

# Nutrition and Brain Health on Our Sleeves - Approach of Life Saving

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## Abstract

Human brains have unique nutritional needs. A lifetime of experience-driven remodeling of the brain begins during the intensive intrauterine environment and the early postnatal years. When this process is at its peak during childhood, the brain may account for 50% of the body's basic nutritional requirements. Nutrition plays a long-term role in brain health. It was our goal to refocus nutritional programs on the brain in order to move it into a more central position. Throughout life, the human brain needs macro- and micro-nutrients, and they are delivered in different ways. This review emphasizes assessing success in meeting the brain's nutritional needs and how nutrition can influence brain development, brain performance and cognition.

**Keywords:** Nutrition; Brain health; Nutritional requirements

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**Citation:** Nichanametla SR, Ujwala M, Vissa SK (2024) Nutrition and Brain Health on Our Sleeves - Approach of Life Saving. J Food Nutr Health, Volume 5.1. DOI: <https://doi.org/10.47275/2692-5222-124>

**Received:** April 09, 2024; **Accepted:** July 4, 2024; **Published:** July 12, 2024

## Introduction

In comparison with other organs of the body, the brain has very high energy requirements. There has been a correlation between nutritional activity of the brain and a reduction in mental and physical disorders. Numerous studies have demonstrated that nutritional activity is effective in preventing colon and breast cancer, cardiovascular disease, obesity, Alzheimer's, depression, and anxiety. Many large, prospective, and cross-sectional studies have found that a dietary profile that benefits cognitive function with aging includes weekly small servings of fish, cereals, darkly colored fruits, and leafy vegetables. The possible negative effects of aging on cognitive function have been reversed with diet and exercise [1].

When researchers like Prof. Kety at the University of Pennsylvania developed quantitative methodologies for measuring whole-brain blood flow and metabolism in the late 1940s, the cost of an adult human brain was first appraised. Human brains consume between 20 and 25% of the body's total energy, despite making up only 2% of an adult's weight. There is no other mammal that devotes so much energy to its brain as humans do. A new human brain costs somewhat less to build than a new adult brain, but glucose consumption, which is the brain's primary energy source, has equaled that of an adult by postnatal age 2 years. A person who believes that the first 1,000 days are the most important for the development of a brain might conclude that the most important work has been done. By the middle of the first decade of life, the brain consumes twice as much glucose as an adult. Since glucose is the sole source of energy for the brain, attention has been diverted from the fact that it has other very important cellular functions in combination with other essential nutrients. Synaptic formation and elimination are two of its most important functions. Approximately 10 - 12% of the brain's

total glucose is used for these and related functions. As the new brain is forming, the formation and elimination of synapse dynamics reach their peak during childhood. Our brains must be built and remodeled throughout our lives. Both synaptic proliferation and elimination genes are balanced in childhood, and this balance is maintained throughout life. Protein structure in the brain, which, amazingly, changes every few minutes, hours, and days, illustrates the importance of this balance. Learning and memory are facilitated by synaptic plasticity. From conception to late adulthood, adequate nutrition is essential for the brain. The purpose of this review is to place the brain at the center of discussions about nutrition by presenting the nutritional requirements that must be met to maintain and develop normal brain function and also how nutrition can influence brain development, brain performance and cognition [2].

A question that needs to be answered: What does the brain need, and how does it meet those needs?

## An Evolutionary Approach and Essentiality

Evolutionary interactions between an organism and its environment have resulted in nutritional requirements and processes. An essential nutrient is a substance found in the environment that is available to the organism for dietary consumption, allowing it to conserve and redirect metabolic energy. Accordingly, essentiality is defined as a diet requirement, resulting from biological requirements and insufficient *de novo* production, for growth, development, and healthy physiological functioning. There is no doubt that vitamin C is an essential nutrient. The enzyme L-gulonolactone is only required in the diets of humans and some primates, guinea pigs, bats, and some passerine birds. Evolutionary nutrient-environment interactions are also evident in brain development in hominids. Hominid groups diverged from



other primates more than 2 million years ago, showing anatomical differences, including larger brains. *Homo erectus* differed from other primates in that it had larger brains, smaller intestines, and smaller teeth [3]. Plant-based foods have been replaced by animal-based foods, resulting in these changes. ASFs contain highly bioavailable nutrients that are important for brain development and functioning. As a result of lacustrine and marine foods being available during the Paleolithic period, the shore-based paradigm explains rapid brain growth. Shallow fish, crustaceans, mollusks, amphibians, seabird eggs, and shore plants provide “brain-selective” nutrients, including iodine, iron, zinc, copper, selenium, and long-chain fatty acids. Archeological evidence supports this paradigm with large-shell middens and fish remains found at earliest human sites in South African Cape sites, Rift Valley lakes, and the Nile corridor, 100-18 kya. Sadly, since the agricultural revolution and, more recently, the industrial revolution, genomic adaptations have outpaced genomic changes, resulting in both undernutrition and overnutrition (Children who are becoming increasingly sedentary and unfit can be a strong indication of this trend, since these lifestyle factors are linked to an earlier onset of chronic diseases like type 2 diabetes and obesity. It has been demonstrated in several cross-sectional and longitudinal studies that overweight and poor academic performance are associated with improper brain development) [4, 5].

### Life-cycle Approach

Throughout the world, considerable attention and resources have been devoted to improving nutrition during the first 1,000 days of life in a baby, from conception to age two. For healthy growth and development, there is widespread consensus that maternal and young-child nutrition is important [6].

Diet taken can substantially influence the development and health of brain structure and function. A healthy diet provides building blocks for the brain to create and maintain neuronal connections, which are critical for improved cognition and performance. Dietary factors have a broad and positive action on neuronal function and plasticity. Due to this 1000-day movement, other phases of the life cycle have been neglected despite the evidence that nutrition plays a vital role in brain development and function. All phases of the neuronal life cycle are affected by nutrients, including neuroanatomy, neurochemistry, and neurophysiology. As mentioned in the statement above, in the early years of life, nutrition plays a significant role. It is critical to provide macro- and micro-nutrients during the late fetal and early neonatal periods for neurons to grow rapidly. There is similarly a strong response in this phase to nutritional insults in specific brain regions, such as the hippocampus, striatum, visual cortex, and auditory cortex. A steady supply of nutrients is necessary for the growth and development of synapses in early and middle childhood, as well as for the selective removal of synapses during adolescence. Through adolescence, there is a continuation of brain development, especially in relation to higher cognitive functions [7-9]. As we age, evidence indicates that a variety of nutrients continue to play an important role in supporting neuroplasticity and behavior. To illustrate the breadth and complexity of processes involved throughout life, we will examine the role of glucose in brain development and nutrition.

### The Brain's Glucose and Oxidative Requirements

In order to grow and function, the human brain requires a lot of glucose. It is estimated that an adult human brain consumes between 20 and 25% of its resting total body glucose consumption rate at rest. We require nearly twice as much energy as our closest evolutionary cousin, the chimpanzee. In order to maintain caloric needs for the brain, humans likely developed dietary, gastrointestinal, and metabolic

adaptations. Often, these analyses ignore the heightened costs of brain development. An analysis of glucose requirements in the developing human brain is presented in this section [10].

In young adults, the brain represents only 2% of body weight but consumes 20% of the body's resting energy. Children are not affected by this. Children's brains make up about 5 - 10% of their body mass, consume 1.5 times as much oxygen as adults' brains, and account for up to 50% of their body's basal metabolic rate. It is largely because the brain grows faster before the body reaches its peak growth rate that these remarkable proportional requirements of the brain arise. Up until recently, ion pumping associated with cellular communication was almost universally thought to be responsible for the energy requirements of the human brain. The situation does not appear to be adequately assessed, however. 60% of the brain's oxygen consumption remains after ion pump activity is inhibited. Several hypotheses regarding other metabolic processes have been proposed as a result of this observation, but few experiments have been conducted to test most of them. In study, examined how glucose is used outside oxidative phosphorylation, the main mechanism for ATP synthesis. Children are the starting point. Children's brains consume approximately 70% of their glucose with oxygen, indicating that even more glucose is being consumed outside of the most efficient means for producing ATP during childhood [2, 11-13]. As opposed to anaerobic glycolysis, which occurs in a hypoxic environment, this excess glucose use is referred to as aerobic glycolysis. What happens to glucose when a child's brain, and to a lesser extent a young adult's brain, uses it for purposes besides oxidative phosphorylation? Despite the fact that there are still many questions to be answered in this area of study, there are some clearly defined hypotheses. A number of nonexclusive possibilities can be derived from studies of aerobic glycolysis in cancer, immune cells, and developing tissues. The primary function of glycolysis is to produce glutathione, NADPH, and substrates for synthesis of nucleic acids. As a result of glycolysis, other biosynthesis pathways rely on carbon fragments of glucose, including amino acid and lipid synthesis pathways, some of which derive further from the TCA cycle. Various homeostatic processes in neural tissue, including synaptic homeostasis, proteostasis, and mitostasis, can be maintained by such biosynthetic pathways. A recent study found that aerobic glycolysis is essential for neurite growth in the mouse brain. To determine the role of aerobic glycolysis in the brain, further mechanistic and labeling studies are needed using advanced flux analysis and metabolomics as well as nuclear magnetic resonance spectroscopy. Nevertheless, these findings reveal that brain metabolism is much more complex than its energy requirements for ion pumping; understanding these requirements is crucial to determining the brain's nutritional needs [14, 15].

Assuming glucose is not fully allocated to the brain, current data suggest that glucose consumption both in absolute terms and relative to oxygen consumption varies significantly over the course of life. According to the previous paragraph, aerobic glycolysis alone is affected by aging. Anatomical and physiological changes accompany these changes, which provide insight into how the human brain develops and ages. From conception to the end of a typical human lifetime, the brain's glucose and oxygen requirements change [16]. Within a few hours after conception, several vesicles are formed at the anterior/rostral end of the neural tube, which later develop into the various components of the mature brain. There are limited studies on the glucose requirements of the brain at this stage. Up to approximately 12 weeks after conception, GLUT1 and GLUT3 expressions are high in the fetal brain but falls during the third trimester. It was demonstrated that about one third of total body glucose consumption occurs in the brain, and approximately half of this is not oxidized, according to a



study that injected 14C-labeled glucose and butyrate into 12- to 21-week preivable human fetuses via the carotid artery. The use of butyrate suggests that ketone bodies, fatty acids, and lactate may also play a role in fetal brain metabolism. In contrast, fetal brain oxygen and ATP needs appear to be significantly lower than those of term and postnatal brains [17, 18]. In fact, premature neonates consume very little oxygen in the brain as measured by cerebral oxygen metabolic rate. According to this evidence, it is likely that the very large biosynthetic requirements of the fetal brain can be met primarily by aerobic glycolysis and other substrates. Myelination along the corticospinal tracts begins to appear in the human brain at term, and folding structures resemble those in more mature brains. When the occipital lobes and thalamus are stimulated with new sensory information, particularly visual or tactile, glucose is up taken more readily. The most vulnerable regions appear to also be those that are most affected by significant and/or prolonged hypoglycemia [19-21].

The body's growth-related metabolic demands increase as a result of evolutionary pressures, suggesting that the body and brain have their own metabolic requirements. Unlike term infants, young adults require similar amounts of glucose and oxygen for their brains. Some brain regions, such as the medial frontal cortex, can have up to 25% aerobic glycolysis, but this is a small amount [22]. The gene expression profiles of regions with high aerobic glycolysis in young adults retain juvenile characteristics, a condition called neoteny. Their persistent high glucose needs, including aerobic glycolysis, may be due to ongoing developmental processes in these regions. There is continued myelination of the white matter tracts connecting these regions. Brain glucose requirements continue to decline as cognitively normal humans continue to age [23]. This indicates that the young adult brain continues to "mature." However, the human brain's oxygen consumption remains virtually constant, suggesting that the decrease in glucose consumption is a result of the loss of aerobic glycolysis. During the development of the young adult brain, the topography of brain glucose metabolism also changes, and the most rapid decline in glucose consumption occurs in regions with high aerobic glycolysis. Researchers do not know the exact causes and consequences of these findings, but they raise the possibility that changes in metabolism may contribute to some of the characteristics of brain aging. There has been no research done on the role of nutrition in these changes in brain metabolism associated with aging (Figure 1) [2, 24].

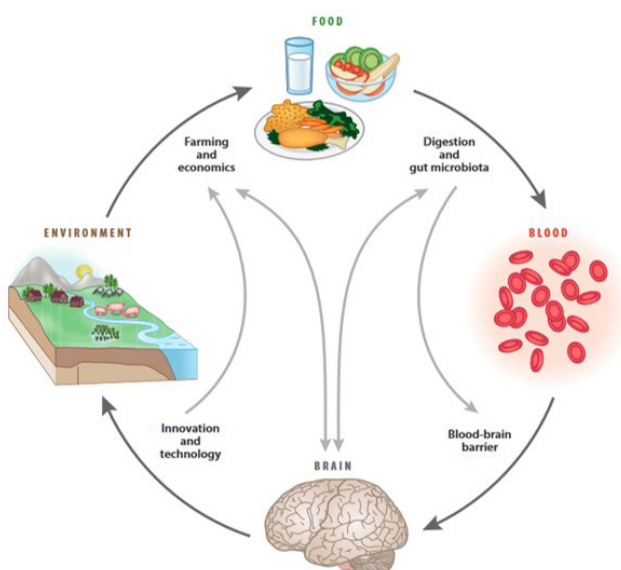


Figure 1: Evolutionary brain nutrition cycle [2].

## The Brain's Other Nutritional Needs

In spite of the fact that glucose is the most important nutrient for the brain, its nutrient needs are complex and largely dependent on age. Brain function, growth, and maintenance require many other nutrients.

The omega-3 fatty acids, for instance, provide building material for the brain. In addition to supporting intercellular signaling events, they also positively influence synaptic function. Sugar, saturated fat, and high-calorie diets, however, are considered deleterious for neural function, as they increase oxidative stress, reduce synaptic plasticity, and impair cognitive function. Certainly, healthy individuals' cognitive function is influenced by short-term variations in the amount and composition of their nutrient intake. It has been shown that well-nourished children who eat breakfast have several positive effects on their cognitive functioning. Dietary interventions and exercise have been shown to interact, with exercise increasing positive effects on brain function and decreasing negative effects associated with high-fat diets. Exercise and dietary management together seem to be the most effective strategies for promoting neural health. Children aged 8 to 11 were also studied to see how a morning meal affected complex mental functions. Electroencephalography was used to assess brain activity while children solved simple addition problems after overnight fasting and after eating or skipping breakfast. Correct responses increased significantly among the fed children compared to those who continued to fast. According to the study, children who eat breakfast have functionally enhanced neural network activity that helps them process numerical information, whereas children who skip breakfast require greater mental effort for this mathematical thinking. An overview of neurophysiology and neurochemistry based on a select group of individual nutrients is presented in this section. As mentioned in the previous paragraph The physiology of nutrition is characterized by a matrix of compounds in complex interactions with each other and with other bioactive factors [10, 25-29]. Based on evidence for greater-known functions of these nutrients in brain development and function and the potential for impaired brain function in deficient states, we include a portion of the more than 40 essential and conditionally essential nutrients. In addition to nutrient deficiencies and overnutrition, gene polymorphisms and nutrient intake overload could also negatively impact metabolism, resulting in brain damage (Figure 2) [1].

Generally known as minerals in human nutrition, iron, zinc, iodine, copper, and selenium are elements that can exist in a variety of forms, either free or as compounds [30]. They catalyze reactions and transmit signals in the brain, among other roles. There is a high concentration of iron, zinc, copper, and selenium within the limbic system, which affects emotions, behavior, memory, and motor coordination. The hippocampus and greater limbic system may also be active in response to iodine, which is largely concentrated in the

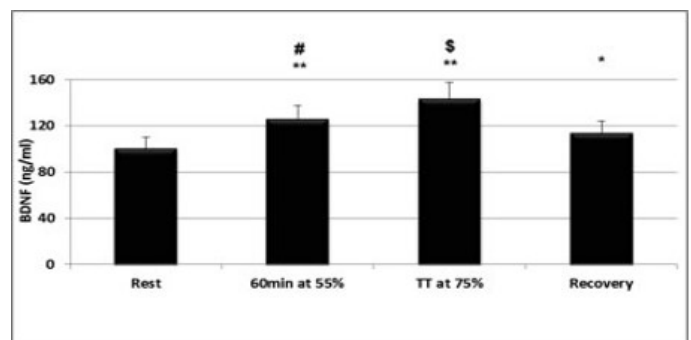


Figure 2: Effects of physical activity, acute exercise/training on the concentration of Brain-derived neurotrophic factor [1].



thyroid gland. An estimated 2 billion people worldwide suffer from iron deficiency, according to the World Health Organization [31]. The majority of iron in the human body is incorporated into heme (65%) for oxygen transport, with the remainder being incorporated into myoglobin and other proteins for enzyme activity. An array of genes regulates absorption and metabolism to maintain a delicate balance [32]. For oxygen transport, myelination synthesis, and neurotransmitter metabolism, iron is concentrated in white matter oligodendrocytes in the brain. Myelin production and dopaminergic dysfunction are associated with iron deficiency in childhood. Several neurodegenerative diseases associated with aging, such as Alzheimer's and Parkinson's, are associated with iron accumulation in the brain [2, 33]. There is a high prevalence of zinc deficiency in low-resource settings where diets lack ASFs or include phytate-containing maize, which interferes with zinc absorption. Generally, zinc deficiency results in stunted growth, but it can also impair development as well. Because zinc regulates growth hormones and delivers neurotransmitters to synaptic clefts, a zinc deficiency can negatively impact the development and function of the brain. Synaptic vesicles of glutamatergic neurons contain 5 - 15% of brain zinc [34]. During fetal and neonatal development, zinc is essential for DNA and RNA synthesis, transcription, and structural maintenance. However, evidence now suggests that zinc is essential for these processes throughout adulthood as well as stem cell proliferation and neuronal differentiation as well. The hippocampus concentrates zinc, but it may be found free in the cortex, amygdala, and olfactory bulb as well. Globally, iodine deficiency has been actively eradicated, but it remains the leading cause of preventable brain damage [35]. Iodine's association with impaired child development and the more severe disorder of cretinism is well established from epidemiological evidence, but its effects on the brain are still poorly understood. In the thyroid gland and throughout the body, iodine is essential for the production of the hormone's thyroxine and triiodothyronine. The neurochemical processes involved in myelination, synaptogenesis, and dendritic arborization are influenced by iodine deficiency via thyroid hormones. A vital cofactor for antioxidant enzymes, selenium protects against free radicals and reduces cell death among other essential trace minerals that contribute to brain health. In addition to antioxidant activity, copper is an important component of dopamine metabolism in the brain [36]. Motor function, balance, and coordination have been affected by copper deficiency modeled in utero in rats. Astrocytes play a critical role in copper storage, metabolism, and homeostasis, according to more recent research [37].

Vitamin A, vitamin B, and choline vitamins are chemical compounds that are necessary for an organism to function properly. There are varying nutrient delivery methods in foods, and different levels of absorption and metabolism in the human body for each category of vitamin. Preformed ASFs, including fish and other animal-based foods, may provide all-transretinol, a more bioavailable form of vitamin A, and plant-based foods may provide carotene, a preformed structure of vitamin A. As coenzymes in energy production, DNA/RNA synthesis, repair, and methylation, as well as neurotransmitter production, all eight essential B vitamins play critical roles in brain function. Blood-brain barrier turnover rates of B vitamins are high, but brain levels of these vitamins are tightly regulated and tend to be higher than plasma levels. Diets deficient in folate and vitamin B12 are associated with health consequences in global nutrition literature. In low-resource populations, cobalamin (vitamin B12) can be expensive and inaccessible due to its synthesis by bacteria. In certain populations, whether vegans or those facing poverty due to lack of access, B12 consumption should be targeted for ASF consumption. Globally, folic acid fortification and supplementation programs are more likely to help prevent foliate deficiency (vitamin B9) [39-41]. Deficits of these two B

vitamins compromise gene expression and transcription in the brain through the methionine cycle. A lack of them also affects the conversion of amino acids to monoamine neurotransmitters, which are involved in the folate cycle. Symptoms of vitamin B12 deficiency include sensory disturbances, motor dysfunction and memory loss, among other effects in the central nervous system caused by demyelination of the posterior and pyramidal tracts of the spinal cord [42, 43]. Brain metabolism is also affected by the remaining six B vitamins, and deficiency has detrimental consequences. Human diets tend to be deficient in these water-soluble vitamins because they are dispersed across a variety of foods. Thiamine (vitamin B1) is needed as a coenzyme in the pentose phosphate pathway, which arises early from glycolysis. In brain energy production, riboflavin (vitamin B2) is essential for generating flavoproteins that participate in fatty acid metabolism [44]. The antioxidant properties of niacin also play a vital role in immune modulation and brain health. The body must produce coenzyme A for the metabolism of brain cells as well as fatty acids from pantothenic acid (vitamin B5). A number of neurotransmitters are synthesized via amino acid metabolism from pyridoxine, pyridoxal, and pyridoxamine (vitamin B6). The metabolism of glucose relies heavily on biotin (vitamin B7) [45]. There are also several brain-related conditions caused by insufficient levels of several of these B vitamins, such as Wernicke's encephalopathy (thiamine) and dementia (niacin), neuropathy and personality disorders (vitamin B6), and depression (biotin). Since vitamin A deficiency is linked to preventable blindness, infection, and child mortality, there has been considerable interest in vitamin A deficiencies in low-resource countries [46-48]. In recent years, choline, a nutrient that has been identified as an essential nutrient, has become increasingly recognized for its importance in brain development, learning, memory, and cognition. It is essential for the production of phospholipids, the integrity of cell membranes, and the synthesis of acetylcholine and sphingomyelin in the brain. Ultimately, it affects epigenetic processes through the conversion of homocysteine to methionine in one-carbon metabolism [49]. A deficiency of choline during pregnancy has been shown to have enduring effects on long-term memory and cognition. Hippocampal development and function can be studied in animal models, but more research in humans is needed.

Several essential fatty acids are needed in human nutrition to synthesize omega-3 and omega-6 polyunsaturated fats. A lot of attention has been focused on omega-6-to-omega-3 fatty acids in the diet, with less attention paid to inadequate intakes. Eicosapentaenoic acid, docosahexaenoic acid (DHA), and arachidonic acid are long-chain fatty acids that are produced when the ratio is too high because they compete with enzymes elongase and desaturase [50]. The recommended 10:1 ratio may be exceeded by populations that consume large amounts of corn or peanut oils. Most of the lipids in the human brain are omega-3 fatty acids, and omega-6 fatty acids, primarily phospholipids, are omega-3 fatty acids. Multiple functions of membranes, including signaling and structure, are well established to be influenced by DHA [51-54]. The effects of DHA deficiency in early life may include impaired cognitive function and poor behavioral development. Acuity of vision is also dependent on DHA, which is found in the retina and visual cortex.

## A Brain's Energy and Nutrient Flow

In spite of the fact that we have described some nutrients and their roles in the brain individually, we want to stress that nutrients generally come from a food matrix and act in concert with other nutrients and compounds. In human nutrition, individual nutrients have been considered historically and this framework has been perpetuated [55, 56]. There has been a connection between nutrients and disease conditions since the 1700s, when citrus fruit consumption was linked



to scurvy (vitamin C was discovered later). Iodine and goiter are examples of other interactions between thiamine and Beri Beri, vitamin D and rickets, and thiamine and Beri Beri. As a result of technological advancements, single nutrients can also be fortified and biofortified to counteract population deficiencies, such as vitamin A, folic acid, iodine, and others. Despite the fact that single nutrients may serve important health needs, good nutrition for the brain is best sustained through high-quality diets [57-61]. Humans have adapted to different environments and diets as a result of migration around the world. Throughout the world, complex food systems and cultures have created a plethora of different diets. Food systems, health behaviors, and the environment should be considered in nutrition interventions for populations who are at risk for deficiencies in brain-selective nutrients. Many food systems around the world produce and consume more maize, but it contains high levels of phytates, which can interfere with zinc absorption and brain development [62, 67]. There are a number of brain-specific nutrients that can be provided by ASFs, including vitamins A and B12, choline, iron, and zinc in highly bioavailable matrices, but their availability and affordability prevent them from being included in many low-resource populations' diets. In many parts of the world, fish and other seafood are depleted, despite their importance for brain development and function [68].

## Gut and Microbiota

Food must first be digested and filtered by the gastrointestinal system before the brain can obtain the nutrient and energy substrates it requires. Over the past few years, remarkable advances have revolutionized our understanding of this process, particularly as it relates to the microbiota of the gut [69]. It is now recognized that the gut microbiota is much more than a collection of commensal and potentially pathogenic bacteria that assist the gastrointestinal tract in its nutritional and immune functions. As well as nutrient uptake and energy homeostasis being modulated by gut-brain axis, the gut-brain axis has been increasingly recognized. The gut microbiota is briefly discussed in this article in the context of brain development, but readers are referred to several excellent reviews of this topic for further reading [70]. Microbes have colonized the intestines in large numbers, mainly bacteria. From the studies performed so far, it is now known that the immune system plays a variety of roles including nutrient metabolism, gut physiology, and recognizing safe environments from pathogenic ones. Diet plays a significant role in influencing gut microbiota composition. Despite differences between cultures, recent studies indicate that over the first few years of life, the gut microbiota accumulates in a fairly stereotypical manner. A high rate of glucose uptake and other nutrients are needed by the brain shortly after this assembly is completed. Children who suffer from malnutrition may be impacted by impairments in gut microbiota assembly, an intriguing possibility [2, 71].

The blood-brain barrier and gut microbiota work together to maintain relationships between them. There are several transporters that regulate the uptake of nutrients through the blood brain barrier. It is also possible that nutrients are also required for the maintenance of the blood-brain barrier.

## Conclusion and Future Directions

We aimed to demonstrate in this review the rich complexity of brain nutrition requirements. It is partly for the purpose of dispelling claims that certain periods of brain development or certain aspects of nutrition are more crucial than others. A variety of interdependent systems are involved in brain nutrition, and they play out differently throughout a person's lifetime. Although a great deal of research

has been conducted on human brain metabolism and rodent brain nutrition to date, our understanding of the complex interactions among the systems involved in maintaining brain nutrition remains limited. There are still many questions to be answered regarding human brain nutrition. We need to multiply our efforts in order to unravel what the brain needs and how those requirements are met in humans, not just mice. The importance of a healthy and functioning brain to the wealth of a nation should be well-recognized by policy makers of every country. Social policies can influence brain development in a number of ways, as illustrated by research performed on different foods like Fish. Based on concerns that mercury contamination may harm the development of a child's brain, the United States (US) Food and Drug Administration and the Environmental Protection Agency issued a statement in 2001 recommending pregnant women limit their fish consumption to one meal per week. There has been significant evidence linking fish consumption during pregnancy to better neurodevelopmental outcomes over the following years. Thus, the US government agencies have revised their recommendations for pregnant women to include more fish in their diets. The purpose of this case study is not only to demonstrate the importance of policies in shaping nutritional habits, but also to demonstrate the potential of scientific studies to inform those policies, thereby improving neurodevelopment outcomes. In light of advances in our understanding of nutrition and the brain, such policies may need to be revisited. A policy or program addressing nutrient deficiencies that affect brain development and function may also be needed for some populations. If ASF is not included in a child's diet during early development, either through choice or lack of access, the long-term effects on their brains and other biochemical functions could be irreversible. There may be a need to supplement nutrients such as B12, iron, zinc, and long-chain fatty acids in vegetarian or vegan diets. Through programs and policies that increase consumption of ASFs, especially during pregnancy, lactation, and childhood, we can also ensure access to ASFs for those without access to them due to poverty and infectious diseases. It is crucial that multinational/global research efforts account for the cultural, agricultural, and socioeconomic differences among nations. Malnutrition is largely seen as a resource-allocation problem, however those who believe it is primarily a brain problem are clearly unaware of the growing problem caused by overnutrition.

## Acknowledgements

None.

## Conflict of Interest

None.

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