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Depression and Diets: The Interconnected Relationship Between Lifestyle and Depression Status-An Updated Review

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Abstract

Background: Depression is a widespread and debilitating mental health condition affecting millions globally. Despite the availability of first-line antidepressant treatments, a significant portion of individuals with major depressive disorder (MDD) fails to respond to conventional therapies. Additionally, lifestyle factors such as stress, sleep patterns, exercise, and diet play a critical role in the development and progression of depression. While stressful life events are common triggers, individual resilience influenced by lifestyle choices is a key area for intervention.

Aim: This review aims to explore the interconnected relationship between lifestyle factors—specifically diet—and depression. By analyzing existing research on dietary patterns and their association with depressive symptoms, the review seeks to understand how dietary interventions might serve as alternative or complementary treatments for depression.

Methods: The review synthesizes evidence from various studies, including original research and meta-analytic investigations, focusing on the links between diet, obesity, metabolic syndrome, and depression. Studies covering meal timing, nutrient deficiencies, and dietary patterns such as the Mediterranean diet were also examined for their impact on depression.

Results: Research highlights that poor dietary habits, including excessive caloric intake and the consumption of ultra-processed foods, are associated with an increased risk of depression. Diets rich in omega-3 fatty acids, vegetables, and fruits, such as the Mediterranean diet, show protective effects against depression. Furthermore, meal timing, such as skipping breakfast or late eating patterns, also correlates with higher depressive symptoms. Additionally, interventions targeting obesity and metabolic disorders, such as calorie restriction or bariatric surgery, have shown improvements in both physical health and depressive symptoms.

Conclusion: Lifestyle modifications, particularly diet, play a crucial role in the prevention and management of depression. The evidence supports the implementation of nutritional interventions, including adopting healthier eating patterns, reducing the intake of ultra-processed foods, and maintaining balanced meal timings, to alleviate depressive symptoms and improve overall well-being.

Keywords: Depression, diet, lifestyle factors, obesity, Mediterranean diet, meal timing, metabolic syndrome, nutritional psychiatry.

Introduction

Persistent sadness, decreased interest or enjoyment in activities, changes in appetite, disturbed sleep patterns, psychomotor agitation or retardation, exhaustion, poor concentration, feelings of guilt or worthlessness, and suicidal thoughts are all signs of depressive disorder, a severe mental illness [1]. According to estimates, the disorder's global point prevalence is 4.4% [2]. A considerable percentage of patients with major depressive disorder (MDD) do not respond well to first-line antidepressant treatments or do not achieve remission, according to extensive clinical studies like the STAR*D (Sequenced Treatment Alternatives to Relieve

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Depression) trial [3]. Additionally, because of the unpleasant side effects, MDD patients frequently do not take their antidepressants as directed, which calls for the investigation of alternate treatment approaches [4]. Stressful life events, like increasing work obligations [5], interpersonal disputes [6], and other negative events [7], are often the cause for depressive disorder. However, the effects of these stressors differ according on personal lifestyle choices. While some people exhibit higher resilience to the detrimental effects of stress, others are more susceptible, which may be influenced by their coping methods, sleep patterns, exercise routines, and eating habits [8]. In fact, a number of lifestyle choices have been found to be important risk factors for the onset of depression [9]. It would be therapeutically advantageous to alter lifestyle characteristics in order to improve stress resilience. With an emphasis on diet, nutritional concerns, and related behaviors, this review aims to analyze research on lifestyle factors linked to depressive illness and therapy approaches for changing these characteristics. The review integrates the results of the author's original study as well as meta-analytic investigations.

Diet and Nutritional Challenges in Modern Society

Research on dietary habits and nutritional status in relation to depressive disorder, particularly since the early 21st century, suggests that depression shares strong associations with dietary patterns, much like other lifestyle-related diseases, including cardiovascular diseases and stroke [10]. Two main nutritional concerns in contemporary society are excessive caloric intake in an age of abundance and nutritional imbalances resulting from the "Westernization" of food products, where natural ingredients lose micronutrients and polyphenols during commercialization. Both of these issues have been linked to depression, as discussed below.

Excessive Caloric Intake and Depression

Obesity and depression are significantly linked, according to recent research, and they share molecular pathways [11,12]. There is growing evidence that depression and obesity, diabetes, and metabolic syndrome—diseases largely caused by consuming too many calories—are correlated. Obesity raised the risk of depression (odds ratio [OR], 1.55), and depression increased the chance of obesity (OR, 1.58), according to a meta-analysis of 15 longitudinal studies done more than ten years ago [13]. Similar, if marginally weaker, correlations have been found in more recent meta-analyses, which show that obesity increases the likelihood of depression (RR, 1.18), and depression increases the risk of obesity (RR, 1.37). These results imply that there might be a larger correlation between depression and obesity. Additionally, it seems that obesity affects how depression manifests clinically. For example, a study by Toups et al. [15] looked at 662 patients with MDD and discovered that a lower body mass index (BMI) was linked to higher rates of substance abuse and PTSD, while a higher BMI was linked to increased medical comorbidities, social phobia, and bulimia. In contrast to their non-obese counterparts, our study showed that obese MDD patients (BMI ≥30 kg/m2) had noticeably worse impairments in cognitive abilities, such as working memory, fine motor skills, and executive function [16]. Obesity was associated with decreased gray matter volume in areas related to cognition (such as the orbitofrontal cortex and thalamus) and impaired white matter neural connections, according to brain imaging. This suggests that obesity adds to the cognitive load and prevents MDD patients from recovering functionally. In euthymic bipolar illness individuals, a similar finding was noted [17].

It is also commonly known that type 2 diabetes and depression are correlated. According to a 1980–2002 meta-analysis, people with type 2 diabetes had a significantly higher prevalence of depression than those without the disease (17.6% vs. 9.8%; OR, 1.6) [18]. According to a Japanese study, depressed symptoms were present in 36.4% of ambulatory diabetic patients, especially those with pain, microvascular problems, and neuropathy [19]. Another study found a reciprocal relationship between hemoglobin A1c levels and depressed symptoms [21], and depression itself raises the risk of type 2 diabetes (RR, 1.18). The relatively high risk of diabetes in depressed people in Japan, possibly as a result of inadequate interventions encouraging physical activity, was highlighted by a Japanese cohort study that found that people with depressive symptoms had a 2.3-fold higher risk of developing diabetes over an 8-year period [22]. The metabolic syndrome raises the likelihood of depression (OR, 1.49) and vice versa (OR, 1.52), according to a meta-analysis of data on the condition [23].

The Importance of Meal Timing

The importance of meal timing for both physical and mental health has been highlighted by recent studies. Three meal timing patterns were distinguished by Wilson et al. [24]: grazing, which involves eating throughout the day; traditional, which involves eating most meals at regular intervals; and late, which involves skipping or postponing breakfast in favor of bigger evening meals. While the typical mealtime pattern was linked to a much lower risk of developing mood disorders, the late meal timing pattern was linked to a higher risk. This implies that irregular eating habits, especially skipping or postponing breakfast, could be a factor in mood problems. Those with a history of depression were more likely to be obese, have dyslipidemia, and snack at night, according to our own study, which polled 11,876 Japanese people [25]. Although causality cannot be established due to the cross-sectional design of the study, these people also reported skipping breakfast more frequently.

Skipping breakfast is frequently linked to late meals and bedtime munchies, which raises the risk of weight gain and obesity, according to a number of research, including those done in Japan [26–28]. Low breakfast consumption was linked to a higher risk of obesity (OR, 1.48) and abdominal obesity (OR, 1.31) than people who ate breakfast more frequently, according to a meta-analysis of 45 studies [29]. In addition, a recent meta-analysis of 14 studies with 399,550 participants revealed a significant positive correlation between skipping breakfast and psychological distress (OR, 1.55), stress (OR, 1.23), and depression (OR, 1.39). However, there was no significant correlation between skipping breakfast and anxiety in any age group (OR, 1.31), with adolescents being the only exception (OR, 1.51) [30].

According to new research, fasting interventions—which frequently entail calorie restriction and skipping breakfast—may also improve metabolic health and stress-related illnesses like anxiety and depression [31–34]. According to a meta-analysis, one well-known fasting method, intermittent fasting (also known as time-restricted eating), which entails fasting for 24 hours or less, significantly lowers body weight (mean difference, −2.49 kg), BMI (mean difference, −1.56 kg/m2), and related metabolic indices like fat mass and waist circumference when compared to non-fasting people [31]. Furthermore, whereas six non-randomized investigations revealed no discernible effect on anxiety or mood, a meta-analysis of eight randomized controlled trials revealed that intermittent fasting had a moderately beneficial effect on depression ratings when compared to control groups [32]. After implementing intermittent fasting, a patient with mood dysregulation, including depression, and gestational diabetes in a case study demonstrated improvements in body weight, plasma glucose, and psychological distress [33]. According to a different meta-analysis, stress, anxiety, and depression scores decreased during Ramadan when compared to pre-Ramadan levels; however, the effects might be impacted by things like quitting smoking [34].

Interventions for Obesity and Related Conditions

A reinforcing loop is suggested by the reciprocal association between physical disorders brought on by excessive energy intake and depression. By treating physical diseases including obesity, metabolic syndrome, and diabetes, people with concomitant depression may be able to break the cycle and improve their cognitive performance and depressive symptoms. In both people and animals, calorie restriction—defined as a 30% to 40% reduction in caloric intake without resulting in malnutrition—has been suggested to have depressive and antidepressant-like effects [35–37]. Additionally, a meta-analysis of 14 prospective studies revealed that bariatric surgery reduces anxiety and depression symptoms in very obese people (BMI ≥35) for at least 24 months [38]. Although one meta-analysis did note that post-bariatric surgery depression is still common in about 15% of patients, two later meta-analyses examining the effect of bariatric surgery on depressive symptoms produced consistent results [39, 40]. Antidiabetic drugs including metformin and glucagon-like peptide-1 agonists have shown promise in reducing depression symptoms and cognitive deficits in people with diabetes, including those at risk of developing diabetes (prediabetes) [42, 43]. In a clinical experiment examining the effects of metformin in individuals with type 2 diabetes and major depressive disorder (MDD), for example, Guo et al. [44] discovered that, in comparison to a placebo, metformin improved cognition and depression ratings. According to a meta-analysis, psychosocial therapies have also been shown to be helpful for depression in diabetic patients [45]. The fact that some antidepressant drugs cause weight gain while others do not should not be overlooked. According to a meta-analysis, medications like paroxetine, amitriptyline, and mirtazapine significantly increase weight gain, while bupropion is linked to weight loss after maintenance therapy [46]. This implies that a patient's body mass index (BMI) could be a significant factor in deciding which antidepressant is best for them. Accordingly, it seems that bupropion works better for treating MDD in fat people than in non-obese ones [47].

Diet Style and Depression

The nutritional imbalances brought about by the Westernization of diet have become a growing area of research interest. A lower incidence of depression has been associated with the Mediterranean diet, which is characterized by a high intake of fruits, vegetables, legumes, grains, fish, and olive oil and a low intake of meat and dairy products. Those who followed a Mediterranean diet regularly had a considerably lower risk of depression than those who followed it sparingly (RR = 0.67), according to a meta-analysis of longitudinal studies [49]. Chronic inflammation is less likely to be triggered by this healthy eating pattern, and diets that are considered "less inflammation-prone" according to the eating Inflammation Index have also been linked to a lower risk of depression (RR = 0.76) [49]. Ultra-processed foods (UPFs), which are frequently heavy in unhealthy elements such snacks, sugary drinks, ready meals, and other food products mostly made from food extracts, have become more popular in modern diets, especially in industrialized nations. The COVID-19 pandemic has made this change worse, which has led to more inflammation and weight gain [52]. Every 10% increase in UPF consumption per daily calorie intake was linked to an 11% higher risk of depression in adults, according to a recent meta-analysis that found a significant correlation between UPF consumption and an increased risk of depression (RR = 1.28) [53]. Increased junk food consumption is

associated with greater rates of depression (OR = 1.62), stress (OR = 1.34), anxiety (OR = 1.24), sleep dissatisfaction (OR = 1.17), and decreased happiness (OR = 0.83) in the younger population, according to a meta-analysis [54]. The International Society for Nutritional Psychiatry Research (ISNPR) suggests five important dietary behaviors in light of these findings: (i) adopt conventional dietary patterns, like the Norwegian, Japanese, or Mediterranean diets; (ii) consume more fruits, vegetables, legumes, whole grains, nuts, and seeds; (iii) give priority to foods high in omega-3 polyunsaturated fatty acids (PUFAs); (iv) replace unhealthy foods with wholesome, nutritious ones; and (v) limit consumption of processed foods, fast food, commercial bakery goods, and sweets [55]. In addition to being acknowledged for its role in the Japanese population's longer lifespan, the traditional Japanese cuisine has also been thought to have positive effects on mental health. Although there aren't many studies that specifically look at the connection between diet and depression in Japanese people, Nanri et al. [56] discovered that in a work environment, people with higher scores on the Healthy Japanese Food Pattern—a diet high in fruits, vegetables, soy products, mushrooms, and green tea—had significantly lower rates of depressive symptoms.

Nutrients and Depression

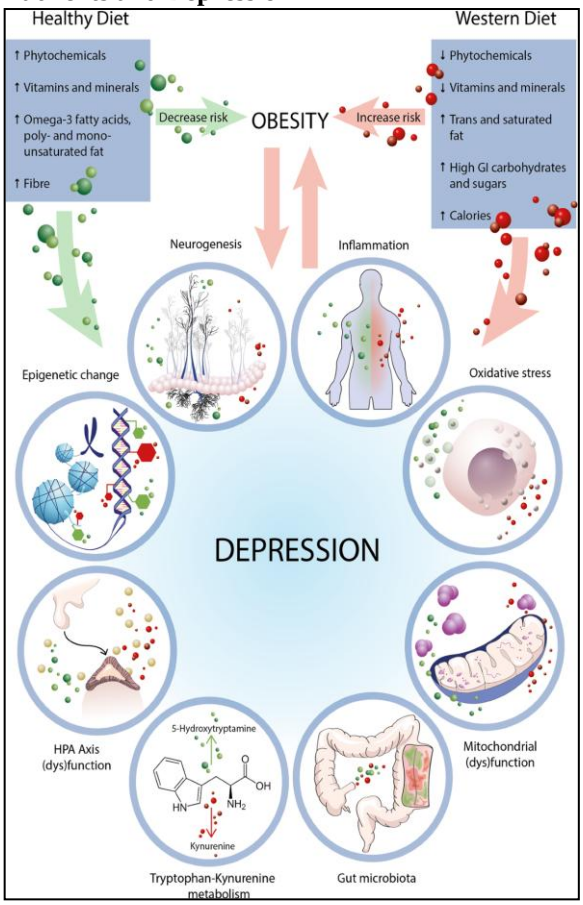

Figure 1: Diets and Depression.

Ω3 PUFAs

Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), two of the ω3 polyunsaturated fatty acids (PUFAs), are often lacking in human diets unless they come from fish. The ability of these nutrients to prevent cardiovascular events has long been known [57]. Lower fish consumption was linked to a higher incidence of depression (relative risk [RR], 0.83 between maximum and lowest consumption), according to a meta-analysis that included 26 trials with a total of 150,278 participants [58]. According to a meta-analysis of 14 investigations, blood levels of ω3 PUFAs were considerably lower in depressed people (N = 648) than in controls (N = 2670) [59]. The effectiveness of EPA and DHA supplementation in treating depression has been documented in a number of meta-analyses; however, the effect sizes are modest and should be interpreted with caution because of possible publication bias [60–64]. According to Sublette et al. [60], supplements that contained EPA at ≥60% of the total EPA and DHA, at a dose range of 200 to 2200 mg/day, were particularly effective in treating primary depression. According to the International Society for Nutritional Psychiatry Research (ISNPR) standards, major depressive disorder (MDD) can be effectively treated with doses of 1 to 2 g of net EPA per day, either pure EPA or an EPA/DHA ratio higher than 2:1 [66]. To determine the ideal dosage and use of ω3 PUFAs for treating depression, more research is required, as Liao et al. [63] found that even doses less than 1 g/day could have positive effects.

In addition to depression, EPA and DHA therapy has demonstrated promise for a number of other mental illnesses. For mood, impulsive control, and psychotic problems, the American Psychiatric Association suggests eating fish at least twice a week and taking supplements of EPA + DHA [67]. Consistent with this, our team discovered that EPA and DHA plasma levels were lower in bipolar depression patients than in healthy people, and that EPA concentrations (but not DHA) were inversely connected with plasma levels of inflammatory cytokines like tumor necrosis factor α (TNF-α) and interleukin 6 (IL-6) [68]. This research demonstrates the value of EPA in the treatment of inflammatory diseases and supports its anti-inflammatory properties. Additional research in populations affected by disasters, including those afflicted by the Great East Japan earthquake, showed a negative relationship between blood EPA concentrations and PTSD symptom scores, indicating that EPA may have a protective effect against PTSD [69]. The positive effects of EPA in treating PTSD are also supported by research on Croatian war veterans [70].

Vitamins

Two important vitamins that have been repeatedly linked to the risk of depression are folate and vitamin D. Depressed people had considerably lower serum

and red blood cell folate levels, according to a meta-analysis of 43 trials including 8519 depressed people and 27,282 controls [71]. In a Japanese workplace (N = 530), employees in the lowest serum folate quartile were more likely to have depression symptoms than those in the higher quartiles [72]. In a meta-analysis of four trials, the effectiveness of folate replacement therapy for depressed patients receiving antidepressant treatment has been documented; nevertheless, its usefulness is still up for question, mainly because of one big study (N = 475) that produced unfavorable results [62]. On the other hand, a more recent meta-analysis of nine studies with 6707 participants suggested that individuals with MDD receiving antidepressant treatment might benefit somewhat from additive L-methylfolate, the active form of folate [76]. Patients with depression should have their folate levels checked, and supplements should be given if needed, since folate preparations are frequently used in clinical practice to treat folate insufficiency. To improve clinical results, foods high in folate, such as green vegetables, dietary liver, and soy products, should be promoted. Furthermore, blood levels of other B vitamins should be tracked, especially in depressed individuals who drink too much alcohol or have severe appetite loss. Inadequate thiamine (vitamin B1) intake was found to be significantly associated with depression in a nationwide cross-sectional research conducted in Korea [77]. There have been anecdotal reports of Wernicke encephalopathy brought on by thiamine shortage, which was caused by decreased appetite during depression [78].

Foods like fish and mushrooms are rich in vitamin D, which is created when the skin's 7-dehydrocholesterol is exposed to ultraviolet light. It is essential for the development of bone and teeth and plays a critical role in encouraging the kidneys and small intestine to absorb calcium and phosphorus. Conditions like osteomalacia and osteoporosis can result from a vitamin D deficiency. For the prevention of osteoporosis, blood levels of 25-hydroxyvitamin D ≥30 μg/L, 20-30 μg/L, and <20 μg/L are categorized as sufficient, inadequate, and deficient, respectively [79]. There is growing evidence that depression and vitamin D deficiency are related. According to a meta-analysis, blood vitamin D levels are typically lower in depressed people than in healthy controls [80]. Similarly, a study conducted in a Japanese workplace found that employees with vitamin D levels ≥20 μg/L were far less likely to experience depression symptoms than those with lower levels (OR, 0.6–0.8) [81]. However, there was no discernible preventative effect of vitamin D on depression in a major randomized controlled study (RCT) that included 25,871 individuals in the United States [82]. Furthermore, oral vitamin D supplementation did not show a significant effect on the treatment of depression, according to a meta-analysis of 10 RCTs involving 1393 individuals [83]. However, when vitamin D was administered as a supplement to antidepressant medication, two additional thorough investigations found beneficial results [84, 85]. Additionally, an RCT comparing vitamin D versus a placebo in Iranian individuals with MDD revealed that vitamin D was beneficial [86]. It is thought that less daylight may play a role in the emergence of seasonal depression since human vitamin D levels show significant seasonal change, especially in high-latitude areas with little exposure to sunlight in the winter and early spring. There is conflicting information about the effectiveness of vitamin D in treating seasonal affective disorder, despite some early research suggesting that vitamin D supplementation may improve mood and reduce seasonal depression in healthy people during the winter [89, 90]. To sum up, more research is needed to ascertain whether vitamin D supplementation can successfully cure depression, especially in those who are vitamin D deficient. It is recommended that vitamin D levels be measured in individuals with depression and that supplementation be considered, especially for those with deficiencies, since a sizable portion of the population is in the inadequate or deficient vitamin D range.

Amino Acids

Significant changes were discovered between the blood amino acid concentrations of individuals with Major Depressive Disorder (MDD) and healthy controls in a study. In particular, compared to healthy controls, MDD patients had significantly lower levels of tryptophan, phenylalanine, tyrosine, and methionine, and higher levels of glutamate [91]. As necessary amino acids, tryptophan, phenylalanine, tyrosine, and methionine must be obtained from diet. Important monoamines like serotonin, dopamine, and noradrenaline are synthesized using these amino acids as building blocks [92]. Despite not being seen as necessary, glutamate is a neurotransmitter in the neurological system. The idea that eating enough protein in the diet may help prevent depression stems from the fact that MDD patients have lower levels of critical amino acids. Data from the U.S. National Health and Nutrition Examination Survey (2007–2014), which included 17,845 people aged 18 and older, indicate an inverse relationship between total protein intake and the risk of depressive symptoms (OR, 0.34 for quartile 4 vs. quartile 1 of total protein intake), despite the paucity of research investigating this possibility [93].

Since it has long been known that tryptophan deficiency can cause depressive symptoms in people who have experienced depression in the past or are at risk of developing the disorder, tryptophan merits special consideration among these amino acids [94]. Our meta-analysis has confirmed several studies that have found lower blood levels of tryptophan in

depressive patients than in healthy controls [95]. Prior to 2000, a number of randomized controlled studies (RCTs) examined the use of tryptophan as an adjuvant antidepressant treatment, in line with the early tryptophan depletion theory. One trial that used 5-hydroxy tryptamine also revealed positive findings, and four of the seven studies produced positive results. To make firm conclusions on tryptophan's role in depression, more research is required, even in light of the paucity of current data [62]. Since phenylalanine and tyrosine are building blocks for the synthesis of dopamine and noradrenaline, the observed decreases in these amino acids are noteworthy. Our results and meta-analyses that revealed a lower concentration of homovanillic acid, a dopamine metabolite, in the cerebrospinal fluid (CSF) of MDD patients compared to healthy controls may be related to this decrease in peripheral blood levels. These metabolic changes point to a possible dopaminergic system disturbance in depression [96–98].

Another important amino acid of significance is methionine, which initiates the methylation cycle. S-adenosylmethionine (SAM-e), the active form of methionine, contributes methyl groups to a number of metabolic processes, including the creation of neurotransmitters. SAM-e may have antidepressant effects, according to evidence from a meta-analysis [62]. However, SAM-e did not show substantial efficacy as an adjuvant treatment to antidepressants in a more recent RCT of patients with nonremitted MDD, which had a reasonably large sample size (N = 107) [99]. SAM-e is still prescribed in Europe and sold over-the-counter in North America in spite of this. Because of its possible benefits for mental health, theanine, a special amino acid that is rich in green tea (Camellia sinensis), has drawn attention. It seems that theanine, a glutamate derivative, partially inhibits the N-methyl-D-aspartate (NMDA) glutamate receptor [100]. In addition to enhancing sleep quality, theanine has been shown in a number of clinical and preclinical research, including our own, to exhibit calming and antidepressant-like effects [100–103]. High-quality green teas like gyokuro and matcha contain theanine (around 30 mg per cup), and supplements containing theanine are also available.

Minerals

Iron insufficiency is common, especially in women who are fertile. For example, it has been reported that the prevalence of iron deficiency anemia (IDA) in women between the ages of 20 and 44 is 11.4% in Tokyo and 14.8% in Shanghai [104]. Enzymes involved in the synthesis and metabolism of dopamine depend on iron, and a lack of it can affect how well dopamine functions. The fact that patients with restless legs syndrome (RLS), a disorder marked by an insatiable desire to exercise their legs, usually have insufficient iron storage as indicated by decreased ferritin levels lends indirect support to this theory. Furthermore, RLS symptoms can frequently be effectively treated with dopamine agonists [105]. Depressive symptoms (32.5%) and suicidal thoughts (28%) were found to be significantly more common in RLS patients than in controls, by factors of 10 and 3, respectively, in a study involving 549 untreated RLS patients and 549 matched controls [106]. These results are consistent with the established link between iron deficiency and symptoms of depression, including agitation, weariness, apathy, and difficulty concentrating. Iron deficiency anemia was also linked to a history of stress symptoms and depression, according to our study of a large online survey [107]. Additionally, studies indicate that moms with postpartum iron deficiency anemia or depleted iron stores are more likely to have postpartum depression than mothers with normal iron levels [108]. Low ferritin levels within 48 hours after birth were strongly linked to the development of postpartum depression, according to one study by Albacar et al. [109]. According to these results, taking iron supplements and keeping an eye on ferritin and serum iron levels may help reduce depressed symptoms. Iron overdose, on the other hand, should be avoided since it may raise the risk of a number of illnesses by causing oxidative stress, elevated blood viscosity, and compromised immunological response [110].

For more than 20 years, the link between zinc deficiency and depression has been recognized [111]. A widespread zinc deficit may be caused by modern dietary practices, which frequently include phosphorus-containing food additives that prevent the absorption of zinc. According to estimates, almost 30% of Japanese people don't get enough zinc in their diet [112]. A meta-analysis of 17 studies (1,643 depressed patients and 804 controls) found that zinc concentrations were roughly 1.85 μmol/L lower in depressed individuals than in controls, according to a large body of research measuring peripheral blood zinc levels in people with and without depression [113]. Zinc supplementation reduces immobility time in forced swim tests, which is consistent with animal research that suggest it has an antidepressant-like effect [111]. A meta-analysis of five research suggests that zinc supplementation, when combined with conventional antidepressant medication, may be beneficial, despite the paucity of human clinical trials [114]. These results highlight the need of keeping an eye on zinc levels in individuals with depression and offering supplements to those whose levels are below 80 μg/dL [115]. For zinc deficiency, zinc supplements are increasingly being prescribed in therapeutic settings. Dietary advice to eat foods high in zinc, such as beef, eel, and oysters, may also be helpful.

Depression has also been connected to magnesium. Magnesium intake and depressed symptoms were found to be negatively correlated in a research of 5,708 members of the Norwegian general population, with lower magnesium intake being linked to more

depressive symptoms [116]. Seaweed, unrefined seeds and grains, and soy products are rich sources of magnesium, while refining lowers their concentration.

Dietary Fiber:

Dietary fiber is a key component found in whole grains, legumes, vegetables, and fruits. The consumption of dietary fiber plays a pivotal role in fostering the growth of beneficial gut microbiota, including Bifidobacterium and Lactobacillus [117]. The health benefits associated with dietary fiber intake are extensive, encompassing weight management, protection against constipation, irritable bowel syndrome (IBS), cardiovascular disease, type 2 diabetes, metabolic syndrome, and various cancers, such as colorectal and lung cancer [118, 119]. However, the average daily fiber intake in Japan has notably declined since the latter half of the 20th century, from 20.5 g/day in 1952 to roughly 70% of this amount by 1970, with little change thereafter [120]. Although limited research exists on the relationship between dietary fiber intake and depression, a meta-analysis of four case-control studies revealed a significantly lower fiber consumption in individuals with depression compared to healthy controls. Moreover, the study indicated that a higher fiber intake was linked to a lower likelihood of depression, with an odds ratio (OR) of 0.76 [121].

Tea, Coffee, and Other Beverages:

A meta-analysis encompassing 15 observational studies—nine cross-sectional and six prospective—examined the relationship between beverage consumption and depression, involving 20,572 depression cases among 347,691 participants. The findings indicated that high coffee consumption (relative risk, RR, 0.73) and tea consumption (RR, 0.71) were associated with a reduced risk of depression, while the consumption of soft drinks was correlated with an increased risk (RR, 1.36) [122]. Research conducted in Japan explored the relationship between green tea consumption and depression, revealing that individuals with major depressive disorder (MDD) consumed green tea less frequently than healthy individuals. This was not attributable to a decrease in overall water consumption, as depressed patients were found to consume more sweetened beverages and juices than their healthy counterparts, which aligns with the findings of the meta-analysis [122]. Additionally, a study within a Japanese occupational setting demonstrated that increased green tea consumption was linked to a reduced incidence of depressive symptoms [124]. These studies also reported a negative correlation between lower coffee consumption and higher rates of depression [123, 124].

Herbs:

Numerous herbs have been identified as potentially beneficial for alleviating depression [125]. St. John's Wort (Hypericum perforatum) is particularly well known for its antidepressant properties, with substantial evidence supporting its efficacy in treating mild to moderate depression [126]. This herb is widely utilized as a supplement in various countries, and in Germany, it is even prescribed by physicians as a medicine. While it is considered relatively safe, caution is required when used in conjunction with other drugs due to potential interactions. For additional insights into other herbal medicines, refer to reviews, including that by Dai et al. [125].

Alcohol:

A meta-analysis of cohort studies investigating the connection between alcohol consumption and depressive symptoms found that individuals with alcohol use disorder were at an increased risk of developing depressive symptoms. In contrast, individuals without alcohol use disorders, regardless of their alcohol intake, did not show significant associations with depressive symptoms [127]. The potential benefits of moderate alcohol consumption in reducing depression risk remain a subject of debate [128]. However, it is generally advised that alcohol consumption should be avoided in patients undergoing treatment for depression, as alcohol may interfere with therapeutic medications, contribute to alcohol dependence, and exacerbate suicidal behavior or accidents due to its impairing effects on judgment and consciousness. Furthermore, alcohol consumption before sleep can adversely affect sleep quality.

Probiotics:

Recent research has highlighted a growing recognition of the connection between gut microbiota and various diseases, including psychiatric conditions [129, 130]. Probiotics—live microorganisms or food products containing them, such as fermented foods, yogurt, and beverages enriched with Lactobacillus and Bifidobacterium—have been suggested to mitigate stress-induced depression-like behaviors and related brain changes [131]. While evidence regarding the intestinal microbiota in patients with depression is still in its early stages, our research team found that patients with MDD exhibited lower levels of Lactobacillus and Bifidobacterium compared to controls [132]. Although no such differences were observed in patients with bipolar disorder, Bifidobacterium levels were negatively correlated with blood cortisol levels, a stress hormone, while Lactobacillus levels were negatively associated with sleep disturbance scores, indicating a possible link between these bacteria, stress, and sleep [133]. A more recent study by our group further suggested that better outcomes for MDD were associated with a higher abundance of Actinobacteria and Bifidobacterium throughout the treatment period

[134]. Recent clinical trials have provided evidence supporting the efficacy of probiotics in alleviating stress symptoms and depression, with the improvement of the intestinal environment considered a key factor in managing depression. Additionally, a significant proportion of patients with depression also suffer from irritable bowel syndrome (IBS), which presents with chronic abdominal pain, diarrhea, and constipation of unknown etiology (approximately 30% in the authors' study [Aizawa et al.132]). Given the efficacy of probiotics in managing IBS, as demonstrated by several meta-analyses [135, 136], probiotics and fermented foods containing beneficial microbes should be recommended for such cases.

Food Allergy:

Limited research has been conducted on the role of food allergies in the development of depression. However, based on the link between gastrointestinal inflammation and depression, our research group examined the potential connection between food allergies and depression using a large dataset obtained from the internet. The study found a significant, dose-dependent association between food allergens and the risk of depression; specifically, the more food allergens a person was exposed to, the greater their risk of developing depression [137]. Additionally, we discovered that food allergies were associated with impaired quality of life (QOL) and sleep disturbances in psychiatric patients, including those with schizophrenia and mood disorders [138]. Therefore, avoiding allergenic foods may be an effective strategy for alleviating or preventing depression, while also improving QOL and sleep.

Oral Hygiene:

A meta-analysis examining the relationship between anxiety, depression, and dental decay revealed that both conditions were associated with an increased number of decayed, missing, and filled teeth or tooth surfaces, though no link was found with periodontal disease [139]. A more recent meta-analysis, however, demonstrated that depression was associated with an increased likelihood of dental caries (OR, 1.27), tooth loss (OR, 1.31), and edentulism (OR, 1.17) [140]. When oral diseases were examined as an independent variable and depression as the outcome, significant associations were found with edentulism (OR, 1.28) and periodontal disease (OR, 1.73), indicating potential bidirectional relationships between depression and oral health.

Smoking:

It is well established that many individuals with mental illness, including depression, are smokers. However, there has been ongoing debate about whether the high prevalence of smoking among those with depression is a result of smoking increasing the risk of depression or whether smoking serves as a form of self-medication for those who have developed depression. Nicotine, a key component in cigarettes, stimulates the release of dopamine and beta-endorphin, which activate the brain's reward system and promote the secretion of adrenaline, thereby temporarily alleviating depressive symptoms and enhancing cognitive function [141, 142]. Despite these effects, cigarettes also have harmful consequences, such as inducing oxidative stress due to the abundance of free radicals in cigarette smoke. A pooled analysis of six studies reported a 1.7-fold increased risk of depression among smokers [143], and a subsequent analysis of 12 studies indicated that depression increases the likelihood of smoking by 1.4 times. This demonstrates the bidirectional relationship between smoking and depression. A recent analysis of data from the UK Biobank, involving approximately 460,000 individuals, utilized Mendelian randomization methods to further establish this bidirectional association, showing that smoking increases the risk of depression by approximately twofold, while depression also raises smoking rates. Additional studies have also corroborated the link between smoking and an increased risk of depression [145, 146]. Given these findings, smoking cessation should be strongly recommended for individuals with depression, and smoking cessation programs should be considered as part of their treatment.

Other contributing Factors:

The decline in physical activity and exercise has become a significant factor in the onset of depression, particularly with the rise of automobile-dependent lifestyles and industrialization, which encourage sedentary habits. In Japan, the National Health and Nutrition Survey (NHNS) revealed that between 2007 and 2017, the average number of steps taken daily by men decreased from 7,321 to 6,846, while for women, it dropped from 6,267 to 5,867. Furthermore, the proportion of individuals in Japan with a regular exercise habit (30 minutes or more per session, at least twice a week for a year) remains low, particularly among adults in their 20s to 50s. The COVID-19 pandemic, which has forced more people to work from home and restrict their outdoor activities, has worsened this trend. Research has shown that individuals who are less physically active are at a higher risk of developing depression later in life. Long-term studies in the United States found that those who were more active or athletes at the time of graduation had a lower incidence of depression compared to their less active peers. Other studies confirm that regular physical activity reduces the risk of depression. A meta-analysis covering over 191,000 participants highlighted an inverse relationship between physical activity and depression, with more significant benefits seen at lower levels of activity. These findings reinforce the idea that regular physical exercise can protect against the onset of depression.

Exercise is also an effective treatment for depression. In clinical trials, exercise therapy was shown to have similar effects to antidepressant medications in

reducing symptoms of depression. Studies have indicated that those who continued exercise therapy at home, after experiencing improvement, had lower rates of relapse compared to those who continued with medication. Furthermore, other meta-analyses have consistently demonstrated the efficacy of exercise in alleviating depressive symptoms, particularly when combined with other forms of physical activity. The European Psychiatric Association suggests that physical activity not only improves depressive symptoms but also enhances cardiorespiratory fitness and quality of life for individuals with major depressive disorder (MDD). The most effective exercise regimens involve moderate to vigorous intensity activities like walking, jogging, aerobics, or dancing, which are typically performed two to five times a week. Starting with shorter sessions and gradually increasing the duration and intensity of exercise is recommended, especially for those new to physical activity. Resistance training is also beneficial, as it can improve both physical health and quality of life for individuals with depression. Another significant factor affecting mental health is access to nature. Urbanization has led to reduced exposure to green and blue spaces, which are linked to better mental health outcomes. Studies show that regular visits to green spaces can improve well-being and reduce mental distress. Activities like gardening or forest bathing, which involve exposure to natural environments, have been shown to improve mood and alleviate depressive symptoms.

Sleep is another critical determinant of mental health. Disruptions to the sleep-wake cycle, often due to modern lifestyle factors such as artificial light exposure, can negatively affect both physical and mental health. Sufficient sleep, generally considered to be 7-8 hours for adults, plays a vital role in preventing depression. Disruptions to sleep patterns are common in individuals with depression, and there is a bidirectional relationship between sleep disturbances and depressive disorders. Finally, modern issues like screen addiction, especially with excessive use of electronic devices, have been linked to poor sleep and an increased risk of depression. Studies show that excessive screen time, particularly after 9 p.m., disrupts sleep patterns and is associated with depression. Interventions to reduce screen time and promote healthier sleep habits have been shown to improve mood and overall well-being. At the molecular level, depression is linked to several biological systems, including the monoamine systems, the stress response, chronic inflammation, and neurotrophic factor dysfunction. Inflammation, in particular, has been shown to play a significant role in the development of depression. Research indicates that proinflammatory cytokines can influence brain functions and contribute to the development of depression. Additionally, nutritional factors, such as iron deficiency and imbalances in omega-3 fatty acids, may contribute to depression by affecting neurotransmitter production and brain function.

Conclusion:

The review underscores the critical relationship between dietary habits and depression, emphasizing the role of lifestyle factors in the onset, progression, and treatment of depression. A growing body of evidence links poor dietary patterns, including excessive caloric intake and consumption of ultra-processed foods, to an increased risk of depression. The modern Western diet, characterized by high amounts of unhealthy fats and sugars, has been implicated in the rise of depression, suggesting that dietary imbalances may exacerbate the condition. Conversely, nutrient-rich diets, such as the Mediterranean diet, have shown protective effects against depression, reinforcing the importance of dietary choices in mental health. Meal timing, particularly the practice of skipping breakfast or engaging in late-night eating, is also linked to a higher risk of mood disorders. Studies indicate that irregular eating habits can disrupt metabolic and hormonal balances, thereby influencing mental health. For example, skipping meals is associated with increased risk factors for obesity and depression. As such, addressing meal timing and promoting consistent eating schedules could be a simple yet effective strategy for improving mental health outcomes. Furthermore, the reciprocal relationship between obesity, metabolic syndrome, and depression is significant. Obesity not only heightens the risk of depression but also complicates its management, as individuals with both conditions experience worsened cognitive and emotional outcomes. Interventions like calorie restriction and bariatric surgery have shown promise in improving depressive symptoms alongside physical health. These findings suggest that addressing underlying metabolic disorders through dietary changes may offer a dual benefit, alleviating both physical and psychological burdens. In conclusion, the evidence strongly supports the role of diet in managing depression. Lifestyle interventions focusing on healthier dietary patterns, meal timing, and the reduction of processed food intake may complement traditional antidepressant treatments. As research continues to unfold, it becomes clear that a holistic approach integrating both dietary changes and psychological care could offer an effective pathway to better mental health outcomes. The findings highlight the potential for a more personalized and integrative treatment model for depression, where diet and lifestyle adjustments are central to the therapeutic process.

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