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EXPLORING THE LINK BETWEEN DIET AND MENTAL HEALTH: A REVIEW OF RECENT FINDINGS.

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Abstract:

Scientific research is increasingly demonstrating the critical role that nutrients play in maintaining brain health and cognitive performance. This thorough analysis delves into the complex interplay between different nutrients and mental health, highlighting their significant effects on neurotransmitter function, neuroplasticity, and mood regulation. Both micronutrients like vitamins and minerals and macronutrients like fatty acids, proteins, and carbs have a major impact on emotional stability and cognitive function. Polyphenols, B-group vitamins, and omega-3 fatty acids are important components of neuroprotection since they have been shown to improve neurotransmitter regulation and synaptic plasticity. Moreover, the gut microbiota becomes an important mediator, generating bioactive substances that affect oxidative stress and inflammation, two factors linked to mental health issues. The interplay among mental health, inflammation, and oxidative stress highlights the significance of dietary treatments in enhancing brain function. Research indicates that anti-inflammatory and antioxidant-rich plant-based diets may be beneficial in halting cognitive aging and lowering the incidence of neurodegenerative illnesses. On the other hand, diets heavy in sugar, processed foods, and bad fats exacerbate cognitive decline by causing systemic inflammation. To sum up, the combination of lifestyle changes and a well-balanced, nutrient-rich diet is essential for promoting brain health and reducing the likelihood of mental health issues. This study emphasizes how important nutrition is for maintaining cognitive function and how dietary treatments might improve mental health over the life span.

Introduction:

In industrialized countries, mental health issues have become a major cause of disability-adjusted life years (DALYs) lost during the last ten years and worrying patterns have also been seen in developing countries. According to current estimates, over 300 million people worldwide suffer from depression, and over 260 million people suffer from anxiety disorders; these individuals account for 4.4% and 3.6% of the global population, respectively. Together, mental illnesses cause 14% of Years Lived with Disability (YLD) worldwide. In 2015, anxiety disorders accounted for 24.6 million YLD, while depressive disorders caused over 50 million YLD. Notably, anxiety and depression frequently co-occur and are associated with various non-communicable diseases, such as cancer, dementia, and cardiovascular disease. Furthermore, sleep disorders are becoming more and more recognized as new illnesses that may be linked to other health problems [1].

The prevention of serious illnesses that have an expanding influence on communities and future generations is contingent upon the early recognition of mental disorder symptoms, the identification of risk factors, and prompt interventions to minimize chronic exposures. An increasing number of studies in the fields of (paleo)anthropology, human evolution, biology, culture, and environment have investigated possible risk factors for mental illnesses. Throughout the past 50 years, there have been substantial changes in lifestyle, including the adoption of unhealthy eating and sleeping patterns, due to rapid cultural development, technical advancements, global industrialization, and urbanization [2-3].

In the modern period, diet has become a significant risk factor for non-communicable diseases, accounting for millions of deaths and Disability-Adjusted Life-Years (DALYs). The current global "nutrition transition" is the replacement of traditional diets with "Westernized" diets that are high in processed foods, high in energy, refined sugars, high in trans fatty acids, high in sodium, and low in plant-based foods. This change in nutrition, together with sedentary lifestyles, impacts not just the risk of mental health disorders but also cardio-metabolic health and some types of cancer [4].

Due to constant exposure to stimuli including light and noise pollution, rigorous work schedules, and social pressures, urban environments may throw off circadian rhythms. This can lead to anxiety, mood disorders, depression, cognitive decline, and sleep difficulties. Researchers have long been interested in the relationship between behavior and diet, including how it affects mental and physical health as well as how stress and obesity factor into this relationship. Dietary changes may be able to prevent diabetes and cardiovascular disease (CVD) from developing. Simultaneously, stress-related mental health disorders including major depression and posttraumatic stress disorder (PTSD) increase the risk of cardiovascular disease (CVD), however the underlying mechanisms are still not fully understood. In particular, more research is needed to determine the specific impact of diet on mental health and the relationship between stress-related psychiatric disorders and unhealthy dietary outcomes like obesity [5].

Bidirectionality in the relationship between these factors is common. For example, dietary modifications can have a direct impact on mood, and the onset of mental illnesses can influence eating habits. The complex network of relationships between nutrition and psychiatric symptoms is depicted in Figure 1. Path A: Stress makes people overeat, especially during periods of binge eating, and reduces their physical activity, which leads to obesity and/or metabolic syndrome (MetS). Because of the functional and social limitations caused by these illnesses, depression may be made worse. Path B describes how stress-related mental health conditions (such as depression and PTSD) lead to changes in metabolism and obesity. Path C refers to medical conditions such as diabetes and cardiovascular disease, which can be caused by depression and PTSD and thus represent a reciprocal interaction or shared pathways. Overeating brought on by stress leads to obesity, which in turn can alter neurotransmitters, neuropeptides, and inflammatory factors that impact mood and subsequent eating patterns. Path D emphasizes neurotransmitters (like serotonin) and neurohormones (like cortisol), whereas Path E shows inflammatory factors. Path F describes how neuropeptides, such as galanin and ghrelin, are involved in this intricate interaction. Finally, going back to Path A, dietary changes affect the gut flora, which in turn affects mood and engages in complex interactions with inflammation, the brain, and the previously stated neurotransmitters and neuropeptides [6].

In conclusion, the escalating prevalence of mental health disorders, alongside the emergence of sleep disturbances, underscores the urgency of addressing these issues on a global scale. The burden of these conditions extends far beyond individual suffering, significantly impacting public health and straining healthcare systems worldwide. Recognizing the early signs of mental illness, identifying predisposing factors, and implementing timely interventions are crucial steps in mitigating their far-reaching consequences. The nexus between diet, behavior, and mental health is multifaceted and bidirectional. Unhealthy dietary patterns, exacerbated by modern lifestyle changes, contribute significantly to the burgeoning rates of non-communicable diseases and mental health disorders. Understanding the intricate interplay between stress, obesity, and psychiatric ailments is essential for developing effective prevention and treatment strategies. While significant strides have been made in elucidating these complex relationships, gaps in understanding persist, particularly regarding the specific impact of diet on mental health and the mechanisms linking stress-related psychiatric disorders to adverse dietary outcomes like obesity. Further research is warranted to unravel these complexities and inform targeted interventions aimed at promoting mental well-being and overall health. By addressing the interconnected challenges of diet, behavior, and mental health, we can strive towards a healthier future for individuals and communities worldwide, fostering resilience and well-being across generations.

Micro and Macronutrients Effect on the Brain:

Amino Acids:

Different nutritional profiles may be required for somatic cells since they have different metabolic needs. Interestingly, the blood-brain barrier surrounds brain cells and controls the flow of vital nutrients, which affects brain function [7]. Of all the macronutrients, the effect of fatty acids on mental health has received a great deal of scientific study. In particular, brain function greatly depends on polyunsaturated fatty acids (PUFAs). Docosahexaenoic acid (DHA) is essential for the integrity, fluidity, and functionality of the neuronal membrane since it is a structural component of the phospholipids in brain cell membranes. On the other hand, leukotrienes, prostaglandins, and thromboxanes are examples of pro-inflammatory mediators that are inhibited by eicosapentaenoic acid (EPA), which may alter immunological and metabolic processes. EPA also functions as a precursor to anti-inflammatory cytokines. Arachidonic acid (AA), one of the omega-6 PUFA precursors, on the other hand, has been linked to pro-inflammatory reactions. In addition to their anti-inflammatory properties, omega-3 polyunsaturated fatty acids (PUFAs) have been linked to the neuroendocrine regulation of dopaminergic and serotoninergic neurotransmission [8].

Moreover, through possibly affecting glucose metabolism, monounsaturated fatty acids (MUFAs) have been connected to the regulation of brain activity and sleep patterns. These discoveries highlight the complex interplay between dietary fatty acids and brain health, emphasizing their diverse functions in preserving mental health and cognitive performance. The consumption of proteins and amino acids through diet has been associated with increases in the quantity and quality of sleep by affecting neurotransmitter and neuromodulator expression. Tryptophan is an important amino acid that is of particular relevance since it is a precursor to bioactive metabolites like melatonin and serotonin that are involved in regulating sleep. It has been demonstrated that the non-essential amino acid glycine improves the quality of sleep by regulating body temperature and acting on neurotransmission through glycine receptors and N-methyl-D-aspartate-type glutamate receptors, respectively, to produce excitatory and inhibitory effects [9].

Furthermore, another non-essential, non-proteinogenic amino acid called l-ornithine may have a direct effect on the central nervous system, reducing stress and enhancing symptoms related to exhaustion and sleeplessness. This is achieved by lowering blood corticosterone levels, attenuating stress responses mediated by the GABA receptor, and decreasing stress-induced activation of the hypothalamic-pituitary-adrenal (HPA) axis. Through their interactions with neurochemical pathways involved in sleep regulation, our findings highlight the potential of dietary proteins and amino acids in promoting healthy sleep patterns and resolving sleep-related disorders [10].

Carbohydrates:

The brain uses carbohydrates as its main energy source, with glucose acting as the brain's main fuel. However, because mood disorders, such as sadness, increase the synthesis of serotonin in the brain, they can also cause excessive ingestion of carbohydrates, a phenomenon known as "carbohydrate craving." Carbohydrates are absorbed at different rates and times based on their composition and food sources, which affects the release of blood glucose and the insulin response. To keep blood glucose homeostasis, high-glycemic index foods might cause a sharp rise in insulin secretion. Insulin preferentially binds to the large neutral amino acid transporter at the blood-brain barrier, where it is converted to serotonin, but it has no effect on the uptake of tryptophan. Insulin increases the uptake of branched-chain amino acids into skeletal muscle [11].

On the other hand, consuming large amounts of easily available carbohydrates over an extended period of time has been linked to worse hippocampal-related memory, which may be mediated by increased neuro-inflammation in the hippocampus. On the other hand, complex carbohydrates—like the fiber found in fruits, vegetables, legumes, and whole grains—may be advantageous for mental health. Instead of being broken down by human enzymes, these carbohydrates are converted by gut bacteria into short-chain fatty acids (SCFAs), such as butyrate, propionate, and acetate. These SCFAs have anti-inflammatory properties that can affect the brain through immune system activation and the gut-brain axis pathways [12]. In conclusion, the kind and source of carbohydrates ingested can have a substantial impact on mental health. Complex carbohydrates, which are high in fiber, may be beneficial due to their anti-inflammatory qualities and effects on the gut-brain axis, whereas high-glycemic carbohydrates may exacerbate mood disorders and neuro-inflammation.

Micronutrients:

Because they lower homocysteine levels, micronutrients—especially B-group vitamins—are essential for regulating memory retention, cognitive function, and brain health, especially in older adults. One vitamin B3 derivative that shows promise as an adjuvant treatment for schizophrenia is niacin. Alpha-tocopherol, a component of vitamin E, shields nerve membranes from oxidative damage, while vitamin D is linked to the protection of neurodegenerative diseases. Manganese, zinc, and copper are among the minerals that take part in enzymatic processes that fight against oxidative stress. In the brain, iron is necessary for energy production, oxygenation, and neurotransmitter synthesis. Calcium, potassium, and magnesium control sleep by adjusting ion channel activity [13].

The possible importance of bioactive chemicals, particularly polyphenols, which are included in foods such as berries, nuts, green leafy vegetables, and whole-grain cereals, in avoiding cognitive decline and improving cognitive performance has drawn attention. The MIND Diet trial and the PREDIMED trial offer proof of the advantages of foods high in polyphenols for mental well-being. Polyphenols affect brain function through a variety of mechanisms, including increased cerebral blood flow, altered blood-brain barrier transporter activity, and direct impacts on central nervous system neuronal and glial cell activity. The potential of bioactive substances to preserve cognitive health and prevent age-related decline is highlighted by this multimodal activity [14].

When consumed as vegetables, glucosinolates—sulfur-containing chemicals mostly present in Brassicaceae plants—become biologically active molecules such as isothiocyanates or indoles. The neurological effects of these substances have been brought to light in recent study, including their suppression of pro-inflammatory cytokine generation and favorable modulation of the nuclear factor erythroid 2-related factor (Nrf2) antioxidant pathway. The possible cognitive benefits of carotenoids, which are lipophilic chemicals found in large quantities in orange and red vegetables as well as Brassicaceae plants, have also drawn attention. Extensive cohort studies, like NHANES, have found a link between enhanced cognitive function and increased consumption of two well-known carotenoids, zeaxanthin, and lutein [14-15].

Factors Affecting nutrition and Brain Health:

Circadian Rhythm:

Through 24-hour rhythmic patterns, the circadian cycle regulates a number of biological activities, including hormone secretion, glucose management, sleep-wake cycles, and thermogenesis. The circadian cycle is triggered by a variety of environmental and behavioral factors, including hormones, physical activity, dietary intake patterns, eating and fasting states, sleep-wake patterns, and temperature. Because circadian rhythms and metabolic processes are bidirectional, any interference with these cycles may lead to energy imbalances and a higher chance of age-related disorders. The 24-hour cycle is reflected in the physiology of fasting-refeeding, which permits organisms to obtain, store, and use resources effectively without sacrificing fitness. According to current research, the fasting phase may aid in the renewal and repair of cellular constituents since it activates several biochemical processes during resource use as opposed to feeding [16].

Fasting Status:

Sleep, metabolism, and circadian rhythm are all influenced by the hormone adiponectin, which is involved in glucose metabolism. Its expression is circadian regulated, and intermittent fasting markedly increases levels of adiponectin. Increased levels of adiponectin are linked to a lower risk of cardiovascular disease, while sleep deprivation may lower levels of adiponectin and increase the risk of cardiovascular disease. Furthermore, there is evidence that adiponectin plays a complex function in mental health since decreased peripheral adiponectin levels are associated with mood, anxiety, and stress-related affective disorders [17].

Brain-Derived Neurotrophic Factor:

Brain-derived neurotrophic factor (BDNF) has attracted a lot of attention due to its important role in controlling many brain functions, acting as a modulator of neurotransmitters, encouraging the survival and proliferation of neurons, and enabling the plasticity of neurons. Furthermore, because both BDNF and insulin receptors are connected to intracellular signaling pathways including MAP kinase and PI3-kinase/Akt, BDNF is essential for glucose and energy metabolism. Intermittent fasting has been shown in experimental experiments to increase brain-derived neurotrophic factor (BDNF) expression in several brain regions, hence supporting neurogenesis, synaptic plasticity, and neuronal resistance against illness and damage. Additionally, by controlling hunger, peripheral glucose metabolism, and the autonomic processes of the digestive and cardiovascular systems, BDNF regulates the behavioral and metabolic reactions to fasting [189].

Reduced blood levels of BDNF have been linked to sleeplessness and insomnia, with BDNF levels being considerably lower in those with depressive and insomnia symptoms. Furthermore, notable variations in the gut microbiota throughout the day-night cycle imply taxonomic configurations that are specific to the time of day and impacted by dietary habits, biological clocks, and rhythmic food intake. The complex relationship between gut microbiota, circadian rhythms, and mental health is highlighted by this interaction between microbes and circadian genes as well as emotional and physiological stress [19].

Bioactive compounds have emerged as potential regulators of circadian rhythm, with implications for obesity-related outcomes. Epigallocatechin-3-gallate (EGCG), a prominent flavan-3-ol found abundantly in green tea, has been studied for its ability to modulate circadian clock genes such as Clock, Bmal1, and Cry1. These genes, in turn, may regulate key metabolic genes like Sirt1 and PGC1α, which control lipid metabolism in adipose tissue. In addition to daily circadian rhythms, bioactive compounds also influence circannual rhythms. Research suggests that polyphenol-rich fruits and vegetables, consumed in or out of season, can alter the photoperiod-dependent effects on gene regulation related to fatty acid transport and lipolysis in skeletal muscles. Similarly, the consumption of seasonal produce, potentially due to their polyphenol content, can influence the leptin system based on the photoperiod during consumption. These findings highlight the intricate relationship between bioactive compounds, circadian rhythms, and metabolic processes, suggesting their potential as therapeutic targets for obesity and related conditions [20].

Brain-Gut Axis:

The gut microbiota of healthy adults is mostly composed of bacteria from the phylum Firmicutes, which includes genera such as Lactobacillus, Clostridium, and Enterococcus, and the phylum Bacteroidetes, which includes genera like Bacteroides. This composition of bacteria does not change over time. Pathogenic conditions, however, might result from variations marked by an excess of facultative anaerobes such as Escherichia coli, pro-inflammatory Ruminococcus species, or nonbacterial microorganisms. Thus, it is essential for sustaining overall body health that the strains of the gut microbiota remain diverse and in balance [21]. The kind, caliber, and origin of food have a big impact on the makeup and functionality of the gut microbiota. It has been demonstrated that consuming more fiber and probiotics will positively affect gut flora. Increased variety in the gut microbiota is linked to healthy eating habits like the Mediterranean diet and other plant-rich diets. Although research is still in its early stages, some findings point to a possible link between depressive moods or reactions to long-term stress and changes in the composition of the gut microbiota, namely in the Firmicutes/Bacteroidetes/Clostridium ratio [22].

Recent studies highlight the neuronal, endocrine, and inflammatory pathways that are involved in the two-way communication between the gut bacteria and the nervous system. Through the synthesis of several chemicals, such as short-chain fatty acids, secondary bile acids, tryptophan metabolites, folate, and GABA, the gut microbiota can directly affect neurotransmitter metabolism and affect the operation of the central nervous system as well as the enteric system. Interactions between enteroendocrine cells (EECs) and enterochromaffin cells (ECCs) assist this signal transmission. These cells can trigger central responses, such the production of serotonin, through long-distance neural signaling via vagal or afferent nerve fibers that extend into the intestinal villi [23].

Intestinal Microbiomes:

A complicated mechanism known as the gut-brain axis depends on gut peptides, which are modulated in large part by the intestinal microbiota. Neuropeptide Y affects GABA release and contributes to neuronal signaling. It is widely distributed throughout the brain and is strictly controlled by peripheral signaling. By controlling insulin and glucagon release, glucagon-like peptide-1, an incretin hormone, influences the hypothalamic-pituitary-adrenal (HPA) axis, stress responses, and postprandial blood glucose levels. Cholecystokinin (CCK) inhibits anxiety-like behavior by activating the limbic region and controlling pancreatic enzyme release, stomach emptiness, gallbladder contraction, and hunger suppression. A reciprocal association between the composition of the gut microbiota and ghrelin is suggested by the correlation between particular strains of gut bacteria and serum ghrelin, which is implicated in adipogenesis and the stress response [24].

By controlling the release of adrenocorticotropic hormone (ACTH) and the secretion of cortisol, corticotropin-releasing factor (CRF) mediates the stress response. Dysregulation of the CRF system can affect gastrointestinal motility and permeability and is linked to problems related to stress. There is a complicated interplay between CRF, gut microbiota, and stress-related pathways, as evidenced by animal studies that link altered CRF signaling, changes in gut microbiota composition (e.g., reduced Lactobacillus), and variations in the intestinal microbial population. The bacteria's conversion of dietary (poly)phenols into smaller chemicals that can affect the neurological system is an interesting aspect of the interaction between the gut microbiota and the brain. Flavan-3-ol colonic metabolites, including phenyl-γ-valerolactones, have been demonstrated to penetrate the blood-brain barrier and perhaps disrupt the formation of amyloid-β oligomers, providing a possible treatment option for Alzheimer's disease-related neurodegeneration. There is evidence that other metabolites generated from the gut microbiota have anti-inflammatory properties at the neuronal level, indicating a more extensive function for these chemicals in brain function [25].

Supplementing with polyphenol-rich extracts has been shown to improve cognitive function in human intervention trials, especially in areas like working memory and attention. Increased intestinal permeability (also known as a "leaky gut") can result from dysbiosis of the intestinal microbiota, which is characterized by a shift toward harmful bacterial species and a decrease in microbial diversity. This can allow bacterial components such lipopolysaccharides (LPS) to enter the bloodstream. This sets off a cytokine-mediated inflammatory response that exacerbates systemic inflammation. It has been demonstrated that short-chain fatty acids (SCFAs), which are generated by gut bacteria, have anti-inflammatory properties. They do this by attaching G-protein receptors on a variety of cells, including brain glial cells and nerve fibers, and thereby reducing neuroinflammation. Furthermore, SCFAs might directly encourage microglial activation, which would further control inflammatory reactions. The complex interactions between the gut microbiota, neurotransmitters, and inflammatory pathways are illustrated by the roles that gut neurotransmitters like serotonin play in immunological and inflammatory modulation [26].

Oxidative Stress:

The intricate relationship between low-grade inflammation, oxidative stress, and mental health is increasingly acknowledged as a pivotal factor in various non-communicable diseases, including mental illnesses. Pro-inflammatory cytokines, pivotal in the pathophysiology of mental disorders, can perturb neurotransmitter function and regulate brain-derived neurotrophic factor (BDNF) expression. Conversely, deficiencies in anti-inflammatory cytokines like transforming growth factor-β1 (TGF-β1) have been linked to depressive disorders and cognitive impairments. Sleep disturbances, depression, and anxiety are correlated with elevated inflammatory markers, indicating a bidirectional link between mental health, inflammation, and oxidative stress. Suboptimal sleep and mental health issues may heighten levels of cytokines such as IL-6 and CRP. Dietary habits and nutrient intake also shape inflammation, with plant-based foods, extra virgin olive oil, omega-3 fatty acids, and specific polyphenols exerting anti-inflammatory effects and enhancing cognitive function [27].

Conversely, diets rich in calories, added sugars, processed meats, and unhealthy fats contribute to systemic inflammation and cognitive decline. The gut microbiota, through the synthesis of bioactive compounds like phenyl-γ-valerolactones from flavan-3-ols, also modulates inflammation and neuroprotection. These insights underscore the potential for dietary interventions and lifestyle adjustments to mitigate inflammation and oxidative stress, thereby fostering improved mental health outcomes and reducing the risk of neurodegenerative diseases like Alzheimer's [28].

Conclusion:

In conclusion, the discussion highlights the intricate relationship between nutrients and brain health, emphasizing the significant impact of diet on mental well-being. Various nutrients, including macronutrients like fatty acids, proteins, and carbohydrates, as well as micronutrients like vitamins and minerals, play crucial roles in modulating brain function, cognitive performance, and mood regulation. Key findings suggest that specific nutrients, such as omega-3 fatty acids, B-group vitamins, and polyphenols, possess neuroprotective properties and can positively influence neurotransmitter function, neuroplasticity, and cognitive function. Additionally, the gut microbiota emerges as a critical player, influencing brain health through the production of bioactive compounds and the modulation of inflammation and oxidative stress. Furthermore, the bidirectional relationship between mental health, inflammation, and oxidative stress underscores the importance of dietary patterns in mitigating systemic inflammation and reducing the risk of neurodegenerative diseases. Plant-based diets, rich in antioxidants and anti-inflammatory compounds, show promise in promoting brain health and preventing cognitive decline. Overall, the evidence presented suggests that adopting a balanced and nutrient-rich diet, along with lifestyle modifications, can have profound implications for mental well-being and cognitive function. Further research in this field is warranted to elucidate the specific mechanisms underlying the effects of nutrients on brain health and to develop targeted dietary interventions for optimizing cognitive performance and preventing mental disorders.

References:

1. Whiteford, H.A.; Degenhardt, L.; Rehm, J.; Baxter, A.J.; Ferrari, A.J.; Erskine, H.E.; Charlson, F.J.; Norman, R.E.; Flaxman, A.D.; Johns, N.; et al. Global burden of disease attributable to mental and substance use disorders: Findings from the Global Burden of Disease Study 2010. *Lancet* **2013**, *382*, 1575–1586.
2. Clarke, D.M.; Currie, K.C. Depression, anxiety and their relationship with chronic diseases: A review of the epidemiology, risk and treatment evidence. *Med. J. Aust.* **2009**, *190*, S54–S60.
3. Branca, F.; Lartey, A.; Oenema, S.; Aguayo, V.; Stordalen, G.A.; Richardson, R.; Arvelo, M.; Afshin, A. Transforming the food system to fight non-communicable diseases. *BMJ* **2019**, *364*, l296.
4. Pot, G.K. Sleep and dietary habits in the urban environment: The role of chrono-nutrition. *Proc. Nutr. Soc.* **2018**, *77*, 189–198.
5. Vaccarino, V.; Goldberg, J.; Rooks, C.; Shah, A.J.; Veledar, E.; Faber, T.L.; Votaw, J.R.; Forsberg, C.W.; Bremner, J.D. Post-traumatic stress disorder and incidence of coronary heart disease: A twin study. *J. Am. Coll. Cardiol.* **2013**, *62*, 97–978.
6. Mayer, E. *The Mind-Gut Connection: How the Hidden Conversation Within Our Bodies Affects Our Mood, Our Choices, and Our Overall Health*; HarperCollins: New York, NY, USA, 2016.
7. Grosso, G.; Galvano, F.; Marventano, S.; Malaguarnera, M.; Bucolo, C.; Drago, F.; Caraci, F. Omega-3 fatty acids and depression: Scientific evidence and biological mechanisms. *Oxidative Med. Cell. Longev.* **2014**, *2014*, 313570.
8. Glenn, J.M.; Madero, E.N.; Bott, N.T. Dietary protein and amino acid intake: Links to the maintenance of cognitive health. Nutrients 2019, 11.
9. Friedman, M. Analysis, nutrition, and health benefits of tryptophan. Int. J. Tryptophan Res. 2018, 11.
10. Bannai, M.; Kawai, N. New therapeutic strategy for amino acid medicine: Glycine improves the quality of sleep. J. Pharmacol. Sci. 2012, 118, 145–148.
11. Wurtman, J.; Wurtman, R. The trajectory from mood to obesity. Curr. Obes. Rep. 2018, 7, 1–5.
12. Irwin, M.R.; Olmstead, R.; Carroll, J.E. Sleep disturbance, sleep duration, and inflammation: A systematic review and meta-analysis of cohort studies and experimental sleep deprivation. Biol. Psychiatry 2016, 80, 40–52.

13. Hoffer, A.; Prousky, J. Successful treatment of schizophrenia requires optimal daily doses of vitamin B3. Altern. Med. Rev. 2008, 13, 287–291.
14. Bourre, J.M. Effects of nutrients (in food) on the structure and function of the nervous system: Update on dietary requirements for brain. Part 1: Micronutrients. J. Nutr. Health Aging 2006, 10, 377–385. [Google Scholar]
15. Zeng, Y.; Yang, J.; Du, J.; Pu, X.; Yang, X.; Yang, S.; Yang, T. Strategies of functional foods promote sleep in human being. Curr. Signal Transduct. Ther. 2014, 9, 148–155.
16. Longo, V.D.; Mattson, M.P. Fasting: Molecular mechanisms and clinical applications. Cell Metab. 2014, 19, 181–192
17. Longo, V.D.; Panda, S. Fasting, circadian rhythms, and time-restricted feeding in healthy lifespan. Cell Metab. 2016, 23, 1048–1059.
18. Monteiro, B.C.; Monteiro, S.; Candida, M.; Adler, N.; Paes, F.; Rocha, N.; Nardi, A.E.; Murillo-Rodriguez, E.; Machado, S. Relationship between brain-derived neurotrofic factor (Bdnf) and sleep on depression: A critical review. Clin. Pract. Epidemiol. Ment. Health 2017, 13, 213–219.
19. Marine-Casado, R.; Domenech-Coca, C.; Del Bas, J.M.; Blade, C.; Caimari, A.; Arola, L. Cherry consumption out of season alters lipid and glucose homeostasis in normoweight and cafeteria-fed obese Fischer 344 rats. J. Nutr. Biochem. 2019, 63, 72–86.
20. Ibars, M.; Aragones, G.; Ardid-Ruiz, A.; Gibert-Ramos, A.; Arola-Arnal, A.; Suarez, M.; Blade, C. Seasonal consumption of polyphenol-rich fruits affects the hypothalamic leptin signaling system in a photoperiod-dependent mode. Sci. Rep. 2018, 8, 13572.
21. Dawson, S.L.; Dash, S.R.; Jacka, F.N. The importance of diet and gut health to the treatment and prevention of mental disorders. Int. Rev. Neurobiol. 2016, 131, 325–346.
22. Makki, K.; Deehan, E.C.; Walter, J.; Backhed, F. The impact of dietary fiber on gut microbiota in host health and disease. Cell Host Microbe 2018, 23, 705–715.
23. Houghton, D.; Hardy, T.; Stewart, C.; Errington, L.; Day, C.P.; Trenell, M.I.; Avery, L. Systematic review assessing the effectiveness of dietary intervention on gut microbiota in adults with type 2 diabetes. Diabetologia 2018, 61, 1700–1711.
24. Ballaz, S. The unappreciated roles of the cholecystokinin receptor CCK(1) in brain functioning. Rev. Neurosci. 2017, 28, 573–585.
25. Morris, L.S.; Voon, V.; Leggio, L. Stress, motivation, and the gut-brain axis: A focus on the ghrelin system and alcohol use disorder. Alcohol. Clin. Exp. Res. 2018, 42.
26. Fox, J.H.; Lowry, C.A. Corticotropin-Releasing factor-related peptides, serotonergic systems, and emotional behavior. Front. Neurosci. 2013, 7, 169.
27. Caraci, F.; Spampinato, S.F.; Morgese, M.G.; Tascedda, F.; Salluzzo, M.G.; Giambirtone, M.C.; Caruso, G.; Munafo, A.; Torrisi, S.A.; Leggio, G.M.; et al. Neurobiological links between depression and AD: The role of TGF-β1 signaling as a new pharmacological target. Pharmacol. Res. 2018, 130, 374–384.
28. Bauche, D.; Marie, J.C. Transforming growth factor β: A master regulator of the gut microbiota and immune cell interactions. Clin. Transl. Immunol. 2017, 6, e136.