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Nutrition and Mental Health: Advances in Nutritional Cognitive Neuroscience

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Abstract

Accumulating evidence indicates that diet and nutrition are important modifiable risk factors for the prevention and treatment of mental health disorders. However, the neural mechanisms underlying nutrition's effects on mental health remain to be well established. The interdisciplinary field of nutritional cognitive neuroscience integrates methods across the nutritional, cognitive, and brain sciences to understand nutrition's impact on brain health across the lifespan, with recent applications to the study of mood and anxiety-related disorders. In this focused review, we begin by investigating the neural mechanisms underlying mood and anxiety-related disorders, surveying evidence of alterations within specific structural and functional networks. We then review emerging evidence to suggest that the structure and function of these networks are influenced by specific nutrients that may confer beneficial effects, including B-vitamins, omega-3 polyunsaturated fatty acids, polyphenols, and carotenoids. In this effort, we

highlight plausible biological pathways through which diet may influence mood and anxiety-related disorders. We conclude by presenting directions for future research, emphasizing the need for dietary interventions that incorporate contemporary methods from cognitive neuroscience and nutritional epidemiology to promote brain health and reduce the risk of mental illness.

NUTRITION AND THE PROMOTION OF MENTAL HEALTH

The escalating burden of mental health disorders is a major public health concern, with mood and anxiety-related disorders among the most prevalent forms of mental illness worldwide (World Health Organization 2022). Mood refers to a sustained emotional state, such as remaining calm under pressure, that influences how an individual understands and responds to their environment (Sekhon & Gupta 2023). Disruptions in emotion regulation, as found in depression and bipolar disorders, provide the basis for mood disorders (Sekhon & Gupta 2023). Anxiety-related disorders are also characterized by disruptions of emotion regulation, with generalized anxiety disorder and social anxiety disorder evidenced by heightened emotional reactivity and chronic worry (Craske et al. 2017). Although the term "mood and anxiety-related disorders" is applied broadly in the present review, it is important to recognize that their underlying symptom profiles may vary significantly, motivating ongoing research to establish their nature and etiology (American Psychiatric Association 2013, Parker 2014).

Modern approaches to the treatment of mood and anxiety-related disorders in psychiatry have primarily focused on psychotherapy and medications that target neurotransmitter functions. In recent years, a growing body of evidence has emphasized the impact of lifestyle choices on mental health, with evidence to support the role of diet and nutrition (Bayes et al. 2022, Jacka et al. 2017, Parletta et al. 2019, Sánchez-Villegas et al. 2013). Epidemiological studies have shown that a poor-quality diet (i.e., high in ultraprocessed foods, trans fats, refined sugars, and foods with a high glycemic index) is associated with a greater risk of developing mental health conditions such as mood and anxiety-related disorders (Eliby et al. 2023, Firth et al. 2020). In contrast, a high-quality dietary pattern, such as adherence to the Mediterranean diet or MIND diet—which emphasize vegetables, fruits, lean proteins, and healthy fats (e.g., monounsaturated and polyunsaturated fats) and advise limits on red meat and sweets—has shown promise in the reduction and management of these conditions (Corella et al. 2018, Firth et al. 2019, Morris et al. 2015). Emerging evidence further suggests that diet and nutrition influence neuroplasticity and inflammation and may even affect brain networks that are known to regulate emotion and mood (Adan et al. 2019). Thus, diet and nutrition are increasingly recognized as important parts of mental health—key modifiable risk factors for the potential treatment and prevention of mental illness (Adan et al. 2019, Firth et al. 2020).

Among the dietary patterns that have been investigated for their promise in addressing mood and anxiety-related disorders, the Mediterranean diet has emerged as a particularly protective diet—due to an abundance of nutrients that provide anti-inflammatory and neuroprotective properties (Eliby et al. 2023). Adherence to this diet has been associated with preventative and therapeutic effects in the context of depression and other mood disorders (see **Table 1**). Despite emerging evidence to support the promise of diet and nutrition for the promotion of mental health, their mechanisms of action—particularly with respect to brain networks involved in mood and emotion regulation—remain to be well established.

Table 1 The Mediterranean (MEDI) diet has been associated with better mental health outcomes

Study	Population	Primary findings
Godos et al. 2023	Adults aged 18 or more years old	Participants with higher adherence to the MEDI diet were less likely to have depressive symptoms
Soldevila-Domenech et al. 2021	Older adults between 55 and 75 years old, with overweight or obesity	Participants with higher adherence to the MEDI diet exhibited reduced depressive symptoms
Shiraseb et al. 2023	Female adults between 18 and 48 years old	Participants with higher adherence to the MEDI diet had lower mild and moderate anxiety scores
Parletta et al. 2019	Adults between 18 and 65 years old	Participants adhering to the MEDI diet had significant reductions in depression and improved mental health quality-of-life scores
Sadeghi et al. 2021	Adults between 18 and 55 years old	Participants with higher adherence to the MEDI diet had lower odds for depression, anxiety, and psychological distress
Cabrera-Suárez et al. 2024	Adults between 18 and 86 years old	Participants adhering to the MEDI diet showed fewer depressive symptoms in the fourth, eighth, and twentieth months
Mantzorou et al. 2021	Older adults over the age of 65	Participants with higher adherence to the MEDI diet had less depressive symptomatology

NUTRITIONAL COGNITIVE NEUROSCIENCE: AN INTERDISCIPLINARY APPROACH TO INVESTIGATING THE EFFECTS OF DIET AND NUTRITION ON MENTAL HEALTH

Nutritional cognitive neuroscience is an interdisciplinary field of research that seeks to understand nutrition's impact on cognitive performance and brain health across the lifespan (Barbey 2025, Zamroziewicz & Barbey 2016). Emerging research in this field indicates that diet and nutrition may affect the neural mechanisms underlying cognitive function and mental health (Barbey & Davis 2023; Talukdar et al. 2019, 2023; Zamroziewicz et al. 2018; Zwilling et al. 2019, 2024), offering a promising framework for mitigating the risk of mood and anxiety-related disorders.

This perspective aims to redefine nutrition as central to brain health, serving as an active determinant of the brain's adaptive capacity. According to this view, nutrition plays a central role in allostasis, enabling the brain and body to maintain stability (i.e., homeostasis) through the continual adjustment of internal and external demands (rather than from static equilibrium) (Juster et al. 2010, McEwen 2020). Research in nutritional cognitive neuroscience reveals how nutrition influences the signaling pathways that regulate neuroplasticity and inflammation—mechanisms through which the brain anticipates and adapts to life experience and recovers from environmental stressors. From this perspective, nutrition influences not only the efficiency of allostatic processes but also the accumulation of allostatic load—the long-term physiological burden that results when adaptive systems are significantly overworked. Through its effects on neuroplasticity and inflammation, diet shapes whether allostasis remains flexible and resilient or shifts toward a state of chronic overload.

Evidence to support the role of diet and nutrition in allostasis suggests that poor diet can promote allostatic load, increasing inflammation and limiting the brain's ability to adaptively regulate internal states in response to the environment (Juster et al. 2010, McEwen 2020). Previous studies have consistently found that poor diet elevates levels of inflammatory biomarkers such as C-reactive protein, IL-6, and TNF-α (Hart et al. 2021, Koelman et al. 2022). In addition, poor diet has been associated with greater metabolic stress and dysregulation of neuroendocrine

function, all of which contribute to increased allostatic load (Christ et al. 2019, Ramos-Lopez et al. 2022, Romaní-Pérez et al. 2025, Ullah et al. 2021). Chronic activation of stress-response systems due to allostatic load can deplete the body's ability to manage harmful levels of inflammation and oxidative stress, contributing to structural and functional changes in the brain.

A growing body of evidence suggests that allostatic load is linked to two primary brain networks, the salience and default mode networks, which are known to play complementary roles in one's response to stress (Kleckner et al. 2017, Lenart-Bugla et al. 2022). The salience network is a system of interconnected brain regions anchored by two cortical hubs, the anterior insula and the anterior cingulate cortex, and includes regions within the amygdala, hypothalamus, ventral striatum, and thalamus (Seeley 2019). The salience network contributes to one's response to stress by enabling the detection of behaviorally salient external events, integrating this information with internal bodily states, and applying these representations to guide goal-directed behavior. The second network implicated in allostasis is the default mode network. This network comprises the medial prefrontal cortex, posterior cingulate cortex, and angular gyrus, and supports self-referential processing, such as self-directed thought and introspection. Both networks are essential for coordinating adaptive responses to stress (Santamaría-García et al. 2025). Increased allostatic load is known to disrupt normal patterns of functional connectivity within these networks (Arnaldo et al. 2022, Kleckner et al. 2017, Santamaría-García et al. 2025). Structural brain imaging studies further suggest that higher allostatic load is associated with reduced gray matter volume within regions of these networks—for example, the insular cortex, which is central to the salience network, and the parahippocampal and medial temporal cortex, which are part of the default mode network (Palix et al. 2025).

Accumulating evidence in biological psychiatry further demonstrates that these specific networks are directly affected by mood and anxiety-related disorders, providing a potential neurobiological target for dietary intervention. Studies indicate that symptoms of these disorders, such as heightened threat detection and self-referential processing, may reflect alterations within the salience (Bora et al. 2012, Hammoud et al. 2024, Slavich & Irwin 2014) and default mode networks (Son et al. 2023).

Taken together, these findings support a mechanistic cascade in which poor diet and nutrition contribute to increased allostatic load, leading to structural and functional disruptions in key networks involved in stress regulation (**Figure 1**). Specifically, alterations in the salience and default mode networks—critical for identifying and prioritizing salient internal and external stimuli and for monitoring internal mental states, respectively—appear to mediate the impact of chronic stress on brain function. These same networks are consistently implicated in mood and anxiety-related disorders, suggesting that disruptions in their structural and functional connectivity may underlie core symptoms such as altered threat sensitivity and maladaptive self-referential thinking. This research points to allostatic load as a central mediator between lifestyle factors and mental health. Indeed, a healthy diet and nutrition across the lifespan may mitigate the accumulation of allostatic load and thereby lower the risk of developing mood and anxiety-related disorders.

Nutritional cognitive neuroscience provides an interdisciplinary framework for studying this system, suggesting that nutrition is a key part of a dynamic regulatory process that supports brain plasticity and resilience across the lifespan (incorporating environmental, psychological, biological, and lifestyle factors) (see Barbey 2025). In this focused review, we aim to establish neurobiological targets for nutritional interventions that are designed to reduce mood and anxiety-related disorders and promote mental health. We therefore begin by reviewing the literature in biological psychiatry that addresses how mood and anxiety-related disorders affect the brain. We then provide a targeted review of the literature in nutritional epidemiology on the beneficial effects of diet and nutrition on brain health, with a focus on nutritional elements

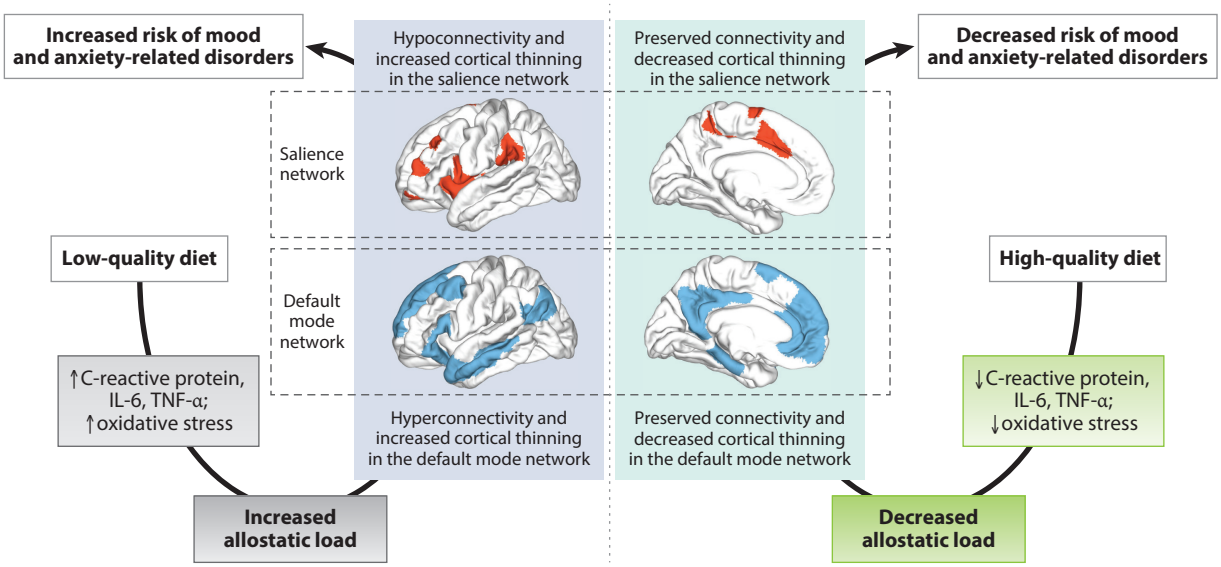

Figure 1

Illustration of the proposed mechanistic cascade underlying nutrition and mental health. Lower dietary quality increases inflammation and allostatic load. Increased allostatic load is associated with changes in brain networks involved in stress and emotion regulation, which may elevate the risk of mood and anxiety-related disorders. Conversely, higher dietary quality decreases inflammation and may mitigate the accumulation of allostatic load. Across the lifespan, a healthy diet and nutrition may reduce the risk of developing mood and anxiety-related disorders. The visualization is generated with codes from Popp et al. (2025) and templates from FreeSurfer (Fischl 2012).

found in the Mediterranean diet. We review evidence to suggest that this dietary pattern may confer benefits to the brain networks that are implicated in mood and anxiety-related disorders. In addition, we present examples of food formulations that contain these beneficial nutrients. Finally, we conclude by highlighting directions for future research, emphasizing the need to establish dietary interventions that integrate modern research in cognitive neuroscience and nutritional epidemiology to promote brain health and reduce the long-term risk of mental illness.

BRAIN NETWORKS IMPLICATED IN MOOD AND ANXIETY-RELATED DISORDERS

Accumulating evidence demonstrates that mood and anxiety-related disorders are characterized by alterations within two intrinsic connectivity networks, the salience and default mode networks. In neurologically healthy individuals, the salience network supports adaptive responses to stress by detecting behaviorally salient external events, integrating them with internal bodily states, and using this information to guide goal-directed behavior (Menon & Uddin 2010). In individuals with mood and anxiety-related disorders, the salience network shows consistent hypoconnectivity (i.e., reductions in the capacity of this network to communicate with other brain networks). For example, Goldstein-Piekarski et al. (2022) found that reductions in connectivity in the salience network significantly predicted symptom scores in mood and anxiety-related disorders. fMRI studies in which participants are not actively engaged in cognitive tasks, also known as resting-state fMRI, have found that individuals with mood and anxiety-related disorders exhibit decreased functional connectivity between the salience network and other regions in the brain (Geng et al. 2016, Magioncalda et al. 2015, Yu et al. 2021). These alterations—reflected by

reductions in connectivity—may signal impairments in the network's ability to appropriately filter and prioritize salient information in the stimuli as well as in the network's ability to integrate salient information with information processed by other parts of the brain.

A second network that is consistently implicated in mood and anxiety-related disorders is the default mode network. This network is responsible for self-referential processing, such as self-directed thought and introspection. In mood and anxiety-related disorders, dysfunction of the default mode network is frequently associated with increased rumination and self-preoccupation (Coutinho et al. 2016, Gillespie et al. 2020). Because these symptoms reflect elevations in processing (e.g., increased rumination and increased negative self-focus), the observed changes in network function reflect hyperconnectivity (i.e., an increase in connectivity). For example, fMRI studies have found that regions of the default mode network, such as the posterior cingulate cortex and parahippocampal and angular gyri, exhibit increased functional connectivity and activation in mood and anxiety-related disorders (Bartova et al. 2015, Janiri et al. 2020, Qiu et al. 2024, Rai et al. 2021, Rolls et al. 2020, Yu et al. 2021, Yuan et al. 2023). Recent brain network dynamics studies have further demonstrated that adults with mood disorders, including major depressive disorder and bipolar disorder, exhibit prolonged activation of the default mode network (Alonso et al. 2023, Piguet et al. 2021). Notably, this prolonged activity is thought to reflect the continued engagement of mental operations for rumination and internalizing, processes that are typically disengaged during task performance in neurologically healthy individuals (Akbar et al. 2022, Menon 2023). As such, hyperactivity and increased duration of activation of the default mode network in mood and anxiety-related disorders may signal the inability to disengage from internally focused thoughts.

Structural MRI studies have also revealed alterations associated with mood and anxiety-related disorders. A meta-analysis found that individuals with mood and anxiety-related disorders exhibited cortical thinning in regions belonging to the salience network, such as the insula, and the default mode network, such as the parahippocampal gyrus (Brandl et al. 2022). In addition, studies have shown that individuals with mood and anxiety-related disorders exhibit greater gray matter volume reductions in regions of the default mode network, such as the precuneus and middle frontal gyrus, as well as in key regions of the salience network, such as the insula (Bai et al. 2020, Okanda Nyatega et al. 2022, Schnellbächer et al. 2022). Similarly, white matter microstructural integrity is known to be compromised in mood disorders. For instance, findings from diffusion-weighted imaging studies indicate that patients with mood disorders exhibit lower structural integrity of the cingulum and fornix, both of which are white matter tracts that support default mode network function (Alves et al. 2019, Hermens et al. 2022, Koshiyama et al. 2020).

Taken together, the neuroimaging literature reveals a consistent pattern of structural and functional disruptions in the salience and default mode networks among individuals with mood and anxiety-related disorders. These disruptions include (*a*) reduced functional connectivity (hypoconnectivity) in the salience network, (*b*) increased functional connectivity (hyperconnectivity) in the default mode network, (*c*) decreased gray matter volume in regions associated with both networks, and (*d*) reduced integrity of white matter pathways that support these networks. The reviewed evidence suggests that disruptions within the salience and default mode networks may contribute to the development and maintenance of mood and anxiety-related disorders. Within the framework of nutritional cognitive neuroscience, these findings highlight potential neurobiological targets for dietary and nutritional interventions to promote mental health. In the following section, we turn to the nutritional science literature to examine whether specific dietary patterns and nutrients may influence the integrity and function of the salience and default mode networks implicated in mood and anxiety-related disorders.

NUTRITIONAL SUPPORT FOR BRAIN NETWORKS IMPLICATED IN MENTAL HEALTH

Emerging evidence in the nutritional sciences demonstrates that nutrients found in the Mediterranean diet may play an important role in maintaining the health and function of brain networks that are implicated in mood and anxiety-related disorders. A stable, sufficient intake of these nutrients may therefore offer a neuroprotective effect against mood and anxiety-related disorders by reducing allostatic load and modulating the default mode and salience networks.

The nutrients and bioactive compounds reviewed here include tryptophan; omega-3 polyunsaturated fatty acids (PUFAs) [with an emphasis on docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA)]; monounsaturated fatty acids (MUFAs); vitamins B_1, B_6, B_9, and B_{12}; vitamin D; lutein and zeaxanthin; and polyphenols. For each type of nutrient and bioactive compound, we provide a brief description, common dietary sources, evidence supporting its potential benefits on mood and anxiety-related disorders, and, lastly, findings suggesting the types of brain changes in mood and anxiety-related disorders the nutrient may help counteract. **Table 2** provides a summary of the nutrients of interest alongside examples of foods that are rich sources of these nutrients. **Table 3** summarizes the ways in which specific nutrients influence brain health biomarkers associated with mood and anxiety-related disorders.

Tryptophan

Tryptophan is an essential amino acid obtained primarily through diet. It can be found in foods such as egg whites, fish, dairy, animal proteins, and legumes (US Department of Agriculture Agricultural Research Service 2025). This essential amino acid serves as a precursor for several biologically important molecules, including serotonin (5-HT), melatonin, and kynurenic acid (Chen et al. 2021, Lukić et al. 2022). Serotonin and melatonin are critical for emotional regulation, circadian rhythm, and stress reactivity—functions commonly implicated in mood and anxiety-related disorders. Traditionally, research has focused on tryptophan's role in increasing serotonin levels to alleviate symptoms of these disorders. For example, an intervention study found that increased intake of tryptophan resulted in improved mood and anxiety-related symptoms in healthy young adults (Lindseth et al. 2015). In this within-subjects experiment, participants followed two separate 4-day dietary treatments: one low in tryptophan and another high in tryptophan. The study reported that participants scored lower on Zung's Self-Rating Anxiety Scale and experienced higher positive mood during the high tryptophan condition compared to the low tryptophan condition (for additional evidence, see Lieberman et al. 2016).

Neuroimaging studies suggest that tryptophan intake is associated with decreased functional connectivity within the default mode network. For example, a double-blind, crossover, randomized controlled trial measured participants' functional connectivity after they consumed a mixture of amino acids that had (*a*) 70 mg/kg body weight of tryptophan, (*b*) 7 mg/kg body weight of tryptophan (the recommended amount), and (*c*) no tryptophan. The study found that participants exhibited decreased functional connectivity between the default mode network and brain regions involved in emotion regulation, such as the putamen, subcallosal cortex, thalamus, and frontal cortex, after consuming the amino acid mixture with the most tryptophan (Deza-Araujo et al. 2019). In the context of mood and anxiety-related disorders, the observed reduction in functional connectivity within the default mode network may serve to mitigate the effects of hyperconnectivity.

Recent studies highlight an additional mechanism through which tryptophan is metabolized into kynurenic acid, a compound with known neuroprotective and anti-inflammatory properties (Chen et al. 2021). Kynurenic acid acts as an antagonist of the N-methyl-D-aspartate receptor,

Table 2 Nutrients in foods

Tryptophan	Omega-3 PUFAs[a]	MUFAs[b]	Vitamin B_1	Vitamin B_6	Vitamin B_9	Vitamin B_{12}	Vitamin D	Lutein and zeaxanthin	Polyphenols[c]
Egg whites	Salmon, mackerel	Extra virgin olive oil	Whole grains and whole-grain products (e.g., oats)	Poultry	Legumes (e.g., chickpeas, pinto beans, lentils)	Clams, oysters	Salmon	Spinach, mustard greens	Berries
Legumes (e.g., soybeans, firm tofu, white beans)	Tuna, herring	Avocado oil	Nuts (e.g., peanuts, macadamia nuts)	Tuna, salmon	Spinach	Mackerel, Herring	Mushrooms	Turnip	Tea
Tuna, salmon	White fish, striped bass	Hazelnuts, pecans	Pork	Pistachios	Asparagus	Tuna, sardines	Mackerel	Sweet corn	Eggplants
Beef, pork	Anchovies	Macadamia nuts	Green peas, chickpeas	Legumes (e.g., chickpeas, pinto beans)	Whole-grain and whole-grain products	Beef	Trout, herring	Kale	Apples, pears, plums
Poultry	Sardines, whitefish	High oleic plant-based oil	Lentils	Potatoes (boiled)	Nuts (e.g., peanuts)	Crab	Fortified milk	Green peas	Broccoli, tomatoes, onions

Examples are sourced primarily from US Department of Agriculture Agricultural Research Service (2025), organized by the abundance of nutrients in whole foods per serving size, and curated to include common foods.

[a]For omega-3 PUFAs, a mix of foods containing docosahexaenoic acid or eicosapentaenoic acid are included.

[b]For monounsaturated fatty acids, a mix of foods, fats, and oils containing oleic acid are included.

[c]For polyphenols, the food items are taken from Manach et al. (2004).

Abbreviations: MUFAs, monounsaturated fatty acids; PUFAs, polyunsaturated fatty acids.

Table 3 Nutrients that are associated with the functions and structures of the key brain regions/networks implicated in mood and anxiety-related disorders

Nutrients	Study	Population	Primary findings
Tryptophan/kynurenic acid	Bravi et al. 2025	Patients with mood disorders	Higher levels of kynurenic acid, a metabolite of tryptophan, were associated with lower levels of baseline neural activity in the default mode network.
	Deza-Araujo et al. 2019	Healthy adults between 20 and 40 years old	Intervention that increases tryptophan plasma levels decreased connectivity between the default mode network and several brain regions involved in emotion and affect regulation (i.e., putamen, subcallosal cortex, thalamus, and frontal cortex).
Omega-3 polyunsaturated fatty acids	Zamroziewicz et al. 2017	Healthy older adults between 65 and 75 years old	Higher levels of long-chain polyunsaturated fatty acid were associated with higher fractional anisotropy in the fornix.
	Talukdar et al. 2019	Healthy older adults between 65 and 70 years old	Omega-3 polyunsaturated fatty acids were significantly associated with functional connectivity patterns of regions in the right cingulate gyrus, right precuneus, right lateral occipital cortex, right primary visual cortex, left amygdala, left frontal pole, and left hippocampus.
	Park et al. 2020	Healthy participants and participants with depressive symptoms between 45 and 69 years old	Functional connectivity of the right middle frontal cortex (default mode network) and the right middle temporal pole (frontoparietal network) was positively associated with depressive symptom scores and negatively associated with omega-3 fatty acid intakes.
	Faulkner et al. 2025	Adults with subthreshold depression between 18 and 29 years old	The connectivity between the orbitofrontal cortex and angular gyrus was negatively correlated with the omega-3 index (calculated as the sum of DHA and EPA, expressed as a percentage of the total measured fatty acids).
	McNamara et al. 2022	Youth between 9 and 21 years old with a current DSM-IV diagnosis of major depressive disorder or depressive disorder	Participants in the fish oil group exhibited a decrease in functional connectivity between the right inferior temporal gyrus and the right amygdala.

(*Continued*)

Table 3 (*Continued*)

Nutrients		Study	Population	Primary findings
B vitamins	B_1	Jannusch et al. 2017	Adults between 55 and 85 years old	Higher vitamin B_1 blood levels were associated with an increase in functional connectivity between left frontal operculum and right dorsal occipital cortex, left middle temporal gyrus and right anterior/posterior superior frontal gyrus, and left and right supramarginal gyri. Participants with higher B_1 were associated with decreased functional connectivity between the left orbitofrontal cortex and left lateral occipital cortex, and left middle temporal gyrus and left supramarginal gyrus; left supramarginal gyrus and left frontal operculum; and right fusiform gyrus and right thalamus as well as right cerebellum.
	B_6	Jannusch et al. 2017	Adults between 55 and 85 years old	Higher B_6 blood levels were associated with stronger functional connectivity between left insula and left middle temporal gyrus.
	B_6, B_{12}	Li et al. 2024	Adults between 40 and 70 years old	Higher intakes of B_6 and B_{12} were associated with less functional connectivity in most networks, including the posterior portion of the default mode network.
	B_6, B_9, B_{12}	Douaud et al. 2013	Older adults over the age of 70	B-vitamin treatment leads to a decrease in gray matter atrophy in posterior brain regions, including bilateral hippocampus and parahippocampal gyrus, retrosplenial precuneus, and lingual and fusiform gyrus as well as in the cerebellum.
	B_{12}	Kaya et al. 2023	Healthy older adults at the age of 65 years old or over	Significantly lower white matter integrity was observed in multiple white matter areas, including superior and middle cerebellar peduncles, cingulum, and genu of corpus callosum in patients with vitamin $B_{12} < 400$ pg/mL.
		Çebi et al. 2022	Healthy middle-aged adults with a mean age of 46.21	Vitamin B_{12} levels were positively correlated with the brain volume of the right fusiform gyrus, left fusiform gyrus, right middle temporal gyrus, and right inferior temporal gyrus.

(*Continued*)

Table 3 (*Continued*)

Nutrients	Study	Population	Primary findings
Vitamin D	Strath et al. 2022	Adults between 45 and 85 years old	Participants with deficient or insufficient levels of vitamin D had significant differences in the gray matter of the left circular insular cortex, left inferior temporal gyrus, and right middle temporal gyrus.
	Beydoun et al. 2020	Adults between 30 and 64 years old	Vitamin D was positively associated with regional fractional anisotropy of the cingulum.
	Zhu et al. 2022	Age-matched healthy controls (with a mean age of 44.24 years old) and patients with major depressive disorder (with a mean age of 44.35 years old)	Vitamin D levels were inversely related to default mode network connectivity.
Monounsaturated fatty acids	Dumas et al. 2023	Older adults between 65 and 75 years old	Participants exhibited increased connectivity between anterior regions of the salience network during the low palmitic acid/high oleic acid diet.
Lutein and zeaxanthin	Mewborn et al. 2018	Healthy older adults between 64 and 86 years old	Serum lutein and zeaxanthin were positively correlated with fractional anisotropy and negatively correlated with radial diffusivity in the cingulum. Serum lutein and zeaxanthin were also positively correlated with fractional anisotropy in the superior and posterior corona radiata, negatively correlated with radial diffusivity in the posterior thalamic radiation and superior corona radiata, and negatively correlated with axial diffusivity in the cingulum, uncinate fasciculus, and corticospinal tract.
	Zamroziewicz et al. 2016	Healthy older adults between 65 and 75 years old	Higher levels of lutein were associated with larger gray matter volume of the right parahippocampal cortex.
Polyphenols	Pachter et al. 2024	Adults of at least 30 years old, with abdominal obesity or dyslipidemia	Greater consumption of polyphenol-rich components (Mankai and green tea) was associated with greater hippocampal and inferior lateral-ventricle volume ratio changes, suggesting the polyphenols may help reduce the loss of hippocampal brain volume.
	Picó-Pérez et al. 2023	Generally healthy Portuguese population	Coffee consumption decreased connectivity of the posterior default mode network in habitual coffee drinkers.

a glutamate receptor implicated in the synaptic plasticity dysregulation observed in mood and anxiety-related disorders (Chen et al. 2021). Notably, a recent neuroimaging study found that higher levels of kynurenic acid were associated with lower baseline neural activity of the default mode network, which is known to demonstrate hyperconnectivity in the context of mood and anxiety-related disorders (Bravi et al. 2025). Thus, the observed findings for kynurenic acid provide a novel pathway through which tryptophan may help mitigate the risk of developing mood and anxiety-related disorders.

Omega-3 Polyunsaturated Fatty Acids

Omega-3 PUFAs have well-documented anti-inflammatory properties and are known to support neuronal membrane integrity and synaptic plasticity (Dyall 2015, Shahidi & Ambigaipalan 2018). The most widely studied omega-3 PUFAs, DHA and EPA, are found primarily in seafood, particularly fatty fish such as salmon, sardines, mackerel, and herring (US Department of Agriculture Agricultural Research Service 2025). Evidence suggests that intake of DHA and EPA is associated with reduced symptoms of mood and anxiety-related disorders (Su et al. 2015). For example, a recent meta-analysis of randomized controlled trials found that EPA interventions may reduce the severity of depression (Kelaiditis et al. 2023), with evidence from the UK Biobank study to further suggest that EPA may be associated with reduced risk of major depressive disorder (Carnegie et al. 2024).

Omega-3 PUFAs have been increasingly linked to brain network function, especially in networks implicated in mood and anxiety-related disorders. For example, Talukdar and colleagues (2019) found that blood-based biomarkers of omega-3 PUFAs were significantly associated with functional connectivity in the anterior cingulate cortex, a key region of the salience network, and in the precuneus, a core region of the default mode network. These findings suggest that omega-3 PUFAs may influence brain networks underlying emotion processing and self-referential thought, functions often disrupted in mood and anxiety-related disorders.

Furthermore, several studies have reported that higher omega-3 PUFA levels are associated with decreased functional connectivity of regions within the default mode network, potentially serving to mitigate the effects of hyperconnectivity observed within this network in mood and anxiety-related disorders. Park and colleagues found that increased omega-3 PUFA intake was linked to decreased connectivity between the default mode network and the right middle temporal pole, as well as lower depressive symptoms scores, in middle-aged women (Park et al. 2020). Similarly, a preliminary study by Faulkner and colleagues (2025) studied young adults with subthreshold depression and found that a lower omega-3 index (i.e., the sum of EPA and DHA as a percentage of total fatty acids in the blood) was associated with reduced connectivity between the angular gyrus, a region within the default mode network, and the orbitofrontal cortex, as well as higher (subthreshold) depression scores. Furthermore, an intervention study in depressed adolescents by McNamara and colleagues (2022) demonstrated that fish oil supplementation reduced functional connectivity between the right inferior temporal gyrus, a region within the default mode network, and the right amygdala (McNamara et al. 2022). In addition to functional connectivity, a study of older adults by Zamroziewicz and colleagues (2017) found that higher plasma levels of omega-3 PUFAs were associated with greater white matter integrity of the fornix, a white matter tract that is essential to memory function and known to influence the default mode network (Zamroziewicz et al. 2017).

Monounsaturated Fatty Acids

MUFAs represent another important class of fatty acids that possess anti-inflammatory properties (Ralston et al. 2017). Along with PUFAs, MUFAs are thought to ameliorate saturated fatty

acid–induced cellular damage (Liu et al. 2024, Rumora et al. 2019). MUFAs, particularly oleic acid, are found in natural oils, such as olive oil (US Department of Agriculture Agricultural Research Service 2025, Wang et al. 2025). Previous findings indicate that higher intake of MUFAs, including oleic acid, was correlated with a lower risk of mood and anxiety-related disorders (Fatemi et al. 2020, Wolfe et al. 2009). Furthermore, neuroimaging evidence suggests that intake of MUFAs, particularly oleic acid, is associated with corresponding changes in functional connectivity within the salience network. A randomized crossover trial compared functional connectivity of participants assigned to a diet high in palmitic acid, a saturated fatty acid, or a diet aimed at replacing saturated fatty acids with MUFAs in the form of oleic acid (Dumas et al. 2023). The MUFA diet was associated with an increase in functional connectivity within anterior regions of the salience network. In the context of mood and anxiety-related disorders, the observed increase in functional connectivity within the salience network may serve to mitigate the effects of hypoconnectivity.

A large body of evidence indicates that MUFA intake can reduce chronic inflammation by increasing insulin sensitivity and lowering insulin resistance (Chen et al. 2023, Vessby et al. 2001). Recent evidence further suggests that insulin resistance is associated with reduced gray matter volume in regions of the default mode network, such as the precuneus (Asano et al. 2023). Although there is currently no direct evidence that MUFAs mitigate cortical atrophy, these findings raise the possibility that reducing chronic inflammation through diet could have downstream effects on brain networks involved in mental health. Future research should examine whether dietary MUFAs may reduce the risk of mood and anxiety-related disorders by increasing insulin sensitivity, lowering insulin resistance, and promoting the integrity of regions within the default mode network.

B Vitamins

The B vitamins are important for energy metabolism, axonal transport, and the synthesis of neurotransmitters, such as serotonin and dopamine (Hanna et al. 2022, Kennedy 2016). Although the B vitamins are often discussed together, each is known to serve a distinct set of functions.

Vitamin B_1 plays a central role in glucose metabolism. As neurons are highly dependent on oxidative metabolism for adenosine triphosphate (ATP) generation, vitamin B_1 is crucial for mitochondrial function and sustaining healthy neurotransmitter levels (Hanna et al. 2022, Mrowicka et al. 2023). Vitamin B_1 is found in most foods but is particularly abundant in whole grains, pork, and legumes (US Department of Agriculture Agricultural Research Service 2025). Clinical findings indicate that adults with lower vitamin B_1 status tend to exhibit more pronounced symptoms of depression (Dhir et al. 2019). Neuroimaging evidence further suggests that vitamin B_1 intake is associated with measures of functional connectivity. In a study of older adults, higher blood vitamin B_1 levels were associated with increased interhemispheric functional connectivity of regions within the salience network, including the left frontal operculum and areas of the right visual cortex (Jannusch et al. 2017). These findings provide preliminary evidence to suggest that vitamin B supplementation may provide an opportunity to counteract the effects of hypoconnectivity within the salience network observed in mood and anxiety-related disorders. In addition, this study found that higher blood vitamin B_1 levels were linked to decreased intrahemispheric functional connectivity between two regions of the default mode network—the left middle temporal gyrus and left supramarginal gyrus—indicating a potential role for vitamin B_1 in reducing default mode network hyperconnectivity (Jannusch et al. 2017).

Vitamin B_6 enables the synthesis of key neurotransmitters, including dopamine, serotonin, gamma-aminobutyric acid (GABA), and noradrenaline, and is also required for the production of melatonin (Kennedy 2016). Vitamin B_6 is found in foods such as tuna, salmon, legumes, beef, poultry, and whole grains (US Department of Agriculture Agricultural Research Service 2025). Recent

clinical findings suggest that vitamin B_6 supplementation in young adults may reduce symptoms of anxiety (Field et al. 2022). Neuroimaging evidence further suggests that vitamin B_6 intake is associated with measures of functional connectivity within brain networks implicated in mood and anxiety-related disorders. For example, a study of the UK Biobank cohort found that increased intake of vitamins B_6 and B_{12} is linked to reduced functional connectivity in the posterior portion of the default mode network (T. Li et al. 2024). Furthermore, evidence indicates that higher blood vitamin B_6 levels in older adults are associated with stronger functional connectivity between the salience network and the left middle temporal gyrus (Jannusch et al. 2017). Together, these findings motivate applications to mental health and future research to examine whether the B vitamins can mitigate the effects of mood and anxiety-related disorders on default mode and salience network function.

Vitamin B_9 (folate) is critical for red blood cell production and converting homocysteine into methionine (Hanna et al. 2022). Notably, the conversion from homocysteine to methionine is important for brain health, as previous studies have shown that a higher methionine to homocysteine ratio is associated with a lower rate of cortical atrophy (Hooshmand et al. 2019). Vitamin B_9 is found in foods such as dark green leafy vegetables, nuts, legumes, meat, poultry, dairy products, and grains (Hanna et al. 2022, US Department of Agriculture Agricultural Research Service 2025). Recent evidence suggests that vitamin B_9 intake is associated with decreased depression symptom scores (Borges-Vieira & Cardoso 2023). Although evidence for the role of vitamin B_9 in brain health is limited, prior research suggests that supplementation of vitamins B_6, B_9, and B_{12} in older adults with mild cognitive impairment is associated with decreased gray matter atrophy of regions tied to the default mode network, such as the parahippocampal gyrus (Douaud et al. 2013). Future research is needed to further establish and validate this finding in the context of mood and anxiety-related disorders.

Vitamin B_{12} plays an important role in myelin formation and the maintenance of healthy brain function (Hanna et al. 2022). Vitamin B_{12} is mostly found in seafood such as clams, tuna, and sardines and in animal products such as beef (Hanna et al. 2022, US Department of Agriculture Agricultural Research Service 2025). Importantly, vitamin B_{12} is functionally associated with vitamin B_9 (folate) in the process of recycling homocysteine into methionine. Evidence suggests that vitamin B_{12} deficiency can lead to a functional folate deficiency, which may serve to compromise brain function and contribute to cortical atrophy and demyelination (for a review, see Kennedy 2016).

A growing body of clinical evidence suggests that vitamin B_{12} deficiency is associated with mood and anxiety-related disorders (Sahu et al. 2022) and that vitamin B_{12} supplementation may mitigate symptoms of depression (Borges-Vieira & Cardoso 2023). Neuroimaging findings further suggest that vitamin B_{12} may help counteract cortical atrophy associated with mood and anxiety-related disorders. For example, a study of healthy middle-aged adults found that blood vitamin B_{12} levels were positively associated with brain volume of the right middle temporal and right inferior temporal gyri, regions of the default mode network (Çebi et al. 2022). Additional evidence suggests that vitamin B_{12} may help promote white matter integrity. A study of older adults found that individuals with low blood levels of vitamin B_{12} exhibited reduced white matter integrity in the cingulum, a key white matter tract that supports the default mode network connectivity (Kaya et al. 2023). Finally, vitamin B_{12} may also play a role in modulating functional connectivity within this network. A recent UK Biobank study found that higher intake of vitamins B_6 and B_{12} was associated with decreased functional connectivity in the posterior portion of the default mode network (T. Li et al. 2024). In the context of mood and anxiety-related disorders, the observed decrease in functional connectivity within the default mode network may serve to mitigate the effects of hyperconnectivity.

Vitamin D

Vitamin D is a neurosteroidal hormone that supports multiple functions, including the regulation of calcium homeostasis, β-amyloid deposition, and antioxidant and anti-inflammatory activities (Anjum et al. 2018). Vitamin D is found in fatty fish, such as salmon, tuna, mackerel, egg yolks, and mushrooms that are exposed to ultraviolet light/sunlight (US Department of Agriculture Agricultural Research Service 2025). Clinical findings suggest that lower vitamin D levels are associated with increased symptoms of mood and anxiety-related disorders (reviewed in Akpınar & Karadağ 2022). A recent review of this literature suggests that higher serum vitamin D levels predict lower risk of depression and severity of depression symptoms (Roșian et al. 2025). Furthermore, neuroimaging evidence suggests that vitamin D may help mitigate cortical atrophy within brain networks associated with mood and anxiety-related disorders. For example, individuals with low levels of vitamin D (either an insufficiency or a deficiency) were found to have significantly lower gray matter volume within regions of the salience network (i.e., the insula) and the default mode network (i.e., the middle temporal gyrus) relative to individuals with healthy levels of vitamin D (Strath et al. 2022). Vitamin D may also play a role in preserving white matter integrity. For example, higher serum vitamin D levels have been associated with greater integrity in the cingulum, a white matter tract supporting default mode connectivity (Beydoun et al. 2020). Finally, recent evidence suggests that higher serum concentrations of vitamin D are associated with lower connectivity within regions of the default mode network, including the right anterior angular gyrus and right posterior angular gyrus (Zhu et al. 2022).

Lutein and Zeaxanthin

Lutein and zeaxanthin are fat-soluble antioxidants from the xanthophyll branch of the carotenoid family that preferentially accumulate in the brain and macula (Johnson 2012, Mrowicka et al. 2022). Lutein and zeaxanthin are found in sweet corn and green leafy vegetables such as spinach, kale, and lettuce (US Department of Agriculture Agricultural Research Service 2025). Recent clinical findings have found that higher lutein and zeaxanthin intake is associated with a lower risk of developing mood disorders (reviewed in Rasmus & Kozłowska 2023). Neuroimaging evidence also suggests that lutein and zeaxanthin may help counteract cortical atrophy. For example, a study of healthy older adults reported that higher lutein serum levels were linked to greater gray matter volume in the right parahippocampal cortex, a region within the default mode network (Zamroziewicz et al. 2016). Additional studies suggest that lutein and zeaxanthin may help preserve white matter integrity. For example, a study found that serum lutein and zeaxanthin levels were positively correlated with the structural integrity of the cingulum, a white matter tract underlying the default mode network (Mewborn et al. 2018).

Polyphenols

Polyphenols are naturally occurring compounds found in many plant products, recognized for their role in modulating cellular signaling pathways involved in neuroplasticity and inflammation (Gomez-Pinilla & Nguyen 2012, Jie et al. 2025). There are four primary classes of polyphenols: phenolic acids, flavonoids, stilbenes, and lignans (Manach et al. 2004). Polyphenols can be found in fruits, vegetables, and legumes. Common dietary sources of polyphenols are derived from plants, including tea, coffee, and red wine (Manach et al. 2004). Clinical studies in animal and human models have demonstrated that polyphenols may reduce the symptoms of mood and anxiety-related disorders (Gomez-Pinilla & Nguyen 2012, Jie et al. 2025, Lin et al. 2021). Neuroimaging findings further suggest that polyphenols may protect the brain against cortical atrophy. For example, evidence from the post-hoc analysis of data from a randomized controlled trial indicates that higher

consumption of polyphenol-rich foods was associated with less atrophy within the hippocampus, a brain region that is closely linked to the default mode network (Pachter et al. 2024). In addition, polyphenol intake has been associated with measures of functional connectivity. A recent study examining the effects before and after coffee consumption in habitual coffee drinkers found that functional connectivity within the posterior default mode network decreased after drinking coffee (Picó-Pérez et al. 2023). These findings motivate applications to mental health and future research to investigate whether the observed decrease in functional connectivity within the default mode network may serve to mitigate the effects of hyperconnectivity in mood and anxiety-related disorders.

FUTURE DIRECTIONS AND CONCLUSIONS

In this focused review, we investigate the neural mechanisms underlying mood and anxiety-related disorders, surveying evidence of alterations within specific structural and functional networks. The neuroimaging literature reveals a consistent pattern of structural and functional disruptions in the salience and default mode networks among individuals with mood and anxiety-related disorders. These disruptions include (*a*) reduced functional connectivity (hypoconnectivity) in the salience network, (*b*) increased functional connectivity (hyperconnectivity) in the default mode network, (*c*) decreased gray matter volume in regions associated with both networks, and (*d*) reduced integrity of white matter pathways that support these networks. Within the framework of nutritional cognitive neuroscience, these findings highlight potential neurobiological targets for dietary and nutritional interventions to promote mental health.

Importantly, nutrients and bioactive compounds commonly found in the Mediterranean diet, including tryptophan, omega-3 fatty acids, MUFAs, B vitamins, vitamin D, lutein and zeaxanthin, and polyphenols, have been shown to demonstrate properties that may counteract the effects of mood and anxiety-related disorders, specifically by (*a*) increasing functional connectivity within the salience network (counteracting hypoconnectivity), (*b*) decreasing functional connectivity (mitigating hyperconnectivity) within the default mode network, (*c*) maintaining gray matter volume in regions associated with both networks (counteracting cortical atrophy), and (*d*) maintaining the integrity of white matter pathways that support these networks (mitigating white matter degeneration). These findings motivate future research to investigate the efficacy of targeted dietary interventions that leverage these findings to decrease the risk of mood and anxiety-related disorders or to reduce the presentation of symptoms.

The reviewed findings offer new insights into how diet exerts its influence on mental health. Here, we posit that poor diet and nutrition contribute to increases in inflammation and oxidative stress, which increases allostatic load and can compromise brain health. The long-term deterioration of brain health is believed to increase the risk of psychopathology, including mood and anxiety-related disorders. Conversely, a healthy diet and nutrition support allostasis by reducing inflammation and lessening the accumulation of allostatic burden. Thus, the maintenance of allostasis may protect the brain from developing mood and anxiety-related disorders and may reduce existing symptoms of mood and anxiety-related disorders (Santamaría-García et al. 2025, Zhou et al. 2022).

There are several promising directions that future research can explore to advance our understanding of how diet and nutrition may combat mood and anxiety-related disorders. First, the gut microbiome, as a part of the gut–brain axis, is an important mediator between diet and brain health. For example, the gut microbiota may play a key role in the metabolism of key nutrients, such as tryptophan (Gao et al. 2020). A healthy gut microbiome can further enhance the effects of nutrition on brain health by promoting nutrient metabolism and absorption. Future research

should explore how effects of diet and nutrition are mediated by gut health. Second, regions across the human brain exhibit varying rates of biological aging (Raz & Rodrigue 2006). Similarly, the metabolic rates of nutrients are also dynamic across the lifespan and exhibit changes with aging (Palmer & Jensen 2022). A lifespan perspective recognizes that two individuals at different stages of life consuming diets of similar quality may be at different levels of risk for developing mood and anxiety-related disorders. Therefore, future research should explore how specific elements of diet and nutrition may selectively affect particular facets of mental health at different stages of the lifespan. Third, brain health is influenced by a multitude of lifestyle factors, including not only diet and nutrition but also physical exercise, social support, sleep quality, and intellectual engagement (Barbey 2025, Pettigrew & Soldan 2019). For instance, prior research suggests that the benefits of diet and nutrition may be amplified by aerobic fitness (Key & Szabo-Reed 2023, Pickersgill et al. 2022, Zwilling et al. 2020). Future research should examine how diet and nutrition interact with other lifestyle factors to elucidate the complex mechanisms of brain health underlying the risk of mood and anxiety-related disorders. Lastly, mood and anxiety-related disorders include both clinical and subclinical symptoms as well as various subtypes (Firth et al. 2020). Advances in the design of personalized treatment approaches motivate future research to examine how specific facets of diet and nutrition may influence clinical symptoms, subclinical presentations, and distinct subtypes of mood and anxiety-related disorders.

Although the available evidence is promising, it is also important to emphasize the limitations of the current review. First, our review of the evidence on the effects of mood and anxiety-related disorders on the brain is not exhaustive. The current review focuses on the salience and default mode networks and their role in mood and anxiety-related disorders. It is important to recognize that there is a much larger literature in biological psychiatry that we do not review here. Second, although the nutritional evidence presented in this review is promising, it is limited by factors such as study heterogeneity, observational design, small sample and effect sizes, and potential confounding variables, which constrain the overall strength, causality, and generalizability of the findings. Third, evidence to support the efficacy of nutritional interventions to promote mental health remains equivocal, with studies that demonstrate benefits for specific mental health symptoms (Jacka et al. 2017, Parletta et al. 2019, Sánchez-Villegas et al. 2013) and others that remain inconclusive (e.g., Bot et al. 2019). Indeed, further research to establish and validate the effects of the reviewed nutrients and bioactive compounds on brain networks underlying mental health is needed. Lastly, many studies reviewed in this article pertaining to cognitive neuroscience, nutritional epidemiology, and nutritional psychiatry are correlational. It is important to recognize that some of the effects may be driven by potential confounding variables or indirect mechanistic pathways. Therefore, further evidence, preferably from randomized controlled trials and meta-analyses, is needed to validate the potential beneficial effects of the reviewed nutrients on mood and anxiety-related disorders.

This focused review synthesizes current evidence on how diet and nutrition may act as effective mediators to enhance specific aspects of brain health commonly implicated in mental health conditions. However, it is important to note that the mechanisms linking diet and mental health are complex, involving interactions between environmental, psychological, biological, and lifestyle factors (Barbey 2025, Bremer et al. 2025). Therefore, to advance the field, future research should prioritize the development of rigorous, multilevel, and multivariate models (Talukdar et al. 2023, Zwilling et al. 2024)—ideally through longitudinal and intervention-based designs—to better understand how specific dietary patterns influence the onset, progression, and alleviation of mood and anxiety-related symptoms.

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J.W. contributed to the development of the outline of the article, original draft preparation, visualization, and editing. J.W. acknowledges the use of generative AI to improve the readability of text during early stages of editing. A.K.B. contributed to reviewing, editing, finalizing, and supervision.

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