ACNM
Annals of Clinical Nutrition and Metabolism

Ann Clin Nutr Metab 2024;16:112-119
https://doi.org/10.15747/ACNM.2024.16.3.112
eISSN 2799-8363

Review

Mental health and micronutrients: a narrative review

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Abstract

Purpose: It aims to summarizes the evidence for the association between specific individual nutrients and mental disorders, focusing on vitamin B12 and related B vitamins, vitamin D, probiotics, and zinc.

Current concept: Vitamin D deficiency is linked to depression, anxiety, and cognitive decline. Vitamin D enhances serotonin synthesis, has anti-inflammatory and neuroprotective effects, and regulates the hypothalamic-pituitary-adrenal axis and circadian rhythms. Vitamin B12 deficiency causes neurological dysfunction, mood disorders, cognitive decline, and psychotic symptoms, especially in the elderly. Vitamin B12 is involved in myelin formation, neurotransmitter synthesis, and preventing homocysteine-related neurodegeneration. Zinc deficiency affects neurotransmitters, neurogenesis, and antioxidant function, contributing to depression, anxiety, and cognitive impairment. Zinc supplementation improves symptoms and increases brain-derived neurotrophic factor levels. The gut-brain axis involves bidirectional communication between the gut microbiome and the central nervous system via the vagus nerve, enteric nervous system, immune system, and neuroendocrine pathways. Probiotics can modulate the gut microbiome to improve depression, anxiety, stress response, and cognitive function by influencing neurotransmitter production, reducing inflammation, and supporting the gut-brain connection.

Conclusion: Nutritional interventions, including vitamin D, B12, zinc, and probiotics, show promise as adjunctive therapies or preventive strategies for mental disorders. These nutrients have specific mechanisms of action on brain function and the gut-brain axis. Further research is needed to establish optimal dosage, timing, and administration methods for these nutritional approaches in supporting mental health.

Keywords: Dietary supplements; Mental health; Micronutrients

Introduction

Nutrition plays an important role in maintaining the functioning of the body's various organs, as well as brain health and even mental health. Westernized dietary habits have led to an abundance of macronutrients and a relative lack of micronutrients such as vitamins and minerals. Especially in the elderly, systemic chronic inflammation and anorexia, which is caused by aging, are often accompanied by poor nutrition and nutritional imbalances. Anxiety, depression, sleep disorders, and cognitive dysfunction are common among the elderly, as is delirium following an acute illness or exacerbation of an underlying condition. Malnutrition and cognitive dysfunction, an important determinant of quality of life in the elderly, are highly correlated in both acute and chronic conditions [1]. In this review, we summarize the evidence for the association of specific individual nutrients with mental disorders, rather than just protein-calorie malnutrition.

Among the individual nutrients known to be associated with mental health, we look at vitamin B12 and related B vitamins, which are essential for brain function; vitamin D, the lack of which is widely associated with depression; probiotics, which activate the gut-brain axis by modulating the gut microbiota to produce neurotransmitters related to gut mucosal health and their effects on immunity; and zinc, which has been meaningfully used in short-term nutrition interven-

Received: November 13, 2024; **Revised:** November 18, 2024; **Accepted:** November 18, 2024

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tions for elderly patients in acute medical conditions.

Vitamin D

Vitamin D is known as a fat-soluble vitamin, but it is also recognized as a steroid hormone and plays a role in regulating calcium metabolism and skeletal homeostasis. In addition to bone health issues, deficiencies have been linked to immune dysfunction, inflammatory responses and cancer development, and have been shown to affect mental health [2-9].

Depression due to vitamin D deficiency is frequently reported in modern urban dwellers and the elderly, especially during the winter months when sun exposure is low. This is called seasonal affective disorder and seems to be related to a decrease in vitamin D synthesis in the skin. Vitamin D is the only vitamin that can be synthesized in the body. In the skin, 7-dehydrocholesterol is produced from pre-vitamin D3 by ultraviolet B (UVB 290–315 nm) light, followed by vitamin D3. After being processed and stored as 25(OH)D3 in the liver, the kidneys produce the active vitamin D metabolite 1,25(OH)2D3, which is utilized by the body [10].

Vitamin D deficiency has been linked to depression, as well as anxiety and cognitive decline [10,11].

Several studies have shown that vitamin D deficiency increases the risk of depression, and vitamin D supplementation therapy has been associated with some improvement in depressive symptoms in meta-analyses [2,3,5,8].

Vitamin D deficiency in older adults is associated with cognitive decline and an increased risk of dementia and Alzheimer's disease, with a 54% increased risk of dementia in the severe vitamin D deficiency group (serum levels <10 ng/mL). Increasing serum vitamin D levels into the optimal range improves memory, concentration, and information processing speed [2].

How vitamin D affects mental health

Neurotransmitter regulation

The active form of vitamin D, 1,25-dihydroxyvitamin D3, enhances the expression of tryptophan hydroxylase type 2, an enzyme essential for serotonin synthesis. Decreased synthesis of serotonin, the most important neurotransmitter for mood regulation, is associated with increased incidence of depression and anxiety. Since most serotonin in the human body is produced by gut cells, we can also consider the possibility of vitamin D's indirect contribution to the gut-brain axis, which has recently gained attention [3]. Vitamin D is involved in the management of dopamine and noradrenaline, which contribute to stress response and mood stabilization.

Anti-inflammatory action and immune modulation

Vitamin D has anti-inflammatory effects by reducing the production of pro-inflammatory cytokines in the brain, which is a major contributor to cognitive decline. Chronic inflammation in the brain can lead to depression, anxiety, cognitive dysfunction, and even damage and degenerative changes in nerve cells. The anti-inflammatory effects of vitamin D can effectively prevent nerve cell damage.

Animal studies have shown that vitamin D deficiency increases radical oxygen species (ROS) production and resting calcium ion concentrations in central nervous system (CNS) terminals, leading to a proinflammatory shift and presynaptic dysfunction. The resulting imbalance of neuronal excitatory and inhibitory activity has been observed, and vitamin D supplementation has been shown to reverse most of these changes [12].

Neuroprotective effects

Vitamin D promotes the release of neurotrophic factors, including nerve growth factor and brain-derived neurotrophic factor (BDNF). Neurotrophic factors play a role in neuronal survival, differentiation, and repair, which are essential for maintaining cognitive function and emotional stability. As a result, vitamin D helps protect neurons in the brain and stimulates the production of new neurons, contributing to the maintenance and improvement of cognitive function.

The antioxidant properties of vitamin D may help prevent and treat cognitive decline and mood disorders caused by oxidative stress. In animal studies, vitamin D deficiency increased ROS production in the periphery and brain and increased concentrations of resting calcium ions in cranial nerve endings. Oxidative stress increased glutamate and unstimulated gamma-aminobutyric acid (GABA) release, which reduced normal neurotransmitter release, but was significantly reversed by vitamin D supplementation, suggesting that vitamin D protects the brain from oxidative stress [12].

Vitamin D is involved in new neurogenesis in the hippocampus, the brain's center for memory and learning. Vitamin D deficiency reduces hippocampal neurogenesis, leading to memory and cognitive decline,

Hypothalamic-pituitary-adrenal axis regulation

Vitamin D manages cortisol levels by managing the hypothalamic-pituitary-adrenal axis. Elevated cortisol is associated with chronic stress, depression, and anxiety. By regulating cortisol levels, it reduces the chronic stress response.

Regulating sleep wakefulness and circadian rhythms

Vitamin D receptors are located in the brain and regulate circadian rhythms. Maintaining adequate vitamin D levels can help maintain regular sleep patterns and improve sleep disorders associated with depression and anxiety.

Supplementing with vitamin D

In addition to dietary intake, serum vitamin D can be increased by UVB exposure through sun exposure for a certain amount of time each day [4]. Adult subjects with depressive symptoms may need additional vitamin D supplementation to ensure adequate levels. On average, vitamin D supple-

mentation with 2,000 units per day or more for at least 12 weeks is effective, but studies have reported that 5,000 units per day or more for 20 weeks is adequate as adjunctive therapy [2,3,4,8].

Vitamin B12

Vitamin B12 is a water-soluble vitamin that contains cobalt, which is why it is also called cobalamin. Along with folic acid, it is involved in DNA synthesis during cell division and is essential for the production of red blood cells and the maintenance of nerve tissue. Along with folic acid, vitamin B12 has been shown to provide some protection against central nervous system developmental disorders, depression, mood disorders, cognitive dysfunction, and dementia [13,14].

Vitamin B12 is available to the body through a combination of intrinsic factors secreted by the stomach and in the upper small intestine, where it is absorbed in the terminal ileum, the last part of the small intestine. The most common causes of vitamin B12 deficiency are pernicious anemia, an immune disorder, and gastrectomy for various gastric diseases, which results in the loss of intrinsic factor production. Inflammation of the terminal ileum, such as Crohn's disease, or resection, which prevents absorption of the vitamin B12 complex, or lack of stomach acid and digestive enzymes to unbind the protein, can cause vitamin B12 deficiency [15].

Vitamin B12 is unique among the B vitamins in that it is found in animal foods such as meat, dairy, and eggs, and is not found in plants. Vegans should be aware of the potential for vitamin B12 deficiency unless they use a supplement.

Vitamin B12 deficiency is best known for its association with pernicious anemia, but relatively little attention has been paid to its neuropsychiatric complications. Neuropsychiatric complications of vitamin B12 deficiency include peripheral neuritis and psychiatric symptoms such as depression and cognitive dysfunction. Megaloblastic anemia associated with vitamin B12 deficiency, regardless of when it occurs, is completely reversible with vitamin B12 supplementation therapy. Neuropsychiatric complications of vitamin B12 deficiency, on the other hand, are likely to resolve and normalize with vitamin B12 supplementation in the early stages of the disease, but prolonged untreated disease may be irreversible despite supplementation [15-17].

Neuropsychiatric symptoms of vitamin B12 deficiency

Neurological dysfunction

Because vitamin B12 is involved in the formation of myelin, the protective sheath that surrounds nerve fibers, vitamin B12 deficiency can lead to peripheral numbness, tingling, and memory problems [14,15,17]. Elevated serum concentrations of methylmalonic acid and homocysteine, which are indirect indicators of vitamin B12 deficiency, as well as low serum vitamin B12 concentrations, are associated with the development of peripheral neuropathy [14]. A variety of peripheral nerve pain conditions benefit from vitamin B12 alone or in combination with conventional therapies [15].

Mood disorders

Vitamin B12 deficiency leads to impaired synthesis of neurotransmitters such as serotonin and dopamine, which can lead to depression [13,18]. Low serum concentrations of vitamin B12 are associated with the development of depressive symptoms, and supplementation with vitamin B12 early in the course of depression may slow the progression of depression and enhance the effectiveness of antidepressants [19].

Cognitive dysfunction

Vitamin B12 deficiency causes cognitive dysfunction, which in turn increases the risk of dementia in the elderly. Homocysteine, recognized in the 1990s as an independent risk factor for atherosclerosis, is elevated in serum concentrations with vitamin B12 deficiency. In addition to vitamin B12, folate and vitamin B6 deficiencies also increase homocysteine levels and are associated with increased risk of cardiovascular and cerebrovascular disease, as well as mental health disorders, including vascular dementia. In several observational studies, elevated homocysteine was associated with increased incidence of Alzheimer's disease and dementia [19-22]. Cerebrovascular ischemia caused by elevated homocysteine leads to focal brain atrophy, neurofibrillary tangles and amyloid plaque formation, neuronal death, and cognitive dysfunction through epigenetic mechanisms [22-24]. Adequate levels of vitamin B12 in the body are important for preventing and maintaining cognitive decline.

Developing psychotic symptoms

Severe vitamin B12 deficiency can cause acute psychotic symptoms, including apathy, agitation, difficulty concentrating, delusions of grandeur, hallucinations, and paranoia. This is caused by subacute combined degeneration of the spinal cord and is largely reversible with adequate injectable vitamin B12 supplementation [25,26].

Vitamin B12 deficiency in the elderly

Vitamin B12 deficiency is common in the elderly, affecting 10%–15% of people over the age of 60 in the Western world [17]. Diagnosis is assessed by measuring serum vitamin B12, methylmalonic acid, and homocysteine concentrations. It is important to note that vitamin B12 deficiency in the elderly can go unnoticed for a long period of time without the typical symptoms of megaloblastic anemia, which are typical of deficiency, and is often diagnosed only after the onset of neurological symptoms. In particular, symptoms such as peripheral neuritis and cognitive dysfunction due to nerve cell damage are difficult to repair if not treated early, and unlike anemia, they are irreversible even if the cause is treated.

In general, vitamin B12 deficiency is caused by pernicious anemia, intrinsic factor deficiency due to gastric resection,

chronic inflammation of the terminal small intestine due to celiac disease or Crohn's disease, malabsorption related to resection, or veganism. The cause of vitamin B12 deficiency in the elderly is a decreased amount and activity of gastric acid and digestive enzymes to digest proteins, unlike in other age groups, and therefore cannot dissociate vitamin B12 from protein. Chronic atrophic gastritis, which is common in the elderly, reduces gastric acid secretion, resulting in poor absorption of vitamin B12 due to the inability to dissociate protein-bound vitamin B12 into its free form, which cannot bind to intrinsic factors [17].

Supplemental treatment with vitamin B12

Vitamin B12 is unique among the B vitamins in that it is found in animal foods such as meat, dairy, and eggs, and is not found in plants. Vegans should be aware of the potential for vitamin B12 deficiency unless they use a supplement.

Because vitamin B12 must be combined with intrinsic factors secreted by the stomach to be absorbed and utilized in the terminal ileum, the end of the small intestine, patients who have undergone gastrectomy or terminal ileal resection need vitamin B12 supplementation just as vegetarians do. While vegetarians can effectively take the recommended dose of vitamin B12 orally, patients with gastrectomy or terminal ileal resection have little gastrointestinal absorption, so parenteral methods of administration, primarily intramuscular injections, are utilized. The elderly, like vegetarians, are not deficient in intrinsic factor nor ileal absorption capacity, enteral supplementation effective. Parenteral vitamin B12 supplementation consists of an initial course of three intramuscular injections of 1 mg once weekly, followed by maintenance therapy of 1 mg intramuscularly every 1 month. In the elderly and vegetarians without intrinsic factor deficiency, oral supplementation is used as maintenance therapy to meet the recommended daily allowance (RDA) of 2 micrograms. On the other hand, patients with pernicious anemia or gastrectomy who lack intrinsic factor and patients with distal small intestinal disease may benefit from a very high oral dose of 1 mg per day to take advantage of absorption by diffusion from the small intestinal cell [13,17].

If homocysteine levels are elevated in blood, a high-dose regimen of three B vitamins—vitamin B12, folic acid, and vitamin B6—can be used to prevent atherosclerosis and neurodegenerative disease such as Alzheimer's disease and dementia.

Zinc

Zinc is an essential mineral for immune function, protein synthesis, DNA synthesis, wound healing, and brain growth and development. It regulates the growth of an individual by affecting cell differentiation, proliferation, and apoptosis. It is the second most abundant micronutrient in the human body after iron, with about 2 to 3 grams of zinc in the human body.

Zinc deficiency affects mucosal and skin tissue composition, which can clinically slow wound healing, dull the sense of smell and taste, and cause diarrhea. Damage to the mucosal membranes impairs immunity and immune function and affects cell membrane composition, resulting in delayed growth and development in pregnancy, infants, and children. Associations with chronic metabolic diseases such as diabetes, malignancies, neurodegenerative diseases, and inflammatory bowel disease, as well as infectious diseases such as tuberculosis, HIV, malaria, and airway infections such as coronavirus disease 2019, have been reported, providing strong evidence for zinc's ability to suppress inflammatory responses and maintain immunity [27]. Zinc deficiency is associated with depression and anxiety, and there is evidence that zinc supplementation improves symptoms [28]. Bipolar disorder, Alzheimer's disease, schizophrenia, anger and violence, ADHD (attention deficit hyperactivity disorder), and Parkinson's disease have been reported to be associated with low levels of zinc in brain cells and serum [29,30].

Zinc is present in every cell in the brain and central nervous system, and it increases the concentration of BDNF, especially in the hippocampus and amygdala, brain regions associated with mood. BDNF exerts its antidepressant effects by regulating various neuropeptides, including neuropeptide Y (NPY), cholecystokinin, substance P, or galanin [31]. A 2022 meta-analysis also found that zinc supplementation consistently increased blood BDNF and zinc concentrations [32].

The role of zinc in mental health

Neurotransmitter coordination

Zinc regulates the neurotransmitters glutamate, GABA, and dopamine, which play a role in cognitive function and emotional regulation.

Neurogenesis

Several studies have shown that zinc contributes to neurogenesis, the creation of new neurons in the brain. Several metal ions, including iron, copper, and zinc, are involved in neurogenesis, but zinc is an essential component of neural stem cell proliferation, neural tissue differentiation, and neural tissue survival throughout the life cycle, from pre- and postnatal life through development and into adulthood. In addition to impaired physical growth, zinc deficiency causes cognitive decline and memory impairment, and perinatal zinc deficiency, in particular, can be irreversible and lead to long-term cognitive dysfunction if zinc supplementation is not timely. As a result, zinc is essential for maintaining learning, memory, and overall cognitive function [33].

Antioxidant benefits

Zinc's antioxidant effects protect brain cells from oxidative stress, which contributes to the prevention of various mental health disorders associated with inflammation. Zinc signals to

immune cells at the molecular level and is required for the differentiation and production of T helper cells. Zinc supplementation in the elderly has been shown to reduce infection rates, decrease both plasma oxidative stress markers and inflammatory cytokine production, and increase plasma zinc levels [34].

Zinc supplementation therapy

The RDA for zinc is 11 mg for adult men. One study reported significant improvements in depression and anxiety in older adults who took a zinc supplement of 30 mg per day for 70 days compared to a control group that did not take the supplement. Zinc supplementation may be considered for the prevention or adjunctive treatment of depression and anxiety, which are common in older adults [35]. As an adjunctive treatment to antidepressants, 25 mg of zinc per day for 6–12 weeks had positive effects on depressive symptoms [36], suggesting that zinc may be recommended as an adjunctive treatment for depression and anxiety, either alone or in combination [28].

Probiotics

The gut-brain axis and the gut microbiome

The role of the digestive system, particularly the gut microbiome, has been emphasized, as neuroinflammation has been implicated in the development of CNS diseases and certain nutrients can prevent or ameliorate depression, anxiety, stress, and cognitive decline [37,38]. The gut microbiome forms a "gut-brain axis," in which the various microbes that live in the gut send and receive signals to and from the central nervous system, creating a system of interaction between the gastrointestinal tract and the central nervous system [39].

Bidirectional communication between the brain and gut microbiota occurs through multiple pathways, including the vagus nerve, enteric nervous system (ENS), immune system, and neuroendocrine system. A variety of neuroactive compounds are at play, including microbial-derived metabolites, peptides, gut hormones, and neuroactive substances. When metabolites reach the brain, they affect neuronal development and regeneration, potentially contributing to a variety of psychiatric disorders and neurodegenerative diseases, including Parkinson's disease, Alzheimer's disease, depression, anxiety, stress, and cognitive dysfunction [39]. There are studies that suggest that probiotics can be used to prevent or improve mental illness by improving signaling in the gut-brain axis.

How the gut-brain axis works

The gut and brain are intimately connected through multiple pathways, and there are four main mechanisms of interaction [40,41].

The first is through the vagus nerve, which is the main pathway directly connecting the gut to the brain, with nerve signals traveling in both directions. It sends autonomic signals from the center to regulate intestinal motility, intestinal secretions, and the permeability of the intestinal mucosa and the gut bacterial environment. Signals from the gut are also transmitted directly to the brain via the vagus nerve, which can affect emotional states and cognitive function.

Second, gut-brain interaction occurs through the coordination of the ENS by the production of neurotransmitters. Gut microbiota contribute to the production of neurotransmitters such as serotonin, dopamine, and GABA gamma-aminobutyric acid. Serotonin is synthesized and stored mostly in enterochromaffin cells, using the essential amino acid tryptophan as a precursor, and sends signals to the brain. Short-chain fatty acids (such as butyric acid), which are metabolites of some gut bacteria, stimulate the production and release of serotonin, which affects the brain and plays an important role in emotional regulation.

Third, hormones secreted by the gut endocrine system send signals to the brain center. Gut enteroendocrine cells regulate appetite and satiety by secreting the anorexigenic hormones NPY and peptide-tyrosine-tyrosine (PYY) and the appetite-inducing hormone ghrelin. Metabolites from gut microbes can affect enteroendocrine cells and alter signals to the brain center.

Overproduction of the stress hormone cortisol activates inflammatory substances such as interferon gamma, interleukin (IL) 6, IL 1 beta, and TNF alpha, which can lead to altered intestinal membrane permeability, gut bacterial imbalance (dysbiosis), nerve damage, and depletion of BDNF, which can lead to brain dysfunction such as memory impairment [42].

Fourth, the gut's immune system is modulated by gut bacteria, which can alter signaling to the brain. The gut is an important part of the human immune system, and an unhealthy gut environment can lead to an increased systemic inflammatory response, which in turn affects the brain. The gut microbiome changes due to diet, alcohol consumption, smoking, stress, and acute systemic illness or infection. The resulting increased permeability of the intestinal mucosa allows lipopolysaccharides, an inflammatory substance derived from the cell membranes of gram-negative bacteria in the gut, to enter the bloodstream as an endotoxin, triggering immune and inflammatory responses throughout the systemic organs. In the bloodstream, it also crosses the blood brain barrier, causing neuroinflammation and degenerative changes in the brain and central nervous system, which can lead to problems such as Parkinson's disease, Alzheimer's disease, depression, and cognitive dysfunction [40].

The gut microbiome and mental health connection

There are reports of attempts to use probiotics, the so-called "good bacteria," to alter the distribution of gut microbiota to improve depression, anxiety stress response, cognitive dysfunction, and schizophrenia through the gut-brain axis.

When it comes to depression, a lack of beneficial bacteria in the gut, or an abundance of harmful bacteria, can lead to increased inflammation and decreased serotonin levels, which can increase depressive symptoms. Probiotics can be administered to improve the gut environment, which in turn can promote the production of neurotransmitters such as serotonin. Probiotics (*Lactobacillus acidophilus*, *Bifidobacterium bifidum*, *Streptococcus thermophilus*) and magnesium given to patients with depression for at least 8 weeks significantly reduced symptoms of depression, anxiety, and stress, making it a safe and effective intervention [43].

The role of the gut microbiota in modulating anxiety and stress responses appears to be supported by the fact that certain microbes respond effectively to certain symptoms. *Lactobacillus rhamnosus* (GG) has been shown in animal studies to reduce anxiety symptoms by modulating the stress response via the vagus nerve [44]. When *Lactobacillus helveticus* and *Bifidobacterium longum* were administered to hamsters, a decrease in anxiety-like behavior and an increase in the anti-inflammatory cytokines IL-4, IL-5, and IL-10 were observed after stress [45].

Gut microbes can help reduce neuroinflammation and relieve oxidative stress, which contributes to improved cognitive function and memory. This may help reduce the risk of neurodegenerative diseases such as Alzheimer's disease.

In summary, as a way to support a healthy gut-brain axis, probiotic intake can help balance the gut microbiome, reducing symptoms of depression and anxiety, relieving stress, and improving cognitive function. Those aiming to improve a specific mental symptom should choose a supplement that contains a specific strain of probiotics, such as *Lactobacillus* or *Bifidobacterium*, that is appropriate for that symptom. Taking a prebiotic, which provides food for the beneficial bacteria, can be synergistic, as it promotes the growth of the beneficial flora. To improve the functioning of the gut-brain axis, eating fermented foods such as probiotic-rich yogurt, kimchi, and sauerkraut, practicing stress management techniques such as meditation and yoga, and exercising regularly can help increase gut microbial diversity and improve the gut environment. Gut microbiota and the gut environment are highly individualized, including dietary habits and genetics, so strain selection and duration of effective use may also vary among individuals.

Probiotics are effective as a complementary therapy for the treatment of depression, anxiety, stress, and cognitive dysfunction, but further research is needed to establish treatment guidelines for the selection of the most effective strains and the duration and method of use.

Conclusion

Despite advances in psychotherapy and psychotropic medications, mental illnesses are not being overcome, and depression, anxiety, and stress disorders are on the rise. The lifestyle and environment of modern, urbanized societies have been blamed for this, and nutritional interventions have been gaining attention as an adjunctive therapy to conventional treatments or as a preventive measure. In particular, the gut-brain axis seems to play an important role in the mutual regulation of the gut, which receives and absorbs nutrients, and the brain, which controls mental disorders through direct and indirect communication. Nutrition and psychiatric disorder research has progressed from exploring the positive effects of dietary patterns, such as the Mediterranean diet, to utilizing various micronutrients and nutraceuticals to prevent mental symptoms and protect function. Among the nutrients that have been reported to have positive effects in psychiatric disorders, particularly depression, anxiety, stress, and cognitive decline, researchers have explored the mechanisms of action and effects of easily accessible vitamin D, vitamin B12, and zinc [46]. These nutrients are effective as stand-alone or adjunctive therapies for depression and anxiety, and can be used to reduce major side effects, shorten treatment duration, and prevent illness by reducing the dose of the main treatment agent. Vitamin B12 is of particular interest because deficiency is associated not only with depression but also with peripheral neuritis, cognitive dysfunction, and psychotic symptoms, and zinc has been associated with psychotic symptoms in some studies and zinc supplementation has been reported to be effective. Probiotics, which have recently been actively studied in relation to the function of the gut-brain axis, seem to be effective by increasing neurotransmitter production and immunity, i.e., regulating brain function by regulating serotonin, which is mainly produced by gut cells, but the relationship between specific strains and depression, anxiety stress, dose, and duration of administration is still unclear.

As depression, cognitive dysfunction, and psychotic symptoms are commonly associated with malnutrition in the elderly due to acute illness, a short-term intensive nutritional intervention of two weeks, including adequate zinc, vitamin D, and antioxidants, is recommended to slow the progression of neuropsychiatric disease rather than simply improve nutritional status.

Further research is needed to determine the effectiveness of these individual nutrients as stand-alone or adjunctive therapies, as well as the dosage, timing, and method of administration.

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Conflict of interest

The author of this manuscript has no conflicts of interest to disclose.

Funding

This study was supported by a clinical research grant (No. 2023-08) from the National Center for Mental Health, Republic of Korea.

Data availability

None.

Acknowledgments

None.

Supplementary materials

None.

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