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Fermented foods as sources of psychobiotics: Implications for gut-brain axis regulation and mental health

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Abstract

The potential of the new field of psychobiotics, live microorganisms that, when consumed in sufficient quantities, have positive effects on mental health, to alter the gut-brain axis and enhance psychological well-being has drawn more and more attention. This review summarises the most recent research on the function of fermented foods as a source of psychobiotics, emphasising their modes of action and prospective applications as treatments for anxiety, depression, and stress-related illnesses. Short-chain fatty acids (SCFAs), which are produced by fermented foods that are high in good bacteria like *Lactobacillus* and *Bifidobacterium*, are essential for preserving the integrity of the gut barrier, lowering inflammation, and controlling neurotransmitter signalling. According to preclinical and clinical research, psychobiotics boost microbial diversity, encourage the expression of neurotrophic factors, and affect the hypothalamic-pituitary-adrenal axis, all of which are linked to mood management and cognitive performance. Though more research is required to maximise their usage and elucidate underlying mechanisms, fermented foods generally constitute a promising, natural supplement to traditional therapy for mental health issues.

1. Introduction

One of the most intricate and diverse ecosystems can be found in the human gut, home to up to 10^{13} - 10^{14} microorganisms, between one and ten times the body's eukaryotic cell count. Up to 500-1000 bacterial species make up the total adult human gut microbiota. The gut microbiota and host have developed a mutual relationship over hundreds of years of co-evolution. In fact, the gut is full of compounds that the microbes can use as food, which promotes the colonisation of the microbiota (Leung and Thuret, 2015). Beginning at birth, gut colonisation develops during the course of the first three years of life. The developmental regulation of intestinal physiology, the neurological system, and the immune system all depend on the first interaction between the host and gut bacteria. At this point, the gut bacteria can also influence the angiogenesis process. Additionally, microbes exhibit antimicrobial properties, which help to preserve a healthy gut ecology. It has been demonstrated that changes in the early-life microbial colonisation of the human gut affect illness risk. The neurophysiology, behaviour, and nervous system function of the host are significantly impacted by microbial colonisation of the intestine later in life (Bermúdez-Humarán *et al.*, 2019).

Prebiotics were first proposed in 1995 by Gibson and Roberfroid as a "nondigestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria already resident in the colon." This idea was first used in relation to probiotics. According to this, they have the capacity to withstand host digestion and exhibit distinct gut microbial activity. This definition has had to change, though, because prebiotics can

also be directly given to other parts of the body, including the skin or vagina that are also colonised by commensal bacteria. Given that dietary prebiotics must not be broken down by host enzymes, the International Scientific Association for Probiotics and Prebiotics (ISAPP) recently proposed a new definition of prebiotics as "a substrate that is selectively utilised by host microorganisms conferring a health benefit" in a consensus panel (Gibson *et al.*, 2017). Plant polyphenols, conjugated linoleic acid, polyunsaturated fatty acids, oligosaccharides (OS), and certain fermentable fibres are examples of substrates that meet this criterion.

The most researched and traditionally recognised prebiotics are, inulin, fructooligosaccharides (FOS), galactooligosaccharides (GOS), xylooligosaccharides (XOS), mannanoligosaccharides (MOS) and human milk oligosaccharides (HMO). The immunological system, gastrointestinal tract bones, mental health, and sugar and lipid metabolism have all been shown to benefit from prebiotics. According to Dinan *et al.* (2013), a psychobiotic is a live organism that helps patients with mental illnesses when taken in sufficient quantities. Certain prebiotics may exert psychobiotic-like effects by modulating gut microbiota, thereby, have been shown to enhance mental well-being and promote the development of specific commensal or beneficial bacteria with psychophysiological effects. The majority of prebiotic substrates examined for their effects on the brain are FOS and GOS, which favourably promote the proliferation of *Lactobacilli* and *Bifidobacteria*.

Fermentation is a biochemical process in which microbes metabolise raw material ingredients to produce final products with improved biosafety effects, nutritional value, and a wide range of organoleptic qualities. Through a variety of food combinations, microbes, and fermentation techniques, more than 5000 different kinds of fermented foods and beverages have been found worldwide too far. The fermented goods are typically made in accordance with the dietary customs of the society, which are based on the availability of plant

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or animal sources and staple meals. Furthermore, every particular fermented product is distinct and differs globally by ethnicity (race, cultural group, and people), culture (religions, customs, social groups, and dietary regulations), and geography. The fermentation process improves the food's nutritional value and biological qualities, such as its antioxidative, anti-inflammatory, antiapoptotic, anticancer, antifungal, antibacterial, immunomodulatory, and hypochol-esterolemic effects, according to numerous studies (Kumar *et al.*, 2022).

Psychobiotics contain good bacteria and prebiotics, which are the food supply for these bacteria and have positive impacts on mental and emotional health in the human gastrointestinal tract. Psychobiotics are known to have antidepressant and anxiolytic effects, and the gut-brain axis mediates these effects. It has been demonstrated that taking psychobiotics can help remedy microbiota dysbiosis and reduce certain symptoms linked to disorders of the central nervous system, including multiple sclerosis, depression, insomnia, anorexia nervosa, diabetic neuropathy, autism spectrum disorders, and Parkinson's disease (Kimse *et al.*, 2024). Despite encouraging results, the lack of mechanistic understanding and variation in strain-specific effects make it difficult to translate psychobiotic therapies from animal models to clinical settings. This review attempts to summarise the most recent research on the effects of psychobiotics, especially those made from fermented foods, on the symptoms of disorders of the central nervous system, including depression, anxiety, and dementia. It also looks into the mechanisms through which these treatments affecting mental well being by modifying the gut-brain axis.

2. Intercommunication between gut, brain and endocrine

The transmission of neural signals from the gut to the brain-also referred to as the "second brain," a term Michael Gershon first used in 1998 to refer to the network of nerves surrounding the gut-that inform the brain of the body's metabolic and physiological states has been the subject of decades of research. Numerous studies have included gut bacteria as a mediator in this context, indicating that the "microbiota-gut-brain axis" is a more plausible hypothesis. According to Casertano *et al.* (2022), the microbiota-gut-brain axis refers to "the interconnected communication between the gut, the brain, and the microbiota that can take place through a variety of systems, including the enteric nervous system (ENS), the gut microbiota, the central nervous system (CNS), and endocrine and immune (including cytokine) pathways" (Figure 1). Gut microbiota may be implicated top-down or bottom-up, delivering signals to the central nervous system and influencing brain function when CNS signals significantly alter the relative abundance of bacteria.

2.1 The vagus nerve

The vagus nerve is the primary component of the parasympathetic branch of the autonomic nervous system. The mixed nerve is composed of 80% afferent nerve fibres (input) that can provide gut information to the CNS and 20% efferent nerve fibres (output) that stretch to the stomach's smooth muscle. The brainstem's caudal nucleus of the solitary tract (cNST), which is involved in reward and pleasure-related brain circuits, receives signals from the gut primarily through this pathway (Bonaz *et al.*, 2018).

Both afferent/sensory and efferent/motor fibres are found in the vagus nerve (cranial nerve X). Mechanoreceptors, gastrointestinal

peptides, neurotransmitters, and microbial metabolites are just a few of the stimuli that the afferent vagal fibres respond to. These peripheral signals are then transmitted to different parts of the brain, including the limbic system, the nucleus tractus solitarius, and others. The nodose ganglia include the vagal afferent neurones and sensory responses that are mediated by different chemosensitive and other gastrointestinal receptors. In fact, behind the brain, the gut contains the highest concentration of nerve endings. Intestinal motility and the endocrine function of the pancreatic and adrenal glands are regulated by the efferent vagal fibres that arise from the nucleus tractus solitarius. Thus, the vagus nerve is crucial for promoting the gut-brain axis's bidirectionality (Verma *et al.*, 2024). Through its many receptors, it reacts to hormonal, pharmacological, and mechanical stimuli. The vagus nerve also controls pro-inflammatory cytokine levels through the vasovagal anti-inflammatory reflex, a process linked to diseases including inflammatory bowel disease (Clerici *et al.*, 2025).

Notwithstanding the significance of vagal pathways, it should be mentioned that the vagus nerve does not extend into the lumen and that enteroendocrine cells (EECs) secrete chemical signals that partially mediate its activation. These cells, which make up 1% of all intestinal epithelial cells, have the ability to interact with receptors expressed on the vagal nerve's afferent fibres, control gastrointestinal (GI) movement, secretion, and dietary intake; detect microbial signals, including SCFAs, *via* toll-like receptors (TLR). Nevertheless, FFARs can also directly activate vagal afferents from SCFAs, sending a signal to the brain. (Foster *et al.*, 2017).

2.2 Hypothalamic-pituitary-adrenal (HPA) axis

One of the primary neuroendocrine systems in the human body is the hypothalamic-pituitary-adrenal axis (HPA), which is also primary non-neuronal communication routes on the microbiota-intestinal-brain axis and is well recognised for being the primary neuroendocrine coordinator in reaction to stress (Mayer, 2000). The paraventricular nucleus of the hypothalamus (PVN) produces corticotrophin releasing factor (CRF) in response to disturbed homeostasis, which in turn triggers the anterior pituitary gland to release adrenocorticotrophic hormone (ACTH). Targeting the adrenal cortex, this hormone is released into the bloodstream and causes the release of glucocorticoids. These glucocorticoids then interact with both low-affinity and high-affinity mineralocorticoid receptors in the brain. The primary purpose of HPA axis activation is to precisely prime the body for the "fight-or-flight" response (Smith and Vale, 2006). One of the primary results of this process is the negative feedback loop, in which glucocorticoids restrict adrenal secretion by acting on the pituitary and brain. Multiple afferent pathways, including limbic, parasympathetic, and sympathetic, simultaneously control PVN activity. In addition, the HPA axis interacts with the vagus nerve and other non-neural pathways that connect the stomach and brain. In rodents, vagal stimulation boosted the production of CRF mRNA in the hypothalamus, and the plasma levels of corticosterone and ACTH were unexpectedly elevated following vagal stimulation. These findings suggest that the HPA axis also interacts with other non-neural routes that connect the stomach and brain, such as the vagus nerve (Demaude *et al.*, 2006). Numerous inflammatory and stress-related conditions are linked to the immune system-HPA axis interactions. For example, psychological stress has been shown in animal models to increase intestinal permeability, which in turn causes bacterial translocation in the host (Kasarello *et al.*, 2023). Again,

emphasising the critical role, the microbiota plays in this interaction, exposure to bacteria and antigens triggers the mucosa's immunological response, which in turn triggers the release of pro-inflammatory cytokines that activate the HPA axis.

According to Schultz and Keita (2020), pathogenic live microbes or bacterial substances such as endotoxins and lipopolysaccharide (LPS) can induce paracellular permeation, penetrate the damaged intestinal epithelium, and result in endotoxemia with a low-grade immune response, and chronically release proinflammatory cytokines like IL-1, IL-6, and TNF- α . These cytokines can communicate with the brain through humoral or vagal pathways. A neuronal cascade is triggered by the signal that reaches the brain, which results in the de novo creation of central proinflammatory cytokines. Crucially, local inflammatory mediators released by stressors have the potential to activate the central immune system by activating vagal afferents that drive central effects and express cytokine receptors.

3. Microbial metabolites

Propionate, butyrate, and acetate are examples of short-chain fatty acids (SCFAs), which are important microbial metabolites generated in the gut. *Roseburia*, *eubacterium*, *Faecalibacterium*, *Lactobacillus*, *Enterobacter*, and *Bifidobacterium* are among the microbial genera from which they are derived. Free fatty acid receptors 2 (FFAR2, designated GPR43) and 3 (FFAR3, designated GPR41) are the best studied among the G-protein coupled receptors (GPCRs) that are activated by SCFAs (Clerici *et al.*, 2025). The heart, different immune cells, and the colon have all been shown to express both receptors. Adipocytes and skeletal muscle express only FFAR2, whereas the blood-brain barrier (BBB) and peripheral nervous system express FFAR3. There is no evidence of FFAR2 expression in the brain (Hoyles *et al.*, 2018). SCFAs have a number of positive impacts. SCFAs suppress the production of cytokines by regulating T helper 1 lymphocyte activity, myeloid cells and regulating T helper 17 cell differentiation. They also control chemotaxis, inflammatory process by neutrophils and modulate immune cells. All things considered, SCFAs affect the immune response by triggering anti-inflammatory pathways and exercising regulatory action. SCFAs support the first line of defence between the microbiota and the host intestinal barrier's permeability by strengthening the mucosal barrier and promoting mucus formation, which is most likely mediated by FFAR3 (Smith *et al.*, 2013).

Furthermore, by binding to a corresponding receptor (such as GPR43 or GPR41) and triggering the release of neuropeptides like glucagon-like peptide (GLP-1) and YY peptide (PYY), SCFAs aid in enteroendocrine signalling. These neuropeptides impact the regulation of energetic homeostasis by activating both enteric and primary afferent vagal pathways. Last but not least, they have the ability to increase the release of the neurotransmitter 5-HT (5-hydroxytryptamine) in the intestinal lumen and the vascular system. This neurotransmitter is crucial for controlling intestinal-brain communication that governs human behaviour; enterochromaffin cells in the gastrointestinal tract and certain microbiota genera, including *Escherichia* spp. and *Enterococcus* spp., produce approximately 90% of serotonin (Cryan *et al.*, 2012).

Short-chain fatty acids (SCFAs) are other bacterial metabolites that have neuroactive properties. The three main SCFAs that are produced by the fermentation of dietary fibre by bacteria in the colon in a 3:1:1

ratio are acetate, butyrate, and propionate. All three metabolites are detectable in the human brain with an average concentration of 17.0 pmol/mg of tissue for butyrate and 18.8 pmol/mg of tissue for propionate (Bachmann *et al.*, 1979). Using special meals that contain acylated starches that can reach the colon without being absorbed in the upper gastrointestinal system, Kimura-Todani *et al.* (2020) investigated the anxiolytic effects of acetate in mice. When measured using the plus-maze and marble-burying (MB) tests, this study revealed a strong correlation between the mice's decreased anxiety-like behaviours and the cecal acetate contents. Colocytes primarily use butyrate as an energy source, and it may affect the gut-brain axis by increasing production of tight junction proteins, which improves the integrity of the intestinal barrier (Casertano *et al.*, 2022).

4. Neurotransmitters

In the central nervous system (CNS), neurotransmitters are essential chemical messengers that let neurones communicate with one another. The main inhibitory neurotransmitter in the central nervous system is gamma-aminobutyric acid (GABA). It is essential for controlling anxiety, muscular tone, and sleep because it lowers neural excitability, avoiding overstimulation. Conditions like epilepsy, anxiety disorders, and sleeplessness are linked to dysregulation of GABAergic signalling. Conversely, acetylcholine (ACh) is an essential excitatory neurotransmitter that plays a role in a number of CNS processes. It has a major impact on learning, memory, attention, and arousal. ACh affects cognitive processes through muscarinic receptors and is necessary for the stimulation of muscular activity through its interaction with nicotinic receptors. Memory loss and cognitive decline are hallmarks of neurodegenerative disorders like Alzheimer's disease, which are linked to disruptions in cholinergic signalling. The precise balance necessary for the best possible CNS function is demonstrated by both GABA and ACh. ACh promotes the excitement required for cognitive functions and muscle control, whereas GABA guarantees inhibitory control to preserve neuronal homeostasis. The intricate nature of neuronal transmission and the exact regulation needed to preserve the best possible CNS health and function are highlighted by the interactions between these neurotransmitters (Ashique *et al.*, 2024).

Serotonin is well known for its role in controlling biological and behavioural processes as a neurotransmitter that plays a role in psychological processes in the central nervous system and shows up in peripheral tissues (such as the stomach and bones). The human gastrointestinal tract produces the majority of it, and enterochromaffin cells are used by the microbiota to aid in its manufacture (Wu *et al.*, 2019). Biogenic amines include catecholamines including dopamine, norepinephrine, and epinephrine. In addition to their effects on the heart, they are involved in cognitive functions like memory formation and learning. In the gut lumen, the gastrointestinal tract's bacteria contribute to the production of free catecholamines. Additionally, it has been documented that the gut microbiota is a source of luminal norepinephrine because it sustains absorption systems for a number of biogenic amines (Asano *et al.*, 2012).

5. Bacterial strains having potential role as probiotics

Numerous research on the probiotic potential of various bacterial strains alone and in certain formulations (combinations) have been published in the literature. Studies on humans and animals have

shown that certain probiotic strains have psychobiotic effects. The most recent research on the potential applications of psychobiotics is compiled in Table 1.

5.1 Effects of fermented foods on mental health: Evidence from clinical and preclinical studies

Foods and drinks produced by microorganisms enzymatically converting major and minor food components are commonly referred to as fermented foods (Marco *et al.*, 2017). Because of extra health advantages beyond nutrition, like improved digestibility, a lower chance of impaired glucose metabolism, a drop in blood pressure and total cholesterol, a boost in immunity, and the preservation of intestinal balance by fostering intestinal barrier integrity, fermented foods and beverages have only recently been considered as potential

functional foods, despite their ancient origins (Marco *et al.*, 2017). Furthermore, even when inactivated, some probiotic lactic acid bacteria (LAB) may still be able to support health through microbial metabolites or parts of bacterial cell walls generated in the matrix (De Filippis *et al.*, 2020). Numerous studies agree that the LAB, of which fermented foods are a possible source that might enter the gut and contribute to the gut microbiota, is responsible for the possible health impacts of these foods (Pasolli *et al.*, 2020). As the number of new fermented food varieties has grown, some of them-such as fermented milk, soybeans, and algae-have been investigated for their possible impacts on brain function. The biological consequences of these fermented foods vary greatly. The particular effects may differ depending on the microorganisms involved, the fermentation process, or the basic ingredients employed.

Table 1: Bacterial strains having potential role as psychobiotics

Bacteria	Potential psychobiotic effects	References
<i>Lactobacillus</i> <i>(Lactiplantibacillus plantarum</i> C29, <i>L. plantarum</i> DR7, <i>L. plantarum</i> P8, <i>L. plantarum</i> PS128, <i>L. plantarum</i> 299v, <i>Limosilactobacillus reuteri</i> DSM 17938, <i>Lactobacillus helveticus</i> CCFM1076, <i>L. helveticus</i> NS8, <i>L. rhamnosus</i> GG, <i>Lactobacillus gasseri</i> CP2305)	Reduced stress and inhibited neurodegenerative processes. Softened opposition/defiance behaviours, improved memory and cognitive traits. Increased the diversity of neurotransmitter-synthesizing/consuming species-level genome bins and the levels of some predicted microbial neuroactive metabolites. Improved cognitive and memory functions, improved the serotonin pathway, and decreased stress and anxiety scores. Reduced Beck Depression Inventory-II scores, fatigue levels, brainwave activity, and awakenings during the deep sleep stage; enhanced self-perceived stress, overall job stress, job burden, cortisol level, general or psychological health, anxiety, depression, sleep disturbances, quality of life, and both positive and negative emotions. Prevented elevated cortisol levels during the test time and decreased the concentration of kynurenine. Enhanced the California Verbal Learning Test and Attention and Perceptivity Test. Improved neurotransmitter homeostasis by balancing the 5-hydroxytryptamine system in the peripheral and central nervous systems, consequently reducing autistic-like behaviours. Altered gut microbiota to regulate immunological responses. Decreased the level of inflammatory markers, decreased serotonin metabolism. The PedsQL Child Self-Report Total Score improved. It stopped the alterations in gene expression linked to mitochondrial functions brought on by stress.	Ma <i>et al.</i>, 2021 Lew <i>et al.</i>, 2019 Chong <i>et al.</i>, 2019 Ho <i>et al.</i>, 2021 Wu <i>et al.</i>, 2021 Liu <i>et al.</i>, 2019 Kong <i>et al.</i>, 2021 Luo <i>et al.</i>, 2014 Sawada <i>et al.</i>, 2019 Kumperscak <i>et al.</i>, 2019
<i>Bifidobacterium</i> <i>(Bifidobacterium breve</i> A1, <i>B. breve</i> CCFM1025, <i>B. longum</i> NCC3001, <i>B. longum</i> 1714, <i>B. infantis</i> 35624, <i>B. bifidum</i> ATCCVR 29521)	Decreased behaviours associated with anxiety and depression enhanced cognitive performance. Avoided cognitive problems, and alleviated anxiety and depressive symptoms. Improved synaptic plasticity and raised the levels of brain-derived neurotrophic factor, fibronectin type III domain-containing protein 5, and postsynaptic density protein. Reduced neurological abnormalities in chronically stressed mice and altered the gut microbiome of chronically stressed mice. Restoration of baseline noradrenaline levels in the brainstem, reversal of behavioural abnormalities, and normalisation of the immunological response It raised acetylcholine and decreased dead cell counts in the brains of AD rats.	Pinto-Sanchez <i>et al.</i>, 2017 Allen <i>et al.</i>, 2016 Wang <i>et al.</i>, 2019, Desbonnet <i>et al.</i>, 2010 Zhu <i>et al.</i>, 2021 Kobayashi <i>et al.</i>, 2017
<i>Bacillus</i> (<i>Bacillus coagulans</i> MTCC 5856)	The reduction of symptoms of IBS and depression.	Majeed <i>et al.</i>, 2018
<i>Clostridium</i> (<i>Clostridium butyricum</i> MIYAIRI 588)	A substantial decrease in depression (when antidepressants are used).	Miyaoka <i>et al.</i>, 2018

The gut microbiota has been implicated in a number of mental processes and disorders related to the nervous system, including mood and anxiety disorders, according to an increasing number of

research. Dairy products may have probiotic microorganisms and bioactive substances that have a number of medicinal uses. The objective of study conducted by Sousa *et al.* (2022) was to look at

potential correlations between university students' anxiety levels and how frequently they consume certain dairy products. With an average age of 20.5 years, the subjects consisted of 311 Azorean university students, 231 of whom were female and 80 of whom were male. A brief version of the spielberger state-trait anxiety inventory (STAI) test and a quantitative questionnaire about the frequency of dairy product use were filled out by the subjects. The most popular dairy items were semi-skimmed milk, followed by matured cheese, sipping yoghurt, skim milk, and set yoghurt; the least popular dairy goods were dairy ice cream, whole milk, and fresh cheese. According to discriminant analysis, the group with low anxiety (scoring < 40 on the STAI test) consumed considerably more fermented foods (cheese and yoghurt) than the group with high anxiety (score $\geq$ 40). According to the frequency of consumption of fermented goods, 62.4% of the cases that were initially categorised in this research were correctly classified. No associations were discovered between unfermented dairy products and anxiety. According to the findings, young Azorean university students' anxiety levels are positively impacted by consuming fermented dairy products.

The effects of fermented foods on mental health, specifically their effects on anxiety, depression, cognitive function, and stress-related outcomes, as mediated through modulation of the gut-brain axis, are summarised in Table 2 based on data from clinical and preclinical studies. Probiotic-rich fermented foods, like kefir and yoghurt, have been shown in numerous clinical trials to reduce symptoms of stress, anxiety, and depression. Júnior *et al.* (2025) found that probiotic kefir supplementation over a 12-week period significantly reduced the severity of depression as measured by HAM-D scores, along with inflammatory markers like IL-6 and CRP and reduced cortisol levels. Özcan and Oskay (2019) found that daily kefir consumption improved sleep quality, quality of life, and depressive symptoms in postmenopausal women, likely through gut-brain axis modulation. Preclinical research has shed light on the mechanisms underlying these effects. In a mouse model of chronic unpredictable mild stress, Sun *et al.* (2025) demonstrated that Tibetan goat kefir decreased depression-like behaviours. This was accompanied by a restoration of gut microbiota diversity, an increase in brain-derived neurotrophic factor (BDNF), and a decrease in hypothalamic-pituitary-adrenal (HPA) axis activity. The gut-brain-immune link was further supported by Van de Wouw *et al.* (2020), who found that kefir enhanced mice's resilience to stress and controlled their immunological responses.

Certain probiotic strains found in fermented dairy products have also showed promise. In individuals with depression and constipation, Zhang *et al.* (2021) discovered that fermented milk containing *Lactocaseibacillus paracasei* strain Shirota decreased inflammatory markers and depressive symptoms. According to Kato-Kataoka *et al.* (2016), medical students' stress reactions under academic stress were reduced and gut microbiota diversity was maintained by

Lactobacillus casei Shirota-fermented milk. According to Ohsawa *et al.* (2018), bioactive peptides in *Lactobacillus helveticus*-fermented milk helped healthy people pay better attention and remember things better. Fermented foods made from soy have been researched for their potential to improve mood and cognition. In a randomised controlled experiment, Hwang *et al.* (2019) found that fermented soybean with *Lactobacillus plantarum* C29 enhanced cognitive performance and elevated serum BDNF in people with mild cognitive impairment. Because of phytoestrogen activity, Nina Estrella *et al.* (2014) found that menopausal women who took soybeans together with antidepressants experienced a higher reduction in depressive symptoms than those who used antidepressants alone.

The effects of fermented rice and garlic have been studied in other studies. Piriyaarasath *et al.* (2023) showed that supplementing stressed mice with rice-koji extract and ergothioneine reduced anxiety- and pain-like behaviours, with normalisation of neural activation patterns and increased BDNF levels. Tyagi *et al.* (2025) showed that in stressed mice, *Limosilactobacillus reuteri*-fermented brown rice reduced anxiety and improved cognition, mediated by gut microbiota modulation and neuroprotection. Numerous probiotic strains found in yoghurt have been demonstrated to improve immunological and mental health. According to Kinoshita *et al.* (2021), *Lactobacillus delbrueckii* OLL1073R-1 yoghurt enhanced the vitality and quality of sleep of female healthcare workers. According to Nishimura *et al.* (2016), in stressed individuals, *Lactobacillus plantarum* HOKKAIDO yoghurt lowered stress indicators and altered immunological function. Yoghurt containing *Bifidobacterium longum* SBT2928 and *Lactobacillus gasseri* SBT2055 boosted natural killer cell activity and reduced mental stress in healthy people, according to Nishihira *et al.* (2014).

Table 2: Effect of fermented foods on mental health: Clinical and preclinical studies

Fermented food	Study design	Population/ model	Mental health outcomes	Proposed mechanisms	Key results	References
Kefir	Case study	Women with MDD (Major depressive disorder)	Reduce depression severity	Decrease in IL-6/ CRP and decrease in cortisol	HAM-D scores and inflammatory markers decreased after 12 weeks	Júnior <i>et al.</i> (2025)
	Randomized control trials	Postmenopausal women	Increase sleep quality, qol (quality of life) decrease in depression	Modulation of gut-brain axis	After eight weeks, there was a noticeable improvement	Özcan and Oskay, (2019)
	Preclinical trials	CUMS (chronic unpredictable mild stress)-induced depression (mice)	Decline in depression-like behaviors	Restoration of gut microbiota, Increase in BDNF, reduced HPA axis activity	Decline in behaviour despair and inflammation	Sun <i>et al.</i> (2025)

Fermented food	Study design	Population/ model	Mental health outcomes	Proposed mechanisms	Key results	References
Fermented Milk	Preclinical trials	Mice stress model	Resilience to stress increased	Gut-brain-microbiome- modulation	Decline in immunological and stress behaviours	Van de Wouw <i>et al.</i> (2020)
	Randomized control trials (lcs-fermented milk)	Patients having depression and constipation	Decline in depression symptoms	Modulation of gut microbiota and decline in IL-6	Reduced BDI and HAMD scores, IL-6 after 9 weeks	Zhang <i>et al.</i> (2021)
	Randomized Control trials (<i>L. casei shirota</i> milk)	Medical students under stress	Reduced abdominal symptoms and stress	Increased microbiota diversity (alpha diversity index) and modulation of stress response	Decreased salivary cortisol and stress VAS (visual analog scale)	Kato-Kataoka <i>et al.</i> (2016)
	Randomized control trials (<i>L. helveticus</i>)	Adults (middle-aged)	Improvement in attention and Memory	Lactononadecapeptide activity	Both the delayed memory and RBANS neuro-psychological test scores increased after 8 weeks	Ohsawa <i>et al.</i> (2018)
	Randomized control trials (<i>Lactobacillus</i> milk drink)	IBS patients having depression	Decline in depression	Modulation of gut microbiota	Significant reduction in depressive scores and improved quality of life after 12 weeks	Sarkawi <i>et al.</i> (2024)
Soybean	Randomized control trials (<i>Lactobacillus plantarum</i> C29-fermented soybean DW2009)	MCI (Mild cognitive impairment) patients	Improved cognitive function	Improve BDNF, gut-brain axis	Attention and memory improved, BDNF increased after 12 weeks	Hwang <i>et al.</i> (2019)
	Randomized control trials (Soybean+antidepressants)	Depressive menopausal women	Reduced depressive scores	Phytoestrogen activity	Greater improvement (soybean+antidepressants) vs. antidepressants alone	Nina Estrella <i>et al.</i> (2014)
Rice	Preclinical (mice) (<i>L. reuteri</i> fermented brown rice)	Stressed mice	Decreased anxiety and improved cognition	Microbiota modulation, neuroprotective	Reduced anxiety-like behaviors and improved cognitive tests	Tyagi <i>et al.</i> (2025)
	Preclinical (mice) (rice-koji extract + ergothioneine)	Psychophysical stress	Decrease anxiety and pain-like behaviors	Neural modulation and improved BDNF	Anxiety and nociception decreased, neural activation normalized	Piriyaprasath <i>et al.</i> (2023)
Yogurt	RCT (OLL1073R-1 yogurt)	Women health-care workers	Increased psychological QoL and sleep	Gut-brain axis, anti-inflammatory	PSQI declined, SF-8 vitality increased	Kinoshita <i>et al.</i> (2021)
	RCT (<i>L. plantarum</i> HOKKAI-DO yogurt)	Stressed adults	Reduced stress markers and immune modulation	Reduced neutrophil-lymphocyte ratio	Stress and immune markers improved	Nishimura <i>et al.</i> (2016)
	RCT (<i>L. gasseri</i> SBT2055 and <i>B. longum</i> SBT2928 yogurt)	Healthy adults	Decrease in mental stress, increase in NK cell activity	Immune modulation, stress reduction	NK cell activity improved, mental stress scores declined	Nishihira <i>et al.</i> (2014)

Garlic	Preclinical (rats) (black garlic)	MSG-exposed adolescent rats	Improved spatial memory and hippocampal neurons	Neuroprotection, anti-oxidant	Improved memory, increase in pyramidal cell count	Hermawati <i>et al.</i> (2015)
	Preclinical (rats) (Aged garlic)	β -amyloid-induced rats	Improve cognitive function, decrease neuroinflammation	Anti-inflammatory, neuroprotection	Improved cognition, decline in neuro inflammation	Nillert <i>et al.</i> (2017)
	Preclinical (rats) (aged garlic)	Amyloid- β induced rats	Increase spatial memory, reduced oxidative damage	Anti-oxidant, neuroprotection	Improved spatial memory, reduction in brain oxidative damage	Wichai <i>et al.</i> (2019)

IL- Interleukins, CRP- C-reactive protein, HAM-D Hamilton depression rating scale, BDNF- Brain derived neurotrophic factor, BDI- Beck depression inventory, RBANS- Repeatable battery for the assessment of neuropsychological status, PSQI- Pittsburgh sleep quality index.

Preclinical models of cognitive impairment have also been used to study extracts from aged and black garlic. Hermawati *et al.* (2015) shown that in adolescent rats exposed to monosodium glutamate, black garlic ethanol extract enhanced spatial memory and raised hippocampus pyramidal cell numbers. In rat models of amyloid- β -induced brain damage, aged garlic extract was shown to enhance cognitive performance, decrease neuroinflammation, and lessen oxidative brain damage (Nillert *et al.*, 2017; Wichai *et al.*, 2019).

5.2 Effect of psychobiotics, probiotics and prebiotics on mental health

Among adults, anxiety and depression are two of the most prevalent psychiatric conditions. Although, the exact causes of these illnesses are still unknown, it is known that abnormalities in serotonergic, noradrenergic, and dopaminergic processes as well as other neuroactive substances like GABA and acetylcholine are implicated (Trzeciak and Herbet, 2021). Drugs known as first-line antidepressants prevent these biological amines from being reabsorbed into nerve terminals, because the cause is frequently linked to a malfunction in the way serotonin and norepinephrine work. The fact that many individuals become resistant to antidepressants and that the gut microbiota plays a significant role in regulating these substances has prompted more research into the role of bacteria in treating mental illnesses (Íimse *et al.*, 2024).

According to recent reports, there is a strong correlation between the gut microbiota and disorders of the central nervous system in humans, such as autism spectrum disorder, major depressive disorders, Parkinson's disease, and Alzheimer's disease (Cai *et al.*, 2023; Cryan *et al.*, 2020). Again, Desbonnet *et al.* (2015) discovered that reducing the gut microbiota caused cognitive impairments, changed the dynamics of tryptophan metabolism, and markedly decreased the expression of vasopressin, oxytocin, and brain-derived neurotrophic factor in adult mice's brains. In a recent study, Xu *et al.* (2023) shown that *L. rhamnosus* zz-1 therapy decreased the expression of pro-inflammatory cytokines (IL-1 β and TNF- α) in the hippocampus and alleviated depression-like behavioural abnormalities in depressed mice. It's interesting to note that even prebiotic-induced gut microbiota modulation has anxiolytic and antidepressant-like effects, reverses the effects of chronic stress in mice, and stops the negative effects of a high-fat diet on the functionality of microglia in ageing mice.

Similar advantages in humans have been documented in certain therapeutic trials. In contrast to control groups that received only the usual treatment, Reiter *et al.* (2020) showed that administering

different species of *Bifidobacterium* and *Lactobacillus* (such as *Bifidobacterium bifidum* W23, *Bifidobacterium lactis* W51 and W52, *Lactococcus lactis* W19, *Lactococcus lactis* W22, *L. acidophilus* W22, *L. casei* W56, *L. paracasei* W20, *L. plantarum* W62, *L. salivarius* W24, and *L. bifidum* W23) in addition to standard treatment resulted in decreased IL-6 gene expression. In patients with major depressive disorder, *L. plantarum* 299v has been shown to improve verbal learning and memory, processing speed, and attention (Rudzki *et al.*, 2019). The symptoms of depression also significantly improved in patients with major depressive disorder who were treated for four weeks with a probiotic cocktail that included *S. thermophiles*, *B. breve*, *B. longus*, *B. infantis*, *L. acidophilus*, *L. plantarum*, *L. paracasei*, and *L. delbrueckii* (Kyei-Baffour *et al.*, 2025). Psychobiotic medication has been associated with a reduction in mental health symptoms in other clinical trials.

The use of dietary changes and gut microbiota-targeted treatments, like prebiotic or probiotic supplements, to enhance mental health is supported by preliminary data. Freijy *et al.* (2023) provide the first randomised controlled study (RCT) to investigate the impact of probiotic supplements and a high-prebiotic diet on mental health. More than hundred adults (119) with poor intake of prebiotic foods and moderate psychological discomfort participated in the 8-week, 2 $\times$ 2 factorial RCT "Gut Feelings." The treatment arms were as follows: (1) probiotic supplement and normal diet (probiotic group); (2) high-prebiotic diet and placebo supplement (prebiotic diet group); (3) probiotic supplement and high-prebiotic diet (synbiotic group); and (4) placebo supplement and normal diet (placebo group). The evaluation of total mood disturbance (TMD; profile of mood states short form) from baseline to eight weeks was the main result. Measures of wellbeing, stress, anxiety, depression, and sleep were secondary outcomes. The prebiotic diet decreased TMD compared to a placebo after 8 weeks, according to a modified intention-to-treat analysis using linear mixed effects models. Probiotic ($d = 0.19$, 95% CI = 0.75, 0.38; $p=0.51$) and synbiotic ($d = 0.03$, 95% CI = 0.59, 0.53; $p=0.92$) therapies did not appear to alleviate symptoms. The prebiotic diet was found to enhance anxiety, tension, and sleep, whereas the probiotic may have improved wellbeing when compared to a placebo. The synbiotic intervention had no positive effects. There were little side effects and all therapies were well tolerated.

Investigating the impact of a chronic (long-term) multispecies probiotic intervention on cognition in healthy ageing individuals was the main goal of the study conducted by Eastwood *et al.* (2025). Secondary objectives included a new study of the acute impact of

supplementation on mood and cognition, as well as an examination of the long-term impact on gut microbiota community and mood outcomes. The study employed a randomised, placebo-controlled, cross-over trial in 30 healthy older adults to examine the short-term (1 day) and long-term (8 weeks) effects of a probiotic supplement on mood measures of anxiety, stress, cognitive reactivity to sad mood and depression as well as the cognitive domains of memory and executive function. To evaluate any impacts on the gut microbiota, stool samples were also subjected to 16s rRNA sequencing both before and after the chronic intervention. Acute probiotic treatment was associated with faster reaction times on cognitively demanding trials during an executive function task. Long-term supplementation has been associated with improvements in cognitive biases such as aggressiveness, hopelessness, and rumination that heighten susceptibility to depression. Additionally, with increased cognitive demands, it might enhance executive function.

6. Conclusion

The integration of fermented foods and psychobiotics into dietary and therapeutic strategies represents a promising paradigm shift in mental health care. Fermented foods, rich in beneficial microorganisms and bioactive metabolites, have demonstrated potential to positively influence mood, cognitive function, and stress resilience through modulation of the gut-brain axis. Emerging preclinical and clinical evidence suggests that psychobiotics may alleviate symptoms of stress, anxiety, and depression through multiple mechanisms, including the production of short-chain fatty acids (SCFAs), regulation of neurotransmitter systems, and modulation of inflammatory and endocrine responses. Although this field remains in its early stages, current findings highlight significant therapeutic potential. However, more rigorous and large-scale human clinical trials are required to establish causal relationships, optimize intervention protocols, and elucidate the precise biological mechanisms involved. As research continues to advance, targeted nutritional interventions and psychobiotic-based therapies may offer innovative, sustainable, and personalized approaches for the prevention and management of mental health disorders. Continued exploration of the gut-brain axis will be essential for unlocking the full therapeutic potential of fermented foods and psychobiotics in mental health care.

7. Future prospects

Future research should focus on conducting large-scale, well-designed randomized controlled clinical trials to establish definitive evidence regarding the efficacy of fermented foods and psychobiotics in preventing and managing mental health disorders. Most available evidence remains limited by small sample sizes, short intervention durations, heterogeneity in fermented food matrices, and variability in microbial strains, making it difficult to derive standardized therapeutic recommendations. Future investigations should prioritize strain-specific characterization, optimal dosage determination, duration of intervention, and long-term safety assessment across diverse population groups. Additionally, integrating multi-omics approaches, including metagenomics, metabolomics, and transcriptomics, will help elucidate the precise molecular mechanisms through which psychobiotics influence neurotransmitter regulation, immune signaling, hypothalamic pituitary adrenal axis modulation, and gut barrier integrity.

Another important direction lies in advancing personalized nutrition-based psychobiotic interventions tailored to individual gut microbiota profiles, dietary habits, and mental health status. The development of functional fermented foods enriched with targeted psychobiotic strains offers significant potential for creating accessible, non-pharmacological adjunct therapies for anxiety, depression, stress-related disorders, and cognitive decline. Future studies should also explore the synergistic role of psychobiotics with prebiotics, synbiotics, and conventional psychiatric treatments to enhance therapeutic outcomes. Furthermore, expanding research toward underexplored traditional fermented foods from diverse cultural systems may uncover novel microbial strains with psychobiotic properties, thereby broadening the scope of dietary strategies for promoting mental resilience and supporting precision mental healthcare.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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