Review



# Above the Sea of Fog: Dietary and Lifestyle Interventions for the Treatment of Depression

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# Above the Sea of Fog: Dietary and Lifestyle Interventions for the Treatment of Depression

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**Abstract:** Antidepressants are among the most used medications in the US, with significant deleterious effects on people's well-being. At any given time, depression impacts approximately 1 in 10 Americans, causing wide and broad societal costs. Interest is developing for non-pharmacological treatments and preventative measures. We summarize the literature on non-invasive dietary and lifestyle approaches for treating depression, including recent work with the psychedelic treatment of depression. This review aims to inform future research and treatment programs for depression. This review provides an evidentiary summary of integrative therapeutic approaches for depression.

**Keywords:** major depression; lifestyle medicine; dietary approaches; antidepressants

## 1. Introduction

Some 17% of the US population experiences clinical depression at some point in their life. It can be a debilitating disease, where many with depression feel a complete lack of joy. It should be noted that depression increases suicide risk, and many suicides can be attributed to depression that way. The population average belies the astronomical rate among some risk cohorts, and the magnitude of the impact of depression is difficult to quantify. Hitting close to home, during the Covid-19 pandemic 1 in 5 doctors experienced depression(1), and doctors experience higher rates of depression than the normal population(2, 3).

Beyond the immediate effects of depression, those with depression are at higher risks for many other conditions, including heart attacks, diabetes, and suicide. The debilitating nature of the condition makes it difficult for one to enjoy a fulfilling life with social connection. Depression has very many multifarious impacts on one's career prospects and one's ability to experience joy from goal pursuit or enacting a hobby.

People with depression often feel alone. Overall, depression while not manifesting as physical symptoms, is a debilitating condition, and one which causes a significant degree of suffering, especially considering its extent. It must also not be underestimated the indirect impact of depression on others, whether through the withdrawal of depressed persons from social life, or from regular interactions with depressed people, which can also depress mood in the phenomenon of mental contagion(4, 5).

In the Netherlands, about 1 of every 13 adults is currently using an antidepressant (6). In recent years, the trend has been towards the increasing duration of antidepressant use (7), and in the US, 2/3 of patients continue antidepressants for at least two years (8, 9).

## 2. Epidemiology

While depression is seen as a condition affecting solely the mind, still, epidemiological factors underly depression on the population level. Authentic spirituality reduces the risk of developing depression by half(10).

Characteristics of one's family of origin can predispose one to depression. While it is unclear the mechanism of causation, the children of parents with major depressive disorder (MDD) are 3 times

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more likely to develop MDD than the children of parents without MDD(11). A history of childhood abuse is associated with a greater risk of depression(12, 13), as well as lack of parental affection(14).

Other factors associated with depression were low education, recent negative life events, loneliness, alcohol consumption, low physical activity(15, 16) and smoking(17). The personality traits of low agreeableness, low extraversion, low openness, low mastery, low conscientiousness and high neuroticism are also associated with depression(17). Internet addiction is also associated with a greater depression risk (18). Significant life disruptions can also precipitate the onset of depression, including heart attacks(19), even childbirth(20). Due to the mental nature of depression, a discussion about its causes traverses many questions about how one is living their life, including work(21, 22), relationships and self-care.

Nutritional associations have also been investigated. Coffee consumption was associated with a lower risk of depression in women(23). Vegetable and fruit consumption is also associated with lower risk of depression(24), and dietary magnesium and calcium significantly lower depression risk(25). A recent umbrella review of the dietary associations with depression prevention and treatment demonstrated a significant protective benefit from healthy diet patterns(26). Unhealthy beverage consumption habits, as parametrized by the Healthy Beverage Index (HBI) score(27), were also associated with an increased depression risk(28).

Specific factors showing strong evidence for decreased depression risk included fish consumption, coffee or tea consumption, dietary zinc, light to moderate alcohol (<40g/day)(26). Consumption of sugar sweetened beverages also raised the risk of depression(26). Moderate quality evidence exists for the association of consumption of probiotics, omega-3 polyunsaturated fatty acid and acetyl-L-carnitine with decreased depression risk(26).

Other dietary factors studied for their anti-depression, revealing equivocal evidence for efficacy include cocoa-rich foods(29), red or processed meat(30), vitamin D(31), folic acid(32) and B-vitamins(33).

Genetic factors can contribute to or protect against the depression phenotype(34-37), and heritability of depression is estimated at 37% from twin studies(38).

Nature exposure is associated with better affective states and lower risk of depression (39-42), an affect which can be mediated by the quality of the urban built environment(43, 44). Sociality can also protect against depression, as evidenced by an interventional study, where women with chronic depression in London made new friends, and observed a significant improvement in their present state examination (PSE) scores(45), an assessment of affect(46). Additionally, having hobbies is associated with a lower risk of depression(47, 48).

High stress environments and jobs can also contribute to depression, though this relationship is mediated by other factors(49), including (perceived) level of support(50) and psychosocial safety in the workplace(51).

## 3. Aims and Methods

This narrative review aims to include non-pharmacological, evidence-based treatments for the treatment of depression. We divide these into the broad categories of interventions: dietary/nutraceutical, lifestyle and experiential therapies. The difference between lifestyle interventions and experiential interventions is the primacy of a singular session, as opposed to a lifestyle change which is continually performed. Experiential interventions are time-bound, though they may be multiple in number, they continue to exert their impact after they are completed.

We perform a manual search for 1) dietary factors impacting depression, including specific supplements and herbal treatments, 2) lifestyle factors influencing depression and 3) psychedelic-based experiential treatments for depression. Our search strategy searches for reviews summarizing the interventions in each category. When reviews are found, the interventions summarized in the review are included in Supplementary Tables S1, S3 and S4 for dietary, lifestyle and psychedelic interventions respectively. These interventions are included in Tables 1–3 respectively in the main text. Some interventions are worthy of note, but are not mentioned in reviews on the topic (Supplementary Tables S1, S3 and S4). These may be included in the main text Tables 1–3.

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In section 5, we include in Table 1 and Supplementary Table S1 any dietary/nutraceutical and herbal factors which have shown evidence for efficacy in meta-analyses of human clinical trials or individual clinical trials for depression. We follow Table 1 by discussing qualitatively the mechanisms behind diet-mediated impacts on depression.

Supplementary Table S2 includes dietary/nutraceutical and herbal factors from our search which have shown efficacy for depression in pre-clinical models.

In section 6, we include in Table 2 and Supplementary Table S3 any lifestyle factors which have shown evidence for efficacy in meta-analyses of human clinical trials or individual clinical trials for depression. After Table 2, we include a qualitative discussion of different promising lifestyle intervention therapeutics.

We include in Table 3 and Supplementary Table S4 any psychedelic interventions which have shown evidence for efficacy in meta-analyses of human clinical trials or individual clinical trials for depression. In this section, we also include a qualitative review of psychedelic use for the treatment of depression.

## 4. Nutritional Support for Depression treatment

As mentioned, the nutritional factors behind depression have been elucidated in meta-analyses. Vegetarian dets are associated with a higher rate of depression in people(52), whereas Mediterranean diets are associated with a lower risk of depression(53, 54). Other specific nutrient deficiencies and their impact on depression are outlined in Table 1.

Nutraceuticals in the context have been reviewed in (32, 55-63). Several nutritional deficiencies may exist in the depressed patient(64), which, if addressed, may positively influence the prognosis of depression.

We searched for reviews on nutritional supplements in depression, and found several reviews providing an evidentiary overview of different nutraceutical and nutritional supplementary protocols for depression (Supplementary Table S1) (55, 65-77). The specific interventions are included in Table 1.

**Table 1.** A summary of dietary agents and their impacts on depression.

| Factor | Impact | Sources |
|---|---|---|
| Zinc | Depression associated with zinc deficiency (78) | Meat, shellfish, dairy, legumes, nuts |
| Magnesium | Consumption associated with lower risk of depression RR=0.81 [0.70,0.92] (25) | Leafy greens, nuts and seeds, legumes |
| Calcium | Consumption associated with lower risk of depression RR=0.66 [0.42,1.02] (25) | Leafy greens, fish with bones, almonds, dairy |
| Caffeine | Associated with reduced depression risk RR=0.72 [0.52,1.00] highest vs lowest consumption (79) | Coffee, tea |
| Coffee | Associated with reduced depression risk RR=0.76 [0.62,0.92] highest vs lowest consumption (79) | Coffee |
| Tea | Lowers depression risk RR=0.69 [0.63,0.75] highest vs lowest consumption (80) | Tea |
| Cocoa | Decrease in depressive symptoms g=-0.42 [-0.67,-0.17] | Cocoa |
| Fish | Lowers depression risk RR=0.89 [0.80,0.99] highest vs lowest consumption (81) | Fish |

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| | | |
|---|---|---|
| | RR=0.83 [0.74,0.93] highest vs lowest consumption (82) | |
| Omega 3 polyunsaturated fatty acids | EPA+DHA consumption associated with lower depression risk (83)<br><br>Lowered depression risk RR=0.87 [0.74,1.04] highest vs lowest consumption (81) | Fatty Fish |
| Selenium | Intake associated with lower risk of postpartum depression OR=0.97 [0.95,0.99] and reduction in depressive symptoms WMD=-0.37 [-0.56,-0.18] (84) | Wheat products, meat (85) |
| B-vitamins | Lower risk of remission (86) | Liver, fish, leafy greens, eggs, seeds |
| Biotin | Associated with lower odds of depression (OR=0.71 [0.55,0.91]) (87) | Organ meat, egg yolk, some vegetables, milk (88) |
| Folic acid | Associated with lower odds of depression OR=0.78 [0.61,0.99] (87) | Legumes, leafy greens, citrus, vegetables, liver, dairy products(89) |
| Vitamin D | In cases of deficiency, vitamin D supplementation may help depressive symptoms (90)<br><br>Inverse correlation between serum vitamin D levels and depression (91) | Sunlight(92), oily fish, fortified foods (93) |
| Probiotics | Small but significant effects for trials lasting at least one month (SMD=-0.28, [-0.44,-0.13] ) (94)<br><br>Significant difference in depression score (SMD=-0.47 [-0.67,-0.27]) (95)<br><br>Other meta-analyses reveal no significant difference, though very close to statistical threshold of p=0.05 (SMD=-0.128, [-0.261,0.005]) (96) | Yogurts, kefir (97), kombucha (98), fermented meat and fish products, sauerkraut, kimchi, natto, miso, sourdough bread (99, 100) |
| Acetyl-L-Carnitine | Significant reduction in depressive symptoms (SMD=-1.10) [-1.65,-0.56] (101) | Meat (102) |
| Creatine | Reduction in depression associated with level of dietary creatine consumption.<br>AOR=0.68 [0.52,0.88] (103) | Meat (104) |
| Amino acids | Positive (105) | Protein rich foods, supplements |
| Niacin | Lower risk with increased consumption up to a point, after which risk increase(106) | Meat products, fish, peanuts, whole grains (107) |
| Methylfolate | Impro<br>vement SMD=-0.38 [-0.59,-0.17] (108)<br><br>SMD=-0.61 [-0.97, -0.24](109) | Leafy greens,<br>Legumes,<br>Fortified cereals, Liver |

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| | | |
|---|---|---|
| 5-HTP | Significant improvements (g=1.11 [0.53,1.69] (110) | Turkey, Chicken, Fish, Dairy products, supplements |
| St. John's Wort | Similar response to SSRI treatment (111) | *Hypericum perforatum* |
| Saffron | Significantly better than placebo g = 0.891 [0.369,–1.412] (112) | Saffron spice derived from the *Crocus sativus* flower |
| Curcumin | Significant clinical efficacy in depression (113) | Turmeric spice, commonly used in curry dishes and various recipes |
| | Effective as adjunctive therapy (114) | |
| Methylene Blue | Reduction in manic depressive attacks (115) | Supplements |
| | Marked improvement in depressive symptoms (116) | |
| Chinese Herbal Medicine | Positive effect (117, 118) | Depends on formulation |
| Nigella Sativa | Decreased depression score (-5.5±2.5, DASS-21 survey) (119) | Black cumin seed |
| S-adenosyl methionine | Low quality evidence for efficacy(120) | Supplements |
| Cannabionoids | Limited evidence (121) | Cannabis |
| | Long term users more likely to develop depression (122) | |
| psilocybin(microdose) | Lower depression scores in retrospective survey (123) | certain species of psychedelic mushrooms. |
| Ayahuasca | Significant Improvement (124) | Banisteriopsis caapi and a DMT containing platn, typically Psychotria viridis |
| LSD | Improvement (125) | Synthesized |
| Psilocybin | Improvement (124) | certain species of psychedelic mushrooms. |
| Bacopa Monnieri | Improved Depressive symptoms (126) | Bacopa Monnieri |
| SHR-5 | Improves depressive symptoms (127) | Rhodiola rosea L. |
| Kava kava | Improvement in symptoms in human subjects(128) | Piper methysticum |
| Inositol | Equivocal evidence(58) | Fruits, beans, grains, and nuts (129) |
| Chromium | RCT shows effectiveness compared to placebo (130) | Meats, grain products, fruits, vegetables, nuts, spices, brewer's yeast, beer, and wine (131) |
| Alpha Lipoic Acid | Equivocal evidence (58) | Muscle meats, heart, kidney, and liver(132) |
| N-acetyl Cysteine (NAC) | Positive evidence from trials (133, 134) | Supplements |
| Ginseng | Improvements in QOL in patients complaining of stressor fatigue (135) | Ginseng |
| Co-enzyme Q10 | (59) SMD=0.97 [0.01,1.93] p<0.00001 | Meat, fish, nuts, and some oils (136) |
| Crocin | (59) MD=6.04 [3.43, 8.65] p=0.01 | Saffron |

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| | | |
|---|---|---|
| Antioxidant supplements | Significant improvement (SMD = 0.40, 95 % CI = 0.28–0.51, $p < 0.00001$) (59) | Supplements |
| Tryptophan | Not significant (32) | Meat and dairy |
| Ethyl-EPA | Positive impact (32) | Fish oils |
| DL-Tryptophan | Positive impact (32) | Supplements |
| Vitamin C | Mixed impact (32) | Citrus fruits, colorful vegetables |
| Catechins | Positive impact (55) | Tea |
| Hydroxytyrosol | Positive impact (56) | Extra virgin olive oil |
| Valerian | Positive impact (137) | Valeriana officinalis |
| Rhodiola | Positive impact (138) | Rhodiola rosea |
| Lavender | Positive impact (138) | Lavandula angustifolia |
| Borage | Mixed (138) | Borago officinalis or Echium |
| Chamomile | Not significant (139) | Matricaria chamomilla or Chamaemelum nobile |
| Dan zhi xiao yao | Positive impact (77) | Mixture of Bupleurum chinense, Scutellaria baicalensis, Paeonia lactiflora, Glycyrrhiza uralensis, Mentha haplocalyx, Zingiber officinale, and Ziziphus jujuba |

Other agents with preclinical data are shown in Supplementary Table S2 (140-201).

### *4.1. The Gut Microbiome and Depression: Exploring the Gut-Brain Axis*

*Depression* is a complex mental health disorder that affects millions worldwide. While the exact causes of depression are not fully understood, emerging research suggests that the gut microbiome may play a significant role in its development and progression. The gut-brain axis, a bidirectional communication system between the enteric microbiota and the central nervous system, is thought to be a key mediator in this relationship and seems to have significant implications for depression.

#### 4.1.1. The Gut-Brain Axis

The gut-brain axis refers to the intricate interactions between the enteric microbiota, the central nervous system (CNS), and the enteric nervous system (ENS)(202), creating a paradigm change in neuroscience(203). The enteric microbiota, consisting of trillions of microorganisms residing in the gastrointestinal tract, influence various physiological processes, including immune function, metabolism, and neurotransmitter production (204). These microorganisms produce neurotransmitters, such as serotonin and gamma-aminobutyric acid (GABA), which are known to regulate mood and emotions (205) and even modify epigenetic processes of the gut-brain axis (206).

#### 4.1.2. The Role of the Gut Microbiome in Depression

Studies have found alterations in the composition and diversity of the gut microbiome in individuals with depression (207). Researchers (208) highlighted the bidirectional communication between the gut microbiota and the CNS, emphasizing the gut microbiome's influence on neurological and psychiatric disorders(209). Additionally, others (210) discussed the impact of the gut-brain axis on mental health, emphasizing the potential therapeutic benefits of modulating the gut microbiota.

#### 4.1.3. Mechanisms

Several mechanisms have been proposed to explain how the gut microbiome may contribute to depression(205). Short-chain fatty acids (SCFAs) (211), produced by the gut microbiota through the fermentation of dietary fibers, have been shown to modulate brain function and behavior (212).

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Scientists (213) discussed the role of SCFAs in microbiota-gut-brain communication, highlighting their potential as therapeutic targets. Moreover, a dysregulated microbiota-gut-brain axis has been observed in patients with bipolar depression (214, 215) and associated with depressive-like behaviors in animal models (207, 209). Emerging evidence suggests that alterations in gut permeability (216) and the subsequent inflammatory response may play a crucial role in the relationship between the gut microbiome and depression(217). It was demonstrated (204) how the gut microbiome influences the production and metabolism of neurotransmitters such as serotonin (218), dopamine(219), and gamma-aminobutyric acid (GABA) (220), and how alterations in these neurotransmitter systems may contribute to depressive symptoms.

#### 4.1.4. Clinical Implications and Treatment Approaches

Understanding the gut-brain axis and its association with depression opens up possibilities for novel therapeutic interventions. In studies, a predominance of some potentially harmful bacterial groups or a reduction in beneficial bacteria in depressive patients(215) has been found in depressive patients. Dietary interventions have been the subject of research and studies examining their potential impact on symptoms of depression. There is emerging evidence that suggests a link between diet and mental well-being, indicating that dietary improvements may positively affect symptoms of depression (61, 221). Probiotics, which are live microorganisms that confer health benefits when consumed, have shown promise in modulating the gut microbiota and improving depressive symptoms. Research (222) reviewed the mechanisms of action of probiotics as potential therapeutic targets for depression and anxiety disorders. For example, Lactobacillus rhamnosus directly regulates the GABAergic system via a vagus nerve-dependent way and mitigates depression- and anxiety-like behaviors in mice (223). Bifidobacterium breve, proven to have an antidepressant-like effect, could stimulate the production of intestinal 5-hydroxytryptophan in mice and then regulate the host's serotonin metabolism (224, 225). Pediococcus acidilactici could mitigate anxiety symptoms in mice by producing lactic acid and inhibiting the over-proliferated gut pathogenic bacteria under stress(226). Fecal Microbiota Transplantation (FMT) is a procedure in which a healthy donor's fecal matter is transplanted into a recipient's gastrointestinal tract to restore a healthy balance of gut bacteria. There is growing interest in the potential therapeutic effects of FMT on various conditions, including depression (227, 228).

Overall, The gut microbiome and the gut-brain axis are emerging areas of research in the field of depression. The bidirectional communication between the gut microbiota and the CNS highlights the potential for microbiome-based interventions in treating depression. While promising, more research is required to elucidate the underlying mechanisms and develop targeted therapies to modulate the gut-brain axis to alleviate depressive symptoms effectively.

### *4.2. The Link Between Depression and Inflammation*

Depression, a prevalent mental health disorder, has long been associated with alterations in the immune system and chronic inflammation. The findings highlight potential therapeutic targets and the importance of a holistic approach to managing depression. The etiology of depression remains multifactorial and complex; emerging evidence suggests a strong connection between depression and inflammation (229). Inflammation, traditionally associated with the immune response to infection or injury, has been implicated in the pathophysiology of various psychiatric disorders. Numerous studies have demonstrated elevated levels of pro-inflammatory cytokines (230), such as interleukin-6 (IL-6) (231, 232) and tumor necrosis factor-alpha (TNF-$\alpha$) (233), in individuals with depression. Conversely, chronic inflammation, often triggered by external factors such as stress, trauma, or medical conditions, has been shown to contribute to developing or exacerbating depressive symptoms. The dysregulation of the immune system, particularly the imbalance in pro-inflammatory and anti-inflammatory cytokines, plays a crucial role in altering neurotransmitter metabolism, neuroplasticity, and neuroendocrine function, ultimately affecting mood regulation (234).

The bidirectional relationship between depression and inflammation suggests a complex interplay between the immune and central nervous systems. Inflammation-induced activation of the

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kynurenine pathway (235), dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis (236), and disruption of the blood-brain barrier(237) are among the proposed mechanisms linking inflammation to depressive symptoms. Moreover, chronic inflammation may impair the efficacy of conventional antidepressant treatments, emphasizing the need for personalized approaches that target both the neurochemical imbalances and the underlying inflammatory processes. It is worth noting that studies indicate that EMF exposure can increase the secretion of pro-inflammatory cytokines (238), including IL-6, TNF-alpha, and IL-1. The increasing intensity of EMF via mobile phones, Wi-Fi, etc, should initiate more research into the potential association between depression and EMF devices. This proinflammatory effect has been shown to be inhibited by curcumin (239).

Curcumin, a compound found in turmeric, has been the subject of scientific research exploring its potential use in depression (240-243). Curcumin has been found to possess anti-inflammatory properties, which, as we can see, may be relevant to depression. Inflammation has been implicated in the development and progression of depression, and curcumin's anti-inflammatory effects may help alleviate depressive symptoms (244). Curcumin has also shown neuroprotective properties in preclinical studies, including antioxidant and anti-apoptotic effects. These effects may help protect against neuronal damage and promote neuroplasticity, essential factors in depression (245). It has been found to modulate various neurotransmitters, including serotonin, dopamine, and glutamate, which are involved in mood regulation. By influencing these neurotransmitter systems, curcumin may impact depressive symptoms (244). BDNF is a protein that plays a crucial role in the growth and maintenance of neurons. Reduced levels of BDNF have been associated with depression. Curcumin has been shown to increase BDNF levels, possibly contributing to its potential antidepressant effects (246). Some studies have explored the combination of curcumin with other antidepressant medications, suggesting possible synergistic effects. Combining curcumin with standard antidepressant treatment may enhance the therapeutic response (242, 243).

### *4.3. The Complex Relationship Between Thyroid Dysfunction and Depression*

Thyroid dysfunction refers to the abnormal functioning of the thyroid gland, which can result in either hyperthyroidism (overactive thyroid) or hypothyroidism (underactive thyroid). Depression, on the other hand, is a mood disorder characterized by persistent feelings of sadness, loss of interest, and a lack of motivation. While the connection between thyroid dysfunction and depression has been the subject of scientific inquiry (247-249) the relationship between these two conditions remains complex and multifaceted (250). Research has shown a bidirectional relationship between thyroid dysfunction and depression, with each condition potentially influencing the other (251) . Several studies have found that individuals with thyroid dysfunction are at a higher risk of developing depression. For instance, a meta-analysis found a significant association between hypothyroidism and depression(252), suggesting that individuals with an underactive thyroid may be more prone to depressive symptoms. Moreover, thyroid hormones play a crucial role in regulating neurotransmitters(253) such as serotonin (251), dopamine (254), and norepinephrine (255), which are involved in mood regulation. Imbalances in these neurotransmitters have been linked to the development of depression. Therefore, disruptions in thyroid hormone levels can impact the functioning of these neurotransmitters, potentially contributing to the development of depressive symptoms (256). Conversely, depression may also affect thyroid function. Chronic stress, a common contributor to depression, can lead to dysregulation of the hypothalamic-pituitary-thyroid (HPT) axis (257) which controls thyroid hormone production. This dysregulation can result in alterations in thyroid hormone levels (258, 259), potentially leading to thyroid dysfunction. Autoimmune thyroiditis is also associated with an increased risk of depression (260). Elevated thyroid-stimulating hormone (TSH), antithyroglobulin (TgAb), and thyroid peroxidase antibodies (TPOAb) levels have all been linked to depression and an increased risk of suicide (251). Moreover, hypothyroidism is known to be one of the leading causes of treatment-resistant depression. Furthermore, chronic inflammation, often observed in individuals with depression, can also impact thyroid function. The complex relationship between thyroid dysfunction and depression necessitates comprehensive treatment approaches that address both conditions. For individuals with thyroid dysfunction,

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appropriate thyroid hormone replacement therapy can help restore hormonal balance and alleviate depressive symptoms. It is crucial to closely monitor thyroid hormone levels and micronutrients like Iodine, Zinc (261), Iron (262) and Selenium (263) and adjust medication dosages as necessary. If an individual with depression also exhibits symptoms of thyroid dysfunction, it is important to assess thyroid function and consider appropriate interventions to optimize treatment outcomes (264). Thyroid dysfunction and depression share a complex and bidirectional relationship. While individuals with thyroid dysfunction may be at a higher risk of developing depression (265) depression can also impact thyroid function (258). Addressing both conditions simultaneously is crucial for effective treatment outcomes. Further research is needed to unravel the precise mechanisms underlying this relationship and develop targeted interventions that can improve the lives of individuals affected by both thyroid dysfunction and depression.

## 5. Psychedelic assisted treatment of depression

Evidence for the treatment efficacy of psychedelics in depression is shown in Supplementary Table S4 (124, 266-278), summaries are shown in Table 2.

**Table 2.** A summary of psychedelic agents and their impacts on depression.

| Substance | Evidence |
|---|---|
| Ketamine | Significant but temporary (1 week) effect (279) |
| MDMA | Hedge's g = -0.71; 95% CI, -1.39 to -0.03 (280) |
| Psilocybin | Hedges' g was 1.289 (95%CI=[1.020, 1.558], heterogeneity $I^2$=50.995%, p<0.001) (272) |
| Ayahuasca | Improvements in depressive symptoms in large cross sectional study (281) |
| LSD | Non significant decrease in depressive symptoms (282) |

The use of psychedelics to treat depression is different from the use of most pharmacological agents and is differentiated. An important factor to consider with psychedelic use is the primacy of the experience. Psychedelics can be thought of as tools which allow one to assume a different frame of mind for the duration of the effects. It can be very helpful for the treatment of various states of disease to see it form an alternative perspective. Even non-pharmacologically, exposing one's self to new ways of thinking, either through hobbies(47, 283), learning(284), engaging with people(285) or traveling(286).

Psychedelics are legally restricted in many jurisdictions, though legalization is increasingly being considered by policymakers(287). A typical psychedelic assisted therapy session involves a facilitator and the person taking the psychedelic. The person taking the psychedelic will typically journal or otherwise clarify their intentions for the session through a conversation or a set of journal prompts(288).

During the session, it is vital to create a safe environment where the recipient is able to fully relax. Psychedelics combined with the introspection encouraged by the facilitator aids the recipient to examine their life from a depatterned frame of mind(289). Many people rate psychedelic experiences as among the most meaningful in their life, and usually overwhelmingly positive (290, 291). Adverse reactions can be minimized through proper set and setting, though psychedelics can be used responsibly with a skilled practitioner and in accordance with local regulations (292).

### *5.1. Ketamine*

Ketamine, derived from phencyclidine (PCP), functions as an N-methyl-D-aspartate (NMDA) receptor antagonist and has been utilized as an anesthetic for over half a century (293). Notably, ketamine demonstrates a rapid and pronounced improvement in mood symptoms and suicidal ideation by directly targeting the glutamate system (293). The pivotal study by Zarate et al. highlighted its potential in patients who do not respond to standard antidepressants, where a single 40-minute ketamine infusion resulted in a very rapid and robust antidepressant effect, with over 50% of patients experiencing a positive response within 24 hours (294). A subsequent collaborative study

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by Murrough et al. in 2013 further supported these findings, revealing a response rate of approximately 67% for participants with treatment-resistant depression (TRD) receiving ketamine, compared to a 28% response rate in the midazolam control group at 24 hours (295). However, the antidepressant effects of ketamine diminished by 7 days. This renewed awareness of the limitations of monoamine-based mechanisms for treating depression has fueled increased interest in ketamine as an alternative (296).

In a 2015 meta-analysis by Newport et al., seven trials involving 147 participants with treatment-resistant depression who underwent a single ketamine infusion demonstrated a rapid and transient antidepressant effect, with odds ratios approaching 10 for treatment response and 14.47 for symptom remission at 24 hours (279). However, the benefits tended to dissipate by 7 days, as indicated in an additional meta-analysis (297). Moreover, ketamine was found effective in reducing suicide ideation for up to 7 days (298). Most ketamine studies have utilized an intravenous dose of 0.5 mg/kg infused over approximately 40 minutes, with a dose-finding study recommending doses within the range of 0.5 mg/kg to 1 mg/kg (299). While single-dose protocols have been prominent in research settings, multi-dose regimens are gaining attention, such as twice-weekly treatments for 2 to 4 weeks or thrice-weekly for 3 weeks. A recent study by Phillips et al. highlighted the potential of maintenance ketamine, indicating lasting antidepressant effects when administered 3 times per week for 6 doses, followed by a weekly dose for 4 additional weeks (300).

Ketamine's use for depression treatment is, however, constrained by the need for administration in a medical facility under strict monitoring, rendering it an expensive and resource-limited option (293). Additionally, treatment-emergent hypertension has been observed in approximately 44% of ketamine infusion cases, with blood pressure increases exceeding 165/100 mmHg, necessitating pharmacological intervention in 12% of patients (301). Despite these limitations, ketamine is increasingly considered as adjunctive therapy for patients with treatment-resistant depression and may also be a valuable option for those with suicidal ideation or severe depression admitted to the hospital.

### *5.2. Psilocybin*

Psilocybin, the active component of psychedelic mushrooms, has been used in human cultures for millennia. While controversy exists over the extent and impact of states induced by psychedelics, they undoubtedly played an important role in the human cultures in which they were adopted as part of ritual, appearing in artworks and sacred locations(302). Species of psilocybin producing mushroom are found in varied geographies, and on all continents (with the exception of Antarctica) (303).

Indigenous relationships with psychedelic plants often regarded them as teachers(304), and their consumption would be performed within a ceremonial setting for such purposes.

Psilocybin has been studied for the treatment of depression, and placebo controlled trials revealed statistically significant reductions in depression and anxiety symptoms, with Hedge's g=0.83 compared to placebo (273).

### *5.3. Ayahuasca*

Ayahuasca is a brew made from the mixture of a DMT containing plant substance, typically the leaves of *Psychotria viridis* (or *chakropanga* species) and a Monoamine oxidase inhibitor (MAOI), typically *Banisteriopsis caapi (281).* The brew is made over multiple days of heating the components together, and the final product is a dark and thick brewed tea, which traditionally, is taken only in the context of ceremony.

The effects of Ayahuasca last for approximately 6 hours (305),wherein the journeyer experiences psychedelic and physical impacts from the psychedelic. Physical experiences can include purging, which is regarded as part of the medicinal action of Ayahuasca(306).

Several trials have explored the therapeutic use of Ayahuasca for depression. Given the salience of the effects, placebo controlled trials are difficult. A survey of 11,912 people who had previously participated in an Ayahuasca ceremony revealed that of the 1571 people reporting depression at the

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time of the ceremony, 46% reported 'very much' improvement and 32% reported that their depression was 'completely resolved' (281). While this study has the limitation of not comparing results to a non-treatment control, still, the results are highly promising.

### *5.4. LSD and MDMA*

Lysergic acid Diethylamide (LSD) has recently been used in the context of psychedelic assisted psychotherapy after a hiatus in research due to regulatory reasons (307). A recent trial demonstrated clinically significant reductions after two LSD assisted psychotherapy sessions compared to placebo(308).

3,4-methylenedioxymethamphetamine (MDMA) is a common party drug which is being adopted in the context of psychotherapy. A recent meta-analysis revealed statistically significant reductions in depressive symptoms with MDMA-assisted psychotherapy (Hegde's g = -0.71; 95% CI, −1.39 to −0.03) (280).

## 6. Lifestyle changes for treatment of depression

There are several changes that one can make in their life to recover from depression. These useful strategies have an evidence base documenting their efficacy. We performed a literature search on lifestyle treatment for depression and found several reviews (Supplementary Table S3) (309-317). These findings are summarized below in Table 3.

**Table 3.** A summary of lifestyle interventions and their impacts on depression.

| Intervention | Effect |
|---|---|
| Hobbies | Dance: effect similar to antidepressants (318)<br>Lower risk (47, 48). |
| Mindfulness | Decreases in depressive symptoms (319) |
| Sleep | Improved sleep quality decreased depressive symptoms (320) |
| Natural environments | increases in positive mood, and lowered feelings of depression(321, 322). |
| Time with animals | reducing depression(323). |
| Socialization | significant improvement in their present state examination (PSE) scores after making a new friend (45) |
| Journaling | Positive impact (324) |
| Gratitude | associated with positive mental health, including alleviating depression (325-329) |
| Deep brain stimulation | small but significant effect(326, 327). |
| Sauna/ whole body hyperthermia | Positive effect (330) |
| Goal setting | Some limited evidence for efficacy (331) |

### *6.1. Exercise*

There is growing recognition that lifestyle behaviors, such as physical activity and exercise can be useful strategies for treating depression, reducing depressive symptoms, improving quality of life, and improving physical health outcomes. Cross-sectional studies have shown that people with higher levels of physical activity present decreased depressive symptoms, and these results are consistent across different countries and cultures. For example, recent evidence using data from the Brazilian National Health Survey, accounting for 59,399 individuals, demonstrated that a lack of physical activity for leisure was associated with depression in young males, middle age, and older adults.(332) A study across 36 countries demonstrated that lower levels of physical activity (defined as less than 150 min of moderate-vigorous physical activity per week) were consistently associated with elevated depression (OR, 1.42; 95%CI, 1.24–1.63). (333) However, mental health benefits have been noted from being physically active, even at levels below the public health recommendations.(334) In The Irish Longitudinal Study on Ageing participants performing 400 to less than 600 MET-min/wk had a

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16% lower rate of depressive symptoms (adjusted incidence rate ratio [AIRR], 0.84; 95%CI, 0.81-0.86) and 43% lower odds of depression compared with 0 MET-min/wk.(335) These findings are consistent with recent meta-analytic data suggesting that salutary mental health benefits among adults can be achieved with physical activity below public health recommendations; specifically, an activity volume equivalent to 2.5 hours per week of brisk walking was associated with a 25% lower risk of depression, and half that activity volume was associated with an 18% lower risk compared with no activity.(334) The findings of The Irish Longitudinal Study on Ageing suggest that accumulating as little as 100 minutes per week or 20 minutes per day for 5 days per week of moderate-intensity activity (eg, brisk walking; 4 METs) may be sufficient to significantly lower the risk of depressive symptoms and odds of major depression over time among older adults

A large body of trials has been performed over the last 40 years evaluating the role of exercise as a therapy for depression. These results have been summarized in several metaanalyses. A Cochrane analysis of 35 trials (1356 participants) comparing exercise with no treatment or a control intervention, the pooled outcome for the primary outcome of depression at the end of treatment was standardized mean difference (SMD) -0.62; 95% CI-0.81 to -0.42, indicating a moderate clinical effect. Schuch et al performed a meta-analysis which included 25 RCTs comparing exercise versus control comparison groups. (336) Overall, exercise had a large and significant effect on depression. Similarly, Krogh et al performed a meta-analysis which included 35 trials enrolling 2498 participants.(337) The effect of exercise versus control on depression severity was −0.66 SMD (95% CI −0.86 to −0.46; $p<0.001$).

Exercise can improve depressive symptoms in people with depression. However, like other treatments, exercise is not a panacea and may not work equally for all. A seminal study by Dunn et al., the Depression Outcomes Study of Exercise, found a response rate of about 40% in depressed people free from other treatments.(338) However, it is likely that when combined with other interventions (i.e vitamin D, L-methyl-folate, etc) the response rate and degree of response will be much greater. In essence, exercise has multiple benefits to several domains of physical and mental health and should be promoted to everyone. To ensure compliance, adapting exercise prescription for people with depression should account for personal preferences and previous experiences in terms of making it the most enjoyable experience possible. Acute exercise should be used as a symptom management tool to improve mood in depression, with even light exercise an effective recommendation.(339) These data suggest that physical activity is beneficial for the depressed patient regardless of the intensity of the exercise.

The neurobiological mechanisms underpinning the antidepressant effects of exercise are largely unclear. However, some hypotheses involving inflammation, oxidative stress, and neuronal regeneration are speculated. Exercise training can promote increases in anti-inflammatory and antioxidant enzymes, referred to as a hormesis response and subsequently decrease IL-6 levels. This effect was demonstrated in the REGASSA trial, where decreases in IL-6 serum levels were associated with reductions in depressive symptoms. (340)

### *6.2. Time in nature*

Time in nature is associated with increases in positive mood, and lowered feelings of depression(321, 322).

#### 6.2.1. Animal-Assisted Therapy

Time spent with animals can be an effective way of reducing depression(323).

### *6.3. Mindfulness*

Several mindfulness based therapies can potently treat depression. The most studied treatments are cognitive behavioral therapy (CBT), mindfulness based stress reduction (MBSR) and mindfulness based cognitive therapy (MBCT), which have important distinctions. Mindfulness based therapies demonstrate significant reductions in depression(319).

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*6.4. Connection with others*

In the middle of depression, one of the things which falls by the wayside are plans and social interactions. Existing in large cities, one lives a largely anonymized existence, where they do not experience connection with others, including seeing others and being seen by others.

6.4.1. Purpose and goals

Positive, goal directed activity is associated with a decrease in depressive symptoms and has the added benefit of providing structure and a reason to positively interact and create with others. Progress in any aspect increases positive self-regard, confidence, and sense of self-efficacy, as well as one's social status. These factors are associated with a decrease in depressive symptoms(341, 342).

Another benefit is that learning positively uses neural pathways and grows new neurons and is also associated with a sense of optimism. Furthermore, a challenging task necessarily takes much of the mental bandwidth, leaving less space for ruminations characteristic of depression. During periods of intense stress including the London Blitz during World War II, there was a paradoxical decrease in psychiatric presentation to hospitals, owing to the dire need of hospital beds(343). The efforts of every man and woman were needed, and this sense of purpose is protective against depression.

Depression is often a reason for introspection into the aspects of one's life that are not working. Often a major life area, such as one's career, or one's close relationships or lack thereof are brought into focus. In these cases where dissatisfaction with one's current life is the proximal cause of one's depression, working with a life coach or otherwise reflecting on one's ideal life (and how to achieve it), is a powerful practice for inspiring hope and action which follows that. A significant proportion of depression is a lack of meaning and purpose.

Interestingly, regular Argentinian tango was comparable to mindfulness meditation in terms of the impact on depression (318), suggesting value in novel pursuits and hobbies.

Indigenous communities living traditional existences do not suffer from psychiatric issues. The differences in the sense of purpose between modern and tribal cultures can be attributed to the tight-knit tribal communities where everybody feels a sense of importance in the eyes of the community. Furthermore, practices such as initiation into manhood and womanhood, most notably the vision quest, provide the individual with a clear role to play in the community.

Over millennia, these practices have corrected wayward youth and to integrate at risk youth into constructive roles within the community. While this review mostly focuses on the individual treatment of depression, it should be noted that initiatives like upward bound, which provide a similar experience for youth on the cusp of adulthood, increase the likelihood of post-secondary education(344).

These programs, involve people getting out in nature, which in itself has positive benefits for mood disorders(345), and additionally provides the benefits of physical activity(346). The program positively impacts self-concept(347).

*6.5. Gratitude*

An outlook of gratitude has been valued by all the major monotheistic religions(348). Furthermore, in modernity, when gratitude is operationalized as an explicit practice, it is associated with positive mental health, including alleviating depression (325-329). Gratitude journaling is one of the most accessible ways that one can practice journaling, which simply involves recording 3-5 things that one is grateful for on a daily basis(349, 350).

*6.6. Deep Brain Stimulation*

Noninvasive brain stimulation methods have been studied for their favorable modulation of a wide variety of neural states. For the treatment of depression, some promising data exists for these therapies, showing a small but significant effect(326, 327).

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Non-invasive brain stimulation (NIBS) using transcranial direct current stimulation or transcranial magnetic stimulation has been demonstrated to be highly effective in the treatment of depression (351-355).

*6.7. Whole-Body Hyperthermia*

Historically, hyperthermia interventions have been utilized to address depressive symptoms, with evidence dating back to ancient times, such as the practices of Galen of Pergamon (129–198 C.E.), who treated melancholia by immersing patients in hot tubs and providing skin massages (330). Contemporary research has highlighted the positive effects of regular sauna bathing, including reductions in all-cause and cardiovascular mortality, increased lifespan, improved exercise performance, and the activation of autophagy through the expression of heat shock proteins (356-359). Heat therapy also enhances cell stress pathways, possesses antioxidant and anti-inflammatory properties, and enhances mitochondrial function. Sauna bathing exhibits physiological similarities to aerobic exercise, increasing heart rate, stroke volume, and cardiac output (360, 361). Furthermore, whole-body hyperthermia (WBH) selectively raises IL-6 levels(362) and shows promise in conditions like chronic fatigue syndrome (363, 364).

Animal studies have indicated that WBH activates portions of the dorsal raphe nucleus associated with mood regulation and produces antidepressant-like responses (365). Clinical studies have shown that a single session of WBH can significantly reduce depressive symptoms when assessed five days post-treatment (366). Additionally, a randomized, double-blind study comparing WBH with a sham condition in depressed patients revealed significant reductions in Depression Rating Scale scores over a six-week post-intervention period in the active WBH group (367). Hanusch et al. conducted a meta-analysis on the effect of WBH on depression indices, encompassing seven studies with a total of 148 subjects. Six out of seven studies reported statistically significant reductions in depressive symptoms between one and six weeks post-intervention. The treatment effect appeared to be independent of the total number of WBH sessions, with target temperatures between 38°C and 39°C and a slower increase in core body temperature during the intervention resulting in larger treatment effects. This suggests potential benefits of near-infrared (NIR) sauna over regular sauna, as NIR sauna sessions can be more controlled, shorter in duration (5-10 mins initially, increasing to 20 mins), and performed two to three times a week for maximal cardiovascular benefit (330).

*6.8. Photobiomodulation*

Photobiomodulation (PBM) is referred to in the literature as low-level light therapy, red light therapy, and near-infrared (NIR) light therapy. Depression is associated with brain hypometabolism and cerebral as well as systemic mitochondrial dysfunction (368-370). In a rat model of depression, vital steps in the production of adenosine triphosphate (ATP) were inhibited in the cerebral cortex and cerebellum (371).

Peripheral blood mononuclear cells of depressed patients were shown to have significantly impaired mitochondrial function (372, 373), and greater mitochondrial dysfunction correlated with severity of neuro-vegetative symptoms, including fatigue and poor concentration (372). Muscle biopsy samples from depressed patients with physical symptoms had a decreased rate of ATP production and more frequent mitochondrial DNA deletions than controls (370).

The most well-studied mechanism of action of PBM centers around enhancing the activity of cytochrome C oxidase (CCO), which is unit four of the mitochondrial respiratory chain, responsible for the final reduction of oxygen to water (374). The theory is that CCO enzyme activity may be inhibited by nitric oxide (NO). This inhibitory NO can be dissociated by photons of light that are absorbed by CCO. These absorption peaks are mainly in the red (600–700 nm) and near-infrared (760–940 nm) spectral regions. When NO is dissociated, the mitochondrial membrane potential is increased, more oxygen is consumed, more glucose is metabolized and more ATP is produced by the mitochondria (375).

PBM has been found to specifically increase CCO activity and expression (374, 376, 377). Studies have also shown increases in complex II, III, and IV activity, as well as upregulation of gene coding

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for subunits of complex I, complex IV, and ATP synthase. (374) Low-level laser therapy has been shown to increase levels of ATP, the rate of oxygen consumption, and cerebral oxygenation (374). Though t-PBM with red and NIR light can include wavelengths from 600 to 1070nm, specific wavelengths have been directly linked to mitochondrial activity. Near Infrared activates CCO, increases mitochondrial oxygen consumption, and leads to higher levels of ATP (378-380).

There is some evidence that PBM applied peripherally, not just transcranially, may have an effect in attenuating depressive symptom (374). There is no clear mechanism proposed explaining this effect. In a recent study, 5 outpatients with low-back pain and concurrent self-reported depression were treated over five weeks with physical therapy (PT) (5-sessions) and concurrent PBM (3-sessions) and matched to five control patients treated with PT alone (5-sessions) (381). Participants receiving s-PBM reported a larger decrease in their depression score. Oron and co-workers have shown that delivering NIR light to the mouse tibia resulted in improvement in a transgenic mouse model of Alzheimer's disease (382).

## 7. Conclusion

More integrative approaches, including diet and lifestyle may improve the quality of life of people with depression and enable them to live a fulfilling life. Currently, practitioner understanding is a barrier, as well as the limited time that primary care physicians spend with patients. Additionally, other systemic issues remain about the cost of therapy, while simultaneously therapists themselves are overburdened and undercompensated. Expectations of one's self can be a barrier to those experiencing depression even acknowledging it, let alone seeking help (383). Much work remains on the public health understanding of depression, and an integrative approach, combining dietary, lifestyle change with other therapies and embracing a trauma-aware perspective can help greatly. Additionally, the resiliency of the person experiencing depression must be acknowledged, and he or she must be captain of the process. Practitioners can help through educating and coaching the person recovering depression, and by pointing them to resources and therapeutics for their specific case.

**Supplementary Materials:** The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

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## References

1. Johns G, Samuel V, Freemantle L, Lewis J, Waddington L. The global prevalence of depression and anxiety among doctors during the covid-19 pandemic: Systematic review and meta-analysis. Journal of Affective Disorders. 2022;298:431-41.
2. Bailey E, Robinson J, McGorry P. Depression and suicide among medical practitioners in Australia. Intern Med J. 2018;48(3):254-8.
3. Outhoff K. Depression in doctors: A bitter pill to swallow. South African Family Practice. 2019;61(sup1):S11-S4.
4. Eisenberg D, Golberstein E, Whitlock JL, Downs MF. SOCIAL CONTAGION OF MENTAL HEALTH: EVIDENCE FROM COLLEGE ROOMMATES. Health Economics. 2013;22(8):965-86.
5. Neumann R, Strack F. "Mood contagion": The automatic transfer of mood between persons. Journal of Personality and Social Psychology. 2000;79(2):211-23.
6. Huijbregts KM, Hoogendoorn A, Slottje P, van Balkom AJLM, Batelaan NM. Long-Term and Short-Term Antidepressant Use in General Practice: Data from a Large Cohort in the Netherlands. Psychotherapy and Psychosomatics. 2017;86(6):362-9.
7. Moore M, Yuen HM, Dunn N, Mullee MA, Maskell J, Kendrick T. Explaining the rise in antidepressant prescribing: a descriptive study using the general practice research database. Bmj. 2009;339:b3999.
8. Olfson M, Marcus SC. National patterns in antidepressant medication treatment. Arch Gen Psychiatry. 2009;66(8):848-56.
9. Mojtabai R, Olfson M. National trends in long-term use of antidepressant medications: results from the U.S. National Health and Nutrition Examination Survey. J Clin Psychiatry. 2014;75(2):169-77.

 doi:10.20944/preprints202402.1273.v1




10. Portnoff L, McClintock C, Lau E, Choi S, Miller L. Spirituality cuts in half the relative risk for depression: Findings from the United States, China, and India. Spirituality in Clinical Practice. 2017;4(1):22-31.
11. Weissman MM, Wickramaratne P, Nomura Y, Warner V, Verdeli H, Pilowsky DJ, et al. Families at High and Low Risk for Depression: A 3-Generation Study. Archives of General Psychiatry. 2005;62(1):29-36.
12. Sneed JR, Kasen S, Cohen P. Early-life risk factors for late-onset depression. International Journal of Geriatric Psychiatry. 2007;22(7):663-7.
13. Comijs HC, van Exel E, van der Mast RC, Paauw A, Oude Voshaar R, Stek ML. Childhood abuse in late-life depression. Journal of Affective Disorders. 2013;147(1):241-6.
14. Parker G. Parental 'Affectionless Control' as an Antecedent to Adult Depression: A Risk Factor Delineated. Archives of General Psychiatry. 1983;40(9):956-60.
15. Zhai L, Zhang Y, Zhang D. Sedentary behaviour and the risk of depression: a meta-analysis. 2015.
16. Mekary RA, Lucas M, Pan A, Okereke OI, Willett WC, Hu FB, Ding EL. Isotemporal Substitution Analysis for Physical Activity, Television Watching, and Risk of Depression. American Journal of Epidemiology. 2013;178(3):474-83.
17. Schaakxs R, Comijs HC, van der Mast RC, Schoevers RA, Beekman ATF, Penninx BWJH. Risk Factors for Depression: Differential Across Age? The American Journal of Geriatric Psychiatry. 2017;25(9):966-77.
18. Kim Y-J, Jang HM, Lee Y, Lee D, Kim D-J. Effects of Internet and Smartphone Addictions on Depression and Anxiety Based on Propensity Score Matching Analysis. International Journal of Environmental Research and Public Health. 2018;15(5):859.
19. Ladwig KH, Ladwig KH, Roll G, Breithard G, Budde T, Borggrefe M. Post-infarction depression and incomplete recovery 6 months after acute myocardial infarction. The Lancet. 1994;343(8888):20-3.
20. Miller LJ. Postpartum Depression. JAMA. 2002;287(6):762-5.
21. Bonde JPE. Psychosocial factors at work and risk of depression: a systematic review of the epidemiological evidence. 2008.
22. Netterstrøm B, Conrad N, Bech P, Fink P, Olsen O, Rugulies R, Stansfeld S. The Relation between Work-related Psychosocial Factors and the Development of Depression. Epidemiologic Reviews. 2008;30(1):118-32.
23. Lucas M, Mirzaei F, Pan A, Okereke OI, Willett WC, O'Reilly ÉJ, et al. Coffee, Caffeine, and Risk of Depression Among Women. Archives of Internal Medicine. 2023;171(17):1571-8.
24. Liu X, Yan Y, Li F, Zhang D. Fruit and vegetable consumption and the risk of depression: A meta-analysis. Nutrition. 2016;32(3):296-302.
25. Li B, Lv J, Wang W, Zhang D. Dietary magnesium and calcium intake and risk of depression in the general population: A meta-analysis. http://dxdoiorg/101177/0004867416676895. 2016.
26. Xu Y, Zeng L, Zou K, Shan S, Wang X, Xiong J, et al. Role of dietary factors in the prevention and treatment for depression: an umbrella review of meta-analyses of prospective studies. Translational Psychiatry. 2021;11(1):478.
27. Duffey KJ, Davy BM. The Healthy Beverage Index Is Associated with Reduced Cardiometabolic Risk in US Adults: A Preliminary Analysis. J Acad Nutr Diet. 2015;115(10):1682-9.e2.
28. Rasaei N, Ghaffarian-Ensaf R, Shiraseb F, Abaj F, Gholami F, Clark CCT, Mirzaei K. The association between Healthy Beverage Index and psychological disorders among overweight and obese women: a cross-sectional study. BMC Women's Health. 2022;22(1):295.
29. Fusar-Poli L, Gabbiadini A, Ciancio A, Vozza L, Signorelli MS, Aguglia E. The effect of cocoa-rich products on depression, anxiety, and mood: A systematic review and meta-analysis. Critical Reviews in Food Science and Nutrition. 2022;62(28):7905-16.
30. Nucci D, Fatigoni C, Amerio A, Odone A, Gianfredi V. Red and Processed Meat Consumption and Risk of Depression: A Systematic Review and Meta-Analysis. International Journal of Environmental Research and Public Health. 2020;17(18):6686.
31. Lázaro Tomé A, Reig Cebriá MJ, González-Teruel A, Carbonell-Asíns JA, Cañete Nicolás C, Hernández-Viadel M. Efficacy of vitamin D in the treatment of depression: a systematic review and meta-analysis. Actas Esp Psiquiatr. 2021;49(1):12-23.
32. Jerome Sarris, Ph.D., M.H.Sc. ,, Jenifer Murphy, Ph.D. ,, David Mischoulon, M.D., Ph.D. ,, George I. Papakostas, M.D. ,, Maurizio Fava, M.D. ,, Michael Berk, M.D., Ph.D. ,, Chee H. Ng, M.D. Adjunctive Nutraceuticals for Depression: A Systematic Review and Meta-Analyses. American Journal of Psychiatry. 2016;173(6):575-87.

 doi:10.20944/preprints202402.1273.v1




33. Young LM, Pipingas A, White DJ, Gauci S, Scholey A. A Systematic Review and Meta-Analysis of B Vitamin Supplementation on Depressive Symptoms, Anxiety, and Stress: Effects on Healthy and 'At-Risk' Individuals. Nutrients. 2019;11(9):2232.
34. Levey DF, Stein MB, Wendt FR, Pathak GA, Zhou H, Aslan M, et al. Bi-ancestral depression GWAS in the Million Veteran Program and meta-analysis in >1.2 million individuals highlight new therapeutic directions. Nature Neuroscience. 2021;24(7):954-63.
35. Niamh Mullins, Ph.D. ,, Tim B. Bigdeli, Ph.D. ,, Anders D. Børglum, Ph.D. ,, Jonathan R.I. Coleman, Ph.D. ,, Ditte Demontis, Ph.D. ,, Divya Mehta, Ph.D. ,, et al. GWAS of Suicide Attempt in Psychiatric Disorders and Association With Major Depression Polygenic Risk Scores. American Journal of Psychiatry. 2019;176(8):651-60.
36. Ni H, Xu M, Zhan GL, Fan Y, Zhou H, Jiang HY, et al. The GWAS Risk Genes for Depression May Be Actively Involved in Alzheimer's Disease. J Alzheimers Dis. 2018;64(4):1149-61.
37. Xie T, Stathopoulou MG, de Andrés F, Siest G, Murray H, Martin M, et al. VEGF-related polymorphisms identified by GWAS and risk for major depression. Translational Psychiatry. 2017;7(3):e1055-e.
38. Patrick F. Sullivan, M.D., F.R.A.N.Z.C.P. ,, Michael C. Neale, Ph.D. , and, Kenneth S. Kendler, M.D. Genetic Epidemiology of Major Depression: Review and Meta-Analysis. American Journal of Psychiatry. 2000;157(10):1552-62.
39. Beute F, de Kort YAW. The natural context of wellbeing: Ecological momentary assessment of the influence of nature and daylight on affect and stress for individuals with depression levels varying from none to clinical. Health & Place. 2018;49:7-18.
40. Jakstis K, Fischer LK. Urban Nature and Public Health: How Nature Exposure and Sociocultural Background Relate to Depression Risk. International Journal of Environmental Research and Public Health. 2021;18(18):9689.
41. Bezold CP, Banay RF, Coull BA, Hart JE, James P, Kubzansky LD, et al. The Association Between Natural Environments and Depressive Symptoms in Adolescents Living in the United States. Journal of Adolescent Health. 2018;62(4):488-95.
42. Dempsey S, Devine MT, Gillespie T, Lyons S, Nolan A. Coastal blue space and depression in older adults. Health & Place. 2018;54:110-7.
43. Galea S, Ahern J, Rudenstine S, Wallace Z, Vlahov D. Urban built environment and depression: a multilevel analysis. Journal of Epidemiology and Community Health. 2005;59(10):822-7.
44. Yang H, Cui X, Dijst M, Tian S, Chen J, Huang J. Association Between Natural/Built Campus Environment and Depression Among Chinese Undergraduates: Multiscale Evidence for the Moderating Role of Socioeconomic Factors After Controlling for Residential Self-Selection. Frontiers in Public Health. 2022;10.
45. Harris T, Brown GW, Robinson R. Befriending as an intervention for chronic depression among women in an inner city: 1: Randomised controlled trial. The British Journal of Psychiatry. 1999;174(3):219-24.
46. Wing JK, Birley J, Graham P, Isaacs A. Present state examination. The British Journal of Psychiatry. 1974.
47. Fancourt D, Opher S, de Oliveira C. Fixed-Effects Analyses of Time-Varying Associations between Hobbies and Depression in a Longitudinal Cohort Study: Support for Social Prescribing? Psychotherapy and Psychosomatics. 2019;89(2):111-3.
48. Li Z, Dai J, Wu N, Jia Y, Gao J, Fu H. Effect of Long Working Hours on Depression and Mental Well-Being among Employees in Shanghai: The Role of Having Leisure Hobbies. International Journal of Environmental Research and Public Health. 2019;16(24):4980.
49. Hammen C. Stress and Depression. Annual Review of Clinical Psychology. 2005;1(1):293-319.
50. Santa Maria A, Wörfel F, Wolter C, Gusy B, Rotter M, Stark S, et al. The Role of Job Demands and Job Resources in the Development of Emotional Exhaustion, Depression, and Anxiety Among Police Officers. Police Quarterly. 2018;21(1):109-34.
51. Hall GB, Dollard MF, Winefield AH, Dormann C, Bakker AB. Psychosocial safety climate buffers effects of job demands on depression and positive organizational behaviors. Anxiety, Stress, & Coping. 2013;26(4):355-77.
52. Ocklenburg S, Borawski J. Vegetarian diet and depression scores: A meta-analysis. Journal of Affective Disorders. 2021;294:813-5.
53. Psaltopoulou T, Sergentanis TN, Panagiotakos DB, Sergentanis IN, Kosti R, Scarmeas N. Mediterranean diet, stroke, cognitive impairment, and depression: A meta-analysis. Annals of Neurology. 2013;74(4):580-91.

 doi:10.20944/preprints202402.1273.v1




54. Sánchez-Villegas A, Martínez-González MA, Estruch R, Salas-Salvadó J, Corella D, Covas MI, et al. Mediterranean dietary pattern and depression: the PREDIMED randomized trial. BMC Medicine. 2013;11(1):208.
55. Nabavi SM, Daglia M, Braidy N, Nabavi SF. Natural products, micronutrients, and nutraceuticals for the treatment of depression: A short review. Nutritional Neuroscience. 2017;20(3):180-94.
56. Alvarez-Mon MA, Ortega MA, García-Montero C, Fraile-Martinez O, Monserrat J, Lahera G, et al. Exploring the Role of Nutraceuticals in Major Depressive Disorder (MDD): Rationale, State of the Art and Future Prospects. Pharmaceuticals. 2021;14(8):821.
57. Bonokwane MB, Lekhooa M, Struwig M, Aremu AO. Antidepressant Effects of South African Plants: An Appraisal of Ethnobotanical Surveys, Ethnopharmacological and Phytochemical Studies. Frontiers in Pharmacology. 2022;13.
58. Mischoulon D, Iovieno N. Supplements and Natural Remedies for Depression. In: Shapero BG, Mischoulon D, Cusin C, editors. The Massachusetts General Hospital Guide to Depression: New Treatment Insights and Options. Cham: Springer International Publishing; 2019. p. 195-209.
59. Wang H, Jin M, Xie M, Yang Y, Xue F, Li W, et al. Protective role of antioxidant supplementation for depression and anxiety: A meta-analysis of randomized clinical trials. Journal of Affective Disorders. 2023;323:264-79.
60. Hoffmann K, Emons B, Brunnhuber S, Karaca S, Juckel G. The Role of Dietary Supplements in Depression and Anxiety – A Narrative Review. Pharmacopsychiatry. 2019;52(06):261-79.
61. Firth J, Marx W, Dash S, Carney R, Teasdale SB, Solmi M, et al. The effects of dietary improvement on symptoms of depression and anxiety: a meta-analysis of randomized controlled trials. Psychosomatic medicine. 2019;81(3):265-80.
62. Subermaniam K, Teoh SL, Yow Y-Y, Tang Y-Q, Lim LW, Wong K-H. Marine algae as emerging therapeutic alternatives for depression: A review. Iranian Journal of Basic Medical Sciences. 2021;24:997 - 1013.
63. Taya C. Varteresian, D.O., M.S. ,, David A. Merrill, M.D., Ph.D. , and, Helen Lavretsky, M.D., M.S. The Use of Natural Products and Supplements in Late-Life Mood and Cognitive Disorders. FOCUS. 2013;11(1):15-21.
64. Petridou ET, Kousoulis AA, Michelakos T, Papathoma P, Dessypris N, Papadopoulos FC, Stefanadis C. Folate and B12 serum levels in association with depression in the aged: a systematic review and meta-analysis. Aging & mental health. 2016;20(9):965-73.
65. Sarris J, Murphy J, Mischoulon D, Papakostas GI, Fava M, Berk M, Ng CH. Adjunctive nutraceuticals for depression: a systematic review and meta-analyses. American Journal of Psychiatry. 2016;173(6):575-87.
66. Alvarez-Mon MA, Ortega MA, García-Montero C, Fraile-Martinez O, Monserrat J, Lahera G, et al. Exploring the role of nutraceuticals in major depressive disorder (MDD): Rationale, state of the art and future prospects. Pharmaceuticals. 2021;14(8):821.
67. Mischoulon D. Popular herbal and natural remedies used in psychiatry. Focus Am Psychiatr Publ. 2018; 16 (1): 2–11.
68. Mischoulon D, Iovieno N. Supplements and natural remedies for depression. The Massachusetts General Hospital Guide to Depression: New Treatment Insights and Options. 2019:195-209.
69. Wang H, Jin M, Xie M, Yang Y, Xue F, Li W, et al. Protective role of antioxidant supplementation for depression and anxiety: A meta-analysis of randomized clinical trials. Journal of affective disorders. 2023;323:264-79.
70. Hoffmann K, Emons B, Brunnhuber S, Karaca S, Juckel G. The role of dietary supplements in depression and anxiety–a narrative review. Pharmacopsychiatry. 2019;52(06):261-79.
71. Varteresian T, Lavretsky H. Natural products and supplements for geriatric depression and cognitive disorders: an evaluation of the research. Current psychiatry reports. 2014;16(8):456.
72. Schefft C, Kilarski LL, Bschor T, Koehler S. Efficacy of adding nutritional supplements in unipolar depression: a systematic review and meta-analysis. European Neuropsychopharmacology. 2017;27(11):1090-109.
73. Dwyer AV, Whitten DL, Hawrelak JA. Herbal medicines, other than St. John's Wort, in the treatment of depression: a systematic review. Alternative medicine review. 2011;16(1):40-9.
74. Szafrański T. Herbal remedies in depression–state of the art. Psychiatr Pol. 2014;48(1):59-73.
75. Ernst E. Herbal remedies for depression and anxiety. Advances in Psychiatric Treatment. 2007;13(4):312-6.

 doi:10.20944/preprints202402.1273.v1




76. Sarris J, Panossian A, Schweitzer I, Stough C, Scholey A. Herbal medicine for depression, anxiety and insomnia: A review of psychopharmacology and clinical evidence. European Neuropsychopharmacology. 2011;21(12):841-60.
77. Sarris J. Herbal medicines in the treatment of psychiatric disorders: a systematic review. Phytotherapy Research. 2007;21(8):703-16.
78. Swardfager W, Herrmann N, Mazereeuw G, Goldberger K, Harimoto T, Lanctôt KL. Zinc in Depression: A Meta-Analysis. Biological Psychiatry. 2013;74(12):872-8.
79. Wang L, Shen X, Wu Y, Zhang D. Coffee and caffeine consumption and depression: A meta-analysis of observational studies. Australian & New Zealand Journal of Psychiatry. 2016;50(3):228-42.
80. Dong X, Yang C, Cao S, Gan Y, Sun H, Gong Y, et al. Tea consumption and the risk of depression: A meta-analysis of observational studies. Australian & New Zealand Journal of Psychiatry. 2015;49(4):334-45.
81. Yang Y, Kim Y, Je Y. Fish consumption and risk of depression: Epidemiological evidence from prospective studies. Asia-Pacific Psychiatry. 2018;10(4):e12335.
82. Li F, Liu X, Zhang D. Fish consumption and risk of depression: a meta-analysis. Journal of Epidemiology and Community Health. 2016;70(3):299-304.
83. Hoffmire CA, Block RC, Thevenet-Morrison K, van Wijngaarden E. Associations between omega-3 poly-unsaturated fatty acids from fish consumption and severity of depressive symptoms: An analysis of the 2005–2008 National Health and Nutrition Examination Survey. Prostaglandins, Leukotrienes and Essential Fatty Acids. 2012;86(4):155-60.
84. Sajjadi SS, Foshati S, Haddadian-Khouzani S, Rouhani MH. The role of selenium in depression: a systematic review and meta-analysis of human observational and interventional studies. Scientific Reports. 2022;12(1):1045.
85. Finley JW. Bioavailability of Selenium from Foods. Nutrition Reviews. 2006;64(3):146-51.
86. Ford A, Almeida OP, Flicker L, Hirani V, McCaul K, Singh U, Van Bockxmeer F. B-vitamins and Depression. European Psychiatry. 2015;30(S1):1-.
87. Mahdavifar B, Hosseinzadeh M, Salehi-Abargouei A, Mirzaei M, Vafa M. Dietary intake of B vitamins and their association with depression, anxiety, and stress symptoms: A cross-sectional, population-based survey. Journal of Affective Disorders. 2021;288:92-8.
88. Said HM. Biotin: Biochemical, Physiological and Clinical Aspects. In: Stanger O, editor. Water Soluble Vitamins: Clinical Research and Future Application. Dordrecht: Springer Netherlands; 2012. p. 1-19.
89. Iyer R, Tomar SK. Folate: A Functional Food Constituent. Journal of Food Science. 2009;74(9):R114-R22.
90. Parker GB, Brotchie H, Graham RK. Vitamin D and depression. Journal of Affective Disorders. 2017;208:56-61.
91. Menon V, Kar SK, Suthar N, Nebhinani N. Vitamin D and depression: a critical appraisal of the evidence and future directions. Indian journal of psychological medicine. 2020;42(1):11-21.
92. Baggerly CA, Cuomo RE, French CB, Garland CF, Gorham ED, Grant WB, et al. Sunlight and Vitamin D: Necessary for Public Health. Journal of the American College of Nutrition. 2015;34(4):359-65.
93. Moore C, Murphy MM, Keast DR, Holick MF. Vitamin D intake in the United States. Journal of the American Dietetic Association. 2004;104(6):980-3.
94. Liu RT, Walsh RFL, Sheehan AE. Prebiotics and probiotics for depression and anxiety: A systematic review and meta-analysis of controlled clinical trials. Neuroscience & Biobehavioral Reviews. 2019;102:13-23.
95. Chao L, Liu C, Sutthawongwadee S, Li Y, Lv W, Chen W, et al. Effects of Probiotics on Depressive or Anxiety Variables in Healthy Participants Under Stress Conditions or With a Depressive or Anxiety Diagnosis: A Meta-Analysis of Randomized Controlled Trials. Frontiers in Neurology. 2020;11.
96. Ng QX, Peters C, Ho CYX, Lim Donovan Y, Yeo W-S. A meta-analysis of the use of probiotics to alleviate depressive symptoms. Journal of Affective Disorders. 2018;228:13-9.
97. Granato D, Branco GF, Nazzaro F, Cruz AG, Faria JAF. Functional Foods and Nondairy Probiotic Food Development: Trends, Concepts, and Products. Comprehensive Reviews in Food Science and Food Safety. 2010;9(3):292-302.
98. Kapp JM, Sumner W. Kombucha: a systematic review of the empirical evidence of human health benefit. Annals of Epidemiology. 2019;30:66-70.
99. Şanlier N, Gökcen BB, Sezgin AC. Health benefits of fermented foods. Critical Reviews in Food Science and Nutrition. 2019;59(3):506-27.

 doi:10.20944/preprints202402.1273.v1




100. Cuamatzin-García L, Rodríguez-Rugarcía P, El-Kassis EG, Galicia G, Meza-Jiménez ML, Baños-Lara MDR, et al. Traditional Fermented Foods and Beverages from around the World and Their Health Benefits. Microorganisms. 2022;10(6).
101. Veronese N, Stubbs B, Solmi M, Ajnakina O, Carvalho AF, Maggi S. Acetyl-l-Carnitine Supplementation and the Treatment of Depressive Symptoms: A Systematic Review and Meta-Analysis. Psychosomatic Medicine. 2018;80(2):154-9.
102. Roseiro LC, Santos C. Chapter 2.5 - Carnitines (Including l-Carnitine, Acetyl-Carnitine, and Proprionyl-Carnitine). In: Nabavi SM, Silva AS, editors. Nonvitamin and Nonmineral Nutritional Supplements: Academic Press; 2019. p. 45-52.
103. Bakian AV, Huber RS, Scholl L, Renshaw PF, Kondo D. Dietary creatine intake and depression risk among U.S. adults. Translational Psychiatry. 2020;10(1):52.
104. Brosnan ME, Brosnan JT. The role of dietary creatine. Amino Acids. 2016;48(8):1785-91.
105. Ille R, Spona J, Zickl M, Hofmann P, Lahousen T, Dittrich N, et al. "Add-On"-therapy with an individualized preparation consisting of free amino acids for patients with a major depression. Eur Arch Psychiatry Clin Neurosci. 2007;257(4):222-9.
106. Zhao L, Guo S, Yang J, Wang Q, Lu X. Association between niacin intake and depression: A nationwide cross-sectional study. Journal of Affective Disorders. 2023;340:347-54.
107. EFSA Panel on Dietetic Products N, Allergies. Scientific opinion on dietary reference values for niacin. EFSA Journal. 2014;12(7):3759.
108. Maruf AA, Poweleit EA, Brown LC, Strawn JR, Bousman CA. Systematic Review and Meta-Analysis of L-Methylfolate Augmentation in Depressive Disorders. Pharmacopsychiatry. 2021;55(03):139-47.
109. Altaf R, Gonzalez I, Rubino K, Nemec EC. Folate as adjunct therapy to SSRI/SNRI for major depressive disorder: Systematic review & meta-analysis. Complementary Therapies in Medicine. 2021;61:102770.
110. Javelle F, Lampit A, Bloch W, Häussermann P, Johnson SL, Zimmer P. Effects of 5-hydroxytryptophan on distinct types of depression: a systematic review and meta-analysis. Nutrition Reviews. 2019;78(1):77-88.
111. Asher GN, Gartlehner G, Gaynes BN, Amick HR, Forneris C, Morgan LC, et al. Comparative Benefits and Harms of Complementary and Alternative Medicine Therapies for Initial Treatment of Major Depressive Disorder: Systematic Review and Meta-Analysis. The Journal of Alternative and Complementary Medicine. 2017;23(12):907-19.
112. Mazidi M, Shemshian M, Mousavi SH, Norouzy A, Kermani T, Moghiman T, et al. A double-blind, randomized and placebo-controlled trial of Saffron (Crocus sativus L.) in the treatment of anxiety and depression. J Complement Integr Med. 2016;13(2):195-9.
113. Ng QX, Koh SSH, Chan HW, Ho CYX. Clinical Use of Curcumin in Depression: A Meta-Analysis. J Am Med Dir Assoc. 2017;18(6):503-8.
114. Fusar-Poli L, Vozza L, Gabbiadini A, Vanella A, Concas I, Tinacci S, et al. Curcumin for depression: a meta-analysis. Crit Rev Food Sci Nutr. 2020;60(15):2643-53.
115. Naylor GJ, Martin B, Hopwood SE, Watson Y. A two-year double-blind crossover trial of the prophylactic effect of methylene blue in manic-depressive psychosis. Biol Psychiatry. 1986;21(10):915-20.
116. Naylor GJ, Smith AH, Connelly P. A controlled trial of Methylene Blue in severe depressive illness. Biological Psychiatry. 1987;22:657-9.
117. Wang Y, Shi Y-h, Xu Z, Fu H, Zeng H, Zheng G-q. Efficacy and safety of Chinese herbal medicine for depression: A systematic review and meta-analysis of randomized controlled trials. Journal of Psychiatric Research. 2019;117:74-91.
118. Yeung W-F, Chung K-F, Ng K-Y, Yu Y-M, Ziea ET-C, Ng BF-L. A systematic review on the efficacy, safety and types of Chinese herbal medicine for depression. Journal of Psychiatric Research. 2014;57:165-75.
119. Zadeh AR, Eghbal AF, Mirghazanfari SM, Ghasemzadeh MR, Nassireslami E, Donyavi V. Nigella sativa extract in the treatment of depression and serum Brain-Derived Neurotrophic Factor (BDNF) levels. J Res Med Sci. 2022;27:28.
120. Galizia I, Oldani L, Macritchie K, Amari E, Dougall D, Jones TN, et al. S-adenosyl methionine (SAMe) for depression in adults. Cochrane Database of Systematic Reviews. 2016(10).
121. Black N, Stockings E, Campbell G, Tran LT, Zagic D, Hall WD, et al. Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis. The Lancet Psychiatry. 2019;6(12):995-1010.

 doi:10.20944/preprints202402.1273.v1




122. Lev-Ran S, Roerecke M, Le Foll B, George T, McKenzie K, Rehm J. The association between cannabis use and depression: a systematic review and meta-analysis of longitudinal studies. Psychological medicine. 2014;44(4):797-810.
123. Rootman JM, Kryskow P, Harvey K, Stamets P, Santos-Brault E, Kuypers KPC, et al. Adults who microdose psychedelics report health related motivations and lower levels of anxiety and depression compared to non-microdosers. Scientific Reports. 2021;11(1):22479.
124. Romeo B, Karila L, Martelli C, Benyamina A. Efficacy of psychedelic treatments on depressive symptoms: A meta-analysis. Journal of Psychopharmacology. 2020;34(10):1079-85.
125. Gasser P, Holstein D, Michel Y, Doblin R, Yazar-Klosinski B, Passie T, Brenneisen R. Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. J Nerv Ment Dis. 2014;202(7):513-20.
126. Calabrese C, Gregory WL, Leo M, Kraemer D, Bone K, Oken B. Effects of a standardized Bacopa monnieri extract on cognitive performance, anxiety, and depression in the elderly: a randomized, double-blind, placebo-controlled trial. J Altern Complement Med. 2008;14(6):707-13.
127. Darbinyan V, Aslanyan G, Amroyan E, Gabrielyan E, Malmström C, Panossian A. Clinical trial of Rhodiola rosea L. extract SHR-5 in the treatment of mild to moderate depression. Nord J Psychiatry. 2007;61(5):343-8.
128. Sarris J, Kavanagh DJ, Byrne G, Bone KM, Adams J, Deed G. The Kava Anxiety Depression Spectrum Study (KADSS): a randomized, placebo-controlled crossover trial using an aqueous extract of Piper methysticum. Psychopharmacology (Berl). 2009;205(3):399-407.
129. Clements RS, Jr., Darnell B. Myo-inositol content of common foods: development of a high-myo-inositol diet. Am J Clin Nutr. 1980;33(9):1954-67.
130. Davidson JR, Abraham K, Connor KM, McLeod MN. Effectiveness of chromium in atypical depression: a placebo-controlled trial. Biol Psychiatry. 2003;53(3):261-4.
131. Swaroop A, Bagchi M, Preuss H, Zafra-Stone S, Ahmad T, Bagchi D. Benefits of chromium(III) complexes in animal and human health. 2019. p. 251-78.
132. Shay KP, Moreau RF, Smith EJ, Smith AR, Hagen TM. Alpha-lipoic acid as a dietary supplement: molecular mechanisms and therapeutic potential. Biochimica et Biophysica Acta (BBA)-General Subjects. 2009;1790(10):1149-60.
133. Berk M, Copolov DL, Dean O, Lu K, Jeavons S, Schapkaitz I, et al. N-acetyl cysteine for depressive symptoms in bipolar disorder--a double-blind randomized placebo-controlled trial. Biol Psychiatry. 2008;64(6):468-75.
134. Berk M, Dean O, Cotton SM, Gama CS, Kapczinski F, Fernandes BS, et al. The efficacy of N-acetylcysteine as an adjunctive treatment in bipolar depression: an open label trial. J Affect Disord. 2011;135(1-3):389-94.
135. Caso Marasco A, Vargas Ruiz R, Salas Villagomez A, Begoña Infante C. Double-blind study of a multivitamin complex supplemented with ginseng extract. Drugs Exp Clin Res. 1996;22(6):323-9.
136. Pravst I, Žmitek K, Žmitek J. Coenzyme Q10 Contents in Foods and Fortification Strategies. Critical Reviews in Food Science and Nutrition. 2010;50(4):269-80.
137. Mischoulon D. Popular Herbal and Natural Remedies Used in Psychiatry. Focus (Am Psychiatr Publ). 2018;16(1):2-11.
138. Dwyer AV, Whitten DL, Hawrelak JA. Herbal medicines, other than St. John's Wort, in the treatment of depression: a systematic review. Altern Med Rev. 2011;16(1):40-9.
139. Szafrański T. [Herbal remedies in depression--state of the art]. Psychiatr Pol. 2014;48(1):59-73.
140. Ahmadpoor J, Chahardahcheric SV, Setorki M. The Protective effect of hydroalcoholic extract of the southern maidenhair fern (adiantum capillus-veneris) on the depression and anxiety caused by chronic stress in adult male mice: an experimental randomized study. Iranian Red Crescent Medical Journal. 2019;21(3).
141. Rabiei Z, Setorki M. Effect of ethanol Adiantum capillus-veneris extract in experimental models of anxiety and depression. Brazilian Journal of Pharmaceutical Sciences. 2019;55.
142. Pedersen ME, Szewczyk B, Stachowicz K, Wieronska J, Andersen J, Stafford GI, et al. Effects of South African traditional medicine in animal models for depression. Journal of Ethnopharmacology. 2008;119(3):542-8.
143. Aderibigbe A. Antidepressant activity of ethanol extract of Albizia adianthifolia (Schumach) WF Wight leaf in mice. African Journal of Medicine and Medical Sciences. 2018;47(2):133-40.

 doi:10.20944/preprints202402.1273.v1




144. Beppe GJ, Dongmo AB, Foyet HS, Dimo T, Mihasan M, Hritcu L. The aqueous extract of Albizia adianthifolia leaves attenuates 6-hydroxydopamine-induced anxiety, depression and oxidative stress in rat amygdala. BMC Complementary and Alternative Medicine. 2015;15(1):1-13.
145. Jahani R, Khaledyan D, Jahani A, Jamshidi E, Kamalinejad M, Khoramjouy M, Faizi M. Evaluation and comparison of the antidepressant-like activity of Artemisia dracunculus and Stachys lavandulifolia ethanolic extracts: an in vivo study. Research in Pharmaceutical Sciences. 2019;14(6):544.
146. Ilkhanizadeh A, Asghari A, Hassanpour S, Safi S. Anti-depressant effect of Artemisia dracunculus extract is mediated via GABAergic and serotoninergic systems in ovariectomized mice. Journal of Basic and Clinical Pathophysiology. 2021;9(2):32-41.
147. Zanelati T, Biojone C, Moreira F, Guimarães FS, Joca SRL. Antidepressant-like effects of cannabidiol in mice: possible involvement of 5-HT1A receptors. British journal of pharmacology. 2010;159(1):122-8.
148. Sales AJ, Crestani CC, Guimarães FS, Joca SR. Antidepressant-like effect induced by Cannabidiol is dependent on brain serotonin levels. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2018;86:255-61.
149. El-Alfy AT, Ivey K, Robinson K, Ahmed S, Radwan M, Slade D, et al. Antidepressant-like effect of Δ9-tetrahydrocannabinol and other cannabinoids isolated from Cannabis sativa L. Pharmacology Biochemistry and Behavior. 2010;95(4):434-42.
150. Selvi PT, Kumar MS, Rajesh R, Kathiravan T. Antidepressant activity of ethanolic extract of leaves of Centella asiatica. Linn by In vivo methods. Asian Journal of Research in Pharmaceutical Science. 2012;2(2):76-9.
151. Rabadia J, Satish S, Ramanjaneyulu J, Narayanaswamy V. An investigation of anti-depressant activity of Cinnamomum camphora oil in experimental mice. Asian Journal of Biomedical and Pharmaceutical Sciences. 2013;3(20):44.
152. Citó M, Silva MIG, Santos LKX, Fernandes M, Melo FHC, Aguiar JAC, et al. Antidepressant-like effect of Hoodia gordonii in a forced swimming test in mice: evidence for involvement of the monoaminergic system. Brazilian Journal of Medical and Biological Research. 2014;48:57-64.
153. Tian J, Zhang F, Cheng J, Guo S, Liu P, Wang H. Antidepressant-like activity of adhyperforin, a novel constituent of Hypericum perforatum L. Scientific Reports. 2014;4(1):5632.
154. Fiebich BL, Knörle R, Appel K, Kammler T, Weiss G. Pharmacological studies in an herbal drug combination of St. John's Wort (Hypericum perforatum) and passion flower (Passiflora incarnata): in vitro and in vivo evidence of synergy between Hypericum and Passiflora in antidepressant pharmacological models. Fitoterapia. 2011;82(3):474-80.
155. Ejigu A, Engidawork E. Screening of the antidepressant-like activity of two hypericum species found in Ethiopia. Eth Pharm J. 2014;30(1):21-32.
156. Benneh CK, Biney RP, Adongo DW, Mante PK, Ampadu FA, Tandoh A, et al. Anxiolytic and antidepressant effects of Maerua angolensis DC. Stem bark extract in mice. Depression Research and Treatment. 2018;2018.
157. Ishaq H. Anxiolytic and antidepressant activity of different methanolic extracts of Melia azedarach Linn. Pakistan journal of pharmaceutical sciences. 2016;29(5).
158. Jedi-Behnia B, Abbasi Maleki S, Mousavi E. The antidepressant-like effect of Mentha spicata essential oil in animal models of depression in male mice. Journal of Advanced Biomedical Sciences. 2017;7(1):141-9.
159. Badr AM, Attia HA, Al-Rasheed N. Oleuropein reverses repeated corticosterone-induced depressive-like behavior in mice: evidence of modulating effect on biogenic amines. Scientific reports. 2020;10(1):3336.
160. Perveen T, Hashmi BM, Haider S, Tabassum S, Saleem S, Siddiqui MA. Role of monoaminergic system in the etiology of olive oil induced antidepressant and anxiolytic effects in rats. International Scholarly Research Notices. 2013;2013.
161. Tariq U, Butt MS, Pasha I, Faisal MN. Neuroprotective effects of Olea europaea L. fruit extract against cigarette smoke-induced depressive-like behaviors in Sprague–Dawley rats. Journal of Food Biochemistry. 2021;45(12):e14014.
162. Machado DG, Bettio LE, Cunha MP, Capra JC, Dalmarco JB, Pizzolatti MG, Rodrigues ALS. Antidepressant-like effect of the extract of Rosmarinus officinalis in mice: involvement of the monoaminergic system. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2009;33(4):642-50.

 doi:10.20944/preprints202402.1273.v1




163. Sasaki K, El Omri A, Kondo S, Han J, Isoda H. Rosmarinus officinalis polyphenols produce anti-depressant like effect through monoaminergic and cholinergic functions modulation. Behavioural Brain Research. 2013;238:86-94.
164. Sasaki K, Ferdousi F, Fukumitsu S, Kuwata H, Isoda H. Antidepressant-and anxiolytic-like activities of Rosmarinus officinalis extract in rodent models: Involvement of oxytocinergic system. Biomedicine & Pharmacotherapy. 2021;144:112291.
165. Abdelhalim A, Karim N, Chebib M, Aburjai T, Khan I, Johnston GA, Hanrahan J. Antidepressant, anxiolytic and antinociceptive activities of constituents from Rosmarinus officinalis. Journal of Pharmacy & Pharmaceutical Sciences. 2015;18(4):448-59.
166. Adebiyi R, Elsa A, Agaie B, Etuk E. Antinociceptive and antidepressant like effects of Securidaca longepedunculata root extract in mice. Journal of ethnopharmacology. 2006;107(2):234-9.
167. Loria MJ, Ali Z, Abe N, Sufka KJ, Khan IA. Effects of Sceletium tortuosum in rats. Journal of ethnopharmacology. 2014;155(1):731-5.
168. Machado DG, Kaster MP, Binfaré RW, Dias M, Santos AR, Pizzolatti MG, et al. Antidepressant-like effect of the extract from leaves of Schinus molle L. in mice: evidence for the involvement of the monoaminergic system. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2007;31(2):421-8.
169. Wado EK, Kubicki M, Ngatanko AHH, Blondelle KDL, Roland RN, Balbine K, et al. Anxiolytic and antidepressant effects of Ziziphus mucronata hydromethanolic extract in male rats exposed to unpredictable chronic mild stress: Possible mechanisms of actions. Journal of ethnopharmacology. 2020;260:112987.
170. Li H, Xiao Y, Han L, Jia Y, Luo S, Zhang D, et al. Ganoderma lucidum polysaccharides ameliorated depression-like behaviors in the chronic social defeat stress depression model via modulation of Dectin-1 and the innate immune system. Brain Research Bulletin. 2021;171:16-24.
171. Mi X, Zeng G-R, Liu J-Q, Luo Z-S, Zhang L, Dai X-M, et al. Ganoderma lucidum triterpenoids improve maternal separation-induced anxiety-and depression-like behaviors in mice by mitigating inflammation in the periphery and brain. Nutrients. 2022;14(11):2268.
172. Nagano M, Shimizu K, Kondo R, Hayashi C, Sato D, Kitagawa K, Ohnuki K. Reduction of depression and anxiety by 4 weeks Hericium erinaceus intake. Biomedical Research. 2010;31(4):231-7.
173. Zhou Y, Ma C, Li B-M, Sun C. Polygala japonica Houtt. reverses depression-like behavior and restores reduced hippocampal neurogenesis in chronic stress mice. Biomedicine & Pharmacotherapy. 2018;99:986-96.
174. Kim N-H, Jeong H-J, Lee J-Y, Go H, Ko S-G, Hong S-H, et al. The effect of hydrolyzed Spirulina by malted barley on forced swimming test in ICR mice. International Journal of Neuroscience. 2008;118(11):1523-33.
175. Suresh D, Madhu M, Saritha C, Shankaraiah P. Antidepressant activity of spirulina platensis in experimentally induced dipression in mice. 2014.
176. Soetantyo GI, Sarto M. The antidepressant effect of Chlorella vulgaris on female Wistar rats (Rattus norvegicus Berkenhout, 1769) with chronic unpredictable mild stress treatment. J Trop Biodivers Biotechnol. 2019;4:72-81.
177. Miyake Y, Tanaka K, Okubo H, Sasaki S, Arakawa M. Seaweed consumption and prevalence of depressive symptoms during pregnancy in Japan: Baseline data from the Kyushu Okinawa Maternal and Child Health Study. BMC pregnancy and childbirth. 2014;14(1):1-7.
178. Allaert F-A, Demais H, Collén PN. A randomized controlled double-blind clinical trial comparing versus placebo the effect of an edible algal extract (Ulva Lactuca) on the component of depression in healthy volunteers with anhedonia. BMC psychiatry. 2018;18:1-10.
179. Guo F, Huang C, Cui Y, Momma H, Niu K, Nagatomi R. Dietary seaweed intake and depressive symptoms in Japanese adults: a prospective cohort study. Nutrition journal. 2019;18(1):1-8.
180. Sasaki K, Othman MB, Demura M, Watanabe M, Isoda H. Modulation of neurogenesis through the promotion of energy production activity is behind the antidepressant-like effect of colonial green alga, Botryococcus braunii. Frontiers in physiology. 2017;8:900.
181. Panahi Y, Badeli R, Karami G-R, Badeli Z, Sahebkar A. A randomized controlled trial of 6-week Chlorella vulgaris supplementation in patients with major depressive disorder. Complementary therapies in medicine. 2015;23(4):598-602.
182. Talbott S, Hantla D, Capelli B, Ding L, Li Y, Artaria C. Astaxanthin supplementation reduces depression and fatigue in healthy subjects. EC Nutrition. 2019;14(3):239-46.

 doi:10.20944/preprints202402.1273.v1




183. Siddiqui PJA, Khan A, Uddin N, Khaliq S, Rasheed M, Nawaz S, et al. Antidepressant-like deliverables from the sea: evidence on the efficacy of three different brown seaweeds via involvement of monoaminergic system. Bioscience, Biotechnology, and Biochemistry. 2017;81(7):1369-78.
184. Abreu TM, Monteiro VS, Martins ABS, Teles FB, da Conceição Rivanor RL, Mota ÉF, et al. Involvement of the dopaminergic system in the antidepressant-like effect of the lectin isolated from the red marine alga Solieria filiformis in mice. International journal of biological macromolecules. 2018;111:534-41.
185. Violle N, Rozan P, Demais H, Nyvall Collen P, Bisson J-F. Evaluation of the antidepressant-and anxiolytic-like effects of a hydrophilic extract from the green seaweed Ulva sp. in rats. Nutritional neuroscience. 2018;21(4):248-56.
186. Wang X, Xiu Z, Du Y, Li Y, Yang J, Gao Y, et al. Brazilin treatment produces antidepressant-and anxiolytic-like effects in mice. Biological and Pharmaceutical Bulletin. 2019;42(8):1268-74.
187. Xu Y, Wang Z, You W, Zhang X, Li S, Barish PA, et al. Antidepressant-like effect of trans-resveratrol: involvement of serotonin and noradrenaline system. European neuropsychopharmacology. 2010;20(6):405-13.
188. Shewale PB, Patil RA, Hiray YA. Antidepressant-like activity of anthocyanidins from Hibiscus rosa-sinensis flowers in tail suspension test and forced swim test. Indian journal of pharmacology. 2012;44(4):454.
189. Ghazizadeh J, Sadigh-Eteghad S, Marx W, Fakhari A, Hamedeyazdan S, Torbati M, et al. The effects of lemon balm (Melissa officinalis L.) on depression and anxiety in clinical trials: A systematic review and meta-analysis. Phytotherapy Research. 2021;35(12):6690-705.
190. Guzmán-Gutiérrez S, Gómez-Cansino R, García-Zebadúa J, Jiménez-Pérez N, Reyes-Chilpa R. Antidepressant activity of Litsea glaucescens essential oil: Identification of β-pinene and linalool as active principles. Journal of ethnopharmacology. 2012;143(2):673-9.
191. Kim M, Nam ES, Lee Y, Kang H-J. Effects of lavender on anxiety, depression, and physiological parameters: Systematic review and meta-analysis. Asian nursing research. 2021;15(5):279-90.
192. Fajemiroye JO, Martins JLR, Ghedini PC, Galdino PM, Paula JAMd, Realino de Paula J, et al. Antidepressive-like property of dichloromethane fraction of Pimenta pseudocaryophyllus and relevance of monoamine metabolic enzymes. Evidence-Based Complementary and Alternative Medicine. 2013;2013.
193. Molina M, Contreras C, Tellez-Alcantara P. Mimosa pudica may possess antidepressant actions in the rat. Phytomedicine. 1999;6(5):319-23.
194. Martínez-Vázquez M, Estrada-Reyes R, Escalona AA, Velázquez IL, Martínez-Mota L, Moreno J, Heinze G. Antidepressant-like effects of an alkaloid extract of the aerial parts of Annona cherimolia in mice. Journal of ethnopharmacology. 2012;139(1):164-70.
195. Gabriela G-C, Javier A-AF, Elisa V-A, Gonzalo V-P, Herlinda B-J. Antidepressant-like effect of Tagetes lucida Cav. extract in rats: involvement of the serotonergic system. The American Journal of Chinese Medicine. 2012;40(04):753-68.
196. Ali SM, Shamim S, Younus I, Anwer L, Khaliq SA. Anxiolytic, antidepressant and inhibitory effect on MAO isoenzymes by Bougainvillea glabra flower extract in rats. Pakistan Journal of Pharmaceutical Sciences. 2021;34(5):1963-8.
197. Sarris J, Kavanagh DJ, Byrne G, Bone K, Adams J, Deed G. The Kava Anxiety Depression Spectrum Study (KADSS): a randomized, placebo-controlled crossover trial using an aqueous extract of Piper methysticum. Psychopharmacology. 2009;205:399-407.
198. Kazemian A, Parvin N, Raisi Dehkordi Z, Rafieian-Kopaei M. The effect of valerian on the anxiety and depression symptoms of the menopause in women referred to shahrekord medical centers. Journal of Medicinal Plants. 2017;16(61):94-101.
199. Tammadon MR, Nobahar M, Hydarinia-Naieni Z, Ebrahimian A, Ghorbani R, Vafaei AA. The effects of valerian on sleep quality, depression, and state anxiety in hemodialysis patients: a randomized, double-blind, crossover clinical trial. Oman Medical Journal. 2021;36(2):e255.
200. Doron R, Lotan D, Einat N, Yaffe R, Winer A, Marom I, et al. A novel herbal treatment reduces depressive-like behaviors and increases BDNF levels in the brain of stressed mice. Life Sciences. 2014;94(2):151-7.
201. Li J-m, Yang C, Zhang W-y, Kong L-d. The effects of banxia houpu decoction on a chronic mild stress model of depression. Zhongguo Zhong yao za zhi= Zhongguo Zhongyao Zazhi= China Journal of Chinese Materia Medica. 2003;28(1):55-9.
202. Mayer EA. Gut feelings: the emerging biology of gut–brain communication. Nature Reviews Neuroscience. 2011;12(8):453-66.

 doi:10.20944/preprints202402.1273.v1




203. Mayer EA, Knight R, Mazmanian SK, Cryan JF, Tillisch K. Gut microbes and the brain: paradigm shift in neuroscience. Journal of Neuroscience. 2014;34(46):15490-6.
204. Cryan JF, Dinan TG. Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour. Nature reviews neuroscience. 2012;13(10):701-12.
205. Foster JA, Neufeld K-AM. Gut–brain axis: how the microbiome influences anxiety and depression. Trends in neurosciences. 2013;36(5):305-12.
206. Stilling RM, Dinan TG, Cryan JF. Microbial genes, brain & behaviour - epigenetic regulation of the gut-brain axis. Genes Brain Behav. 2014;13(1):69-86.
207. 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. Journal of psychiatric research. 2016;82:109-18.
208. Carabotti M, Scirocco A, Maselli MA, Severi C. The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. Annals of gastroenterology: quarterly publication of the Hellenic Society of Gastroenterology. 2015;28((2)):203-9.
209. Zheng P, Zeng B, Zhou C, Liu M, Fang Z, Xu X, et al. Gut microbiome remodeling induces depressive-like behaviors through a pathway mediated by the host's metabolism. Molecular psychiatry. 2016;21(6):786-96.
210. Clapp M, Aurora N, Herrera L, Bhatia M, Wilen E, Wakefield S. Gut microbiota's effect on mental health: The gut-brain axis. Clinics and practice. 2017;7(4):987.
211. Van de Wouw M, Boehme M, Lyte JM, Wiley N, Strain C, O'Sullivan O, et al. Short-chain fatty acids: microbial metabolites that alleviate stress-induced brain–gut axis alterations. The Journal of physiology. 2018;596(20):4923-44.
212. Slyepchenko A, Maes M, Jacka FN, Köhler CA, Barichello T, McIntyre RS, et al. Gut microbiota, bacterial translocation, and interactions with diet: pathophysiological links between major depressive disorder and non-communicable medical comorbidities. Psychotherapy and psychosomatics. 2016;86(1):31-46.
213. Dalile B. Short-chain fatty acids in microbiota-gut-brain communication. Nat Rev Gastroenterol Hepatol. 2019;16:461-78.
214. Li Z, Lai J, Zhang P, Ding J, Jiang J, Liu C, et al. Multi-omics analyses of serum metabolome, gut microbiome and brain function reveal dysregulated microbiota-gut-brain axis in bipolar depression. Molecular psychiatry. 2022;27(10):4123-35.
215. Jiang H, Ling Z, Zhang Y, Mao H, Ma Z, Yin Y, et al. Altered fecal microbiota composition in patients with major depressive disorder. Brain, behavior, and immunity. 2015;48:186-94.
216. Kelly JR, Kennedy PJ, Cryan JF, Dinan TG, Clarke G, Hyland NP. Breaking down the barriers: the gut microbiome, intestinal permeability and stress-related psychiatric disorders. Frontiers in cellular neuroscience. 2015:392.
217. Maes M, Kubera M, Leunis J-C, Berk M. Increased IgA and IgM responses against gut commensals in chronic depression: further evidence for increased bacterial translocation or leaky gut. Journal of affective disorders. 2012;141(1):55-62.
218. 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(2):264-76.
219. Strandwitz P. Neurotransmitter modulation by the gut microbiota. Brain research. 2018;1693:128-33.
220. Strandwitz P, Kim KH, Terekhova D, Liu JK, Sharma A, Levering J, et al. GABA-modulating bacteria of the human gut microbiota. Nature microbiology. 2019;4(3):396-403.
221. Bear TL, Dalziel JE, Coad J, Roy NC, Butts CA, Gopal PK. The role of the gut microbiota in dietary interventions for depression and anxiety. Advances in Nutrition. 2020;11(4):890-907.
222. Slyepchenko A, F Carvalho A, S Cha D, Kasper S, S McIntyre R. Gut emotions-mechanisms of action of probiotics as novel therapeutic targets for depression and anxiety disorders. CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders). 2014;13(10):1770-86.
223. Bravo JA, Forsythe P, Chew MV, Escaravage E, Savignac HM, Dinan TG, et al. Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. Proceedings of the National Academy of Sciences. 2011;108(38):16050-5.
224. Tian P, O'Riordan KJ, Lee Y-k, Wang G, Zhao J, Zhang H, et al. Towards a psychobiotic therapy for depression: Bifidobacterium breve CCFM1025 reverses chronic stress-induced depressive symptoms and gut microbial abnormalities in mice. Neurobiology of stress. 2020;12:100216.

225. Tian P, Chen Y, Zhu H, Wang L, Qian X, Zou R, et al. Bifidobacterium breve CCFM1025 attenuates major depression disorder via regulating gut microbiome and tryptophan metabolism: A randomized clinical trial. Brain, behavior, and immunity. 2022;100:233-41.
226. Tian P, Chen Y, Qian X, Zou R, Zhu H, Zhao J, et al. Pediococcus acidilactici CCFM6432 mitigates chronic stress-induced anxiety and gut microbial abnormalities. Food & Function. 2021;12(22):11241-9.
227. Knudsen JK, Michaelsen TY, Bundgaard-Nielsen C, Nielsen RE, Hjerrild S, Leutscher P, et al. Faecal microbiota transplantation from patients with depression or healthy individuals into rats modulates mood-related behaviour. Scientific Reports. 2021;11(1):21869.
228. Doll JPK, Vázquez-Castellanos JF, Schaub AC, Schweinfurth N, Kettelhack C, Schneider E, et al. Fecal Microbiota Transplantation (FMT) as an Adjunctive Therapy for Depression-Case Report. Front Psychiatry. 2022;13:815422.
229. Miller AH, Raison CL. The role of inflammation in depression: from evolutionary imperative to modern treatment target. Nature reviews immunology. 2016;16(1):22-34.
230. Dowlati Y, Herrmann N, Swardfager W, Liu H, Sham L, Reim EK, Lanctôt KL. A meta-analysis of cytokines in major depression. Biological psychiatry. 2010;67(5):446-57.
231. Ting EY-C, Yang AC, Tsai S-J. Role of interleukin-6 in depressive disorder. International journal of molecular sciences. 2020;21(6):2194.
232. Hodes GE, Ménard C, Russo SJ. Integrating Interleukin-6 into depression diagnosis and treatment. Neurobiology of stress. 2016;4:15-22.
233. Howren MB, Lamkin DM, Suls J. Associations of depression with C-reactive protein, IL-1, and IL-6: a meta-analysis. Psychosomatic medicine. 2009;71(2):171-86.
234. Dantzer R, O'connor JC, Freund GG, Johnson RW, Kelley KW. From inflammation to sickness and depression: when the immune system subjugates the brain. Nature reviews neuroscience. 2008;9(1):46-56.
235. Dantzer R, O'Connor JC, Lawson MA, Kelley KW. Inflammation-associated depression: from serotonin to kynurenine. Psychoneuroendocrinology. 2011;36(3):426-36.
236. Pariante CM, Lightman SL. The HPA axis in major depression: classical theories and new developments. Trends in neurosciences. 2008;31(9):464-8.
237. Kéri S, Szabó C, Kelemen O. Expression of Toll-Like Receptors in peripheral blood mononuclear cells and response to cognitive-behavioral therapy in major depressive disorder. Brain, Behavior, and Immunity. 2014;40:235-43.
238. Isaković J, Gorup D, Mitrečić D. Molecular mechanisms of microglia-and astrocyte-driven neurorestoration triggered by application of electromagnetic fields. Croatian medical journal. 2019;60(2):127-40.
239. He G-L, Liu Y, Li M, Chen C-H, Gao P, Yu Z-P, Yang X-S. The amelioration of phagocytic ability in microglial cells by curcumin through the inhibition of EMF-induced pro-inflammatory responses. Journal of Neuroinflammation. 2014;11(1):1-13.
240. Ng QX, Koh SSH, Chan HW, Ho CYX. Clinical use of curcumin in depression: a meta-analysis. Journal of the American Medical Directors Association. 2017;18(6):503-8.
241. Lopresti AL, Maes M, Maker GL, Hood SD, Drummond PD. Curcumin for the treatment of major depression: a randomised, double-blind, placebo controlled study. Journal of affective disorders. 2014;167:368-75.
242. Yu J-J, Pei L-B, Zhang Y, Wen Z-Y, Yang J-L. Chronic supplementation of curcumin enhances the efficacy of antidepressants in major depressive disorder: a randomized, double-blind, placebo-controlled pilot study. Journal of clinical psychopharmacology. 2015;35(4):406-10.
243. Sanmukhani J, Satodia V, Trivedi J, Patel T, Tiwari D, Panchal B, et al. Efficacy and safety of curcumin in major depressive disorder: a randomized controlled trial. Phytotherapy research. 2014;28(4):579-85.
244. Ramaholimihaso T, Bouazzaoui F, Kaladjian A. Curcumin in depression: potential mechanisms of action and current evidence—a narrative review. Frontiers in psychiatry. 2020;11:572533.
245. Fusar-Poli L, Vozza L, Gabbiadini A, Vanella A, Concas I, Tinacci S, et al. Curcumin for depression: a meta-analysis. Critical reviews in food science and nutrition. 2020;60(15):2643-53.
246. Liu D, Wang Z, Gao Z, Xie K, Zhang Q, Jiang H, Pang Q. Effects of curcumin on learning and memory deficits, BDNF, and ERK protein expression in rats exposed to chronic unpredictable stress. Behavioural brain research. 2014;271:116-21.
247. Lass P, Slawek J, Derejko M, Rubello D. Neurological and psychiatric disorders in thyroid dysfunctions. The role of nuclear medicine: SPECT and PET imaging. Minerva endocrinologica. 2008;33(2):75-84.

 doi:10.20944/preprints202402.1273.v1




248. Kirkegaard C, Faber J. The role of thyroid hormones in depression. European Journal of Endocrinology. 1998;138(1):1-9.
249. Ittermann T, Völzke H, Baumeister SE, Appel K, Grabe HJ. Diagnosed thyroid disorders are associated with depression and anxiety. Social psychiatry and psychiatric epidemiology. 2015;50:1417-25.
250. Bauer M, Goetz T, Glenn T, Whybrow P. The thyroid-brain interaction in thyroid disorders and mood disorders. Journal of neuroendocrinology. 2008;20(10):1101-14.
251. Nuguru SP, Rachakonda S, Sripathi S, Khan MI, Patel N, Meda RT. Hypothyroidism and depression: a narrative review. Cureus. 2022;14(8).
252. Loh HH, Lim LL, Yee A, Loh HS. Association between subclinical hypothyroidism and depression: an updated systematic review and meta-analysis. BMC Psychiatry. 2019;19(1):12.
253. Cleare A, McGregor A, O'keane V. Neuroendocrine evidence for an association between hypothyroidism, reduced central 5-HT activity and depression. Clinical endocrinology. 1995;43(6):713-9.
254. Duval F, Mokrani M-C, Erb A, Danila V, Lopera FG, Foucher JR, Jeanjean LC. Thyroid axis activity and dopamine function in depression. Psychoneuroendocrinology. 2021;128:105219.
255. Swann A. Thyroid hormone and norepinephrine: effects on alpha-2, beta, and reuptake sites in cerebral cortex and heart. Journal of neural transmission. 1988;71:195-205.
256. Haggerty Jr JJ, Prange Jr AJ. Borderline hypothyroidism and depression. Annual review of medicine. 1995;46(1):37-46.
257. Sullivan P, Wilson D, Mulder R, Joyce P. The hypothalamic-pituitary-thyroid axis in major depression. Acta Psychiatrica Scandinavica. 1997;95(5):370-8.
258. Hage MP, Azar ST. The link between thyroid function and depression. Journal of thyroid research. 14 Dec 2011;2012:590648.
259. Hein MD, Jackson IM. Thyroid function in psychiatric illness. General hospital psychiatry. 1990;12(4):232-44.
260. Kotkowska Z, Strzelecki D. Depression and Autoimmune Hypothyroidism—Their Relationship and the Effects of Treating Psychiatric and Thyroid Disorders on Changes in Clinical and Biochemical Parameters Including BDNF and Other Cytokines—A Systematic Review. Pharmaceuticals. 2022;15(4):391.
261. Betsy A, Binitha M, Sarita S. Zinc deficiency associated with hypothyroidism: an overlooked cause of severe alopecia. International journal of trichology. 2013;5(1):40-2.
262. Rayman MP. Multiple nutritional factors and thyroid disease, with particular reference to autoimmune thyroid disease. Proceedings of the nutrition society. 2019;78(1):34-44.
263. Ventura M, Melo M, Carrilho F. Selenium and thyroid disease: from pathophysiology to treatment. International journal of endocrinology. 2017;2017.
264. Trifu S, Popescu A, Dragoi A, Trifu A. Thyroid hormones as a third line of augmentation medication in treatment-resistant depression. Acta Endocrinológica (Bucharest). 2020;16(2):256.
265. Bauer M, Heinz A, Whybrow P. Thyroid hormones, serotonin and mood: of synergy and significance in the adult brain. Molecular psychiatry. 2002;7(2):140-56.
266. Ko K, Kopra EI, Cleare AJ, Rucker JJ. Psychedelic therapy for depressive symptoms: A systematic review and meta-analysis. Journal of Affective Disorders. 2023;322:194-204.
267. Leger RF, Unterwald EM. Assessing the effects of methodological differences on outcomes in the use of psychedelics in the treatment of anxiety and depressive disorders: A systematic review and meta-analysis. Journal of Psychopharmacology. 2022;36(1):20-30.
268. Luoma JB, Chwyl C, Bathje GJ, Davis AK, Lancelotta R. A meta-analysis of placebo-controlled trials of psychedelic-assisted therapy. Journal of Psychoactive Drugs. 2020;52(4):289-99.
269. Galvão-Coelho NL, Marx W, Gonzalez M, Sinclair J, de Manincor M, Perkins D, Sarris J. Classic serotonergic psychedelics for mood and depressive symptoms: a meta-analysis of mood disorder patients and healthy participants. Psychopharmacology. 2021;238:341-54.
270. Goldberg SB, Shechet B, Nicholas CR, Ng CW, Deole G, Chen Z, Raison CL. Post-acute psychological effects of classical serotonergic psychedelics: a systematic review and meta-analysis. Psychological medicine. 2020;50(16):2655-66.
271. Muttoni S, Ardissino M, John C. Classical psychedelics for the treatment of depression and anxiety: A systematic review. Journal of Affective Disorders. 2019;258:11-24.
272. Li N-X, Hu Y-R, Chen W-N, Zhang B. Dose effect of psilocybin on primary and secondary depression: a preliminary systematic review and meta-analysis. Journal of Affective Disorders. 2022;296:26-34.

 doi:10.20944/preprints202402.1273.v1




273. Goldberg SB, Pace BT, Nicholas CR, Raison CL, Hutson PR. The experimental effects of psilocybin on symptoms of anxiety and depression: A meta-analysis. Psychiatry Research. 2020;284:112749.
274. Andersen KA, Carhart-Harris R, Nutt DJ, Erritzoe D. Therapeutic effects of classic serotonergic psychedelics: A systematic review of modern-era clinical studies. Acta Psychiatrica Scandinavica. 2021;143(2):101-18.
275. Bahji A, Lunsky I, Gutierrez G, Vazquez G. Efficacy and Safety of Four Psychedelic-Assisted Therapies for Adults with Symptoms of Depression, Anxiety, and Posttraumatic Stress Disorder: A Systematic Review and Meta-Analysis. Journal of Psychoactive Drugs. 2023:1-16.
276. Sicignano D, Snow-Caroti K, Hernandez AV, White CM. The Impact of Psychedelic Drugs on Anxiety and Depression in Advanced Cancer or other Life-threatening Disease: A Systematic Review With Meta-analysis. American Journal of Clinical Oncology. 2023;46(6):236-45.
277. Vargas AS, Luís Â, Barroso M, Gallardo E, Pereira L. Psilocybin as a New Approach to Treat Depression and Anxiety in the Context of Life-Threatening Diseases—A Systematic Review and Meta-Analysis of Clinical Trials. Biomedicines. 2020;8(9):331.
278. Perez N, Langlest F, Mallet L, De Pieri M, Sentissi O, Thorens G, et al. Psilocybin-assisted therapy for depression: A systematic review and dose-response meta-analysis of human studies. European Neuropsychopharmacology. 2023;76:61-76.
279. Newport DJ, Carpenter LL, McDonald WM, Potash JB, Tohen M, Nemeroff CB. Ketamine and Other NMDA Antagonists: Early Clinical Trials and Possible Mechanisms in Depression. Am J Psychiatry. 2015;172(10):950-66.
280. Bahji A, Lunsky I, Gutierrez G, Vazquez G. Efficacy and Safety of Four Psychedelic-Assisted Therapies for Adults with Symptoms of Depression, Anxiety, and Posttraumatic Stress Disorder: A Systematic Review and Meta-Analysis. Journal of Psychoactive Drugs.1-16.
281. Sarris J, Perkins D, Cribb L, Schubert V, Opaleye E, Bouso JC, et al. Ayahuasca use and reported effects on depression and anxiety symptoms: An international cross-sectional study of 11,912 consumers. Journal of Affective Disorders Reports. 2021;4:100098.
282. Galvão-Coelho NL, Marx W, Gonzalez M, Sinclair J, de Manincor M, Perkins D, Sarris J. Classic serotonergic psychedelics for mood and depressive symptoms: a meta-analysis of mood disorder patients and healthy participants. Psychopharmacology. 2021;238(2):341-54.
283. Dupuis SL, Smale BJA. An Examination of Relationship Between Psychological Well-Being and Depression and Leisure Activity Participation Among Older Adults. Loisir et Société / Society and Leisure. 1995;18(1):67-92.
284. Miyata H. Impacts of reading habits on mindfulness and psychological status: A further analysis. WASEDA RILAS JOURNAL. 2020;8:207-18.
285. Choi NG, Kim J, DiNitto DM, Marti CN. Perceived Social Cohesion, Frequency of Going Out, and Depressive Symptoms in Older Adults:Examination of Longitudinal Relationships. Gerontology and Geriatric Medicine. 2015;1:2333721415615478.
286. Hyun S, Lee Y, Park S. No travel worsens depression: reciprocal relationship between travel and depression among older adults. Annals of General Psychiatry. 2022;21(1):31.
287. Downey LA, Sarris J, Perkins D. Legalization of psychedelic substances. JAMA. 2021;326(23):2434-5.
288. Walsh Z, Thiessen MS. Psychedelics and the new behaviourism: considering the integration of third-wave behaviour therapies with psychedelic-assisted therapy. International Review of Psychiatry. 2018;30(4):343-9.
289. Lebedev AV, Kaelen M, Lövdén M, Nilsson J, Feilding A, Nutt DJ, Carhart-Harris RL. LSD-induced entropic brain activity predicts subsequent personality change. Human brain mapping. 2016;37(9):3203-13.
290. Yaden DB, Griffiths RR. The subjective effects of psychedelics are necessary for their enduring therapeutic effects. ACS Pharmacology & Translational Science. 2020;4(2):568-72.
291. Griffiths R, Richards W, Johnson M, McCann U, Jesse R. Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. J Psychopharmacol. 2008;22(6):621-32.
292. Dyck E, Elcock C. Reframing bummer trips: scientific and cultural explanations to adverse reactions to psychedelic drug use. The Social History of Alcohol and Drugs. 2020;34(2):271-96.

 doi:10.20944/preprints202402.1273.v1




293. Kritzer MD, Mischel NA, Young JR, Lai CS, Masand PS, Szabo ST, Mathew SJ. Ketamine for treatment of mood disorders and suicidality: A narrative review of recent progress. Ann Clin Psychiatry. 2022;34(1):33-43.
294. Zarate CA, Jr., Singh JB, Carlson PJ, Brutsche NE, Ameli R, Luckenbaugh DA, et al. A randomized trial of an N-methyl-D-aspartate antagonist in treatment-resistant major depression. Arch Gen Psychiatry. 2006;63(8):856-64.
295. Murrough JW, Iosifescu DV, Chang LC, Al Jurdi RK, Green CE, Perez AM, et al. Antidepressant efficacy of ketamine in treatment-resistant major depression: a two-site randomized controlled trial. Am J Psychiatry. 2013;170(10):1134-42.
296. Kishimoto T, Chawla JM, Hagi K, Zarate CA, Kane JM, Bauer M, Correll CU. Single-dose infusion ketamine and non-ketamine N-methyl-d-aspartate receptor antagonists for unipolar and bipolar depression: a meta-analysis of efficacy, safety and time trajectories. Psychol Med. 2016;46(7):1459-72.
297. Xu Y, Hackett M, Carter G, Loo C, Gálvez V, Glozier N, et al. Effects of Low-Dose and Very Low-Dose Ketamine among Patients with Major Depression: a Systematic Review and Meta-Analysis. Int J Neuropsychopharmacol. 2016;19(4).
298. Wilkinson ST, Ballard ED, Bloch MH, Mathew SJ, Murrough JW, Feder A, et al. The Effect of a Single Dose of Intravenous Ketamine on Suicidal Ideation: A Systematic Review and Individual Participant Data Meta-Analysis. Am J Psychiatry. 2018;175(2):150-8.
299. Fava M, Freeman MP, Flynn M, Judge H, Hoeppner BB, Cusin C, et al. Double-blind, placebo-controlled, dose-ranging trial of intravenous ketamine as adjunctive therapy in treatment-resistant depression (TRD). Mol Psychiatry. 2020;25(7):1592-603.
300. Phillips JL, Norris S, Talbot J, Birmingham M, Hatchard T, Ortiz A, et al. Single, Repeated, and Maintenance Ketamine Infusions for Treatment-Resistant Depression: A Randomized Controlled Trial. Am J Psychiatry. 2019;176(5):401-9.
301. Rodrigues NB, McIntyre RS, Lipsitz O, Lee Y, Cha DS, Nasri F, et al. Safety and tolerability of IV ketamine in adults with major depressive or bipolar disorder: results from the Canadian rapid treatment center of excellence. Expert Opin Drug Saf. 2020;19(8):1031-40.
302. Sayin HU. Chapter 2 - Psychoactive Plants Used during Religious Rituals. In: Preedy VR, editor. Neuropathology of Drug Addictions and Substance Misuse. San Diego: Academic Press; 2016. p. 17-28.
303. Guzmán G, Allen J, Gartz J. A Worldwide geographical distribution of the Neurotropic Fungi, an analysis and discussion. Ann Mus Civ Rovereto. 1998;14.
304. Narby J, Pizuri RC. Plant teachers: Ayahuasca, tobacco, and the pursuit of knowledge: New World Library; 2021.
305. Kaasik H, Kreegipuu K. Ayahuasca Users in Estonia: Ceremonial Practices, Subjective Long-Term Effects, Mental Health, and Quality of Life. Journal of Psychoactive Drugs. 2020;52(3):255-63.
306. Fotiou E, Gearin AK. Purging and the body in the therapeutic use of ayahuasca. Social Science & Medicine. 2019;239:112532.
307. Schmid Y, Gasser P, Oehen P, Liechti ME. Acute subjective effects in LSD- and MDMA-assisted psychotherapy. Journal of Psychopharmacology. 2021;35(4):362-74.
308. Holze F, Gasser P, Müller F, Dolder PC, Liechti ME. Lysergic Acid Diethylamide–Assisted Therapy in Patients With Anxiety With and Without a Life-Threatening Illness: A Randomized, Double-Blind, Placebo-Controlled Phase II Study. Biological Psychiatry. 2023;93(3):215-23.
309. Sarris J, O'Neil A, Coulson CE, Schweitzer I, Berk M. Lifestyle medicine for depression. BMC psychiatry. 2014;14(1):1-13.
310. Wong VW-H, Ho FY-Y, Shi N-K, Sarris J, Chung K-F, Yeung W-F. Lifestyle medicine for depression: A meta-analysis of randomized controlled trials. Journal of Affective Disorders. 2021;284:203-16.
311. Gómez-Gómez I, Bellón JÁ, Resurrección DM, Cuijpers P, Moreno-Peral P, Rigabert A, et al. Effectiveness of universal multiple-risk lifestyle interventions in reducing depressive symptoms: Systematic review and meta-analysis. Preventive Medicine. 2020;134:106067.
312. Lopresti AL, Hood SD, Drummond PD. A review of lifestyle factors that contribute to important pathways associated with major depression: diet, sleep and exercise. Journal of affective disorders. 2013;148(1):12-27.
313. Berk M, Sarris J, Coulson CE, Jacka FN. Lifestyle management of unipolar depression. Acta Psychiatrica Scandinavica. 2013;127:38-54.

 doi:10.20944/preprints202402.1273.v1




314. Binnewies J, Nawijn L, van Tol M-J, van der Wee NJ, Veltman DJ, Penninx BW. Associations between depression, lifestyle and brain structure: A longitudinal MRI study. NeuroImage. 2021;231:117834.
315. Wang X, Arafa A, Liu K, Eshak ES, Hu Y, Dong J-Y. Combined healthy lifestyle and depressive symptoms: a meta-analysis of observational studies. Journal of affective disorders. 2021;289:144-50.
316. Van Dammen L, Wekker V, De Rooij S, Groen H, Hoek A, Roseboom T. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obesity reviews. 2018;19(12):1679-87.
317. Bruins J, Jörg F, Bruggeman R, Slooff C, Corpeleijn E, Pijnenborg M. The Effects of Lifestyle Interventions on (Long-Term) Weight Management, Cardiometabolic Risk and Depressive Symptoms in People with Psychotic Disorders: A Meta-Analysis. PLOS ONE. 2014;9(12):e112276.
318. Pinniger R, Brown RF, Thorsteinsson EB, McKinley P. Argentine tango dance compared to mindfulness meditation and a waiting-list control: A randomised trial for treating depression. Complementary Therapies in Medicine. 2012;20(6):377-84.
319. McCarney RW, Schulz J, Grey AR. Effectiveness of mindfulness-based therapies in reducing symptoms of depression: A meta-analysis. European Journal of Psychotherapy & Counselling. 2012;14(3):279-99.
320. Gee B, Orchard F, Clarke E, Joy A, Clarke T, Reynolds S. The effect of non-pharmacological sleep interventions on depression symptoms: A meta-analysis of randomised controlled trials. Sleep Medicine Reviews. 2019;43:118-28.
321. Furuyashiki A, Tabuchi K, Norikoshi K, Kobayashi T, Oriyama S. A comparative study of the physiological and psychological effects of forest bathing (Shinrin-yoku) on working age people with and without depressive tendencies. Environmental Health and Preventive Medicine. 2019;24(1):46.
322. Li Q, Ochiai H, Ochiai T, Takayama N, Kumeda S, Miura T, et al. Effects of forest bathing (shinrin-yoku) on serotonin in serum, depressive symptoms and subjective sleep quality in middle-aged males. Environmental Health and Preventive Medicine. 2022;27:44-.
323. Souter MA, Miller MD. Do Animal-Assisted Activities Effectively Treat Depression? A Meta-Analysis. http://dxdoiorg/102752/175303707X207954. 2015.
324. Stice E, Burton E, Kate Bearman S, Rohde P. Randomized trial of a brief depression prevention program: An elusive search for a psychosocial placebo control condition. Behaviour Research and Therapy. 2007;45(5):863-76.
325. Chen Y, Ishak Z. Gratitude Diary: The Impact on Depression Symptoms. Psychology. 2022;13:443-53.
326. Cregg DR, Cheavens JS. Gratitude Interventions: Effective Self-help? A Meta-analysis of the Impact on Symptoms of Depression and Anxiety. Journal of Happiness Studies. 2021;22(1):413-45.
327. Feng L, Yin R. Social Support and Hope Mediate the Relationship Between Gratitude and Depression Among Front-Line Medical Staff During the Pandemic of COVID-19. Frontiers in Psychology. 2021;12.
328. Bryan JL, Young CM, Lucas S, Quist MC. Should I say thank you? Gratitude encourages cognitive reappraisal and buffers the negative impact of ambivalence over emotional expression on depression. Personality and Individual Differences. 2018;120:253-8.
329. Kaniuka AR, Kelliher Rabon J, Brooks BD, Sirois F, Kleiman E, Hirsch JK. Gratitude and suicide risk among college students: Substantiating the protective benefits of being thankful. Journal of American College Health. 2021;69(6):660-7.
330. Hanusch KU, Janssen CW. The impact of whole-body hyperthermia interventions on mood and depression - are we ready for recommendations for clinical application? Int J Hyperthermia. 2019;36(1):573-81.
331. Jacob J, Stankovic M, Spuerck I, Shokraneh F. Goal setting with young people for anxiety and depression: What works for whom in therapeutic relationships? A literature review and insight analysis. BMC Psychology. 2022;10(1):171.
332. de Oliveira GD, Oancea SC, Nucci LB, Vogeltanz-Holm N. The association between physical activity and depression among individuals residing in Brazil. Soc Psychiatry Psychiatr Epidemiol. 2018;53(4):373-83.
333. Stubbs B, Koyanagi A, Schuch FB, Firth J, Rosenbaum S, Veronese N, et al. Physical activity and depression: a large cross-sectional, population-based study across 36 low- and middle-income countries. Acta Psychiatr Scand. 2016;134(6):546-56.
334. Pearce M, Garcia L, Abbas A, Strain T, Schuch FB, Golubic R, et al. Association Between Physical Activity and Risk of Depression: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2022;79(6):550-9.
335. Laird E, Rasmussen CL, Kenny RA, Herring MP. Physical Activity Dose and Depression in a Cohort of Older Adults in The Irish Longitudinal Study on Ageing. JAMA Netw Open. 2023;6(7):e2322489.

 doi:10.20944/preprints202402.1273.v1




336. Schuch FB, Vancampfort D, Richards J, Rosenbaum S, Ward PB, Stubbs B. Exercise as a treatment for depression: A meta-analysis adjusting for publication bias. J Psychiatr Res. 2016;77:42-51.
337. Krogh J, Hjorthøj C, Speyer H, Gluud C, Nordentoft M. Exercise for patients with major depression: a systematic review with meta-analysis and trial sequential analysis. BMJ Open. 2017;7(9):e014820.
338. Dunn AL, Trivedi MH, Kampert JB, Clark CG, Chambliss HO. Exercise treatment for depression: efficacy and dose response. Am J Prev Med. 2005;28(1):1-8.
339. Meyer JD, Koltyn KF, Stegner AJ, Kim JS, Cook DB. Influence of Exercise Intensity for Improving Depressed Mood in Depression: A Dose-Response Study. Behav Ther. 2016;47(4):527-37.
340. Lavebratt C, Herring MP, Liu JJ, Wei YB, Bossoli D, Hallgren M, Forsell Y. Interleukin-6 and depressive symptom severity in response to physical exercise. Psychiatry Res. 2017;252:270-6.
341. Phillips WM. Purpose in life, depression, and locus of control. Journal of Clinical Psychology. 1980;36(3):661-7.
342. Robak RW, Griffin PW. Purpose in life: What is its relationship to happiness, depression, and grieving? North American Journal of Psychology. 2000;2(1):113-9.
343. Jones E. COVID-19 and the Blitz compared: mental health outcomes in the UK. The Lancet Psychiatry. 2021;8(8):708-16.
344. Coverdale BJ. Evaluating the Effectiveness of Upward Bound Programs: The Ohio State University; 2009.
345. Rodiek S. Influence of an outdoor garden on mood and stress in older persons. Journal of Therapeutic Horticulture. 2002;13(1):13-21.
346. Dinas P, Koutedakis Y, Flouris A. Effects of exercise and physical activity on depression. Irish journal of medical science. 2011;180:319-25.
347. Ewert A. The Effects of Outdoor Adventure Activities Upon Self-Concept. 1977.
348. Emmons RA, Crumpler CA. Gratitude as a Human Strength: Appraising the Evidence. Journal of Social and Clinical Psychology. 2000;19(1):56-69.
349. Gogo A, Osta A, McClafferty H, Rana DT. Cultivating a way of being and doing: Individual strategies for physician well-being and resilience. Curr Probl Pediatr Adolesc Health Care. 2019;49(12):100663.
350. Davis DE, Choe E, Meyers J, Wade N, Varjas K, Gifford A, et al. Thankful for the little things: A meta-analysis of gratitude interventions. J Couns Psychol. 2016;63(1):20-31.
351. Liu S, Sheng J, Li B, Zhang X. Recent advances in non-invasive brain stimulation for major depressive disorder. Fronteirs in Human Neuroscience. 2017;11:526.
352. Brononi AR, Sampaio-Junior B, Moffa AH, Aparicio L, Gordon P, Klein I, Rios RM. Noninvasive brain stimulation in psychiatric disorders: a primer. Brazilian Journal of Psychiatry. 2019;4:70-81.
353. Dunlop K, Hanlon CA, Downar J. Noninvasive brain stimulation treatments for addiction and major depression. Annals of the New York Academy of Sciences. 2017;1394:31-54.
354. Mutz J, Edgcumbe DR, Brunoni AR, Fu CH. Efficacy and acceptability of non-invasive brain stimulation for the treatment of adult unipolar and bipolar depression: A systematic review and meta-analysis of randomised sham-controlled trials. Neuroscience and Biohevioral Reviews. 2018;92:291-303.
355. McClure D, Greenman SC, Koppulu SS, Varvara M, Yaseen ZS, Galynker II. A pilot study of safety and efficacy of cranial electrotherapy stimulation in treatment of bipolar II depression. J Nerv Ment Dis. 2015;203:827-35.
356. Hussain J, Cohen M. Clinical effects of regular dry sauna bathing: A systematic review. Evidence-Based Complementary and Alternative Medicine. 2018;2018:1857413.
357. Laukkanen JA, Laukkanen T, Kunustor SK. Cardiovascular and other health benefits of sauna bathing: A review of the evidence. Mayo Clin Proc. 2018;93:1111-21.
358. Laukkanen T, Khan H, Zaccardi F, Laukkanen JA. Association between sauna bathing and fatal cardiovascular and all-cuase mortality. JAMA Intern Med. 2015;175:542-8.
359. Laukkanen T, Kunutsor S, Kauhanen J, Laukkanen JA. Sauna bathing is inversely associated with dementia and Alzheimer's disease in middle-aged Finnish men. Age & Ageing. 2017;46:245-9.
360. Kunutsor SK, Khan H, Laukkanen T, Laukkanen JA. Joint associations of sauna bathing and cardiorespiratory fitness on cardiovascular and all-cause mortality risk: a long-term prospective cohort study. Annals of Medicine. 2018;50:139-46.
361. Scoon GS, Hopkins WG, Mayhew S, Cotter JD. Effect of post-exercise sauna bathing on the endurance performance of competitive male runners. Journal of Science and Medicine in Sport. 2007;10:259-62.

 doi:10.20944/preprints202402.1273.v1




362. Flux MC, Smith DG, Allen JJB, Mehl MR, Medrano A, Begay TK, et al. Association of plasma cytokines and antidepressant response following mild-intensity whole-body hyperthermia in major depressive disorder. Transl Psychiatry. 2023;13(1):132.
363. Amano K, Yanagihori R, tEI c. Waon therapyis effective as the treatment of myalgic encephalomyelitis/Chronic fatigue syndrome. J Jpn Soc Balneol Climatol Phys Med. 2015;78:285-302.
364. Soejima Y, Munemoto T, Masuda A, Uwatoko Y, Miyata M, tEI c. Effects of Waon therapy on chronic fatigue syndrome: A pilot study. Intern Med. 2015;54:333-8.
365. Lowry CA, Hale MW, Evans AK, Heerkens J, Staub DR, Gasser PJ, Shekhar A. Serotonergic systems, anxiety, and affective disorder: focus on the dorsomedial part of the dorsal raphe nucleus. Ann N Y Acad Sci. 2008;1148:86-94.
366. Hanusch KU, Janssen CH, Billheimer D, Jenkins I, Spurgeon E, Lowry CA, Raison CL. Whole-body hyperthermia for the treatment of major depression: associations with thermoregulatory cooling. Am J Psychiatry. 2013;170(7):802-4.
367. Janssen CW, Lowry CA, Mehl MR, Allen JJ, Kelly KL. Whole-body hyperthermia for the treatment of major depressive disorder.A randomized Clinical Trial. JAMA Psychiatry. 2016;73:789-95.
368. Drevets WC, Bogers W, Raichle ME. Functional anatomical correlates of antidepressant drug treatment assessed using PET measures of regional glucose metabolism. Eur Neuropsychopharmacol. 2002;12(6):527-44.
369. Bansal Y, Kuhad A. Mitochondrial Dysfunction in Depression. Curr Neuropharmacol. 2016;14(6):610-8.
370. Gardner A, Johansson A, Wibom R, Nennesmo I, von Döbeln U, Hagenfeldt L, Hällström T. Alterations of mitochondrial function and correlations with personality traits in selected major depressive disorder patients. J Affect Disord. 2003;76(1-3):55-68.
371. Rezin GT, Cardoso MR, Gonçalves CL, Scaini G, Fraga DB, Riegel RE, et al. Inhibition of mitochondrial respiratory chain in brain of rats subjected to an experimental model of depression. Neurochem Int. 2008;53(6-8):395-400.
372. Karabatsiakis A, Böck C, Salinas-Manrique J, Kolassa S, Calzia E, Dietrich DE, Kolassa IT. Mitochondrial respiration in peripheral blood mononuclear cells correlates with depressive subsymptoms and severity of major depression. Transl Psychiatry. 2014;4(6):e397.
373. Hroudová J, Fišar Z, Kitzlerová E, Zvěřová M, Raboch J. Mitochondrial respiration in blood platelets of depressive patients. Mitochondrion. 2013;13(6):795-800.
374. Askalsky P, Losifescu DV. Transcranial photobiomodulation for the management of depression: Current perspectives. Neuropsychiatric Disease and Treatment. 2019;15:3255-72.
375. Hamblin MR. Shining light on the head: Photobiomodulation for brain disorders. BBA Clinical. 2016;6:113-24.
376. Salehpour F, Ahmadian N, Rasta SH, Farhoudi M, Karimi P, Sadigh-Eteghad S. Transcranial low-level laser therapy improves brain mitochondrial function and cognitive impairment in D-galactose-induced aging mice. Neurobiol Aging. 2017;58:140-50.
377. Wang X, Tian F, Reddy DD, Nalawade SS, Barrett DW, Gonzalez-Lima F, Liu H. Up-regulation of cerebral cytochrome-c-oxidase and hemodynamics by transcranial infrared laser stimulation: A broadband near-infrared spectroscopy study. J Cereb Blood Flow Metab. 2017;37(12):3789-802.
378. Sanderson TH, Wider JM, Lee I, Reynolds CA, Liu J, Lepore B, et al. Inhibitory modulation of cytochrome c oxidase activity with specific near-infrared light wavelengths attenuates brain ischemia/reperfusion injury. Sci Rep. 2018;8(1):3481.
379. Oron U, Ilic S, De Taboada L, Streeter J. Ga-As (808 nm) laser irradiation enhances ATP production in human neuronal cells in culture. Photomed Laser Surg. 2007;25(3):180-2.
380. Wu Q, Xuan W, Ando T, Xu T, Huang L, Huang YY, et al. Low-level laser therapy for closed-head traumatic brain injury in mice: effect of different wavelengths. Lasers Surg Med. 2012;44(3):218-26.
381. Gabel CP, Petrie SR, Mischoulon D, Hamblin MR, Yeung A, Sangermano L, Cassano P. A case control series for the effect of photobiomodulation in patients with low back pain and concurrent depression. Laser Ther. 2018;27(3):167-73.
382. Oron A, Oron U. Low-Level Laser Therapy to the Bone Marrow Ameliorates Neurodegenerative Disease Progression in a Mouse Model of Alzheimer's Disease: A Minireview. Photomed Laser Surg. 2016;34(12):627-30.

 doi:10.20944/preprints202402.1273.v1



383. Real T. I don't want to talk about it: Overcoming the secret legacy of male depression: Simon and Schuster; 1998.