zinc and iron are additional nutrients with significant impacts on cognitive impairment (6, 7). Here's a summary of recent findings on the effect of key nutrients impacting brain function and development.

Omega-3 Fatty Acid

Omega-3 enhances mental function, protects neurons from degeneration, and preserves them. Types of omega-3 fatty acids i.e Eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and alpha-linolenic acid (ALA) are essential for brain functions (8). Human milk is a common and natural source of Docosahexaenoic Acid DHA (9). The Alpha Linoleic Acid (ALA), is also present in soybean and canola oil, flaxseed oil and walnuts, and the EPA and DHA are found in seafood (10). Preferable neurocognitive development of the offspring is linked to the ingestion of commercially available fish during pregnancy (11). Less than 20% of the world's population is thought to ingest more than 250 mg/day of seafood-origin n-3 LCPUFA. The recommended amount of omega-3 fatty acid consumption is 0.6-1.2% of total calorie intake (12). For the processing of LLC-n3-Fatty acids, astrocytes in the brain are a key location. Due to the body's inability to synthesize either omega-3 and omega-6 PUFA endogenously, both are considered essential fatty acids that must be obtained through diet (13) while long-chain (LC) PUFAs, EPA, and DHA can be synthesized endogenously from their precursor omega-3 or omega-6 PUFA or obtained through direct dietary consumption or supplementation (14).

Lipids make up about 50–60% of the brain's weight, and 35% of those lipids are omega-3 polyunsaturated fatty acids (PUFAs). Over 40% of all omega-3 PUFAs, especially in the grey matter, are made up of docosahexaenoic acid (DHA) in neural tissue(8). The brain lipid composition is unique and exceedingly diverse (13). Beginning during gestation, the brain begins to accommodate both omega-3 and omega-6 PUFAs, a process known as "accretion" The third trimester of pregnancy is when DHA accumulation begins in humans (12). The brain accumulates a significant amount of DHA during the first two years of life (12). Pregnant and lactating mothers are advised to consume enough n-3 fatty acids, increased n-3 LCPUFA consumption during pregnancy and lactation promotes the development of fetus brain (15). The brain's most prevalent fatty acids, specifically docosahexaenoic acid (DHA; omega-3 PUFA) and arachidonic acid (AA; omega-6 PUFA),are crucial for the formation and growth of the brain (16). DHA, is one of the most studied LCPUFA (9), which is accumulated during the brain growth spurt beginning in the second half of pregnancy, especially in the first two years of life, which are crucial for the development of the central nervous system and other functional organs (12). After weaning, n-3 PUFA supplementation cannot repair the negative effects of PUFA deficiency that occur during pregnancy and breastfeeding on the brain neurogenesis and apoptosis of the adult offspring (17)

DHA has been reported to affect cognitive functions such as working memory, mental agility, information processing rate and motor-neuronal preservation, and protection against neurodegeneration (8). DHA, although being a highly unsaturated fatty acid, can act as an antioxidant in a brain that is prone to oxidation. Detoxifying enzymes support DHA's antioxidant defense in brain cells (15). Omega-3 (EPA and DHA), have attracted great attention for their ability to prevent cognitive decline as a result of the anti-inflammatory and anti- amyloidogenic properties of PUFAs. The balance of n-6/n-3 PUFAs during prenatal development has an impact on the hippocampus by influencing neurogenesis (18).

Human neuroimaging research's most recent findings imply that gray matter shrinkage in healthy, middle-aged, and elderly persons is associated with decreased intake of omega-3 PUFAs (19). Parkinson's disease (PD) and Alzheimer's disease (AD), neurodegenerative diseases, were protected against by a higher intake of omega-3 PUFA specially DHA (20). Lack of omega-3 PUFAs disrupts neurotransmission, neurogenesis, and synaptic fine-tuning, resulting in a variety of neurobehavioral disorders. Numerous studies show that elderly people's brain health and cognition are improved by LC-n3-FA ingestion through fish or fish oil supplements (21).

Vitamin A

Vitamin A deficiency can negatively impact the hypothalamus, which may result in a decreased appetite and growth (22). The hippocampus, which is important for learning and memory, as well as the hypothalamus, which is important for maintaining the body's internal physiological equilibrium, all depend on vitamin A availability (22). It is well-known that both vitamin A deficiency and excess during prenatal and postnatal life can lead to birth defects, also known as teratogenic effects (23). The mother needs vitamin A and the compounds that are derived from it during pregnancy for the maintenance of the placenta, and the embryo needs it for the formation and development of many different organs, including spinal cord, and brain. Vitamin A is stored in the placenta and is released to the developing fetus during pregnancy. This storing process helps ensure adequate supply to protect the developing fetus in situations where mothers don't consume enough (24).

Vitamin A cannot be synthesized by the body, it must be consumed through diet, vitamin A is fat-soluble and can be obtained from both plant and animal-based sources (25). Functional vitamin A concentrations are highest in liver and fish oil. The liver has around 90% of vitamin A (23). Glandular meat, red palm oil, milk , egg yolk, carrots, tomatoes, apricots, green vegetables, fortified processed food that may include cereals, condiments and fats are all rich in Vitamin A. Breast milk is one of the primary sources of vitamin A for infants (26).

Vitamins B

Vitamins of the B group are water-soluble vitamins with many positive effects on the nervous system. Numerous mental illnesses have been connected to vitamin B deficiency like Parkinson's and Alzheimer's disease (27). In later life, vitamin B insufficiency and elevated total plasma homocysteine levels have been related to poor cognitive function, cognitive decline, and dementia (28); (29). In both the cognitive-domain and global cognition trials, allocating to B vitamins was linked to a 28.4% and 26.1% decrease in homocysteine plasma concentrations (30). Evidence shows that vitamin B supplementation may lower the homocysteine level that reduce cognitive decline (31). In particular, the metabolism and transport of glucose are sensitive to the brain. The function of pancreatic beta cells, (gluconeogenesis and lipogenesis), insulin receptor transcription, and hepatic glucose uptake are all significantly regulated by B vitamins (32).

The B vitamins B6 (Thiamin) folate (B9), and B12 have drawn the most attention as they have role in functionality by improving neurological conditions and maintaining a healthy nervous system (33). Vitamin B6 (Thiamine) can be consumed in its purest form through fish, liver, pork, fortified cereals, eggs, nuts, oats, oranges, dried beans, yeast, powdered milk, potatoes, dark leafy greens, and chickpeas (34); (35).

Folate, also known as Vitamin B9 has special importance in pregnancy. Studies have shown that a lack of folate is associated with changes in offspring's neurodevelopment, include changes in neurogenesis and neuronal death and decreased overall brain volume. These modifications have been associated with alterations in brain activity in children, including memory, motor function, linguistic abilities, and psychological problems (36). To prevent neural tube development problem, which affect about 50% of the population, folic acid supplementation at least 400 µg (mcg) has been frequently recommended to expectant mothers (37). (38), preferably a month before conceiving (39). Folate is naturally found in many food sources. Leafy greens, seeds, fortified cereals, and folic acid supplements are all natural sources of dietary folate, meanwhile liver is recommended as plentiful source (34).

Vitamin B especially B12 has greater importance in brain function and its supplementation reduce cognitive decline. The main dietary source of vitamin B12 is found in foods including meat, milk, eggs, fish, and shellfish that are sourced from animals (40). Liver in particular is a very rich source of Vitamin B12, followed by kidney and heart. Compared to non-vegetarians, vegetarians are more susceptible to vitamin B12 insufficiency (41).

Vitamin D

The nervous system's health and disease are affected by vitamin D (VD) and its metabolites in a variety of ways (42, 43). During fetal development, growth, and senescence, vitamin D may be essential for improving neuro-cognition (44). Vitamin D may influence particular neurotransmitters and cortical function (45). Vitamin D has crucial roles in the brain's calcium signaling, proliferation and differentiation, as well as neurotrophic and neuroprotective activities. It may also change synaptic plasticity and neurotransmission (46).

Vitamin D can impact the brain through different mechanisms, such as regulating neurotrophic growth factors, influencing inflammation, and thrombosis (47). Numerous researches have examined the associations between maternal Vitamin D (VD) insufficiency and the brain health of offspring.

(46). Numerous studies have found a connection between adult vitamin D insufficiency and some neurodegenerative diseases (45). Dementia, Alzheimer's disease, and Parkinson's disease have all been associated with low vitamin D levels (48). Interestingly, some studies have shown that VD deficiency is linked to reduced hippocampus volumes, which is a brain region that has a crucial role in memory and learning (48). The placenta allows vitamin D to pass from the mother to the fetus, thus, the mother is the sole source of vitamin D substrate for her developing child. Studies have suggested that low maternal VD levels could affect neuronal development and lead to the beginning of mental disorders like schizophrenia and autism (49).

Worldwide, there is a high prevalence of vitamin D insufficiency. By exposing skin to sunlight, vitamin D can be produced internally in the body (48) and from foods and supplements that include the vitamins D2 and D3 ergocalciferol and cholecalciferol, respectively (50). The primary nutritional source of vitamin D2 is mushrooms (51), along with fatty fish and eggs, whereas most of vitamin D3 is synthesized within the body (52). Natural dietary sources of vitamin D3 is also present in small amounts in the diet of animal origin and include fatty fish, egg yolks, liver oils, dairy products, and supplements (53). Vitamin D supplements is readily available and affordable and should be integrated into the care management of older adults with cognitive disorders (46).

Vitamin E and C.

There is evidence that antioxidants may reduce the incidence of age-related cognitive decline and Alzheimer's disease especially in aging. They protect against oxidative stress, which can damage brain cells (54). Vitamin C and E have antioxidant activity are vital to brain function. Research has indicated that vitamin C helps lessen the neurodegeneration linked to Parkinson's disease, traumatic brain injury, as well as dementia (55). The brain maintains high levels of vitamin C a depression and cognitive impairment are hallmarks of neuropsychiatric scurvy, which is caused by a vitamin C shortage (56).

Likewise, vitamin E is the first line of defense against lipid peroxidation. Vitamin E has anti-inflammatory and neuroprotective properties, and it can help prevent neurodegenerative illnesses brought on by oxidative stress (57). It has been demonstrated that vitamin E supplementation can increase the levels of important neurotransmitters, such as acetylcholine, serotonin, dopamine, and glutamate, which are necessary for cognitive processes, emotional processing, and fear conditioning (58). According to research, vitamin E is essential for maintaining the neurochemical equilibrium.

Vitamin E has been shown to preserve the structural integrity of the cerebral cortex in addition to its neurotransmitter-modulating and antioxidant properties. According to studies, vitamin E supplementation can prevent stress-induced neuronal damage, age-related cortical shrinkage, maintain synaptic connection, and retain dendritic morphology (56).

Iron

The brain uses only 2% of the total amount of iron in the human body. It specifically contributes to the synthesis of myelin and neurotransmitters as well as it is a cofactor used for the facilitation of chemical reactions by attaching itself to the substrate of enzymes. (59). Iron is necessary for myelination, neurotransmitter synthesis, and cognitive development in order for the brain to function correctly. The development of the highly specialized myelin membrane around axons is a characteristic of myelination. The first two years of postnatal life are the most rapid and dramatic times for this process (60). One of the most common dietary deficits worldwide is iron deficiency (ID). Despite iron replacement, poor cognitive function and emotional regulation brought on by an iron shortage in the late fetal and neonatal stages can last into adulthood (Bastian *et al.*, 2020). Iron-rich foods include red meat, beans, poultry, fish, and fortified cereals. Iron supplements may be necessary for children who are at risk of iron deficiency, such as those with certain medical conditions or inadequate food intake (61)

Zinc

Zinc, a necessary trace element, is crucial for brain growth, synaptic plasticity, and overall brain health (62); The cerebral cortex, amygdala, olfactory bulb, and hippocampal neurons are among the regions of the brain that contain free zinc ion (Zn^{2+}) neurons. The presence of zinc is crucial for adult brain neurogenesis, which has profound effects on the hippocampal structure and function, including memory and learning as well as emotion and mood control (35). Recommended daily intake of Zn for men are 11mg and 8 mg for women (63). Various illnesses, such as Alzheimer's disease, Parkinson's disease, and mood disorders, have been hypothesized to be influenced by changes in the amount of zinc in the brain (64). Inadequate zinc during development can also disrupted brain function in the offspring, which might show as altered behavior, motor and cognitive function, and attention symptoms, e.g. depression, and altered child psychomotor development (65). Because the body cannot store zinc, it must be consumed regularly through diet to meet physiologic requirements (66). The main sources of zinc include dark green and dark yellow vegetables, shellfish, meat, eggs, cereals, peanuts, dairy products, and whole grains (67). Both excess and deficiency is associated with cognitive decline. Approximately 150 µmol/L is the average concentration of zinc ions (68). Zinc supplementation (15 or 30 mg/day) was tested in 387 healthy individuals between the ages of 55 and 87 in a study on the relationship between zinc and cognitive function in adults. Each zinc dose taken over a three-month period, the study found, improved spatial working memory. One of the few studies on the relationship between zinc and cognitive function in adults looked at the effects of zinc supplementation (15 or 30 mg/day) in 387 healthy individuals aged 55 to 87 years and found that each dose had a beneficial impact on spatial working memory over the course of three months (35). Lack of zinc is linked to a number of different mental illnesses. Inadequate levels of zinc affect behaviour, mental health, and brain development since it is essential for neuronal impulses. A number of diseases, including Alzheimer's, Parkinson's, and mood disorders, have been associated to changes in brain zinc levels (64). There is a higher risk of zinc insufficiency throughout pregnancy and older infancy (69).

To achieve nutritional demands for zinc, which cannot be stored by the body, one must consume it frequently (66). Dietary Reference Intakes (DRIs) for Zn is daily consumption of 8 mg for women and 11 mg for men. These values can be increased during pregnancy. The vast majority of Zinc intake comes from food (63). The highest amounts of zinc were found in oyster, fortified breakfast cereals, beef meat, pumpkin and squash seed kernels (70); (63).

Magnesium (Mg2+) is an essential mineral that is involved in many cellular processes that are critical for the health and function of neurons. (71). Magnesium plays a crucial role in over 600 enzymatic reactions in the human body (72). It plays a crucial modulating role for many aspects of social behavior, including aggression, memory and cognition, eating behavior, addictions, and others (73). The main mechanisms by which magnesium is involved in neurons activity include: the modification of the presynaptic release of certain brain neurotransmitters, synaptic neuroplasticity (74), the alteration of the affinity of certain neuronal receptors for their agonists, the transduction of the biological signal after stimulating the receptors, the activity of certain neuronal enzymes, reducing the intensity of addictions and the susceptibility of individuals at risk for addiction, enhances children's attention deficit, and lowers anxiety (75).

Amino Acids

Tryptophan and Tyrosine

Precursors for neurotransmitters like serotonin and dopamine. They influence mood, cognition, and behavior. Tryptophan and tyrosine are a indispensable amino acid that the body cannot synthesize; both are obtained through various food sources as L-tryptophan. And L-tyrosine they are the precursor of serotonin and melatonin and has been shown to have therapeutic benefits in enhancing mood, behavior, and cognition, with a focus on depression (76). As a precursor to neurotransmitters, they can cross the BBB and become a functional neurotransmitter (77). Additionally, research indicates that after adding tryptophan and tyrosine to a deficient diet, patients' depressive symptoms significantly improved (78). L-tryptophan can be used to treat parasomnias in children. Tryptophan has very few side effects, as might be expected from a dietary component (79).

Maternal nutritional Impact on brain Development and Function

The role of maternal nutritional factors in fetal development appeared as an important research during the 20th century. Maternal nutrition has a direct impact on fetal neurodevelopment, as diet and food choices play a significant role in defining maternal nutritional status (80). For a healthy pregnancy and successful fetal development, the maternal diet is crucial (81). Around 22 days after conception, fetal neurodevelopment starts, and it progresses quickly in the second and third trimesters (82).

It's essential to have proper nutrition from the start of pregnancy as it interferes with the neural tube's and plate's development. Nutrients like folic acid, copper, and vitamin A play a crucial role in this process. The specific neurodevelopmental processes are also dependent on a number of nutrients. Different parts of the brain engage in each process at various, overlapping times. For instance, myelination of the brainstem auditory pathway starts from week 26 of pregnancy and lasts for at least a year after delivery. The formation of myelin requires fatty acids like docosahexaenoic acid (DHA) (81). Maternal malnutrition during pregnancy can negatively impact placentation, resulting in changes to placental size, shape, and blood flow, which may lessen the fetus's access to nutrition. Later, the fetal nutrition status is disturbed, which has dramatic consequences on organogenesis, growth, and programming and has been linked to both short- and long-term effects on development and morbidity (39).

Fatty acids such as docosahexaenoic acid (DHA, C22:6 n-3) are necessary for myelination(83). Human studies suggest that prenatal inflammation and low consumption of n-3 polyunsaturated fatty acids (PUFAs) can have a negative impact on neurodevelopment, leading to long-lasting consequences on behavior (84).

Malnutrition in mothers can alter the brain development of the embryo, leading to changes in developmental tendencies that may impact learning, memory, and social-emotional processes. Deficiencies that occur in the postnatal period can persist throughout adulthood, and may increase the possibility of developing schizophrenia, personality problems, and other psychiatric illnesses including depression (85).

Healthy foods for Brain

The findings suggested that eating more 'healthy' foods such fruit, vegetables, seafood, and whole grains was associated with a lower risk of depression (86). Healthy eating habits have been demonstrated to be inversely associated to the likelihood of, or risk for, depression in recent systematic studies looking at the connection between nutrition and common mental diseases. Such diets emphasize eating fruit, vegetables, whole grains, nuts, seeds, and seafood while limiting the intake of processed foods. On the other hand, it has been demonstrated that unhealthy diets high in processed, high-fat, high-sugar meals during adolescence and adulthood are positively connected with mental disorders (86). Walnut diet can enhance memory and cognitive level, consuming walnuts in diet might reduce oxidative stress by lowering the production of free radicals and improving antioxidant defense (87). Walnut extracts could decrease Amyloid-ß fibrillation and aggregation, indicating their positive impact on memory and cognition (88). English walnuts are abundant in linoleic acid (LA), alpha linolenic acid (ALA), polyphenolics, phytosterols, and micronutrients which, regardless of age, have been found to enhance brain health and function (89).

The research suggests that eating a balanced diet that prioritizes consuming fish, while limiting the consumption of added sugars will significantly slow and reduce cognitive decline (90). Dairy products have been extensively studied and are considered nutrient-dense and affects cognition (91). Several countries dietary guidelines have recommended a serving of dairy products, at least one, per day. However, a large number of people do not consume the recommended 3 cups of dairy products each day (92). Diets with a low glycemic index have been shown to improve cognition, memory, and functional capacity, whereas diets high in simple sugars have been connected to attention and concentration problems. The manufacture of neurotransmitters, especially serotonin and catecholamines, requires a steady supply of amino acids in the brain. Reduced memory, thinking, and learning have been linked to low serotonin levels (93). Low serotonin levels and impaired brain function are both likely to be linked to excessive sugar consumption (25).

CONCLUSION

The current review highlights recent progress in explaining complex connections between diet, brain function, and mental health. Critical analysis of numerous clinical and experimental investigations reveals that omega-3 fatty acids, vitamins (A, B, C, D and E) and minerals (iron zinc and magnesium have crucial roles in disorders of mental health and neurology.

The brain's most prevalent fatty acids, specifically docosahexaenoic acid and arachidonic acid are crucial for the formation and growth of the brain. Likewise vitamin A deficiency and excess during prenatal and postnatal life can lead to birth defects. Numerous mental illnesses have been connected to vitamin B deficiency like Parkinson's and Alzheimer's disease. To prevent neural tube development problem, folic acid supplementations has been frequently recommended to expectant mothers. Vitamin D has crucial roles in the brain's calcium signaling, proliferation and differentiation, as well as neurotrophic and neuroprotective activities. Vitamin C and E has anti-inflammatory and neuroprotective properties, and it help prevent neurodegenerative illnesses brought on by oxidative stress. Iron is necessary for myelination, neurotransmitter synthesis, and cognitive development in order for the brain to function correctly. Zinc and Magnesium are necessary trace elements, crucial for brain growth, synaptic plasticity, and overall brain health. L-tyrosine and L-tryptophan they are the precursor of neurotransmitters and has been shown to have therapeutic benefits in enhancing mood, behavior, and cognition, with a focus on depression. For a healthy pregnancy and successful fetal development, the maternal diet is crucial. Maternal diets should emphasize eating fruit, vegetables, whole grains, nuts, seeds, and seafood while limiting the intake of processed foods. On the other hand, it has been demonstrated that unhealthy diets high in processed, high-fat, high-sugar meals during adolescence and adulthood are positively connected with mental disorders.

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