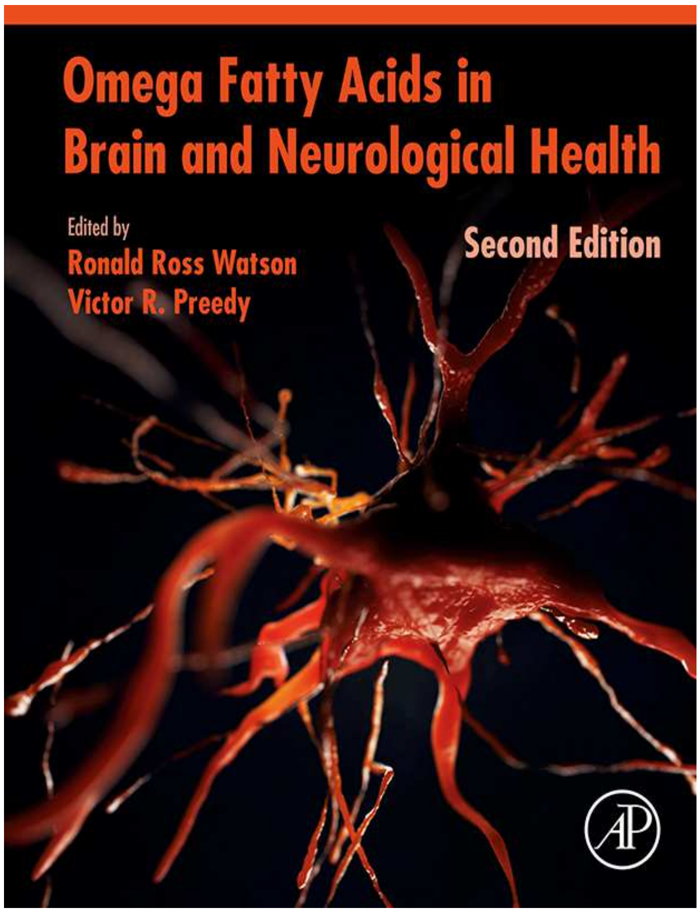

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CHAPTER

10

Omega-3 and Cognition in Children with Malnutrition

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OMEGA-3

Malnutrition generally refers to deficiencies, excesses, or imbalances in energy and/or nutrient intake and encompasses three categories including undernutrition, overweight/obesity, and micronutrient malnutrition.[1,2] The consequences of malnutrition have significant and lasting effects which impact economic, social, and healthcare systems globally.[3] The magnitude of the negative impact of malnutrition may be greatest when considering one of the most affected populations, children. According to the World Health Organization, 224 million children under the age of 5 are under nourished, where 41 million are overweight or obese.[4] Likewise, 45% of deaths of this group are linked to undernutrition and obesity is in the rise in almost every country worldwide.[4] Malnutrition is not only related to a range of noncommunicable diseases but is considered to cause a range of issues which negatively impact the individual over their entire lifespan[5,6] and future generations via epigenetic mechanisms.[7] One of the primary concerns with child malnutrition is the negative impact it has on brain development and cognitive functioning altering physical and psychological characteristics and wellbeing of the child and their future self.

During development, the central nervous system (CNS) and brain are susceptible to a variety of factors which influence brain development and cognitive functioning.[8] These factors include both environmental and biological factors (i.e., genes and cellular mechanisms) and their interaction.[9] Nutrition is an especially significant environmental factor because of the influence it has on gene expression and epigenetics[10] and the specific cellular and developmental mechanisms which depend on essential nutrients for proper function and growth.[11] Likewise, with increasing duration of malnutrition, these problems are exacerbated increasing the long-term and more serious consequences and lifelong residual effects.[12]

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Specific nutrients are critical during different developmental epochs and for specific cellular mechanisms which underlie brain development and cognitive functioning. One nutrient of significant importance to both development and day-to-day functioning is omega-3 fatty acids. The following chapter reviews the specifics of how malnutrition in children can impact development and cognitive performance. Details are provided on the specific influence of both undernutrition and overweight/obesity on cognitive performance. Moreover, the bulk of the following specifically highlights the empirical evidence demonstrating the effect that Omega-3 fatty acid consumption or supplementation has on cognition and neuropsychological performance in children with malnutrition.

MALNUTRITION AND COGNITION IN CHILDREN

The World Health Organization (WHO) defines malnutrition as "the cellular imbalance between the supply of nutrients and energy and the body's demand to ensure growth, maintenance and specific functions"[13] resulting in accumulated energy, protein, or micronutrient deficits that may negatively affect growth, development, and other pertinent outcomes.[14] It has been demonstrated that children who experience retardation in growth during early childhood have increased probabilities of cognitive, motor, and language deficits along with poorer outcomes in academic performance and slowed cognitive development.[15]

In comparison to the body, the brain develops rapidly during the first years of life reaching 80% of adult weight by age 2,[16] but this rapid growth increases vulnerabilities to the negative effects of nutritional deficiencies.[17] Animal models have demonstrated that malnutrition during this period of rapid development can alter the number of cell,[18] the migration of cells,[19] neuronal myelination,[20] formation of synapses,[21] hippocampal formation,[22] and neurotransmission.[23] In addition, undernourished children may have less energy which may result in less exploratory behaviors and interest in learning which also impacts cognitive development.[24] This association between malnutrition and development of cognition is well established by cross-sectional studies, however, only a few longitudinal studies have been conducted and no international statistics exist which demonstrate the actual progress of cognitive development in children.[25]

Various findings which demonstrate the influence malnutrition has on child development and cognition have arisen from specific geographical incidents, such as famine or lacking a specific nutrient in a local area. However, it is important to consider that nutrients do not act in isolation but act within complex system and sequences which are integral to specific and general mechanisms which require the provision of other micronutrients.[15] This is especially true when considering the impact of nutrition on brain development and cognitive functioning.

IMPACT OF UNDERNUTRITION ON COGNITIVE FUNCTION

The impact of undernutrition, that is, lacking in energy and/or specific micronutrients, had been demonstrated to impact brain development and cognitive function starting during pregnancy through adolescence. The nutritional guidelines for pregnant mothers and infants have been greatly influenced by findings showing theses critical effect of nutrition. Malnutrition may begin before the child is even born, when the mother is undernourished, as is often the case in low-income countries.[26] However, in western countries, delays in fetal growth is often the result of a medical conditions for example with severe hypertension,[27] or if the mother consumes higher levels of alcohol.[28]

Also undernourishment during this period is associated with decreased birth weight, delays in cognitive development and with a decrease of 4–8 points in IQ scores compared to children with normal birth weight.[29] Frequently malnutrition during pregnancy is also followed by poor nutrition during the first months and years of life further resulting in severely stunted growth.[30] Stunting of growth in early childhood caused by a nutritional deficiency is associated with poorer cognitive development, academic performance in later childhood,[25] and specifically protein-energy malnutrition can cause delays in growth of the hippocampus and cortex.[31] Furthermore, reviews of the both animal and human studies have shown that mild but persistent malnutrition during the first 2 years of life negatively affects reasoning, visuospatial functions, language development, attention, academic achievement, IQ, and learning.[32] Research on brain development and cognition have demonstrated that some nutrients may more influential than others, including proteins, energy, certain fats, iron, zinc, copper, iodine, selenium, vitamin A, choline, and folic acid. Micronutrient deficiencies are a major concern among children in developing countries, which affect their growth and cognitive development.[33] The specific profiles or lack of resources with regional diets which have little variation may result in lack of important micronutrients essential for development.[34]

IMPACT OF OVERWEIGHT/OBESITY ON COGNITIVE FUNCTION

Obesity is a special form of malnutrition considered as over nutrition, as opposed to undernutrition, but it is considered malnutrition because it is likely that the diet has a low density of nutrients along with a high content of fats and carbohydrates.[35] Obesity represents a rapidly growing problem greatly affecting developed regions and is steadily increasing in developing countries[36] and is considered a world pandemic[37]. Childhood obesity and the associated burden of associated diseases and disorders are greatly impacting healthcare systems in the United States and abroad, and the increase in prevalence continues to rise.[38] In 2010, it was estimated that 43 million children worldwide, including 35 million in developing countries, were overweight or obese, and it is expected that this number will continue to grow to 60 million by 2020.[39]

Childhood obesity is not only associated with many major adverse health consequences but predisposes them as adults to hypertension, dyslipidemia, diabetes, cardiovascular disease (CVD), stroke, and many types of cancer.[39] Correspondingly, childhood obesity is associated with poorer cognitive function and future outcomes such as academic performance and cognitive functioning.[40] Dietary components such as high saturated fats and sugars may also have a detrimental impact on brain function although much of this evidence is derived from animal models.[41] Brain-derived neurotrophic factor (BDNF) appears to function at the crossroads of cognitive and metabolic regulation.[42] BDNF modulates insulin resistance and glucose metabolism and deletion or polymorphisms of BDNF are related to abnormal hippocampal function among rodent and human studies.[43] Exposure to a diet high in saturated fat and sucrose, independent of obesity, was related to decreased BDNF in the hippocampus and poorer learning and memory performance.[44]

A recent review of the literature concluded that overweight and obesity may result in lower academic performance as measured as literacy, numeracy, and school grades,[45] but only a few studies have investigated a possible connection between being obesity and/or overweight and cognitive performance in children. Associations have been demonstrated between overweight status and poor school performance among all children from 7th to 9th grade, but not from 3 to 6.[46] It has been found that obese children have a worse performance in mental updating, understanding of language and memory in comparison with normal weight children.[47] Likewise, others have observed that, among Chinese elementary school children, children with severe obesity had a significantly lower IQ than controls.[48] An association between the BMI percentile category and cognitive impairment in the visuospatial organization and general mental capacity, the importance of these findings can be judged by noting that the adverse effects of increasing body weight status on the functioning of cognition begin to play as early as in childhood.[49]

DEFICIENCIES OF SPECIFIC MICRONUTRIENTS AND BRAIN DEVELOPMENT

It is well established that nutritional deficiencies can affect the brain and alter development and subsequent behavior permanently as seen with the prime examples of iron, folic acid, zinc, and iodine deficiency. Studies of these micronutrients have established evidence which has been used to inform public policy and community interventions to better health outcomes and promote healthy development in children. Furthermore, this area of research demonstrates the increased need to better understand the influence of malnutrition, especially considering the influence of specific nutrients, on important outcomes which impact may affect the individual over their whole lifespan and even future generations.

The importance of nutrition to development is highlighted by the following specific micronutrients and their impact on cognitive functioning, likewise, it is important to consider the implications of malnutrition where the child or the pregnant mother is lacking basic sustenance. Any of the micronutrient deficiencies may occur alone or concurrently in individuals lacking sufficient caloric intake exacerbating the impact of malnutrition on development and cognition, especially in the epochs of development where specific micronutrients and energy are critical.

Iron deficiency anemia is the most prevalent nutritional deficiency worldwide, and it is estimated that up to half of all children worldwide are deficient in iron.[50] In children, the relationship between iron and cognitive development has been well researched, however, there are mixed results.[15] Meta-analysis has demonstrated that short-term iron treatment for anemia in children under 3 did not improve cognitive development, however in older children, there have been results indicated that supplementation did increase IQ.[51–53] Iron appears to modify the development processes in hippocampal neurons by altering dendritic growth[54] which may cause long-lasting effects on neural structure and behavior.[55] If a deficiency of iron occurs in the 6–12 months of life, the damage may be irreversible.[56]

Folic acid is another example of a nutrient vital to brain development. Deficiency of folic acid between 21 and 28 days after embryo is fertilized and implanted, when the neural tube is closed, predisposes the fetus to a congenital malformation, called a neural tube defect.[57] If there is not enough folic acid, in this critical period, there is an irreversible change in the structure and function of the brain, supplementation of folic acid can prevent this and associated fetal mortality.[58] Furthermore, vitamin B12 is often given alongside folic acid because of its critical and connected roles in metabolism mechanisms. Since folate and vitamin B12 are metabolically associated, deficiency of one can influence the functioning of the other.[59] Like folic acid, B12 deficiency has been showed to cause brain atrophy and demyelination of nerve cells that directly affect cognitive and language development in the long term.[60] An important function of B12 in the nervous system is the metabolism of the fatty acids necessary for the maintenance of the myelin sheath surrounding the axon and with long-term deficiency can cause irreversible brain damage.[59]

Another major problem worldwide is zinc deficiency, affecting 40% of the world's population.[61] Zinc is involved in the process of neurogenesis,[62] maturation and migration of neurons,[63] and overall in motor functioning[64] and cognitive development.[65] Likewise it is plays a critical role in in synaptic transmission[66] especially in hippocampal neurons, involved in learning and memory[67] and is known to modulate neurotransmitters, including glutamate and gamma-aminobutyric acid receptors (GABAs).[68] Evidence has demonstrated changes motor development and cognitive performance,[69–71] however some have demonstrated no benefits[72,73] and the exact mechanism which zinc is acting on behavior and cognitive development is undecided.[74]

Additionally, iodine deficiency is a significant global problem, which is especially important in developing children and during pregnancy[75] and can result in hypothyroidism, causing an insufficient production of thyroid hormones.[76] These hormones play a critical role in brain development and neurological processes, including differentiation of neuronal cells, maturation and migration, myelination, neurotransmission, and synaptic plasticity.[77,78] Past meta-analysis of the importance of iodine to cognitive development has shown significant effects on measures of cognition.[79] Similarly, a more recent meta-analysis using more advanced techniques and only studies from China, where the soil has a severe iodine deficiency, show similar results. It was found that there was a decrease of 12.3 points in the IQ of those children whose mothers lived in regions with iodine deficient soil as compared to those who lived in regions with sufficient soil iodine concentrations.[80] However, the association between mild to moderate maternal iodine deficiency and cognitive development is not as clear as it is when iodine deficiency is severe.[81]

As seen with iron, folic acid, zinc, and iodine micronutrients deficiencies of essential fatty acids are now considered to play a major role in development and cognitive function. Of interest are omega-3 polyunsaturated fatty acids (PUFAs) and its importance in biological mechanisms, brain structure, and behavior. The primary role that omega-3 plays in brain and behavior can further be demonstrated by the findings from studies in which supplement of omega-3 in children with malnutrition.

OMEGA-3, BRAIN DEVELOPMENT, AND COGNITION IN MALNUTRITION

The role of omega-3 fatty acids has been the focus for a broad range psychological issues and pathologies in children ranging from behavioral problems, attention deficit hyperactive disorder (ADHD), psychotic mania, autism spectrum disorder, and mood disorders.[82]

The basis of this area of research is that omega-3 polyunsaturated fatty acids (PUFAs) are important for physiological functioning especially in the CNS and have been shown to associate with decreased neuroinflammation.[83] Like the previously mentioned micronutrients, humans depend on dietary sources for essential fatty acids including omega-3 and omega-6 fatty acids. Linoleic acid (LA), the omega-6 precursor, and α-linoleic acid (ALA), the omega-3 precursor, are major essential fatty acids. ALA can be modified by the body into eicosatetraenoic acid (EPA) and docosahexaenoic acid (DHA), however, these conversions are slow and inefficient.[84] The main dietary sources of EPA and DHA are fatty fish such as salmon, herring, tuna and halibut, while ALA comes mainly from plant sources such as canola oil, walnuts, and flaxseed.[85]

Both omega-3 and omega- 6 are beneficial for health, however omega-6 is more prevalently consumed in western diets, while omega-3 is consumed less[86] and children who consume high levels of omega-6 are at risk of consuming low levels of omega-3.[87] The ratio of omega-6 to omega-3 consumption is of concern in westernized diets, as ratios are as high as 10:1 to 20:1 and are a large departure from the 1:1 ratio proposed by evolutionary perspectives.[88] This ratio is thought to be important to proper balance of lipids in brain tissues and brain functioning.[89] Increased blood serum level ratios of omega-6 to omega-3 have also been found to associate with increased risk for obesity, increased symptoms of ADHD, and increased symptoms of Autism Spectrum Disorder.[90] Lack of omega-3 from dietary sources produces deficiencies in the biological systems because of the inefficient conversion, which promotes inflammation, pathogenesis of disease, and hinders optimal brain functioning.[91]

The role of fatty acids in development and cognition is important as apparent when looking at brain tissue composition and the role that fatty acids play in brain cellular functioning and structure.[92] Sixty percent of brain tissue is composed of lipids[93] and is unique in its levels of specific fatty acids, with high levels of AA and DHA and lower levels of EPA.[94] The consumption of these essential fatty acids helps to conserve the neuronal membranes of this unique lipid composition which vital for the proper functioning of the CNS.[95] Specifically, 30%–40% of the lipids which comprise the cellular membranes in gray matter are DHA and higher concentrations are found synaptic membranes.[96] Omega-3 PUFAs have been associated with the integrity of the CNS and are important for development and functioning of the CNS.[97]

Essential fatty acids, especially DHA, contribute to the optimal functioning of neuronal membranes and neurotransmission, including the influence on inflammation, deficiencies of fatty acids are associated with problems with behavior, learning, and cognition.[98,99] Likewise, studies have shown that deficiency of omega-3 is associated with problems of the endocannabinoid system which helps regulate neuronal activities associated with mood and behavior.[100] Animal models demonstrate that maternal deficiency of omega-3 during gestation affects the development of the brain in the offspring and was associated with offspring spatial memory problems.[101] Omega-3 deficiency has also be associated with problems in learning and brain functioning and these behavioral deficits are thought to be the result of problems with the synthesis of phospholipids (which make up brain cell membranes), transportation and utilization of glucose, and decreased neuron size in the hippocampus, hypothalamus, and cerebral cortex.[98]

The regulation of membrane fluidity and gene expression is believed to be particularly important during infant and childhood development.[102] Likewise, problems in the fatty acid metabolism are also related with neurodevelopmental disorders such as attention deficit hyperactivity disorder, dyslexia, dyspraxia, and autistic spectrum disorder.[103] However, most research on the association between omega-3 intake and cognitive development has focused on preterm or low-birth-weight babies.[8]

The accumulation of DHA in the brain begins in the uterus, mainly in the second half of pregnancy, when gray matter growth accelerates.[104] In the last trimester of gestation and the first months of life DHA storage in the brain continues to increase, this is when neurogenesis is very active and neuroblast migration, differentiation and synaptogenesis occur.[105] Therefore preterm infants, who do not receive the intrauterine supply of DHA in the third trimester, they may have DHA deficiencies which will make them vulnerable to reductions in neuronal growth and decreased regional cortical gray matter volumes.[105]

As realized with other micronutrients, Omega-3 deficiency has been the focus of investigations to improve health and psychological functioning associated with the bulk of these studies have centered around the first couple years of life when development is rapidly occurring. However, it is important to consider that development is an ongoing process and is not uniform across individuals, especially when considering cognitive development.[106] Likewise, effects from early malnutrition are seen to cause lasting effects on cognitive abilities into adolescence and even young adulthood.[106,107]

When considering normal cognitive development, research has demonstrated beneficial effects from nutritional supplementation of omega-3. A recent systematic review and meta-analysis conducted by Shulkin and colleagues demonstrated that omega-3 supplementation improves child cognitive development.[108] Their meta-analysis included 15 randomized controlled trials including 2525 children with 20 different intervention types (supplementation with different combinations of DHA, EPA, AA at different time periods). They demonstrated that these studies, which had an average supplementation duration of about 7 months and measures taken after an average of 16 months, that both material and infant supplementation improved cognitive development as measured by the Bayley Scales of Infant Development (BSID) having a standard mean difference (SMD) of 0.21 and 0.24, respectively. The effect size was greatest (SMD = 0.40), on the psychomotor development subscale of the BSID when DHA and/or EPA was used. However, the combined use of DHA and AA had the greatest effect size (SMD = 0.17) on the mental development index used. The use of high-quality RCTs and differential intervention types aids in bettering the understanding of the effects of omega-3 supplementation in normal development, showing that there are clear benefits. Likewise, it is equally important to explore the differences in children with malnutrition, as this population represents one that is highly susceptible to cognitive deficits which are caused by lack of energy and nutrients to ensure optimal growth and development.

SUPPLEMENTATION AND IMPACT ON COGNITION WITH UNDERNUTRITION

In respect to undernutrition, it is important to explore avenues to aid children with the associated health and cognitive issues which may arise, especially in respect to cognitive functioning. This large, growing, and underserved population characterizes a unique group where early intervention aids development and functioning throughout the lifespan.

However, there is limited research on the direct effects of only omega-3 supplementation on cognitive function in undernourished children, especially when it comes to studies which use high-quality methodology such as randomized controlled trials. Furthermore, many of the results from studies connecting changes in cognition are controversial.

The use of other types of supplementation methods has been explored as well. Dalton et al. used a fish-flour spread to deliver omega-3 PUFAs to children to better understand the influence on cognitive outcomes.[109] One hundred and eight three children ages 7–9 who attended a primary school which served low SES community in Northern Cape Province of South Africa were randomized into two groups. Of the children who were participated in the study, anthropometric indices indicated that malnutrition was present, approximately 26% were classified as having stunting, 23.6% were classified as underweight, and 9.7% were classified as having wasting. No significant differences were seen between control or treatment groups in any demographic or anthropometric measurements. Both groups received two slices of bread with a 25 g of spread one which had marine fish flour and was designed to deliver 892 mg of DHA per week. This was provided to the children over a 6-month period for 104 days only taking place when school in session. Children were evaluated using the Hopkins Verbal Learning test (HVLT), a Reading test, and a Spelling test. This single-blind study found that for two of the subtests of the HVLT, that there were marginally significant treatment effects and for two others significant treatment effects, demonstrating that the treatment group was able to recall and recognize more words from the learning phase of the test. Likewise, it was seen that the treatment group had a significant increase in the Reading test, however, for the Spelling test did not change significantly from baseline. However, the control groups scores on the Spelling test actually declined significantly from baseline, which may have been due to high temperatures experienced during the follow-up testing. The authors indicate that this increase in cognitive performance is likely due to the community have no intake of fatty fish and very low consumption of lean fish and the supplementation increasing blood levels of DHA in the treatment group. However, these findings come from children with and without undernutrition, so it makes it difficult to indicate the true effect that omega-3 is having on children with undernutrition. About 20% of their low SES community sample could be classified as having undernutrition but similar studies have found mixed results of omega-3 using such samples.

Muthayya and colleagues conducted research with children ages 6–10 in two primary schools serving low SES communities in Bangalore, India. This double-blind randomized controlled trial used four different treatment groups to determine the effects of high and low micronutrient supplementation and high and low omega-3 PUFA supplementation. A total of 598 children participated and intervention lasted 12 months. After the intervention all four groups had significant improvements in weight and height, however, there were no significant differences between low and high omega-3 PUFA supplements. Likewise, measures of cognitive performance increased in all treatment groups as well. Low micronutrient treatment was the most beneficial on cognitive performance at 12 months, however, no significant effects or interactions were found when exploring the differences between low and high omega-3 PUFA treatments. The authors purport that the use of only 100 mg of omega-3 might be too low to see effects and that the use of a placebo control group would aid in making comparisons. Likewise, the children from this study were not all malnourished, inclusion criteria stated that they must not be severely malnourished, which makes it difficult to make clear conclusions about the effects of omega-3 on cognition in malnourished children. Only a small percentage of children who were included in the study could be classified as undernourished with 15% being classified as stunting and 20% being classified as underweight. The effect of omega-3 supplementation on cognition has likewise been studied in combination with iron supplementation, in similar samples of children, who have iron deficiency and come from low-income villages in eastern South Africa.

To better understand the combined effect of iron and omega-3 supplementation, Baumgartner and colleagues employed a randomized placebo-controlled double-blind design.[110] They used this design to investigate the effects of iron supplementation, DHA/EPA, and the combination of Iron and DHA/EPA supplementation in 321 children ages 6–11 who had iron deficiency. Four treatment groups were used Iron and placebo, Placebo and DHA/EPA, Iron and DHA/EPA, and Placebo and Placebo. The intervention lasted for 8.5 months and cognitive performance was assessed using four subtests of the Kaufman Assessment Battery for children (KABC-II) and the HVLT at baseline and conclusion of treatment. The groups were assessed using anthropometric indices, but all different categories were included in the study. Notably, their sample had a wider variation in the sample proportion classified as having malnutrition. The largest proportion of the sample, 31.5% had mild stunting (height for age z-scores less than −1 SD but greater than −2 SD), next 21.5% were overweight, 7.2% obese, 6.2% stunting, and 2.1% as underweight. Mixed results were found treatment effects regarding changes in cognitive performance, iron supplementation showed small significant effects on recall for HVLT, however, DHA/EPA supplementation had a large negative effect for working memory and for girls with iron deficiency a large negative effect on long-term memory subtests. Boys in the DHA/EPA group tended to benefit from supplementation having higher scores on the long-term memory subtest. The authors support this finding by the example of an animal study which found that using DHA/EPA or iron alone in rats which are deficient in both leads to poorer performance on working memory and memory tasks. Furthermore, they state that both the mechanisms which iron and PUFAs play in neurotransmission and in inflammation may influence their findings. However, again their study did not specifically determine the impact of omega-3 on undernutrition, their sample had a large mixture of children with differential nutritional status and anthropometric categorization. With this in consideration, it is important to acknowledge that their findings may be imprecise when trying to make conclusions about the effects of omega-3 on cognition in children with undernutrition.

Portillo Reyes et al. addressed this gap in the literature by determining the effects of omega-3 supplementation in children ages 8–12 classified as having mild to moderate levels of malnourishment as defined by being 85%–95% in height/age and 70%–90% in weight/height.[111] The study used a randomized double-blind placebo-controlled and case-controlled designed which supplemented children over a 3-month period using a daily dose of 180 mg of DHA and 270 mg of EPA. The children who received the omega-3 supplementation at conclusion showed significant changes in tests of processing speed, visuoperceptual integration, visuoconstructive integration, attention, and executive functioning. When comparing the treatment group with the placebo group, 63% (12 of 19) of the neuropsychological measures showed changes indicating moderate to large effect sizes, as measured by Cohen's d, whereas the placebo group only showed changes in 10.5% (2 of 19) of measures. Likewise, when unique change for each participant was calculated as an index of clinical significant, it was found that 70% or more of children in the omega-3 supplementation treatment group had large improvements ($d > 0.80$) in processing speed (Symbol Search), coordination visuomotor (Block Design), perceptual integration (Embedded Figures), attention (Letter Cancellation), and executive functioning (Letter/Number Sequencing & Matrix Reasoning). Even though blood serum levels of omega-3 or the omega-6/3 ratio were not obtained, nutritional questionnaires indicated that this sample of mild to moderate malnourished children was not frequently consuming foods rich in omega-3; 8% indicated consuming a portion of fish two or more times per week, 39% one portion per week, and 19% one portion per 2 weeks. Likewise, typical Mexican diets, especially in northern regions, are high in omega-6. Considering this, the supplementation of omega-3 in this sample of children and the effects which are seen in cognitive functioning are in line with studies demonstrating the importance to physiological brain functions.

The improvements in visuoperception may be due to the effect of omega-3 that has on biological mechanisms underlying vision and visual processing, such as seen with newborn children.[112] Furthermore, electrophysiology studies also demonstrate that supplementation of omega-3 improves direct measures of neuro functioning underlying visual processing.[113] Findings of increased processing speed with omega-3 may point to the effect which it has on brain structure, brain cell membranes and myelin, and neurotransmission. Witte et al. found that omega-3 supplementation improved the structural integrity of white matter in older adults which others have found as related to the cognitive speed of processing.[114] Likewise, the importance of omega-3 to the composition of neuronal membranes may be driving the enhancement seen in processing speed via its influence on membrane fluidity in membrane protein incorporation and function,[115] signal transduction speed, and neurotransmission.[102] These same physiological benefits of omega-3 supplementation also may be driving improves in attention and executive functioning which rely heavily on the integration of information from different brain areas and quick processing speed to produce improvements in cognitive measures. These improvements are in line with findings from studies showing that omega-3 improves symptoms of attention deficit disorder[116,117] and reductions in decline seen in older adults.[118]

The effect of omega-3 consumption in undernourished children is substantial to aid in the development process and lifelong functioning when it comes to both physiological and psychological well-being. Early intervention with omega-3 or nutritional education may be able to aid these children's functional role in society. This large and underserved population is important however, it is also important to understand how omega-3 consumption may influence the deficits which are seen with overnutrition. Childhood obesity is a growing problem and the long-term physiological, psychological, and societal consequences are just being revealed, however, the small number of studies available does seem to indicate that omega-3 is just as important to the overweight and obese children as it is with undernourished child populations in the same and other unique ways.

SUPPLEMENTATION AND IMPACT ON COGNITION WITH OVERWEIGHT/OBESE CHILDREN

The consumption of more omega-3 fatty acids has been associated with enhancements in cognition (depending on the population) while on the other hand consumption of a westernized diet (high in saturated fats and calories) has been associated with brain physiology[119,120] and is associated with poorer cognitive function.[121] Researchers have started to fill the gap on how omega-3 fatty acids influence cognitive functioning, especially concerning childhood obesity, where early prevention and treatment can maximize individual and societal benefits by deterring lifetime concurrency of disease and comorbid conditions. However, there are large gaps in the literature concerning the effects of omega-3 fatty acids or the ratio of omega-6 to omega-3 with respect to cognitive performance in children who are overweight or obese. Furthermore, the evidence is now growing which demonstrates that increased dietary intake of omega-3 fatty acids may aid in prevention and treatment of obesity via actions on the mechanisms underlying appetite.[122]

Regarding the relationship of omega-3 and cognitive functioning in childhood obesity, very limited evidence exists. Haapala and colleagues conducted a study with 386 normal weight and 58 overweight children ages 6–8 years old and found that higher levels of EPA and DHA in blood plasma of the obese children were associated with higher scores on the nonverbal reasoning (as measured by Raven's Colored Progressive Matrices).[122] However, they did not find any significant associations between normal-weight children's level of blood EPA and DHA and scores. They point out that earlier studies which investigated the levels of EPA and DHA have had mixed results in respect to cognition in normal weight children, only combined levels of blood EPA and DHA had an association with working memory in one study[123] whereas another study found no association.[124]

They highlight that their study included child weight status as a modifying factor, which have a stronger influence on cognitive performance via reductions in inflammation, which is known to be associated with excess body fat. However, their study only found associations with levels of EPA and DHA in plasma triacylglycerols, which reflect recent fatty acid consumption and not with fatty acids in plasma cholesteryl esters or phospholipids, which reflect consumption over the prior months. However, their findings of these direct associations do reflect findings from Harris and colleagues which found that children who had increased levels of palmitic acid and arachidonic acid had associated biomarkers of increased low-grade inflammation, whereas omega-6 and total polyunsaturated fatty acids were associated with decreased inflammation.[125] Furthermore, the findings from Haapala et al. also agree with findings from studies using animal models, adult populations, and aging populations.[126–128]

CONCLUSIONS

The investigation of cognitive development and the relationship between diet and cognition are both emerging fields. However, some clear connections have been made concerning normal development and nutrition which has arisen from observations of the consequences when diets are restricted, deficient, or have excesses. The role that essential fatty acids play in the brain and cognition, especially concerning omega-3, biological are critical to structure and function; however, mixed results have been seen with normal populations. Even though the research on child development is large, the exact timeline of cognitive development has no standards making it hard to compare and indicate how omega-3 is influencing developmental mechanisms and the observable cognitive performance.

However, when examining the studies which explore populations with malnutrition, the small amount of evidence seems to indicate a large benefit to development and cognition. However, there is a definite lack of research which uses high-quality designs and methodologies and specific populations of malnourished to determine the differential effects of omega-3 in this varied umbrella category. Future investigations should consider looking at specific profiles of malnourished children (i.e., mild undernourished, severely undernourished) to better determine the influence of omega-3 consumption on cognitive functioning. Many of the studies try to use omega-3 supplementation as a community intervention with low SES children to better cognitive outcomes, however, fail to make specific comparisons within the different profiles of these children.

Public policy and nutritional agencies are taking heed to the evidence with suggestions about omega-3 consumption as expert committees have started recommending it during pregnancy[129] and for adult populations for cardiovascular health.[130] Likewise, nutritional agencies are including omega-3 suggestions.[131] However, the greatest magnitude of impact may be in the growing number of children who consume a western diet or those who live in low SES communities. With the growing rates of childhood obesity, due partly to the consumption of calorie-dense but nutritionally deprived foods,[132] there is a great concern, especially when considering the effects of malnutrition on cognitive functioning. The deficits in cognitive function along with long-term epigenetic consequences may be impossible to factor in when calculating the overall impact malnutrition is having globally.

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