Review Article

Impact of Nutrition on Depression: A Review of Some Dietary Components with Antidepressant Effects and Their Mechanism of Action

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Abstract

Recent years have seen a surge in psychiatric diseases, which has resulted in considerable disease distress and considerably decreased living conditions. Many considerable synthetic medications have been used to treat these illnesses throughout the years, but they have been found to have limited effects and substantial recurrence risks in many individuals. Mental illnesses such as depression and anxiety are persistently on the rise around the world, posing serious challenges to the affected person's and their family members' personal lives. There is mounting evidence that suggests the gut–brain axis (GBA) contributes to the genesis and development of psychiatric diseases. This review focuses on contemporary dietary therapies such as Mediterranean diets and dietary supplements and emphasizes nutrition's critical role in psychiatric care through the GBA. Several research have indicated that dietary quality affects mental health because it controls metabolic processes, has anti-inflammatory and antiapoptotic characteristics, and promotes neurogenesis and synaptogenesis. This study demonstrates many dietary components, their relationships to depression, and how they work. The use of dietary recommendations to support mental health appears to be a novel, affordable, useful, nonpharmacological intervention for people with mental problems.

Keywords: *Dietary supplements, gastrointestinal connection, lifestyle, mental health, mental illnesses*

Introduction

With more diet-related or nutrient-oriented supplement treatment being put in place and the availability of a wealth of preclinical and epidemiological data, nutritional psychiatry has recently undergone a rapid evolution. Much work has been done recently to establish a strong connection between nutritional quality and mental health. This emerging paradigm entails using nutrient-based supplements or proper clinical inspection to modify or improve prescribed diets to prevent or treat mental health issues.[1] It is intriguing to see that the expense of numerous noncommunicable diseases, including mental illnesses, is expected to total US$47 trillion by the year 2020.[2] Because of this, there has to be a change in clinical practice and policy in the area of mental health that emphasizes the importance of nutrition.[3]

Nutritional psychiatry, the discipline of employing diets and nutrient-based dietary supplements as a treatment option for mental health issues, has developed into a viable option for clinical intervention for patients with depression and anxiety.[4] Given how frequently these illnesses occur and how they are becoming an issue for public health, it is highly likely that the prevalence of depressive illnesses will be on the rise, in the coming years. They are prevalent across all cultural contexts and pose a significant challenge to the families of those who are affected, leading to extreme suffering, impairment, and increased mortality, especially if left untreated.[5] In future, depression is anticipated to overtake cardiac diseases as the primary source of disease burden, surpassing depression as the current primary reason for disability in the world.[6] Depression is a prevalent psychological state characterized by reduced mood, loss of enjoyment or interest, decreased vitality, self-blame or sense of inferiority, disrupted eating or sleeping, and trouble focusing. These issues might intensify over time or repeat,

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which significantly impairs one's capacity to handle daily responsibilities.[7] Around the world, depression impacts over 264 million individuals across all age groups,[8] whereas Nigeria has a prevalence rate of 3.9% or 7 million people.[9] The prevalence of depression is considerable, and it may have a significant effect on one's life. Medical care and counseling can help ease symptoms in many cases, but lifestyle changes, including eating a healthy diet, can also improve one's well-being.[10]

Causes of Depression

Even though ongoing research in neurophysiology and neuropsychiatry has helped us grasp the pathophysiology of depression, the specific mechanism (s) through which it arises is still unknown. This is because depression is a diverse condition with a complicated phenomenon and a wide range of possible etiologies. Although the underlying neurobiology of depression has not yet been fully elucidated, aberrations at the molecular and cellular levels are thought to combine with hereditary and environmental variables to cause depression.[11] The development of depressive mood diseases is influenced by several factors, including environmental, psychological, and genetic factors.[12] Typically, genetics account for a sizable portion of the risk of depressed mood illnesses.[13]

Pathophysiology of Depression

The hypothalamic–pituitary–adrenal (HPA) axis dysfunction, the biogenic amine hypothesis, and genetic and environmental variables are all part of the way depression affects the body's normal functioning. Other conceivable factors comprise neurogenesis, elevated amounts of corticotrophin-releasing factor (CRF), anomalies of second messenger systems, enhanced synthesis of inflammatory cytokines (immunologic factors),[11] and alterations in the mechanisms for oxidative and nitrosative stress. No single theory fully accounts for all the indications and manifestations of depression, and it is probable that depression entails various interconnected pathological mechanisms that present as a combination of indications and manifestations that define depression. This makes it difficult to understand the pathophysiologic mechanisms by which depression occurs.[11]

Nutritional Psychiatry

A growing area known as nutritional psychiatry establishes diet and mental health relationships.[14] It is a rapidly expanding field that focuses on using diet and supplements to deliver necessary nutrients as part of an integrated or alternative approach to treating mental well-being conditions.[15] The foods we eat can affect our physical well-being, and diseases and dietary modifications may have an impact on the progression of many chronic diseases.[16] An article in the journal *Nutrients* claims that individuals who consume more fruits and vegetables are happier and more confident in their abilities.[17]

Nutritional Psychiatry and Depression

It is possible that changes to our food do not directly impact our mood or depression symptoms.[18] However, possibly a connection exists connection between diet and emotional state, which is encouraging information for the estimated over 264 million individuals globally who suffer from depression.[19] The development, intensity, and course of depression can all be significantly influenced by nutrition. Many readily observable dietary habits present before depression also exist during the depression, including things such as reduced appetite, missing meals, and a predominance of sweet food cravings.[18]

According to studies, those who adopt an improved eating pattern, such as a Mediterranean-style diet, appear to have the ability to protect against the onset of depression with time, whereas individuals who consume more fast food, sweets, and sugary beverages are at a higher risk of getting depression.[20] Lack of key nutrients, such as omega-3 fatty acids, B Vitamins, Vitamin D, magnesium, and zinc, is linked to an increased danger of depression.[21] Diets high in B vitamins, particularly folate, pyridoxine (B-6), and methylcobalamin (B-12), may be particularly useful in treating depression. They are cofactors for enzymes that make it easier for neurotransmitters that control mood, such as norepinephrine, serotonin, and dopamine, to be made. There are various processes by which nutrients improve mood. Some minerals, including omega-3 fatty acids, magnesium, and zinc may boost enhanced brain-derived neuro factor (BDNF) production, which improves neuroplasticity and increases the brain's resilience to stress, lowering the risk of depression. It is a commonly accepted fact that omega-3 fatty acids and a few B vitamins play significant anti-inflammatory and neuroprotective roles; this could potentially have an impact on the antidepressant effects of these nutrients. According to research, the microbiome, which comprises bacteria found in the large and small intestines, may influence inflammatory chemicals and neurotransmitters involved in mood regulation as well as general physical and mental health.[22] Furthermore, according to Senra,[23] there is proof that certain dietary habits and minerals have a preventative influence on the development of depression. A reduction in oxidative stress, a drop in inflammatory indicators, a rise in the endothelial role, and alterations to serotonin synthesis and function are a few of the processes underlying this association.

The Relationship between the Gut and the Brain

The relay pathway that links the gut and the brain is known as the "gut–brain axis (GBA)." This arrangement is for exchanging information between the digestive system and the brain. The digestive system-brain has a two-way transmission channel that involves central and enteric neural systems that unite the brain's expressive and intellectual regions to peripheral digestive activities.[24]

Numerous associations exist between the digestive and the brain, anatomically and enzymatically;

Neurological System and the Vagus Nerve

The central nervous system and the brain of an individual have around 100 billion neuronal cells, which are cells that provide the body with behavioral instructions.[25] Around 500 million neuronal cells in the digestive system relay with the brain through nervous system nerves.[26] The vagus nerve, the most significant nerve that relieson the digestive tract and the brain, carries impulses both ways.[27]

Neurotransmitters

The brain and the digestive tract are likewise related by neurotransmitters, which control feeling and emotion. Serotonin, for instance, is a neurotransmitter that aids to regulate the body clock and is connected to positive feelings.[28] It is crucial to understand that countless of these neurotransmitters are created by the billions of microbes that live in our digestive tract and other cells there. In the case of the brain neurotransmitter serotonin, the digestive tract produces 90% of it.[29] In addition, gut microbes create the neurotransmitter gamma-aminobutyric acid (GABA), which aids in reducing nervousness and panic.[30]

Elements with Antidepressant Effects

Selenium

Selenium is a vital nutrient that is found in most natural foods and is sometimes obtainable as a dietary additive. Selenium performs significant roles in the metabolism of thyroid hormone, oxidative stress, DNA synthesis, and reproduction.[31] Selenium exists in organic (selenomethionine and selenocysteine) and inorganic (selenate and selenite) forms.[32] About 28%–46% of selenium is deposited in the skeletal muscle, which makes up the total selenium content.[33] Brazil nuts, organ meats, and shellfish are rich sources of selenium.[31] Diets such as dairy products, meats with muscle, grains, and cereals also contain selenium.[34] Lean pork, mushrooms, beef, turkey, chicken, eggs, yogurt, beans, spinach, milk, cashews, and bananas are selenium are other foods that contain selenium.[35]

The link between selenium and depression

Eating more selenium might enhance emotion and lessen anxiety, which may lead to a lower prevalence of depression.[10] Selenium has a protective effect against free radicals by sustaining greater enzyme activity. This is because it is associated with the glutathione peroxidase enzyme.[36] Selenium prevents the liver's glutathione peroxidase from decreasing with low selenium intake because the brain has to capacity to store selenium.[37] Low selenium intake may implicate certain brain functions, including memory or feeling,[38,39] suggesting that low levels of selenium may be detrimental to depression. Selenium has a role in the onset time of depression by enhancing endothelial function, lowering oxidative stress and inflammatory indicators, and altering the synthesis of serotonin and its activity.[23] Selenium also modulates thyroid metabolism and the activities of selenoproteins on the serotonergic, dopaminergic, and noradrenergic systems disturb a person's propensity to experience depression.[40]

Mechanism of action of selenium

Selenium increases mood by sustaining the health of the metabolic, oxidative, and central nervous systems. Interference of selenium with the modulation of metabolism can predispose an individual to depression. Iodothyronine deiodinases (DIOs), which contain selenium, are necessary for the proper synthesis and metabolism of thyroid hormones. The correlation linking selenium amounts and depression may lead to an imbalance of oxidative and inflammatory pathways. Studies have shown that selenium proteins protect against lipoperoxidation and oxidative cell injury (thioredoxin reductases, glutathione peroxidases, and selenoprotein). Decreased levels of C-reactive protein (CRP), growth differentiation factor-5, and interleukin-6 (IL-6) have been associated with lower amounts of selenium.[41,42] The pathophysiology of depression is marked by more and oxidative stress inflammation.[42]

Selenium modulates the actions of several neurotransmitter systems, suggesting its antidepressant properties. It also significantly modulates the serotonergic, dopaminergic, and noradrenergic systems.[43] This contributes to the physiopathology of mental illnesses such as depression.[44] Neurochemical evidence shows that m-CF3-PhSe2 disturbs the serotonergic system by specifically hindering an enzyme, monoamine oxidase A, associated with 5-HT breakdown ensuing in 5-HT raising its entire availability in the synaptic cleft.[45] Furthermore, selenium control dopaminergic neurons' defense against oxidative stress through selenoprotein, thereby offering neuroprotection against neurodegeneration.[46]

Vitamin D

Vitamin D is a fat-soluble secosteroid that has biological effects that boost the absorption of calcium, phosphate, and magnesium.[47] Vitamin D3 (cholecalciferol) and Vitamin D2 (ergocalciferol) are the two vital classes of this vitamin in humans.[48] On exposure to the sun, lower layers of the skin epidermis produce cholecalciferol, which is a natural source of this vitamin.[49] Ergocalciferol and cholecalciferol can be obtained from supplements or as part of a healthy diet.[50] Fatty fish such as tuna, mackerel, and salmon, as well as fortified foods such as orange juice, soybeans, cereals, liver, cheese, beef, milk, and egg yolks, are examples of foods that naturally contain Vitamin D.[51] A slight genetic objective occurs for Vitamin D that is generated by the skin or taken through diet. First, protein is hydroxylated in the liver before occurring in the kidneys.[52] Cholecalciferol is converted into calcifediol, whereas ergocalciferol is changed into 25-hydroxyergocalciferol in the liver.[53]

25(OH)D levels in the serum of an individual determines the person's vitamin D level.[54]

The link between Vitamin D and depression

Vitamin D, an important neurosteroid hormone, can be a significant component in lessening depression. In Vitamin D lacking patients, Vitamin D additives can efficiently cure depression, as stated by many studies.[55] Generation and advancement of depression have been hypothesized to be accompanied by a shortage of vitamin D among other factors. Shortage of Vitamin D may lead to advanced-age depression.[56,57] A high level of Vitamin D in the serum can reduce the danger of having depression and other neurological conditions.[58,59] According to Mohammad Zahedi *et al*.,[60] consuming foods high in Vitamin D can aid in lowering the indications of depression because of the Vitamin D receptors present in the cingulate cortex and the hippocampus. Neuroplasticity, neuroimmunomodulation, the control of neurotrophic factors, brain growth, and neuroprotection are some of the neurological actions that can be impacted by Vitamin D. Studies suggest that consuming Vitamin D additives can mitigate both depression and lessen an individual's threat of having it.[61] The huge number of Vitamin D receptors in the human brain are responsible to regulate several neurotransmission pathways, such as those for serotonin, noradrenaline, glutamine, and dopamine.[62]

Mechanism of action

Regulation of the expression of the elements of the Ca2 + signaling toolkit, one of Vitamin D's most significant functions, helps to sustain and reduce latent Ca2 + levels in the cytosol. According to stability theory, the maintenance of Ca2 + and redox balance is maintained by Vitamin D.[63] Vitamin D has been revealed to decrease brain Ca2 + levels, which may help relieve depression.[64] Lack of Vitamin D results in increased amounts of Ca2 + and reactive oxygen species (ROS) in brain cells,[63] which may give an understanding association between depression and this disease.

Tyrosine hydroxylase and tryptophan hydroxylase, the rate-limiting enzymes in the production of serotonin and dopamine respectively, are also associated with Vitamin D, which elucidates the connection between a Vitamin D deficit and depression.[65] Since Vitamin D regulates serotonin production, depression and Vitamin D deficit are connected.[66] Vitamin D suppresses the expression of the tryptophan hydroxylase action and stimulates the growth of the serotonin-producing gene tryptophan hydroxylase 2. Serotonin is formed by tryptophan hydroxylases 1 and 2, respectively. As a result, Vitamin D capacity to retain fixed levels of serotonin may aid in the prevention of depression.[67]

Omega-3 fatty acids

Omega-3 fatty acids, which are polyunsaturated fatty acids, are also known by various names, such as omega-3 oils and omega-3 oils, omega-3 fatty acids, and n-3 fatty acids.[68] The chemical structure of omega-3 fatty acids has three atoms distant from the final methyl group.[69] They are broadly found in nature, and they play a significant function in animal lipid metabolism. Besides, omega-3-fatty acids also show a significant role in human food and composition.[70] Omega-3 fatty acids occur in three forms: docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and linolenic acid (ALA). The first is seen in plant oils, whereas the other two are seen in marine oils. Walnut, hemp oil flaxseed oil, edible seeds, algal oil, sacha inchi oil, and clary sage seed oil are common sources of ALA oil-containing plants, whereas sources of animal omega-3 fatty acids, EPA, and DHA are squid oils, fish, krill oil, fish oils, and eggs from hens.[69]

The link between omega-3 fatty acids and depression

Growing body of studies reveals that mega-3 polyunsaturated fatty acids, also called omega-3 PUFAs, can be used to manage depression.[71] The combination of DHA[72] and EPA[73] can help alleviate the symptoms of depression. They can also play a significant role in sustaining the fluidity of the membrane and its structure. In addition, they have anti-inflammatory property.[74]

Mechanism of action in depression

The possible association between omega-3 consumption and dopaminergic and serotoninergic transmission, including release, metabolism, absorption, and receptor function, has been theorized to have a promising impact on depressive status. DHA and EPA are known to remarkably affect the organization of several cell types' fluidity due to their extensive unsaturation.[75] Membrane-bound enzymes, such as omega-3 PUFA and Na/K-dependent ATPase, likewise regulate signal transduction by improving protein kinase C[76] and G-protein-mediated signal transmission.[77] Dopaminergic and serotonergic neurotransmission could be enhanced by omega-3 PUFA consumption that regulates membrane changes, which are usually malfunctioned in depressed patients. Hypothetically, the current receptor and neurotransmitter concepts of depression are connected to fatty acids by variations in dopamine receptor and serotonin (5-HT) amount and function brought on by variations in PUFA.[78] Violent suicide attempts during depression have been related to lesser levels of 5-hydroxyindoleacetic acid (5-HIAA), a metabolite that characterizes serotonin turnover, in the cerebrospinal fluid (CSF).[79] Healthy individuals with higher plasma DHA concentrations have increased serotonergic neurotransmission (higher CSF 5-HIAA), according to several studies.[80] Contrarily, a lack of omega-3 leads to a rise in frontal cortex serotonin receptor (5HT2) density, likely as a result of the body's response to a reduced serotonergic activity.[81] Several evidence from research show reduced amounts of the prefrontal cortex dopamine turnover and up to 6-fold greater of nucleus accumbens amounts of dopamine from animal model studies.[82]

Proinflammatory cytokines that are influenced by eicosanoid release and linked to depression, such as IL-1, IL-2, and

IL-6, tumor necrosis factor-42, can be significantly reduced by EPA and DHA consumption. Furthermore, through their precursor arachidonic acid, DHA and EPA can both lessen inflammation. Arachidonic acid levels are reduced in both the cells and plasma as EPA and DHA interact with arachidonic acid to produce membrane-based phospholipids.[83]

Due to the overactivity of the HPA axis, which is largely caused by over secretion of CRH, depression has been connected to an increased amount of cortisol in the blood. EPA may bring to normal the dysfunction of the HPA axis linked to depression by causing a reduction of how corticotrophin-releasing factor is expressed and the secretion of corticosterone.[84] Studies have shown that omega-3 PUFA reduces P-glycoprotein activity from a molecular perspective,[85] which are transport proteins in charge of the increased blood–brain barrier cortisol trafficking in depressed individuals.[86] The HPA axis's feedback control would be restored to normal once cortisol disseminated into the brain returns to normal.[87]

Antioxidants

Antioxidants are constituents that avert oxidation, a chemical process that can result in free radicals and cascade actions that could cause injury to the cells of an organism.[88] Carrots asparagus, broccoli, apricots, maize, green peppers, beets, cantaloupe, mangoes, pink grapefruit, nectarines, peaches, kale, spinach, sweet potatoes, tangerines, tomatoes, and watermelon all contain Vitamin A. Kale, cantaloupe, mango, Brussels sprouts, cauliflower, snow peas, honeydew, kiwi, nectarine, papaya, sweet potato, grapefruit, tomatoes, orange, strawberries, berries, broccoli, and red, green, or yellow peppers are foods that contain high amounts of Vitamin C. Foods high in Vitamin E include broccoli (boiled), pumpkin, mustard, chard, papaya, mangoes, turnip greens, nuts, avocado, and red peppers.[89]

The link between antioxidants and depression

The inverse relationship between (dietary total antioxidant capacity) DTAC and anxiety and depression can be elucidated by the antioxidative and anti-inflammatory properties of antioxidant-rich diets. It is been established that inflammation and weakened antioxidant defense are strongly correlated with sad mood.[90] Free radicals are the byproducts of normal human functions that can accumulate in the body and are removed by antioxidants. Oxidative stress can occur if the body is unable to remove enough free radicals. Numerous health issues, such as anxiety and depression, may follow.[10]

Mechanism of action

Antioxidants are known to be able to eliminate reactive nitrogen species (RNS) and ROS in the body by clearing free radicals and inhibiting the oxidative stress pathway. This further guards against injury to neurons triggered by nitrosative or oxidative stress causes in the brain, expectantly leading to the remission of anxiety or depression symptoms.[91] Flavonoid exerts their depressive action similarly to traditional antidepressants by making current neuropharmacology more readily available.[92]

B Vitamins

B vitamins, often known as the Vitamin B complex, are a collection of water-soluble vitamins that are critical for cell metabolism. These vitamins, which are chemically diverse, often coexist in some meals. Dietary additives that contain all eight of these vitamins are called Vitamin B complexes.[93]

They are vital to the preservation of health and well-being. B vitamins, which are the basis of a healthy body, unswervingly affect brain function, turkey, energy levels, and cell metabolism.[94] Salmon, fortified cereals, liver, eggs, oysters, clams, leafy greens, cattle, beans, milk, chicken, yogurt, pork, mussels, trout, and sunflower seeds are all good sources of B vitamins.[95]

The link between antioxidants and depression

Chemicals that impact mood and other neurological processes, produced by the brain are assisted by Vitamin B-12 and other B vitamins. Vitamin B-12 deficiency, along with other B vitamins such as Vitamin B-6 and folate, could be linked to depression.[96]

Mechanism of action

Vitamin B-12 has an impact on the levels of other neurotransmitters and serotonin in the brain. An individual mood is controlled by serotonin, and depression is associated with low serotonin levels.[97]

Zinc

Zinc is a significant mineral that is added to some meals, inertly found in others, and sold as a dietary additive. Zinc involves several processes in cellular metabolism. The catalytic activity of nearly 100 enzymes is dependent on it,[98] and it has a role in DNA synthesis and cell division,[99] immunological function, protein synthesis,[99] and wound healing.[100] Meat, whole grains, shellfish, eggs, legumes, seeds, nuts, dairy, vegetables, and fruits are foods that naturally contain zinc.[101]

The link between zinc and depression

Numerous receptors or transporters, including those for monoamines, are modulated on the postsynaptic side by zinc released from the presynaptic vesicles.[102] Individuals with depression have reportedly been linked to reduced serum amounts of zinc. Zinc amount drops in depressed patients.[103] Numerous studies show lower serum zinc amounts in depressed people in relation to healthy subjects, and a meta-analysis shows depressive symptoms at serum zinc amounts of 1.8 um or below.[104]

Mechanism of action

Zinc regulates the pathways of neurogenesis, neurotransmitter, and endocrine. Zinc ions serve as neurotransmitters in the cortex and the hippocampus and control synaptic

transmission,[105] altering voltage- and ligand-gated ion channels.[106] Zinc has an impact on serotonergic receptors producing antidepressant-like characteristics, which are seen in both preclinical and clinical investigations[102] and also linked to the endocrine pathway of depression is zinc insufficiency. The antioxidant and anti-inflammatory qualities of zinc augmentation may also contribute to the depressive properties of zinc. Previous research has shown that humans' CRP levels are reduced by zinc supplementation.[107] Zinc has preventive properties against lipid peroxidation.[108] Current research confirms the link between serious depression and lipid peroxidation,[109] indicating that zinc's antioxidant actions contribute to its observed antidepressant benefits. Finally, zinc's role as an antagonist of the glutamatergic N-methyl-d-aspartate (NMDA) receptor and its participation in the l-arginine-nitric oxide pathway as a nitric oxide synthase inhibitor may be related to its putative antidepressant qualities. Since glutamate homeostasis and neurotransmission are impaired in depressed individuals, the therapeutic targeting of NMDA has been applied in depression treatment during clinical and preclinical trials.[110]

Magnesium

More than 300 enzyme processes in the body of humans contain magnesium, making it a crucial component. One of its many functions is controlling blood pressure, helping to maintain healthy muscle and neuron function, and enhancing the immune system.[111] Avocados, nuts (almond, cashew, and Brazil nuts), legumes, seeds (pumpkin, flax, and chia), bananas, whole grains, fatty fish, and leafy greens are foods high in magnesium.[112]

The link between magnesium and depression

Depression development has also been connected to low levels of magnesium. Magnesium contributes to the control of NMDA glutamate receptor activity in the brain. Glutamate is an excitatory neurotransmitter that is important for normal function in the brain. Cells may become overstimulated if it is used excessively, though. Anxiety and depression are also associated with high levels of glutamate. Magnesium inhibits glutamate's effects on NMDA receptors. Cell injury and overexcitation may result from this. Magnesium may therefore be helpful in the treatment and prevention of depression.[113]

Mechanism of action

Magnesium modulates response to stress and is one of the potential mechanisms for magnesium's antidepressant effects. Magnesium can inhibit the overactivation of the HPA axis by modulating adrenocorticotropic sensitivity to ACTH and lowering the secretion of adrenocorticotrophic hormone (ACTH). Dysregulated HPA activity and high levels of cortisol are significantly observed in depressed patients, and irregular regulation of the HPA axis in adults has been strongly associated with depression and stress.[114] Magnesium's function in the gut microbiota (GM) has recently attracted attention since changes in GM have been associated with mood disorders.[115] In addition, fluctuations in the inflammatory and oxidative response, indicated by an increase in cytokines and indicators of cellular stress, have been connected to modifications caused by magnesium in the microbiota.[116] By contributing to serotonergic and dopaminergic neurotransmitters and increasing BDNF expression, magnesium may also have antidepressant effects[117] and regulation of the sleep-wake cycle through augmentation of the production of melatonin.[118]

Proteins

It is a vital component of every diet and a component of every body cell. It aids the body's cellular and tissue repair and growth. One of the three macronutrients the body needs in larger amounts is protein. Twenty amino acid long chains make up its structure[119] (Brazier, 2020). Soy products, legumes, seeds, eggs, seafood, legumes (beans and peas), nuts, lean meats and poultry, and dairy products are all natural sources of protein (milk, cheese, and yogurt).[119]

The link between protein and depression

A protein diet helps build important neurotransmitters that fight depression and anxiety because it contains amino acids. Protein-rich foods can aid with energy levels, giving you the drive to move around and feel better. Amino acids, which are the building blocks of protein, play a significant function in the creation of neurotransmitters. The brain uses chemicals known as neurotransmitters to converse with each other. As an illustration, when someone eats protein-containing food, the body digests the protein and produces dopamine from the amino acid L-tyrosine. Several illnesses, including depression, are linked to reduced dopamine levels. Tryptophan, an amino acid included in dairy products, poultry, nuts, and fish, acts as a precursor to serotonin. The consumption of foods that contain high levels of L-tryptophan can enhance mood and boost the efficacy of antidepressants such as selective serotonin reuptake inhibitors.[120]

Mechanism of action

Tryptophan, an important amino acid that the brain uses to make serotonin, is known to be present in proteins. Reduced levels of the neurotransmitter serotonin are known to cause depression and are linked with depression in the brain. Foods high in protein help the brain produce more serotonin.[10]

Probiotics

Probiotics are living bacteria that, by supporting a healthy digestive system, may be able to prevent and treat several diseases. They are also frequently referred to as beneficial, healthy, or friendly bacteria. Beverages, foods, and dietary supplements can all include probiotics.[121] Certain products

made from maize, cassava, yam, millet, soybeans, and locust beans can also serve as sources of probiotics.[122]

The link between probiotics and depression

Studies have revealed a close relationship between the gastrointestinal system, and the brain, also known as the GBA. It connects the gastrointestinal tract to the central nervous system, which contains the spinal cord and brain. By creating and expressing neurotransmitters that might influence feeling, hunger, or sleep patterns and by lowering inflammation in the body, which can contribute to depression, microorganisms in the gut, particularly probiotics, play a critical function in the GBA.[123]

Mechanism of action

It has been established that the GM can synthesize neurotransmitters such as GABA, glutamate, serotonin, dopamine, norepinephrine, histamine, and acetylcholine.[124] In addition, it protects against depression through its anti-inflammatory function.[125] It has been demonstrated that probiotics have anti-inflammatory capabilities by either unswervingly reducing the plasma concentration of proinflammatory cytokines or by inhibiting the pathway of kynurenine and reinstating gut permeability, both of which have been connected to depression etiopathology. It has been demonstrated that administering probiotics can increase and restore the amounts of the neurotransmitters of interest, including 5-HT, GABA, dopamine, and norepinephrine, which have been linked to the development of depression.[126] Through the decrease of cortisol level, a stress biomarker in human patients, and cortisone level in animal models of depression, the role of probiotics in the improvement of the hyperactive HPA-axis linked to depression has been demonstrated[127] and a change in the HPA-axis-related neurotransmitter circuitry.[128]

Conclusion

For patients with depression and anxiety, nutritional psychiatry is becoming a viable option for treatment management. Healthy eating habits such as the Mediterranean diet or avoiding items that cause inflammation seem to offer some protection against depression. Nutritional psychiatry fills this gap by giving patients helpful, actionable instructions, and it has the possibility to be a potent tool for doctors and other health-care professionals. The GBA, a channel for information between the brain and the gut, is important in psychiatric disease and aids in our understanding of the relationship between disease and nutrition.

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There is no need for patient informed consent.

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- Ekpo Ubong Udeme (40%): developed the idea, drafted the outline, drafted the manuscript, and edited the manuscript
- Uduak Emmanuel Umana (30%): edited, revised, and organized the manuscript
- Abubakar Adamu Sadeeq (30%): edited, revised, and organized the manuscript.

References

1. Sarris J. Nutritional psychiatry: From concept to the clinic. Drugs 2019;79:929-34. [doi: 10.1007/s40265-019-01178-3].
2. World Health Organization. Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013-2020. World Health Organization; 2013. Available from: https://www.who.int/nmh/events/ncd_action_plan/en/. [Last accessed on 2023 Mar 18].
3. Mozaffarian D. Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: A comprehensive review. Circulation 2016;133:187-225. doi: 10.1161/circulationaha.115.018585].
4. Hanon-Baiden J. What is Nutritional Psychiatry? News Medical and Life Sciences; 2022. Available from: https://www.news-medical.net/health/What-is-Nutritional-Psychiatry.aspx. [Last accessed on 2023 Mar 18].
5. Sartorius N. Physical symptoms of depression as a public health concern. J Clin Psychiatry 2003;64 Suppl 7:3-4. [doi: 10.4088/jcp.v64n0511].
6. Tucci V, Moukaddam N. We are the hollow men: The worldwide epidemic of mental illness, psychiatric and behavioral emergencies, and its impact on patients and providers. J Emerg Trauma Shock 2017;10:4-6.
7. Sabic D, Sabic A, Bacic-Becirovic A. Major depressive disorder and difference between genders. Mater Sociomed 2021;33:105-8. [doi: 10.5455/msm.2021.33.105-109].
8. Khan AS, Alalawi AH, Alalawi MH, Alsahaf HA, Albahrani MS, Alhasawi FA. Screening for depression, anxiety, and obsessive-compulsive disorders among secondary school students in Al-Hasa Region, Saudi Arabia. J Family Community Med 2021;28:28-34. [doi: 10.4103/jfcm.jfcm_470_20].
9. Adeomi A, Obiajunwa C, Oduntan O, Ogbukwo E. Is nutritional status associated with depression? Evidence from a cross-sectional study among workers in tertiary educational institutions in Southwestern Nigeria. Pan Afr Med J 2021;39:94. [doi: 10.11604/pamj.2021.39.1.26363].
10. Johnson J. What Foods are Good for Helping Depression? Medically Reviewed by Katherine Marengo. Medical News Today; 2019. Available from: https://www.medicalnewstoday.com/articles/325497. [Last accessed on 2023 Mar 18].
11. Jesulola E, Micalos P, Baguley IJ. Understanding the pathophysiology of depression: From monoamines to the neurogenesis hypothesis model – Are we there yet? Behav Brain Res 2018;341:79-90. [doi: 10.1016/j.bbr.2017.12.028].
12. Han XM. Depression – Treatment and Research. Beijing, China: People's Health Publishing House; 2012.

13. Fan T, Hu Y, Xin J, Zhao M, Wang J. Analyzing the genes and pathways related to major depressive disorder via a systems biology approach. Brain Behav 2020;10:e01502. [doi: 10.1002/brb3.1502].
14. Sass C. What Is Nutritional Psychiatry, and Can It Help You Feel Healthier? Here's What an Expert Says. Health; 2020. Available from: https://www.health.com/nutrition/nutritional-psychiatry. [Last accessed on 2023 Mar 18].
15. Cavaye J. Why Nutritional Psychiatry is the Future of Mental Health Treatment. The Conversation; 2018. https://theconversation.com/why-nutritional-psychiatry-is-the-future. [Last accessed on 2023 Mar 18].
16. World Health Organization. Diet, Nutrition, and the Prevention of Chronic Diseases: Report of a Joint WHO/FAO Expert Consultation. Geneva: World Health Organization; 2003.
17. Głąbska D, Guzek D, Groele B, Gutkowska K. Fruit and vegetable intake and mental health in adults: A systematic review. Nutrients 2020;12:115. [doi: 10.3390/nu12010115].
18. Rao TS, Asha MR, Ramesh BN, Rao KS. Understanding nutrition, depression and mental illnesses. Indian J Psychiatry 2008;50:77-82. [doi: 10.4103/0019-5545.39761].
19. World Health Organization. Depression. Fact Sheet; 2020. Available from: https://www.who.int/news-room/fact-sheets/detail/depression. [Last accessed on 2023 Mar 18].
20. Rahe C, Unrath M, Berger K. Dietary patterns and the risk of depression in adults: A systematic review of observational studies. Eur J Nutr 2014;53:997-1013. [doi: 10.1007/s00394-013-0568-3].
21. Shakoor H, Feehan J, Al Dhaheri AS, Ali HI, Platat C, Ismail LC, *et al.* Immune-boosting role of Vitamins D, C, E, zinc, selenium and omega-3 fatty acids: Could they help against COVID-19? Maturitas 2021;143:1-9. [doi: 10.1016/j.maturitas.2020.08.003].
22. Needham BD, Kaddurah-Daouk R, Mazmanian SK. Gut microbial molecules in behavioural and neurodegenerative conditions. Nat Rev Neurosci 2020;21:717-31. [doi: 10.1038/s41583-020-00403-5].
23. Senra ICR. Nutrition and depression. 1st Cycle in Nutrition Sciences, Faculty of Nutrition and Food Sciences, University of Porto 2017;1-25.
24. Carabotti M, Scirocco A, Maselli MA, Severi C. The gut-brain axis: Interactions between enteric microbiota, central and enteric nervous systems. Ann Gastroenterol 2015;28:203-9. [doi: 10.20524/aog.2015.0031].
25. Herculano-Houzel S. The human brain in numbers: A linearly scaled-up primate brain. Front Hum Neurosci 2009;3:31. [doi: 10.3389/neuro.09.031.2009].
26. Mayer EA. Gut feelings: The emerging biology of gut-brain communication. Nat Rev Neurosci 2011;12:453-66. [doi: 10.1038/nrn3071].
27. Breit S, Kupferberg A, Rogler G, Hasler G. Vagus nerve as modulator of the brain-gut axis in psychiatric and inflammatory disorders. Front Psychiatry 2018;9:44. doi: 10.3389/fpsyt.2018.00044].
28. Anguelova M, Benkelfat C, Turecki G. A systematic review of association studies investigating genes coding for serotonin receptors and the serotonin transporter: II. Suicidal behavior. Mol Psychiatry 2003;8:646-53. [doi: 10.1038/sj.mp.4001324].
29. Yano JM, Yu K, Donaldson GP, Shastri GG, Ann P, Ma L, *et al.* Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis. Cell 2015;161:264-76. doi: 10.1016/j.cell.2015.02.047].
30. Mazzoli R, Pessione E. The neuro-endocrinological role of microbial glutamate and GABA signaling. Front Microbiol 2016;7:1934. [doi: 10.3389/fmicb.2016.01934].
31. Wang J, Um P, Dickerman BA, Liu J. Zinc, magnesium, selenium and depression: A review of the evidence, potential mechanisms and implications. Nutrients 2018;10:584. [doi: 10.3390/nu10050584].
32. Sunde RA, Ross AC, Caballero B, Cousins RJ, Tucker KL, Ziegler TR. Selenium. In: Caballero B, Allen L, Prentice P, editors. Modern Nutrition in Health and Disease. 11th ed. Philadelphia: Lippincott Williams and Wilkins; 2012. p. 225-37.
33. Sunde RA, Bowman B, Russell R. Selenium. In: Bowman B, Russell R, editors. Present Knowledge in Nutrition. 9th ed. Washington, D.C.: International Life Sciences Institute; 2006. p. 480-97.
34. Terry EN, Diamond AM, Erdman JW Jr., Macdonald IA, Zeisel SH. Selenium. In: Caballero B, Allen L, Prentice A, editors. Present Knowledge in Nutrition. 10th ed. Hoboken, NJ: Wiley-Blackwell; 2012. p. 568-87.
35. Chun OK, Floegel A, Chung SJ, Chung CE, Song WO, Koo SI. Estimation of antioxidant intakes from diet and supplements in U.S. Adults. J Nutr 2010;140:317-24. doi: 10.3945/jn.109.109595].
36. Purdie J. Can a B 12 Deficiency Cause Depression? Healthline; 2017. Available from: https://www.healthline.com/health/mental health/ b12 deficiency and depression. [Last accessed on 2023 Dec 18]. [doi: 10.1155/2014/951762].
37. Gosney MA, Hammond MF, Shenkin A, Allsup S. Effect of micronutrient supplementation on mood in nursing home residents. Gerontology 2008;54:292-9. [doi: 10.1159/000140332].
38. Behne D, Kyriakopoulos A. Mammalian selenium-containing proteins. Annu Rev Nutr 2001;21:453-73. [doi: 10.1146/annurev.nutr. 21.1.453].
39. Gao S, Jin Y, Hall KS, Liang C, Unverzagt FW, Ji R, *et al.* Selenium level and cognitive function in rural elderly Chinese. Am J Epidemiol 2007;165:955-65. [doi: 10.1093/aje/kwk102].
40. Maes M, Galecki P, Chang YS, Berk M. A review on the oxidative and nitrosative stress (O and NS) pathways in major depression and their possible contribution to the (neuro) degenerative processes in that illness. Prog Neuropsychopharmacol Biol Psychiatry 2011;35:676-92. [doi: 10.1016/j.pnpbp.2010.05.004].
41. Colangelo LA, He K, Whooley MA, Daviglus ML, Morris S, Liu K. Selenium exposure and depressive symptoms: The coronary artery risk development in young adults trace element study. Neurotoxicology 2014;41:167-74. [doi: 10.1016/j.neuro.2014.02.004].
42. Prystupa A, Kiciński P, Luchowska-Kocot D, Błażewicz A, Niedziałek J, Mizerski G, *et al.* Association between serum selenium concentrations and levels of proinflammatory and profibrotic cytokines-Interleukins IL-6 and IL-4, TNF-α, TGF-β1, and IFN-γ in patients with psoriasis vulgaris. Biol Trace Elem Res 2017;175:76-83. [doi: 10.1007/s12011-016-0821-1]
43. Spallholz JE. On the nature of selenium toxicity and carcinostatic activity. Free Radic Biol Med 1994;17:45-64. [doi: 10.1016/0891-5849(94)90009-4].
44. Castaño A, Ayala A, Rodríguez-Gómez JA, Herrera AJ, Cano J, Machado A. Low selenium diet increases the dopamine turnover in prefrontal cortex of the rat. Neurochem Int 1997;30:549-55. [doi: 10.1016/S0197-0186(96)00117-8].
45. Nogueira CW, Rocha JB. Toxicology and pharmacology of selenium: Emphasis on synthetic organoselenium compounds. Arch Toxicol 2011;85:1313-59. [doi: 10.1007/s00204-011-0704-8].
46. Brüning CA, Prigol M, Roehrs JA, Nogueira CW, Zeni G. Involvement of the serotonergic system in the anxiolytic-like effect

caused by m-trifluoromethyl-diphenyl diselenide in mice. Behav Brain Res 2009;205:511-7. [doi: 10.1016/j.bbr. 2009.08.006].
47. Chaudhary PK, Patel SA. Status of Vitamin D and its correlation with diabetes in North Gujarat, India. World J Pharm Sci. 2021;9:159-79. [doi: 10.20959/wjpps20216-20221]
48. MacDonald J. How Does the Body Make Vitamin D from Sunlight? JSTOR Daily; 2019. Available from: https://www.jstor.org/stable/26928233. [Last accessed on 2023 Dec 18].
49. Holick MF, MacLaughlin JA, Doppelt SH. Regulation of cutaneous previtamin D3 photosynthesis in man: Skin pigment is not an essential regulator. Science 1981;211:590-3. [doi: 10.1126/science.6256851].
50. Calvo MS, Whiting SJ, Barton CN. Vitamin D intake: A global perspective of current status. J Nutr 2005;135:310-6. [doi: 10.1093/jn/135.2.310].
51. DerSariankiss C. Top Foods for Calcium and Vitamin D. Food and Recipe; 2020. Available from: https://www.foodandrecipe.com/nutrition/top-foods-for-calcium-and-vitamin-d/. [Last accessed on 2023 Dec 18].
52. Bikle DD. Vitamin D metabolism, mechanism of action, and clinical applications. Chem Biol 2014;21:319-29. [doi: 10.1016/j.chembiol.2013.12.016].
53. Hollis BW. Assessment of Vitamin D nutritional and hormonal status: What to measure and how to do it. Calcif Tissue Int 1996;58:4-5. [doi: 10.1007/BF02509523].
54. Norman AW, Myrtle JF, Midgett RJ, Nowicki HG, Williams V, Popják G. 1,25-dihydroxycholecalciferol: Identification of the proposed active form of Vitamin D3 in the intestine. Science 1971;173:51-4. [doi: 10.1126/science.173.3991.51].
55. di Michele F, Talamo A, Niolu C, Siracusano A. Vitamin D and N-acetyl cysteine supplementation in treatment-resistant depressive disorder patients: A general review. Curr Pharm Des 2020;26:2442-59. [doi: 10.2174/1381612826666200514082042].
56. Okereke OI, Singh A. The role of Vitamin D in the prevention of late-life depression. J Affect Disord 2016;198:1-14. [doi: 10.1016/j.jad.2016.03.044].
57. Cui X, Gooch H, Groves NJ, Sah P, Burne TH, Eyles DW, *et al.* Vitamin D and the brain: Key questions for future research. J Steroid Biochem Mol Biol 2015;148:305-9. [doi: 10.1016/j.jsbmb. 2014.11.004].
58. Jääskeläinen T, Knekt P, Suvisaari J, Männistö S, Partonen T, Sääksjärvi K, *et al.* Higher serum 25-hydroxyvitamin D concentrations are related to a reduced risk of depression. Br J Nutr 2015;113:1418-26. [doi: 10.1017/S0007114515000689].
59. Stokes CS, Grünhage F, Baus C, Volmer DA, Wagenpfeil S, Riemenschneider M, *et al.* Vitamin D supplementation reduces depressive symptoms in patients with chronic liver disease. Clin Nutr 2016;35:950-7. [doi: 10.1016/j.clnu.2015.08.019].
60. Mohammad Zahedi A, Razavi A, Sajjadi M, Nasirzadeh A. The effect of Vitamin D on depression in individuals. Int J Med Rev 2019;6:77-80. [doi: 10.29252/ijmr-060301]
61. Eyles DW, Smith S, Kinobe R, Hewison M, McGrath JJ. Distribution of the Vitamin D receptor and 1 alpha-hydroxylase in human brain. J Chem Neuroanat 2005;29:21-30. [doi: 10.1016/j.jchemneu. 2004.08.006].
62. Kesby JP, Turner KM, Alexander S, Eyles DW, McGrath JJ, Burne TH. Developmental Vitamin D deficiency alters multiple neurotransmitter systems in the neonatal rat brain. Int J Dev Neurosci 2017;62:1-7. [doi: 10.1016/j.ijdevneu.2017.05.001].
63. Berridge MJ. Vitamin D: A custodian of cell signalling stability in health and disease. Biochem Soc Trans 2015;43:349-58. [doi: 10.1042/BST20150018].
64. Kalueff AV, Eremin KO, Tuohimaa P. Mechanisms of neuroprotective action of Vitamin D (3). Biochemistry (Mosc) 2004;69:738-41. [doi: 10.1023/B:BIRY.0000041938.4386223].
65. Kaneko I, Sabir MS, Dussik CM, Whitfield GK, Karrys A, Hsieh JC, *et al.* 1,25-Dihydroxyvitamin D regulates expression of the tryptophan hydroxylase 2 and leptin genes: Implication for behavioral influences of Vitamin D. FASEB J 2015;29:4023-35. [doi: 10.1096/fj.15-273862].
66. Patrick RP, Ames BN. Vitamin D hormone regulates serotonin synthesis. Part 1: Relevance for autism. FASEB J 2014;28:2398-413. [doi: 10.1096/fj.14-268342].
67. Petric D. The importance of Vitamin D in seasonal affective disorder and other depressive disorders. Psychiatry Danub 2015;27 Suppl 1:S355-7.
68. National Institutes of Health. Omega-3 Fatty Acids. Office of Dietary Supplements, US; 2021. Available from: https://ods.od.nih.gov/factsheets/Omega3FattyAcids-Consumer/. [Last accessed on 2023 Dec 18].
69. Micronutrient Information Center. Essential Fatty Acids. Linus Pauling Institute, Oregon State University; 2019. Available from: https://lpi.oregonstate.edu/mic/other-nutrients/essential-fatty-acids. [Last accessed on 2023 Dec 18].
70. Scorletti E, Byrne CD. Omega-3 fatty acids, hepatic lipid metabolism, and nonalcoholic fatty liver disease. Annu Rev Nutr 2013;33:231-48. [doi: 10.1146/annurev-nutr-071812-161230].
71. Mocking RJ, Harmsen I, Assies J, Koeter MW, Ruhé HG, Schene AH. Meta-analysis and meta-regression of omega-3 polyunsaturated fatty acid supplementation for major depressive disorder. Transl Psychiatry 2016;6:e756. [doi: 10.1038/tp.2016.29].
72. Mischoulon D, Best-Popescu C, Laposata M, Merens W, Murakami JL, Wu SL, *et al*. A double-blind dose-finding pilot study of docosahexaenoic acid (DHA) for major depressive disorder. Eur Neuropsychopharmacol 2008;18:639-45. [doi: 10.1016/j.euroneuro.2008.03.003].
73. Mozaffari-Khosravi H, Yassini-Ardakani M, Karamati M, Shariati-Bafghi SE. Eicosapentaenoic acid versus docosahexaenoic acid in mild-to-moderate depression: A randomized, double-blind, placebo-controlled trial. Eur Neuropsychopharmacol 2013;23:636-44. [doi: 10.1016/j.euroneuro.2012.06.002].
74. Deacon G, Kettle C, Hayes D, Dennis C, Tucci J. Omega 3 polyunsaturated fatty acids and the treatment of depression. Crit Rev Food Sci Nutr 2017;57:212-23. [doi: 10.1080/10408398.2013.781505].
75. Grosso G, Galvano F, Marventano S, Malaguarnera M, Bucolo C, Drago F, *et al.* Omega-3 fatty acids and depression: Scientific evidence and biological mechanisms. Oxid Med Cell Longev 2014;2014:313570. [doi: 10.1155/2014/313570].
76. Bowen RA, Clandinin MT. Maternal dietary 22: 6n-3 is more effective than 18: 3n-3 in increasing the 22: 6n-3 content in phospholipids of glial cells from neonatal rat brain. Br J Nutr 2005;93:601-11. [doi: 10.1079/bjn20051424].
77. Vaidyanathan VV, Rao KV, Sastry PS. Regulation of diacylglycerol kinase in rat brain membranes by docosahexaenoic acid. Neurosci Lett 1994;179:171-4. [doi: 10.1016/0304-3940(94)90992-8].
78. Mann JJ, Malone KM. Cerebrospinal fluid amines and higher-lethality suicide attempts in depressed inpatients. Biol Psychiatry 1997;41:162-71. [doi: 10.1016/S0006-3223(96)00092-8].
79. Hibbeln JR, Linnoila M, Umhau JC, Rawlings R, George DT, Salem N Jr. Essential fatty acids predict metabolites of serotonin and dopamine in cerebrospinal fluid

among healthy control subjects, and early- and late-onset alcoholics. Biol Psychiatry 1998;44:235-42. [doi: 10.1016/S0006-3223(97)00453].

80. Vines A, Delattre AM, Lima MM, Rodrigues LS, Suchecki D, Machado RB, *et al.* The role of 5-HT A receptors in fish oil-mediated increased BDNF expression in the rat hippocampus and cortex: A possible antidepressant mechanism. Neuropharmacology 2012;62:184-91. [doi: 10.1016/j.neuropharm.2011.07.010].
81. McNamara RK, Able J, Liu Y, Jandacek R, Rider T, Tso P, *et al.* Omega-3 fatty acid deficiency during perinatal development increases serotonin turnover in the prefrontal cortex and decreases midbrain tryptophan hydroxylase-2 expression in adult female rats: Dissociation from estrogenic effects. J Psychiatr Res 2009;43:656-63. [doi: 10.1016/j.jpsychires.2008.09.003].
82. Zangen A, Overstreet DH, Yadid G. Increased catecholamine levels in specific brain regions of a rat model of depression: Normalization by chronic antidepressant treatment. Brain Res 1999;824:243-50. [doi: 10.1016/S0006-8993(98)01187-5].
83. Caughey GE, Mantzioris E, Gibson RA, Cleland LG, James MJ. The effect on human tumor necrosis factor alpha and interleukin 1 beta production of diets enriched in n-3 fatty acids from vegetable oil or fish oil. Am J Clin Nutr 1996;63:116-22. [doi: 10.1093/ajcn/63.1.116].
84. Schiepers OJ, Wichers MC, Maes M. Cytokines and major depression. Prog Neuropsychopharmacol Biol Psychiatry 2005;29:201-17. [doi: 10.1016/j.pnpbp.2004.11.003].
85. Song C, Li X, Leonard BE, Horrobin DF. Effects of dietary n-3 or n-6 fatty acids on interleukin-1beta-induced anxiety, stress, and inflammatory responses in rats. J Lipid Res 2003;44:1984-91. [doi: 10.1194/jlr.M300189-JLR200].
86. Pariante CM, Makoff A, Lovestone S, Feroli S, Heyden A, Miller AH, *et al.* Antidepressants enhance glucocorticoid receptor function *in vitro* by modulating the membrane steroid transporters. Br J Pharmacol 2001;134:1335-43. [doi: 10.1038/sj.bjp.0704392].
87. Juruena MF, Cleare AJ, Pariante CM. The hypothalamic pituitary adrenal axis, glucocorticoid receptor function and relevance to depression. Braz J Psychiatry 2004;26:189-201. [doi: 10.1590/S1516-44462004000400003].
88. Dabelstein W, Reglitzky A, Schutze A, Reders K. Automotive Fuels. In: Ullmann's Encyclopedia of Industrial Chemistry, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim; 2007 [doi: 10.1002/14356007.a16_719].
89. Dunkin MA. Super Foods for Optimal Health. Food and recipes; 2021. Available from: https://www.webmd.com/food-recipes/antioxidants-your-immune-system-super-foods-optimal-health. [Last accessed on 2023 Dec 18].
90. Milaneschi Y, Bandinelli S, Penninx BW, Corsi AM, Lauretani F, Vazzana R, *et al.* The relationship between plasma carotenoids and depressive symptoms in older persons. World J Biol Psychiatry 2012;13:588-98. [doi: 10.3109/15622975.2011.587476].
91. Ying Z, Roy RR, Edgerton VR, Gómez-Pinilla F. Exercise restores levels of neurotrophins and synaptic plasticity following spinal cord injury. Exp Neurol 2005;193:411-9. [doi: 10.1016/j.expneurol.2014.01.010].
92. Bouayed J, Bohn T. Exogenous antioxidants – Double-edged swords in cellular redox state: Health beneficial effects at physiologic doses versus deleterious effects at high doses. Oxid Med Cell Longev 2010;3:228-37. [doi: 10.4161/oxim.3.4.12858].
93. Kaur A. Biological functions of Vitamin B complex and effects on human health in both excess and deficiency levels. Pharma Tutor 2015;3:40-7. [doi: 10.29161/PT.v3.i11.2015.40-47]
94. Cronkleton E. Why is Vitamin B Complex Important, and Where Do I Get it? 2019. Available from: https://www.healthline.com/nutrition/vitamin-b-foods. [Last accessed on 2023 Dec 18].
95. McCulloch M. 15 Healthy Foods High in B Vitamins. Healthline; 2018. Available from: https://www.healthline.com/nutrition/vitamin-b-foods. [Last accessed on 2023 Dec 18]. [doi: 10.1155/2014/951762]
96. Hall-Flavin MD, Daniel K. Vitamin B-12 and depression: Are they related? Health information; 2018. Available from: https://www.mayoclinic.org/diseases-conditions/depression/expert-answers/vitamin-b12-and-depression/faq. [Last accessed on 2023 Dec 18]. [doi: 10.1155/2014/951762].
97. Purdie J. Can a B-12 Deficiency Cause Depression? Healthline; 2017. Available from: https://www.healthline.com/health/mental-health/b12-deficiency-and-depression. [Last accessed on 2023 Dec 18]. [doi: 10.1155/2014/951762].
98. Sandstead HH. Understanding zinc: Recent observations and interpretations. J Lab Clin Med 1994;124:322-7.
99. Prasad AS. Zinc: An overview. Nutrition 1995;11:93-9.
100. Simmer JP, Thompson JH. Effect of zinc on DNA synthesis and cell division *in vitro*. J Cell Physiol 1985;125:175-80. [doi: 10.1002/jcp.1041250124]
101. West H. The 10 Best Foods that are High in Zinc. Healthline; 2018. Available from: https://www.healthline.com/nutrition/best-foods-high-in-zinc. [Last accessed on 2023 Mar 18].
102. Satała G, Duszyńska B, Stachowicz K, Rafalo A, Pochwat B, Luckhart C, *et al.* Concentration-dependent dual mode of Zn action at serotonin 5-HT1A receptors: *In vitro* and *in vivo* studies. Mol Neurobiol 2016;53:6869-81.
103. Dobosz B, Drzewiecka K, Waskiewicz A, Irzykowska L, Bocianowski J, Karolewski Z, *et al.* Free radicals, salicylic acid and mycotoxins in asparagus after inoculation with *Fusarium proliferatum* and *F. oxysporum*. Appl Magn Reson 2011;41:19-30.
104. Swardfager W, Herrmann N, Mazereeuw G, Goldberger K, Harimoto T, Lanctôt KL. Zinc in depression: A meta-analysis. Biol Psychiatry 2013;74:872-8.
105. Huang EP. Metal ions and synaptic transmission: Think zinc. Proc Natl Acad Sci U S A 1997;94:13386-7. [doi: 10.1073/pnas.94.25.13386].
106. Veran J, Kumar J, Pinheiro PS, Athané A, Mayer ML, Perrais D, *et al.* Zinc potentiates GluK3 glutamate receptor function by stabilizing the ligand binding domain dimer interface. Neuron 2012;76:565-78. [doi: 10.3945/ajcn.2010.29354].
107. Bao B, Prasad AS, Beck FW, Fitzgerald JT, Snell D, Bao GW, *et al.* Zinc decreases C-reactive protein, lipid peroxidation, and inflammatory cytokines in elderly subjects: A potential implication of zinc as an atheroprotective agent. Am J Clin Nutr 2010;91:1634-41. [doi: 10.3945/ajcn.2010.29354].
108. Irmisch G, Schlaefke D, Richter J. Zinc and fatty acids in depression. Neurochem Res 2010;35:1376-83. [doi: 10.1007/s11064-010-0233-4].
109. Sowa-Kućma M, Styczeń K, Siwek M, Misztak P, Nowak RJ, Dudek D, *et al.* Lipid peroxidation and immune biomarkers are associated with major depression and its phenotypes, including treatment-resistant depression and melancholia. Neurotox Res 2018;33:448-60. [doi: 10.1007/s12640-017-9803-4].
110. Pittenger C, Sanacora G, Krystal JH. The NMDA receptor as a therapeutic target in major depressive disorder. CNS Neurol Disord Drug Targets 2007;6:101-15. [doi: 10.1111/j.1527-3458.2007.00001.x].
111. Ware M. Why do we Need Magnesium? Med News Today; 2020. Available from: https://www.healthdirect.gov.au/magnesium#:~:text=Magnesium%20is%20

important%3A,bone%20and%20DNA%20(genetic%20material). [Last accessed on 2023 Mar 18]. [doi: 10.1016/j.biopsych.2013.05.008].

112. Spritzler F. 10 Evidence-Based Health Benefits of Magnesium. Healthline. Available from: https://saltfloatstudio.com.au/healthline-10-evidence-based-health-benefits-of-magnesium/. [Last accessed on 2023 Mar 18, Last updated on 2018 Dec 13]. [doi: 10.1007/s11064-010-0233-4]
113. Kendra K. The role of magnesium in depression and anxiety. Clin Psychol Today 2021;4:1-7. [doi: 10.37532/cpt. 2021.4(2).102].
114. Guerry JD, Hastings PD. In search of HPA axis dysregulation in child and adolescent depression. Clin Child Fam Psychol Rev 2011;14:135-60. [doi: 10.1007/s10567-011-0097-9].
115. Kelly JR, Borre Y, O' Brien C, Patterson E, El Aidy S, Deane J, *et al.* Transferring the blues: Depression-associated gut microbiota induces neurobehavioural changes in the rat. J Psychiatr Res 2016;82:109-18. [doi: 10.1016/j.jpsychires.2016.07.019].
116. Pachikian BD, Neyrinck AM, Deldicque L, De Backer FC, Catry E, Dewulf EM, *et al.* Changes in intestinal bifidobacteria levels are associated with the inflammatory response in magnesium-deficient mice. J Nutr 2010;140:509-14. [doi: 10.3945/jn.109.114389].
117. Pochwat B, Szewczyk B, Sowa-Kucma M, Siwek A, Doboszewska U, Piekoszewski W, *et al.* Antidepressant-like activity of magnesium in the chronic mild stress model in rats: Alterations in the NMDA receptor subunits. Int J Neuropsychopharmacol 2014;17:393-405. [doi: 10.1093/ijnp/pyu019].
118. Billyard AJ, Eggett DL, Franz KB. Dietary magnesium deficiency decreases plasma melatonin in rats. Magnes Res 2006;19:157-61. [doi: 10.1684/mrh.2006.0095].
119. Brazier B. Protein: Why it's Important, How Much you Need, and How to Get Enough. Harvard Health Publishing, Harvard Medical School; 2020. Available from: https://www.health.harvard.edu/blog/protein-how-much-you-need-and-how-to-get-enough-2020091721087. [Last accessed on 2023 Mar 18].
120. Sandwood J. The Connection between Protein and Your Mental Health. Mental Health. Available from: https://www.mentalhealth.org.uk/a-to-z/p/protein-and-mental-health. [Last accessed on 2023 Mar 18, Last updated on 2019 Feb 20].
121. Lordan R, Rando HM, COVID-19 Review Consortium, Greene CS. Dietary supplements and nutraceuticals under investigation for COVID-19 prevention and treatment. mSystems 2021;6:e00122-21. [doi: 10.1128/mSystems.00122-21].
122. Uzogara GA, Agu LN, Uzogara EO. Review of traditional fermented foods, condiments, and beverages in Nigeria: Their benefits and possible problems. J Agric Food Chem 1990;38:267-88. [doi: 10.1021/jf00092a001]
123. Raypole C. Can Probiotics Help With Depression? Medically reviewed by Alan Carter. Healthline; 2019. Available from: https://www.healthline.com/health/depression/probiotics-for-depression. [Last accessed on 2023 Mar 18].
124. Oleskin AV, Shenderov BA. Neuromodulatory effects and targets of the SCFAs and gasotransmitters produced by the human symbiotic microbiota. Microb Ecol Health Dis 2016;27:30971. [doi: 10.3402/mehd.v27.30971].
125. Park C, Brietzke E, Rosenblat JD, Musial N, Zuckerman H, Ragguett RM, *et al.* Probiotics for the treatment of depressive symptoms: An anti-inflammatory mechanism? Brain Behav Immun 2018;73:115-24. [doi: 10.1016/j.brainres.2019.02.026].
126. Wei CL, Wang S, Yen JT, Cheng YF, Liao CL, Hsu CC, *et al.* Antidepressant-like activities of live and heat-killed *Lactobacillus paracasei* PS23 in chronic corticosterone-treated mice and possible mechanisms. Brain Res 2019;1711:202-13. [doi: 10.1016/j.brainres.2019.02.026].
127. Kazemi A, Noorbala AA, Azam K, Eskandari MH, Djafarian K. Effect of probiotic and prebiotic versus placebo on psychological outcomes in patients with major depressive disorder: A randomized clinical trial. Clin Nutr 2019;38:522-8. doi: 10.1016/j.clnu.2018.02.015].
128. Dhaliwal J, Singh DP, Singh S, Pinnaka AK, Boparai RK, Bishnoi M, *et al. Lactobacillus plantarum* MTCC 9510 supplementation protects from chronic unpredictable and sleep deprivation-induced behaviour, biochemical and selected gut microbial aberrations in mice. J Appl Microbiol 2018;125:257-69. [doi: 10.1111/jam.13834].