

The Role of Diet in Maintaining Strong Brain Health by Taking the Advantage of the Gut-brain Axis

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Abstract A healthy and diverse gut microbiota is essential for host health. Recent studies indicate that the gut microbiota play a significant role in signaling the gut-brain axis, and thereby having a significant impact on the brain, which is a part of the central nervous system (CNS). As the concept of the gut-brain-axis is now relatively well-established, attention has turned to the effects of diets on the gut-brain-axis. While functions of the gut-brain-axis have been studied, the potential impact of diet on brain health, as part of the gut-brain-axis, remains underexplored. Indeed, a limited body of evidence supports a role for diet, prebiotics, and probiotics in influencing the gut-brain-axis. This review focuses on nutrients and bio-active substances such as iron, fiber, short chain fatty acids, vitamins, polyphenols, zinc, and probiotics and their protective effects on brain health. Understanding the influence of diet on the gut-brain-axis will shed light on the conditions wherein brain health can be maintained by altering diet.

Keywords: *microbiota, gut-brain axis, nutrition, diet, brain, fatty acids*

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1. Introduction

There are multiple bacterial species in the gut and they play a crucial role in the metabolism of various categories of food materials [1,2]. Although the "normal" gut microbiota is predominantly bacterial, variety of other microorganisms is also present and include yeasts, archaea, single-celled eukaryotes, and viruses, such as bacteriophages [3,4,5]. There are approximately 100 trillion commensal bacteria residing within the human gastrointestinal (GI) tract and they continually stimulate the intestinal mucosal surface [6]. These microorganisms perform various functions that are important for host health, such as synthesis of vitamins, digestion of the complex indigestible polysaccharides, and food processing [7]. This review aims to explore multiple aspects of the role of diet, gut microbiota, and health of the gut microbiota population, to provide indications on the opportunities as well as the knowledge gaps in this field.

2. Gut Microbiota

At the basic level, the association between the gut microbiota and the human host is a symbiotic relationship wherein the host intestine offers an environment for the bacteria to grow while the bacteria help homeostatic control in the host body [8]. The gut microbiota are essential for digestion as well as absorption, and energy,

vitamin K2, short chain fatty acids (SCFAs), and folate [9,10,11] production for the host. In addition, complex carbohydrates digested in the human large intestine are fermented by anaerobic intestinal microbiota to form SCFAs such as propionate, acetate, and N-butyrate [12]. The gut microbiota also modulates intestinal motility, neutralize carcinogens and drugs, and enhance host immune system [13]. In the absence of healthy microbiota, this relationship between the microbiota and the host deteriorates and may finally lead to conditions such as neuropsychological [14], metabolic, and gastrointestinal disorders [15]. Several studies on metabolic, gastrointestinal, and neuropsychological disorders have identified an association between the gut-brain axis, and dysfunction and disease [16,17]; specifically, associations have been reported between altered microbiota and neuropsychological disorders such as depression [14] and autism spectrum diseases [18], gastrointestinal disorders such as irritable bowel syndrome and inflammatory bowel disease, and metabolic disorders such as obesity [15,19].

3. The Gut-brain Axis

Communication between the brain and the gut, also referred to as the gut-brain axis, refers to a bi-directional communication system that involves neural pathways, such as the enteric nervous system, spinal and sympathetic nerves, and the Vagus and the humoral pathways, and comprises hormones, cytokines, neuropeptides, and other signaling molecules [20,21,22]. The enteric nervous

system controls all the functions of the gut such as absorption, motility, secretion, and blood flow and, therefore, is a crucial element of the gut-brain axis that is strategically located at the interface between the brain and the gut [21,23]. Recent studies have demonstrated that gut microbiota control the host brain functions via the gut-brain axis, thereby having a significant impact on maintaining the mental health [24,25,26].

4. Role of Gut Microbiomes in Brain Health

Gut bacteria can directly stimulate the afferent neurons of the enteric nervous system to signal the human brain through the Vagus nerve [27]. Gut microbes can affect mood, memory, as well as cognition [28], and are therapeutically and clinically related to various disorders such as chronic fatigue syndrome, alcoholism, restless legs syndrome, and fibromyalgia [29,30]. Equally, any changes in the gut microbiome composition are relayed to the CNS via the Vagus nerve and such communication can have an impact on cognition, behavior, and stress reactivity [31]. Moreover, gut microbiota can synthesize and degrade various neurotransmitters such as noradrenaline, serotonin, acetylcholine, and gamma-aminobutyric acid (GABA) [32,33]. The production of neurotransmitters may affect neurotransmitter levels in the CNS, thereby affecting the performance of the central nervous system [34].

Importantly, the effects of microbiota on the gut-brain axis are being increasingly implicated in conditions such as depression and anxiety [35,36,37,38]. Currently, various findings regarding sociability, anxiety, depression, stress, among others, are becoming essential for a comprehensive understanding of metabolic and eating disorders. For example, a research study has reported a strong correlation between the composition and diversity of gut microbiota in people with anorexia nervosa at inpatient admission and levels of anxiety, depression, and eating disorder psychopathology [39]. Moreover, various food-related behavioral outcomes influenced by the microbiota-gut-brain axis are always mediated via pathways that are similar to those of the gut microbiota interactions with host appetite and metabolism, along with immune system modulation [40], signaling via the vagus nerve, and neurochemical production [41].

5. Impact of Diet on Gut Microbiomes and Brain Health

Gut microbiota are essential as they facilitate the break-down of specific nutrients, which are further metabolized by the host cells, and it is quite interesting that most of these products have functions that are closely related to the nervous system. Specifically, gut bacteria generate amino acids, such as tryptophan, GABA, as well as monoamines, such as histamine, dopamine, and serotonin; these molecules play crucial roles within the brain as either precursors to or as neurotransmitters [42,43]. Although they are likely to target the central nervous system (CNS) after transport through the blood

stream, it is also highly possible that these neuroactive molecules affect neurons in the enteric nervous system, which is part of the peripheral nervous system [44,45]. Currently, there is an increasing recognition of the role played by diet as well as other environmental factors in regulating both the composition and the metabolic activities of human gut microbiota, which then ultimately affect human health [46,47].

Epidemiologic and experimental evidence indicate that dietary factors play a crucial role in the development of depression [48,49]. Probiotics and gut microbiota can alter cytokine levels, which may affect brain function [50]. Moreover, the vagus nerve as well as tryptophan, a precursor of serotonin, signal changes in gut microbiota to the human brain [51,52]. It is well-established that diet significantly alters the composition and function of host gut microbiota [53]. However, the health of the gut also determines what the host can extract from the diet consumed and this ranges from nutrients to bio-active signaling molecules such as vitamins, neuro-metabolites, and SCFAs [54]. Most of these molecules, including GABA and serotonin, can not only modulate neural signaling in the enteric nervous system (ENS) but also influence both host behavior and brain function [55].

The brain experiences a high nutrient- and metabolic turnover, and it is considered a high maintenance organ, based on the optimal intake of nutrients [56]. Compared to diets with a single nutrient, balanced diets are beneficial to brain function [57]. Nutrients also encompass bio-active compounds that are crucial for human health and functioning [58,59]. In the entire life of a human being, adequate nutrition plays a crucial role in ensuring continued brain health as increasing evidence indicates that specific dietary patterns, such as greater consumption of vegetables and fruits, fish and fish products, are especially beneficial [60,61]. Moreover, proper consumption of Mediterranean diets (characterized by consumption of whole grains, fruits, fish, olive oil, and vegetables) is associated with lower risks of Alzheimer's disease as and slower progression of symptoms from the mild cognitive impairment to overt Alzheimer's disease [62]. Reports also indicate that nutrients like B vitamins and omega-3 fatty acids are beneficial to brain health and its functioning [63,64,57]. Furthermore, the deficiency of these nutrients may adversely affect cognitive performance of an individual. Multiple nutrients need to be acquired from food as adequate amounts cannot be synthesized internally in the body [65].

6. Role of Fiber

Many studies have demonstrated that the gut microbiota is associated with depression as it can affect inflammation, stress response, oxidative stress, and neurotransmitters such as serotonin [66,67]. Fiber consumption patterns can change intestinal flora composition, and bacteria along the gastrointestinal tract communicate effectively with CNS [68]. Moreover, neuroactive bacterial metabolites of dietary fibers and saturated chain fiber acids can modulate behavior and the brain of an individual [69]. Many reports also indicate that diets with high fiber content enhance circulatory levels of butyrate, which can then affect CNS functioning

[70,71], and foods with lower dietary fiber content are associated with lesser microbial diversity, anti-pathogenic bacterial numbers, and short chain fatty acid levels; elements that have unhealthy long-term effects on the host [72,73].

Multiple studies have evaluated the significance of high dietary fiber on cognition and the memory [74,75] and have reported that the microbiome and/or the diet can be manipulated to improve the brain function. For instance, children consuming diets with high fiber exhibit better cognition control compared to children whose diet has low fiber content [76]. Additionally, studies that have examined the relationship between individual dietary patterns and depression have partially supported the observed lower odds for the development of symptoms of depression in individuals with greater dietary fiber intake (e.g., fruits and vegetables) [77,78]. Fruit and vegetable intake has also been linked to lower risk or prevalence of depression in some prospective and cross-sectional studies [79,80] and fruits and vegetables are considered key contributors of dietary patterns that exhibit an inverse relationship with depression [81].

Dietary modifications, especially in intake of fiber from vegetables, fruits, and other plants, are likely to change intestinal microbiotic profile [82]. The SCFAs that are generated by fermentation of dietary fiber by intestinal microbiota have been reported to prevent inflammation, which is a factor that controls depression [83]. People can achieve adequate intake of dietary fiber by increasing the intake of plant foods, such as nuts, legumes, whole grains, fruits, and vegetables, which also reduce energy consumption from processed diets that are rich in sugar, fat, and refined carbohydrates. Moreover, intake of dietary fiber and higher intake of plant-based foods also appears to prevent bacteria from generating toxic metabolites from proteins [84]. Some of the sources of fiber includes beans, whole grains, brown rice, popcorn, nuts (almonds, pecans, walnuts, etc.), baked potato, berries, bran cereal, oatmeal, and vegetables [85].

7. Role of Vitamins

Studies have reported an association between intake of diets with higher vitamin E content and a reduction in risk or prevalence of AD and cognitive decline [86]. Various observational studies have also indicated that lower levels of vitamin B6, vitamin B12 and folate are linked to cognitive reduction in aging [87,88,89]. Moreover, low dietary intake and status of vitamin B12 levels have been associated with greater risk of depression [90] and published studies shown the significance of vitamin B12 supplementation in lowering the prevalence of neurodevelopmental disorders [91,92]. It has been reported that there is a relation between maternal vitamin B12 status and the offspring cognition abilities [93]. Vitamin B12 is predominantly derived from food of animal origin [94,95] and vegetarians may be at risk of deficiency. This micronutrient is a crucial for proper brain development and is linked to one-carbon metabolism that is essential for transmethylation reactions. Moreover, vitamin B12 is popular for its significant role in enhancing brain function across ages and for the prevention of CNS development disorders, mood disorders, and dementias such as vascular dementia and Alzheimer's disease in the elderly [96,97].

Vitamin D is a nuclear steroid hormone that has various physiological roles [98,99]. Epidemiological studies have also associated vitamin D levels to various brain-related outcomes [100]. Notably, while low concentrations of vitamin D levels are linked to impaired cognitive functions, including orientation and memory, Alzheimer's disease, and dementia diagnosis [101], higher dietary vitamin D intake is linked to lower self-reported psychotic experiences [102]. Multiple studies also indicate that there is a relation between lower levels of vitamin D status and depressive symptoms [103,104].

8. Role of Polyphenols

Damage to brain macro-molecules and oxidative stress are significant processes in neurodegenerative disease development [105]. As polyphenols are naturally highly antioxidative, their intake may offer protection against neurological disease development [106]. In addition, dietary polyphenols and antioxidant vitamins can be beneficial in oxidative stress regulation [107,108]. Polyphenols are ubiquitous and diverse non-nutritious compounds found in plant foods that have various physiological effects on the body [109,110]. Studies have indicated that polyphenol administration offers protection against Parkinson's disease [111], and ferulic acid, a maize bran-derived polyphenol, has been reported to be beneficial in reducing Alzheimer's disease, because of its anti-inflammatory and antioxidant properties [112].

Table 1. Sources of Polyphenol [115]

| Type | Source (Serving size:100g) | Polyphenol content (mgs) |
|-----------------------|-------------------------------|-----------------------------|
| Chocolate or cocoa | Dark chocolate | 1,664 |
| | Cocoa powder | 3,448 |
| Cloves and seasonings | Cloves | 15,188 |
| | Dried peppermint | 11,960 |
| | Star anise | 5,460 |
| Non-berry fruits | Plums | 377 |
| | Black currants | 758 |
| | Apples | 136 |
| | Sweet cherries | 274 |
| Berries | High bush blueberries | 560 |
| | Black chokeberry | 1700 |
| | Strawberries | 235 |
| | Blackberries | 260 |
| | Red raspberries | 215 |
| Nuts | Hazelnuts | 495 |
| | Almonds | 187 |
| | Walnuts | 28 |
| | Pecans | 493 |
| Beans | Black beans | 59 |
| | white beans | 51 |
| Tea | Black tea | 102 |
| | Green tea | 89 |
| Vegetables | Chicory | 166–235 |
| | Artichokes | 260 |
| | Spinach | 119 |
| | Red onions | 168 |
| Soy | Soy tempeh | 148 |
| | Soybean sprouts | 15 |
| | Soy yogurt | 84 |
| | Tofu | 42 |
| | Soy flour | 466 |
| Wine | Red wine | 101 |

Polyphenols are derived from vegetables, fruits, beverages, and other plant-derived foods. Significant quantities of polyphenols are found in colorful fruits such as tomatoes, blueberries, and grapes, herbs, tea, spices, and olive oil. Fruit and vegetable polyphenols seem to be invaluable agents of neuro-protection, as they can modulate various cellular processes such as apoptosis, signaling, differentiation, proliferation, and redox balance [113,114]. Table 1 shows the amount of polyphenol available in various foods. Unless stated otherwise, the amounts are presented in milligrams (mg)/ 100 grams (g) of the food.

9. Role of Zinc

Zinc is considered as one of the most predominant metal ions in the brain as it plays a role in neuronal migration, regulation of both neurogenesis and differentiation, thereby shaping cognitive development and maintaining normal brain functioning [116,117]. Moreover, zinc serves not only in intra-glial and intra-neuronal functions but also in synaptic neuro-transmission. Zinc homeostasis in the human brain is modulated by the blood-cerebrospinal fluid and blood brain barriers, and is not easily altered due to dietary zinc deficiency [118].

Table 2. Sources of Zinc [124]

| Type, food (serving size 100 gr) | Zinc content (mgs) |
|--|--------------------|
| Mollusks, oyster, eastern, canned | 90.95 |
| Mollusks, oyster, eastern, wild, cooked | 78.6 |
| Beverages, chocolate powder, no sugar added | 13.64 |
| Beef, chuck, short ribs, boneless, cooked | 12.28 |
| Seeds, sesame flour, high-fat | 10.67 |
| Seeds, pumpkin and squash seeds, roasted | 10.3 |
| Lamb, shoulder, trimmed to 1/4" fat, cooked | 8.06 |
| Spices, poppy seed | 7.9 |
| Seeds, sesame seeds, whole, dried | 7.75 |
| Egg, yolk, dried | 7.73 |
| Mushrooms, shiitake, dried | 7.66 |
| Spices, cardamom | 7.47 |
| Pork, fresh, cooked, braised | 6.72 |
| Peanuts, oil-roasted, with salt | 6.62 |
| Chicken, broilers or fryers, giblets, cooked | 6.27 |
| Spices, mustard seed, ground | 6.08 |
| Nuts, cashew nuts, raw | 5.78 |
| Chicken, broilers or fryers, giblets, cooked | 6.27 |
| Ostrich, oyster, cooked | 4.94 |
| Tofu, dried-frozen | 4.9 |
| Soybeans, mature seeds, raw | 4.89 |
| Turkey, all classes, heart, cooked | 4.6 |
| Nuts, pecans | 4.53 |
| Nuts, cashew nuts, raw | 5.78 |
| Seeds, flaxseed | 4.34 |
| Spices, paprika | 4.33 |
| Cheese, American, nonfat or fat free | 4.11 |
| Milk, dry, nonfat, regular | 4.08 |
| Spices, onion powder | 4.05 |
| Egg, whole, dried | 3.15 |
| Nuts, almonds | 3.12 |
| Barley, hulled | 2.77 |
| Turkey, whole, meat and skin, cooked | 2.48 |

Deficiency of zinc can have an impact on cognitive development as it alters attention, neuro-psychological behavior, activity, and motor development [119,120]. Zinc deficiency and gut inflammation are also associated with psychological and physiological stress as animal studies have indicated that psychological stress reduce the levels

of serum zinc [121]. Alterations in zinc homeostasis in the brain may be due to neurological disorders such as Parkinson's disease, Alzheimer's disease, or amyotrophic lateral sclerosis, wherein oxidative stress is implicated as the cause [122]. A study conducted on elderly adults involved more than 800 elderly patients in Europe and reported that there is an association between higher zinc levels and the aging of healthy brain [123]. Commonly, zinc in the diet is derived from consumable foods such as grains, beans, nuts, as well as high protein diets such as lamb, beef, and pork. Table 2 shows some of the foods reported to have high zinc content (in milligrams).

10. Role of Iron

Iron plays a crucial role in ensuring normal glial and neuronal energy metabolism, neurotransmitter production, as well as myelination [125,126]. Iron is crucial for multiple processes in the body [127,128], including mitochondrial function, oxygen transport, synthesis of DNA, ATP production (energy transfer and storage molecule within a cell), and cellular protection from oxidative damage [129]. Moreover, iron is needed as a co-factor for enzyme activity [130] involved brain functions such as myelination, neurotransmitter synthesis such as serotonin (tryptophan hydroxylase) and dopamine (tyrosine hydroxylase), the latter is a precursor to both norepinephrine and adrenaline [131].

Table 3. Sources of Iron [134]

| Type, food (serving size 100 gr) | Iron content (mgs) |
|--|--------------------|
| Spices, thyme, dried | 123.6 |
| Spices, basil, dried | 89.8 |
| Spearmint, dried | 87.47 |
| Spices, cumin seed | 66.36 |
| Spices, turmeric, ground | 55 |
| Beef, variety meats and by-products, raw | 44.55 |
| Lamb, variety meats and by-products, raw | 41.89 |
| Spices, anise seed | 36.96 |
| Cocoa, dry powder, unsweetened | 36 |
| Spices, fenugreek seed | 33.53 |
| Seaweed, spirulina, dried | 28.5 |
| Spices, coriander seed | 16.32 |
| Soy protein isolate | 14.5 |
| Spices, cardamom | 13.97 |
| Mushrooms, morel, raw | 12.18 |
| Chocolate, dark, 70-85% cacao solids | 11.9 |
| Fish, caviar, black and red, granular | 11.88 |
| Egg, yolk, dried | 9.56 |
| Turkey, all classes, cooked, simmered | 6.96 |
| Mollusks, oyster, eastern, cooked | 6.95 |
| Beans, kidney, red, mature seeds, raw | 6.69 |
| Nuts, cashew nuts, raw | 6.68 |
| Lentils, raw | 6.51 |
| Rice, white, long-grain, precooked | 6.3 |
| Spices, garlic powder | 5.65 |
| Ostrich, oyster, cooked | 4.9 |
| Tofu, fried | 4.87 |
| Barley malt flour | 4.71 |
| Pork, fresh, variety meats, raw | 4.68 |
| Soybeans, mature seeds, dry roasted | 3.95 |
| Nuts, almonds | 3.71 |
| Bread, wheat | 3.6 |
| Mushrooms, Chanterelle, raw | 3.47 |
| Pasta, dry, enriched | 3.3 |
| Fish, anchovy, raw | 3.25 |

Iron supplementation acts as an illustration of the emerging complex association between host immune system, diet, as well as the gut microbiota, which has further downstream consequences for gut homeostasis [132]. Studies have shown that most depressive symptoms in iron deficiency anemia patients may be resolved through supplementation of iron and that this occurs before improvements in indicators such as red blood cell count, among others, are visible. Seemingly, this phenomenon is caused by enhanced neurotransmitter levels as well as improvement in iron-dependent enzyme activity, which is different from hemoglobin concentration [133]. Beans and lentils, whole-grain, baked potatoes, enriched breads, cashews, Tofu, fortified breakfast cereals, and dark green leafy vegetables such as spinach are most recommended plant sources of iron. Other sources include split peas, nuts, whole grains, seeds, and dried fruits. Table 3 shows foods that contain the highest quantities of iron.

11. Role of Fat

Essential fatty acids (EFAs) are indispensable for normal brain development [135]. EFAs are also constituent molecules of cellular phospholipid membranes. EFAs such as alpha linolenic and linoleic acids should be provided through the diet as they cannot be synthesized by the body [136]. Several studies have established that dietary saturated fatty acid consumption (SFAs) can influence brain neurochemistry and function [137,138]. Most importantly, saturated fatty acids have been proven to impair several mood-regulating circuits in the brain, e.g. feeding behavior and neuro-inflammation [139]. On the other hand, polyunsaturated fatty acids are essential for maintaining cognitive function and are also preventive against dementia via their anti-inflammatory and antithrombotic properties, along with their effect on neural functions [140].

Polyunsaturated fatty acids (PUFAs) play a number of important roles in the CNS, and these include glucose homeostasis and food intake regulation, and regulating neurotransmission, apoptosis, emotional behavior, and neuroinflammation [141,142]. Omega-3 PUFAs help in brain development, behavioral functions, and enabling cognitive development and they regulate several neurotransmitter functions, including signal transduction, responsivity, and phospholipid turnover [143]. Fatty acids have been reported to play a significant role in psychiatric disorders but are also involved in preventing neuronal death and prevention or reduction of neuroinflammation [144]. Reports also indicate that when adults consume Omega-3 PUFAs as part of their diet, their depressive symptoms may be lowered [145].

Like Omega-3 PUFAs, omega-6 PUFAs are essential as they influence brain function, growth, and development [146,147]. Brain EFA metabolites such as docosahexaenoic acid (DHA) [148], eicosapentaenoic acid (EPA), and arachidonic acid (AA) are also essential [149]. Sufficient omega-3 polyunsaturated fatty acid status is required for the maintenance of neuronal function and integrity. DHA may directly be involved in the enhancement of an aging brain's neuronal health [150]. DHA may also alter gene

expression that regulates various potentially essential biological functions in cognitive health, including neuronal function and neurogenesis. It should be noted that any changes in the composition of brain fatty acids that are predominantly caused by alterations in the amount of fat consumed through the diet, are closely related to the impaired emotional behavior [151].

High-fat diets increase anxiety with discerning interruptions in cognitive and exploratory behaviors [152,153]. In addition, they increase circulatory lymphocyte numbers and endotoxin expression [154]. However, studies suggest that the consumption of monounsaturated fatty acids can improve overall functioning of the brain. For instance, observations made by Sartorius and collaborators show that exposure of a diet enriched with monounsaturated fatty acids (MUFA) for a period of eight weeks led to an improvement in insulin signaling in the mouse brain [155].

The main dietary source of DHA and EPA is fatty fish. In fact, DHA and EPA synthesis occurs in animals and phytoplankton but not in plants [156]. Furthermore, EPA and DHA are absent in all vegetable oils and fats, including seeds, grains, and nuts, and in ruminant fats, including in milk and dairy products. Fish and sea foods are the richest dietary sources, but poultry and eggs are also important sources that provide lower levels of DHA and EPA [157]. Major dietary sources of alpha linolenic acid (ALA) are canola oils and soybean; some nuts and flax seed oils are also high in ALA, but usually these latter sources are consumed neither consistently nor in large quantities or consistently [158]. The primary sources of SFAs in the modern diet are eggs, dairy products, and fatty meats [159]. Food sources of SCFAs include: (a) pectin from apricots, apples, carrots, blackberries, and oranges, (b) resistant starches from barley, whole-grain, lentils, brown rice, beans, pasta or cooked and cooled potatoes, and green bananas, (c) guar gum, (d) arabinoxylan, and (e) inulin and fructooligosaccharides (FOS) from onions, wheat, Jerusalem artichokes, leeks, rye, and asparagus. MUFAs are present in a variety of foods and oils such as canola and olive oil, hazelnuts, avocados, pecans, and almonds [160]. Major sources of N-3 PUFAs are fatty fish, walnuts, green leafy vegetables, and a variety of seeds whereas n-6 PUFAs are found in seeds of most oils and plants, such as sunflower, cottonseed, and corn, among others [161]. Processed liquid cooking oils are the most damaging PUFAs, for example soybean oil, canola oil, corn oil, generic vegetable oil, grape seed oil, sesame oil, walnuts oil, flaxseed oil, cottonseed oil, margarine, and peanut oil.

12. Role of Probiotics

Probiotics are live microorganisms which when consumed in sufficient numbers provide a specific benefit to health [162]. Most of the probiotics belong to one of two types-*Bifidobacteria* or *Lactobacillus*. Some of *Bifidobacteria* and *Lactobacilli* strains act as antioxidants that protect brain cells from free radical damage [163]. These live bacteria in probiotics provide many benefits which include effects on the ENS present in the GI tract [164]. Symptoms of depression, anxiety, obsessive-compulsive disorder, and autism have been reported to be reduced by

probiotics, thereby leading to memory improvement, according to a review of 38 studies [165], and a meta-analysis of 96 trials found that significant reduction in depression was associated with probiotic consumption [166].

Evidence also exists to show that regular probiotic consumption may positively modify gut microbiota profile and population, which may then influence immune function, proliferation of intestinal epithelium cells, and their protection and function [167]. Consumption of probiotics and fermented foods enriched with *Bifidobacteria* spp. and *Lactobacillus* spp. may cause specific changes in gut activity suggesting that the diet may be a feasible means of modifying the gut microbiota profile [168].

The most sustainable way to increase the number of healthy gut bacteria is consumption of probiotic foods (foods containing beneficial microbes). Virtually all traditional healthy diets wisely contained fermented foods having *Bifidobacterium*, and *Lactobacillus* spp., which are the mainstays of psychobiotic and probiotic supplements [169]. To naturally boost friendly flora, one needs to add these to their diet; (a) fermented vegetables such as pickles, kimchi, and sauerkraut, (b) fermented soy foods, including miso, tamari, and tempeh, and (c) fermented dairy products such as kefir and yogurt [170]. *Prebiotics alone may also reduce perceived levels of depression, stress, and anxiety [132]. Whereas all plant foods contain fiber, foods with particularly high prebiotic fiber content include bamboo shoots, artichokes, bananas, asparagus, barley, chicory coffee, black pepper, dark chocolate, beets, fennel root, broccoli, endive, Jerusalem artichokes, mustard greens, ginger, onions, garlic, tomatoes, jicama, yacón (a natural sweetener), leeks, and legumes (especially lentils and lima beans).*

13. Conclusion

Gut microbiota serve a crucial role in the gut-brain axis and have a significant impact on the CNS. The GI tract and the brain are connected through the Vagus nerve and more information is sent to the brain by the gut than what the gut receives from the brain. Therefore, disturbances in the gut can directly lead to issues such as depression, autism, and anxiety. This review presented the effects of nutrients such as iron, fiber, SCFAs, vitamins, polyphenols, zinc, and probiotics on the gut-brain-axis, which in turn can affect the health of the brain. Understanding the role of diet and its influence on the gut-brain-axis will provide important insights into maintaining brain health.

Conflicts of Interest

The authors declare that there is no conflict of interest.

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