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Enhancing Cognitive Health with Psychobiotics

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ABSTRACT

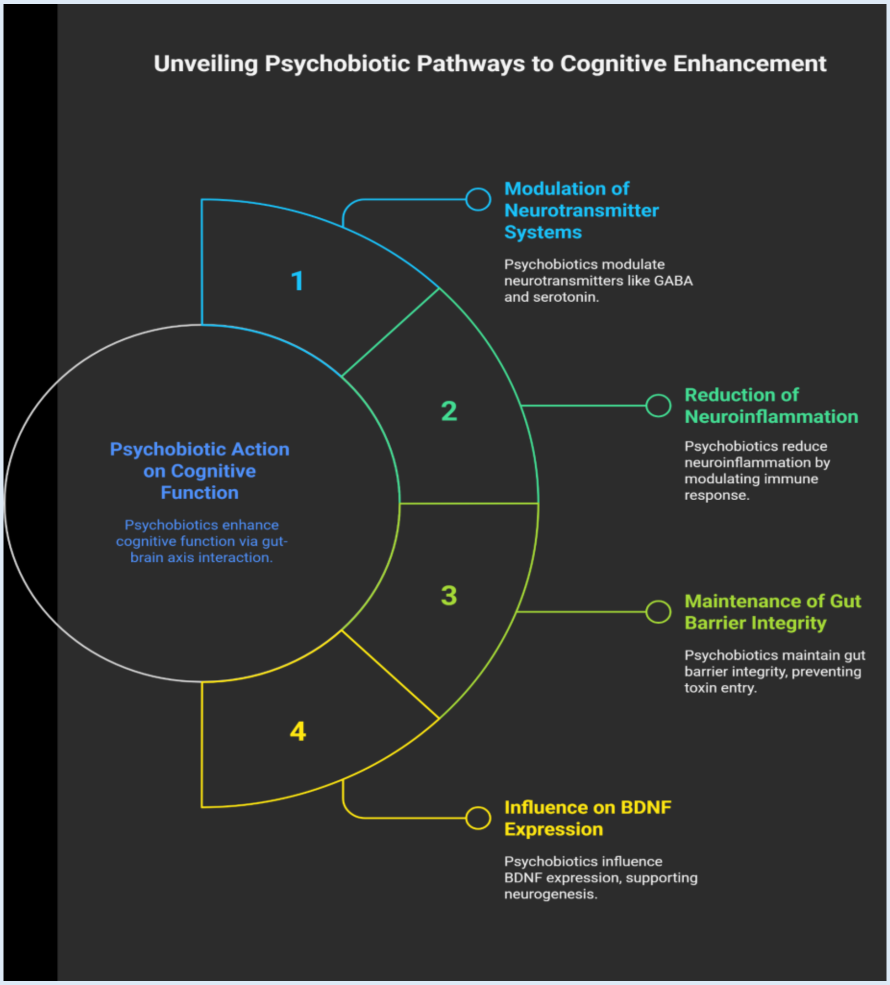
The intricate connection between the gut microbiota and brain function, known as the gut-brain axis, has opened novel avenues for addressing cognitive health challenges. **Psychobiotics**, defined as probiotics or prebiotics that confer mental health benefits, are gaining considerable attention for their potential therapeutic roles. This review comprehensively explores the emerging landscape of psychobiotics found in fermented foods, focusing specifically on their mechanisms of action via bioactive compounds and their utility in managing cognitive disease-related symptoms and preventing neurodegenerative conditions.

We synthesize current research on how specific psychobiotic strains and the bioactive molecules they produce or modulate (e.g., short-chain fatty acids, neurotransmitters, amino acids, polyphenols) interact with the gut-brain axis to influence neuroinflammation, oxidative stress, and neural plasticity, thereby impacting cognitive function. The review highlights evidence from in vitro, in vivo, and preliminary human studies that underscore the promise of fermented food-derived psychobiotics as a novel, diet-based strategy for supporting cognitive health and potentially mitigating the onset or progression of cognitive decline.

While significant advancements have been made, further rigorous clinical trials are essential to elucidate optimal strains, dosages, and long-term efficacy, paving the way for developing targeted functional foods for cognitive support.

Novelty of the Study: This review is among the first to comprehensively analyze the role of psychobiotics explicitly derived from fermented foods in supporting cognitive function through the gut-brain axis. It uniquely highlights how these food-based microorganisms influence neuroinflammation, oxidative stress, and neurotransmitter pathways via bioactive compounds. The work also introduces the emerging concept of functional fermented foods as viable dietary tools for early cognitive support and neurodegenerative disease prevention.

Keywords: Psychobiotics, Fermented Foods, Cognitive Health, Gut-Brain Axis, Bioactive Compounds, Neurodegeneration, Functional Food, Probiotics, Prebiotics



Graphical Abstract: Enhancing Cognitive Health with Psychobiotics

INTRODUCTION

With recent projections indicating that nearly 42% of Americans over the age of 55 may experience symptoms of dementia in their lifetime [1] and over 23.1% of the US population living with some form of mental illness [2], the importance of early, non-invasive interventions has become increasingly apparent. Dietary strategies that enhance gut microbial balance, such as consuming fermented or fiber-rich functional foods, can play a preventative role in the rising burden of cognitive and mental health disorders. As such, leveraging the gut-brain axis through nutrition may offer a promising avenue for preserving brain health across the lifespan.

Recent research has highlighted the critical role of the gut-brain axis (GBA)—a complex, bidirectional communication network linking the gastrointestinal tract, the microbiome, and the central nervous system—in supporting cognitive function and mental health. This system facilitates the exchange of neural, hormonal, and immunological signals, allowing the gut and brain to influence one another's physiology and behavior. Disruptions to this axis, particularly through dysbiosis, an imbalance in gut microbial composition, have been increasingly associated with a range of neuropsychiatric conditions, such as depression, anxiety disorders, and autism spectrum disorder [3]. Furthermore, specific strains of probiotic and commensal bacteria have demonstrated the ability to modulate stress-related gut-brain axis symptoms, such as cognitive performance, memory retention, and even patterns of resting brain activity [4]. These findings emphasize the potential of targeting the gut microbiome as a novel strategy for supporting neurological health.

Although treatments for cognitive and neuropsychiatric disorders have become increasingly accessible to the global population and have rapidly advanced as a result of growth in technology and biomedical knowledge, conventional methods of treatment possess multiple limitations. For instance, in Alzheimer's disease, one of the most common neurodegenerative diseases worldwide, administering treatment is crucial in the early stages, as these studies have shown there to be no statistically significant clinical improvement nor impediment of disease progression when anti-amyloid immunization is dispensed during advanced stages [5]. In terms of major depressive disorders, recent research demonstrates that, in placebo-controlled studies of tricyclic antidepressants, 69% of studies did not find a substantial benefit in comparison to placebo [6]. Alongside the slow onset of therapeutic response and issues with compliance and sleep disturbances [6], antidepressants exhibit several issues that indicate other forms of treatment must be investigated.

A newly emerging perspective on improving cognitive health can be found in the field of psychobiotics, a form of probiotic that, when given in the correct dosage, has the potential to be beneficial in subjects with neurological or psychiatric illnesses [7]. Recent research has illustrated that psychobiotics can survive in fermented food and can have a direct impact on the production of neurotransmitters (i.e. GABA, serotonin, and dopamine), activation of gut-brain neural pathways, and modulation of neurotrophic chemicals such as the brain-derived neurotrophic factor (BDNF) [7.] Psychobiotic diets have been shown to decrease perceived stress in a human cohort [8] and even demonstrate efficacy in treating depression with some strains [9]. As such, further investigation into the mechanisms of psychobiotics and their ability to survive in fermented foods is valuable as it can uncover novel ways of treating cognitive disorders.

This short review will synthesize current research and findings on the benefits and limitations of psychobiotics in fermented foods. Specifically, this review will focus on the bioactive compounds and biological mechanisms utilized by psychobiotics that are relevant to managing and preventing neurological and psychiatric disorders and symptoms.

The Gut-Brain Axis: A Foundation for Cognitive Health: The colonization of the gastrointestinal (GI) tract by commensal microbiota and their impact on the gut-brain axis has been the subject of much attention in recent years [10]. The pathophysiology of numerous neurological and psychological diseases, such as schizophrenia, epilepsy, migraine, depression, Parkinson's disease, and autism spectrum disorder (ASD), has been linked to psychological stress and inflammation and has shared comorbidities with gut diseases such as inflammatory bowel disease or irritable bowel syndrome [10].

Gut microbiota have been shown to interact with the immune system through microbial-derived metabolites, namely short-chain fatty acids (SCFAs), secondary bile acids, amino acid metabolites, and other bioactive molecules. Since bacteria must travel through the intestinal barrier to enter the circulation, gut microbiota are regulators of enteric immunity. They also play a role in translocating immune cells from the gut to the brain, wherein they interact with immune cells through paracrine signaling and "train" them to relocate to the central nervous system (CNS) to perform their designated functions [11]. Gut microbiota can also synthesize vitamins, specifically vitamin K and vitamin B12 [7], alongside the capacity to ferment complex carbohydrates such as cellulose and starch to produce short/branched-chain fatty acids that are a necessary energy source for colonocytes, epithelial cells lining the colon. Regarding contributions to cognitive health, specific intestinal microbiota can produce and release neuroactive compounds, namely neurotransmitters (GABA, dopamine, serotonin, and glutamate), cytokines, chemokines, and neuropeptides. These molecules can reach the brain through blood circulation, transporter molecules, or other cells, which profoundly influence gut flora on cognitive function and mental health [12].

Dysbiosis, or gut microbiome disruptions, is linked to mood disorders and a severe disruption of the gut-brain axis [3]. Imbalanced gut microbiota interferes with the hypothalamic-pituitary-adrenal (HPA) axis, which leads to elevated cortisol levels and adrenocorticotropic hormone levels. This hormone imbalance is associated with increased intestinal permeability, resulting in heightened stress and anxiety levels [13]. It has also been shown that gut-brain axis activity is regulated by calcitonin gene-related peptide (CGRP). Following gut microbiota disruption from pathogenic microorganisms, neurons may release CGRP into the gut, which activates host immune responses via the calcitonin receptor-like receptor (CRLR). Probiotic organisms can help rebalance the intestinal microbiota and support gut-brain signaling, including CGRP-mediated pathways. CRH enhances intestinal permeability and ACTH levels during neurological stress, linking gut dysbiosis to altered cognitive function and emotional health [13]. Given the importance of the gut-brain axis, modifying the gut microbiota through targeted interventions may aid in treating and managing neurological and psychiatric disorders.

Psychobiotics from Fermented Foods: Sources and Bioactive Compounds. There is a wide range of bacterial strains that have the potential to serve as psychobiotics, with each having unique psychiatric effects and differing dosages. For instance, the strain *B. longum* 1714, when taken at a dosage of 1 x 10^9 CFU/day mixed into milk drunk in the morning for 4 weeks, was observed to decrease stress and enhance memory in subjects [13]. A multi-strain probiotic, containing *Bacillus coagulans* Unique IS2, *L. rhamnosus* UBLR58, *B. lactis* UBBLa70, *L. plantarum* UBLP40, *B. breve* UBBr01, and *B. infantis* UBBI01, at a dosage of 1 x 10^9 CFU/capsule taken twice daily for 28 days, was demonstrated to reduce rating on a depression-anxiety-stress scale significantly [13].

Food fermentation dates back to 7000 B.C., between the late Neolithic period and the Shang Dynasty in China [14]. Following the domestication of livestock such as goat, sheep, and cattle, alongside the cultivation of crops following the Agricultural Revolution in the Fertile Crescent of Southwestern Asia, it was found that meat and milk possessed a short storage period before they began to spoil. Fermentation allowed milk to have an extended shelf life in the form of cheese, which saved food for times of scarcity [15]. Fermentation has also been utilized for plants (fruits, seeds, tubers, vegetables) and animal byproducts (meat, fish, eggs) [16].

Fermented foods are a suitable environment for probiotic bacteria to thrive. Many fermented foods have probiotics purposefully added during the manufacturing process, or spontaneously develop, such as non-starter lactic acid bacteria found in cheese [17,18]. In terms of the presence of psychobiotics, fermented foods such as yogurt, kefir, fermented soy, fermented milk, fermented seaweed, and fermented rice bran are high in psychobiotic strains, such as *L. acidophilus, B. lactis BB12, L. reuteri, L. kefiranofaciens, L. brevis, L. plantarum C29, L. helveticus, L. casei, L. brevis BJ20,* and *S. cerevisiae IFO 2346*, which have been demonstrated to provide mental health benefits such as reduced anxiety, improved memory, enhanced cognition, reduced stress, and protection against cognitive decline [13].

Among the key bioactive compounds in psychobiotics that allow them to contain beneficial therapeutic effects, some of the most significant are the microbial metabolites they produce through fermentation. One primary class of metabolites is short-chain fatty acids (SCFAs), such as acetate, propionate, and butyrate [19]. SCFAs can serve as signaling molecules, as evidenced by butyrate's (and to a lesser extent, propionate's) ability to act as histone deacetylase (HDAC) inhibitors, allowing them to have a role in gene regulation and expression [20]. SCFAs can also regulate the permeability of the blood-brain barrier, thereby significantly impacting brain function and behavior, as studies in mice have shown that increased blood-brain barrier permeability can result in hyperactivity and spatial memory impairment [20,21].

Psychobiotics also produce neuroactive metabolites in the form of neurotransmitters, namely gamma-aminobutyric acid (GABA), serotonin (5-HT), dopamine, acetylcholine, and norepinephrine. While they are produced in the gut, they can directly influence the CNS through the vagus nerve, alongside immune signaling through cytokines and through the circulatory system by entering the bloodstream and crossing the blood-brain barrier [22]. Psychobiotics can regulate host tryptophan metabolism, crucial for serotonin production, as nearly 90% of the body's serotonin is produced in the gut [23]. Certain bacterial strains, such as *Lactobacillus* and *Bifidobacterium*, can produce GABA, which helps regulate neuronal excitability and reduces anxiety and depression [23]. Changes in neurotransmitter levels are linked to alterations in behavior, such as anxiety, depression, and stress, and cognitive functions, namely memory and learning [22].

In addition to the previously mentioned microbially produced metabolites, certain strains of psychobiotics (*Bifidobacterium* and *Lactobacillus*) can also synthesize neuroactive vitamins, such as: vitamin B1 (thiamine), which is necessary for neuronal energy metabolism; vitamin B6 (pyridoxine), crucial for synthesizing neurotransmitters, namely serotonin and dopamine; vitamin B9 (folate), which is involved in the methylation process for gene expression in the brain; and vitamin B12 (cobalamin), which plays a vital role in myelin formation and thus cognitive function [24]. Understanding the vitamin-producing capabilities of gut flora can profoundly impact the development of targeted psychobiotics aimed at enhancing mental health through nutritional pathways.

Alongside the metabolites they produce through fermentation, psychobiotics and gut microbiota play a crucial role in enhancing the bioavailability and efficacy of plant-derived bioactives, particularly polyphenols. A recent study emphasizes that polyphenols (naturally occurring compounds in fruits, vegetables, tea, and cocoa) undergo microbial metabolism in the colon, transforming into smaller phenolic acids with significantly improved absorption and biological activity [25]. This biotransformation boosts their antioxidant and anti-inflammatory properties and modulates the gut microbiota composition itself, fostering the growth of beneficial bacteria such as Bifidobacteria and Lactobacilli. These microbial changes, in turn, influence host physiology, including neuroimmune signaling pathways linked to the gut-brain axis. Such findings are directly relevant to the discussion of psychobiotics and cognitive health, as they suggest that dietary interventions rich in polyphenols, when paired with a healthy, diverse gut microbiome, may enhance neuroprotection, reduce neuroinflammation, and support mental well-being through improved gut-brain communication [25].

Mechanisms of Psychobiotic Action on Cognitive Function: Psychobiotics exert multifaceted effects on cognitive function by interacting with the gut-brain axis. One key mechanism involves the modulation of neurotransmitter systems; certain psychobiotic strains, such as *Lactobacillus plantarum*, have been shown to influence the production of gamma-aminobutyric acid (GABA) and serotonin, which are neurotransmitters integral to mood regulation and cognitive processes [23]. Additionally, psychobiotics can impact neuroinflammation by modulating the immune response; they may reduce the production of pro-inflammatory cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), thereby mitigating inflammation-related cognitive impairments [26].

In tandem with their abilities to regulate neurotransmitters, psychobiotics play a crucial role in maintaining gut barrier integrity and function. A condition known as “leaky gut syndrome,” also known as intestinal hyperpermeability, occurs when the lining of the small intestine is disrupted, resulting in substances intended to remain in the gut, such as food particles and toxins, entering the bloodstream. This results in inflammation and irritation as an immune response is incurred [27]. By preserving gut integrity through maintaining tight junctions in the intestinal lining, preventing toxins from entering the bloodstream, psychobiotics can safeguard brain function [28]. Specifically, psychobiotics can regulate the gene expression of tight junction (TJ) proteins, which play a crucial role in sustaining the selective permeability of the intestinal epithelium. TJ proteins such as occludin, claudins, and zonula occludens (ZO-1) form complexes that seal the spaces between epithelial cells, preventing the translocation of harmful substances into systemic circulation [29]. Specific psychobiotic strains of psychobiotics, such as Lactobacillus plantarum MB452, demonstrate the ability to upregulate genes encoding TJ proteins, thereby strengthening the intestinal barrier. Additionally, in vitro studies using Caco-2 cell monolayers illustrate that treatment with *L. plantarum* MB452 increases the expression of occludin and ZO-1, resulting in enhanced barrier function and reduced permeability [30].

While more in-depth research is still ongoing, psychobiotics can potentially influence brain-derived neurotrophic factor (BDNF), potentially supporting neurogenesis and the repair of neurons. In a study conducted in 2023, n=60 patients diagnosed with major depressive disorder (MDD) underwent a 4-week high-dose probiotic regimen alongside their usual depression treatment. The study found that the probiotic group exhibited significant enhancements in immediate verbal recall, as measured by the Verbal Learning Memory Test (VLMT), immediately following the intervention, supporting the notion that probiotics and thus psychobiotics may bolster hippocampus-dependent memory functions. Additionally, fMRI scans revealed a normalization of hippocampal activation during working memory tasks in the probiotic group, indicating improved neural efficiency in regions associated with memory processing. While the study depicted a slight, non-significant increase in serum BDNF levels in the probiotic group and a decrease in the placebo group, the change direction aligns with previous studies suggesting that probiotics can affect BDNF concentrations [31]. The properties of psychobiotics, namely their abilities to restore the gut microbiota balance and modulate the HPA axis, may lead to improved hippocampal function and increased BDNF expression [31].

Evidence for Cognitive Support: Multiple in vivo studies have been conducted on animal models and have illustrated the potential applications of psychobiotics in fermented food products. For instance, in a clinical trial administering fermented soybean containing a strain of *Lactobacillus plantarum* C29 to mice at 800 mg/day for 12 weeks, the subjects demonstrated improved cognitive function in individuals with mild cognitive impairment [32]. In a similar study, administering kefir containing *Lactobacillus reuteri* to mice every 1 hour through oral gavage for a total of 3 weeks, the mice had increased GABA production in their gut microbiota [33]. Another murine study focused on fermented milk containing *Lactobacillus brevis* FPA 3709 at a dosage of 35-70 mg/kg body weight by oral gavage for 28 days demonstrated effects mirroring those of antidepressants, sans typical side effects in rat models [34]. Given the success rate of psychobiotics producing statistically significant clinical impact in mice, there is clear evidence that these effects can be translatable to human subjects on a broader scale, especially if given further focus and development on discovering the most effective strains at counteracting particular neurological and psychiatric conditions.

Preliminary human studies have been conducted, and while the results are not as conclusive as those of the animal models, they generally show similar outcomes. One clinical trial focusing on the strain *Lactobacillus casei* Shirota that administered 100 mL of a fermented beverage containing > 1×10^9 CFU/mL/day to medical students experiencing academic examination stress shows that the experimental group had higher fecal serotonin levels and a lower rate of subjects experiencing abdominal and cold symptoms, alongside a reduction in the average duration experiencing these symptoms, compared to the placebo group [35]. Another clinical trial involving *Bifidobacterium longum* taken at a dosage of 1×10^{10} CFU/g/trial on patients with irritable bowel syndrome resulted in a reduction in depression scores in the Hospital Anxiety and Depression Scale, alongside reduced responses to negative emotional stimuli [36]. The mechanism was speculated to be the release of neuroactive compounds through signaling pathways in the vagus nerve, alongside BDNF regulation [37].

Several psychobiotic strains and fermented foods appear to be more promising than others as a result of numerous research studies and have been identified as possessing significant cognitive benefits that are worth further investigation. These strains include *Lactobacillus plantarum* C29, which is associated with improved cognitive function in MCI patients; *Lactobacillus brevis* FPA 3709, which has demonstrated prominent antidepressant effects in animal studies; and *Lactobacillus gasseri* CP2305, which has been linked to stress alleviation and improved sleep quality [37]. Regarding fermented foods, kimchi, fermented soy products, and kefir all contain diverse probiotic strains linked to improved emotional regulation, reduced depressive symptoms, enhanced cognitive function, reduced neuroinflammation, and improved memory and executive function [37].

Table 1 presents a summary of key findings regarding particular psychobiotic strains and their reported effects on mental health disorders.

Table 1. Summary of Psychobiotic Strains, Fermented Food Sources, and Mental Health Effects

Strain/Species	Fermented Food Source	Reported Effect	Reference
Lactobacillus plantarum **MB452**	Probiotic supplement	Enhances intestinal barrier function via tight junction genes	[30]
Lactobacillus casei **Shirota**	Fermented milk	Prevents physical stress symptoms under academic examination stress	[35]
Lactobacillus brevis **FPA 3709**	Black soybean milk	Antidepressant effect without side effects in a forced swimming rat model	[34]
Lactobacillus reuteri	Kefir	Increased GABA production in the gut microbiome	[33]
Bifidobacterium longum	Powder in lactose-free milk, soy milk, or rice milk	Reduction in depression scores in the Hospital Anxiety and Depression Scale; reduced responses to negative emotional stimuli	[36]
Lactobacillus plantarum C29	Fermented soybean	Improved cognitive function in individuals with mild cognitive impairment	[32]
Bacillus coagulans **Unique IS2, *L. rhamnosus* UBLR58, *B. lactis* UBBLa70, *L. plantarum* UBLP40, *B. breve* UBBr01, and *B. infantis* UBBI01**	Capsule	Reduce rating on a depression-anxiety-stress scale	[13]
Lactobacillus gasseri **CP2305**	Fermented milk	Stress alleviation and improved sleep quality	[37]

Future Perspectives and Challenges: After reviewing recent studies and literature, future researchers must consider numerous challenges when investigating the potential of psychobiotics in fermented foods.

The breadth of probiotic strains available to study makes standardizing and characterizing different strains, doses, and formulations difficult, causing issues for researchers hoping to cross-compare against other studies. Since the efficacy and specific properties of psychobiotics differ wildly even across strains in the same species, it can be tough to replicate and validate findings properly. As a result, it is necessary to thoroughly compare the effects of different strains and replicate strain-level conclusions from earlier studies to make more statistically significant conclusions about the results of a study [38].

Another limitation of current literature is the nature of human clinical trials, which lack clinical efficacy compared to their animal model counterparts, which show much more definitive results. Since human trials tend to have a much smaller sample size and possess high heterogeneity among their participants, there tends to be significant inconsistency in the degree of statistical significance between in vivo human and animal studies. Although the gut microbiota of rats and mice tends to resemble the human gut microbiota highly, there is enough diversity in human microbiota and the symptoms of various neuropsychiatric disorders, such as depression, to warrant a method of standardizing or characterizing specific gut microbiome profile composition to make the results of studies more conclusive [39].

Effective dosage, method of delivery of psychobiotics, and the wide variety of fermented foods cause high variation between studies, which makes it challenging to draw concise conclusions on the potency and effectiveness of psychobiotics. Given that the effects of psychobiotics are highly strain-specific, studies require precise dosing to achieve therapeutic benefits. However, a lack of standardization across studies makes it challenging to determine optimal dosages. Ensuring the viability of psychobiotic strains through effective delivery methods is also a significant hurdle, as factors like stomach acidity can compromise their survival.

Formulation strategies, such as encapsulation and pairing with prebiotics, are suggested to enhance stability and efficacy. Researchers stress the need for rigorous clinical trials to refine dosage and delivery protocols and highlight the potential for personalized approaches based on individual gut microbiota differences [40].

Evaluation as a Functional Food: The classification of psychobiotic-rich fermented foods as functional foods has garnered increasing attention due to their potential to confer health benefits beyond basic nutrition, specifically mental health. According to the Functional Food Center, functional foods are defined as those that provide health benefits beyond their nutritional value through bioactive compounds that positively impact physiological functions [41].

Fermented foods such as kimchi, sauerkraut, and tempeh are rich sources of beneficial bacteria, including strains like Lactobacillus plantarum, Leuconostoc mesenteroides, and Bifidobacterium species. These psychobiotic strains have been associated with mental health benefits through mechanisms such as neurotransmitter modulation (e.g., serotonin and GABA production), inflammation reduction, and HPA axis regulation [42].

An emerging area of interest within this framework is the identification of specific psychobiotic strains, such as those derived from human breast milk, which exhibit pronounced mental health benefits. When incorporated into fermented food matrices like yogurt, these strains may enhance probiotic viability and activity, thereby strengthening their functional role in supporting emotional and cognitive health [43]. As such, psychobiotics exemplify functional foods by delivering measurable, condition-specific outcomes, which fit the Functional Food Center's definition through their targeted action on the gut-brain axis.

Another example of psychobiotics aligning with the definition of functional foods is the probiotic yeast Saccharomyces cerevisiae var. boulardii, which offers diverse health-promoting effects. Historically consumed unintentionally through fermented foods, this eukaryotic probiotic is now deliberately incorporated into diets and functional products due to its antimicrobial, anti-inflammatory, immunomodulatory, and gut-supportive properties. Its clinical efficacy in treating gastrointestinal and systemic conditions underscores its potential as a functional food component, especially when delivered through fermented carriers that amplify biological and sensory benefits [44].

Recent studies have further elucidated the role of fermented foods rich in psychobiotics in modulating mental health through the gut-brain axis. For instance, a 2022 study demonstrated that probiotics found in fermented foods like kimchi and miso can positively influence gut bacteria and neurotransmitter levels, leading to reduced anxiety and depression symptoms in animal models. These findings suggest that incorporating such fermented foods into the diet may offer mental health benefits, although more human studies are needed to confirm these effects [45].

Moreover, recent research has highlighted the potential of specific psychobiotic strains in modulating mental health through the gut-brain axis. Lactobacillus plantarum PS128, for instance, has demonstrated promising effects in both animal models and human studies. In murine models, chronic administration of PS128 led to increased levels of dopamine and serotonin in the striatum, correlating with reduced anxiety-like behaviors [46]. Furthermore, a randomized, double-blind, placebo-controlled pilot trial involving self-reported insomniacs found that PS128 supplementation resulted in decreased depressive symptoms and fatigue, as well as improved sleep quality [47]. These findings suggest that PS128 may exert its psychotropic effects by modulating neurotransmitter levels and improving sleep parameters [48].

Similarly, Bifidobacterium longum 1714 has been investigated for its impact on stress and cognitive function. Bifidobacterium longum 1714 has been shown to reduce perceived stress and improve sleep quality in healthy adults [49]. In a study involving healthy volunteers, consumption of B. longum 1714 was associated with reduced cortisol output and subjective anxiety in response to a socially evaluated cold pressor test. Additionally, participants exhibited subtle improvements in hippocampus-dependent visuospatial memory performance and enhanced frontal midline electroencephalographic mobility. Similarly, Lactobacillus plantarum PS128 has been associated with decreased depressive symptoms and fatigue and improved sleep quality in individuals with insomnia [50]. In patients with anxiety disorders, PS128 supplementation alongside standard treatment resulted in greater symptom improvement compared to treatment alone [51]. These results indicate that B. longum 1714 and L. plantarum PS128 may modulate stress responses and cognitive processes, further supporting its classification as a functional food component with psychobiotic properties [52,53].

Recent research highlights the potential of fermented foods to modulate neuroinflammation by influencing microglial activity, which plays a critical role in the development and progression of neuropsychiatric disorders such as depression, anxiety, and neurodegeneration [37,54]. Microglia are the brain's resident immune cells responsible for maintaining neural homeostasis and responding to inflammatory stimuli. Their dysregulation is linked to heightened neuroinflammatory states associated with mental health disorders [55]. Certain psychobiotic strains found in fermented foods, including Lactobacillus and Bifidobacterium species, have attenuated microglial activation and reduced pro-inflammatory cytokine production in vitro and in animal models [56-57]. For example, supplementation with Lactobacillus plantarum and Bifidobacterium longum has been demonstrated to decrease levels of IL-6 and TNF-α in the brain, improving anxiety- and depression-like behaviors [58]. These findings suggest that fermented foods could serve as functional dietary interventions that support mental health by targeting neuroinflammatory pathways and promoting microglial regulation, thus offering a novel angle for psychobiotic application beyond traditional neurotransmitter modulation. These neuroinflammation-modulating effects of psychobiotic strains found in fermented foods further support their classification as functional foods, as they provide targeted health benefits beyond basic nutrition by promoting brain health through the gut-brain axis.

Emerging evidence suggests that psychobiotics found in fermented foods may enhance neuroplasticity and cognitive resilience, offering protective effects against cognitive decline and stress-related impairments. Studies have shown that certain strains, such as Lactobacillus rhamnosus and Bifidobacterium breve, can upregulate BDNF expression, a key modulator of synaptic plasticity and neuronal survival [59,60]. This neurotrophic support correlates with learning, memory, and mood regulation improvements observed in animal models and clinical trials [61,62]. Additionally, fermented foods containing psychobiotics have been reported to modulate neurogenesis in the hippocampus, a brain region crucial for memory and emotional regulation [63]. The enhancement of gut barrier integrity and reduction of systemic inflammation further contribute to an optimal environment for neuroplasticity [64,65]. These multifactorial benefits underscore the potential of psychobiotic-rich fermented foods as functional foods that support brain health and cognitive function through diverse biological pathways.

Table 2 summarizes key psychobiotic-rich fermented foods, their associated strains, mechanisms of action, mental health benefits, and supporting references.

Table 2. Psychobiotic-Rich Fermented Foods as Functional Foods for Mental Health

Food Source/Matrix	Psychobiotic Strains	Mechanism of Action	Health Outcomes	References
Kimchi, Sauerkraut, Tempeh	Lactobacillus plantarum, Leuconostoc mesenteroides, Bifidobacterium spp.	Neurotransmitter modulation (e.g., serotonin, GABA), anti-inflammatory, HPA axis regulation	Reduced anxiety and depression symptoms, improved gut-brain axis signaling	[42], [45]
Yogurt (with human-derived strains)	Human breast milk-derived Lactobacillus, Bifidobacterium	Enhanced probiotic viability, gut-brain modulation	Support for emotional and cognitive health	[43]
Fermented food carriers	Saccharomyces cerevisiae var. boulardii	Antimicrobial, immunomodulatory, anti-inflammatory, gut barrier protection	Gastrointestinal support, potential mental health benefit	[44]
Miso, Kimchi	Mixed Lactobacillus and Bifidobacterium spp.	Neurotransmitter production, microbial diversity enhancement	Reduced anxiety/depression in animal models	[45]
Yogurt, capsules (PS128)	Lactobacillus plantarum PS128	Dopamine and serotonin elevation, sleep quality improvement	Reduced anxiety, depression, and fatigue; improved sleep	[46-48]
Yogurt, capsules (B. longum 1714)	Bifidobacterium longum 1714	Cortisol reduction, improved EEG patterns, memory support	Reduced stress and anxiety; enhanced cognitive flexibility	[49-53]
Fermented soy (tempeh)	Rhizopus oligosporus plus Lactobacillus spp.	Gut barrier enhancement, cytokine reduction	Cognitive improvement, anti-inflammatory	[58], [63]
Kombucha	Mixed bacterial and yeast cultures	Antioxidant effects, gut microbiota modulation	Mood improvement, stress reduction	[64], [65]

While fermented foods containing psychobiotics hold promise as functional foods for mental health support, further research is needed to fully understand their efficacy, optimal strains and dosages, and the mechanisms underlying their effects. Standardization of fermentation processes and comprehensive clinical trials will be essential in establishing clear guidelines for their use in promoting cognitive and emotional well-being.

Scientific Innovation: The paper brings forward an interdisciplinary synthesis linking microbiology, neuroscience, and nutrition to spotlight fermented psychobiotics as innovative, non-invasive alternatives to pharmacological cognitive therapies. By focusing on strain-specific mechanisms and emphasizing the importance of developing robust biomarkers and standardized interventions, the review lays a foundation for advancing personalized psychobiotic nutrition.

Practical Implications: Fermented foods enriched with targeted psychobiotic strains could become a widely accessible, cost-effective strategy to enhance mental well-being, especially in populations at risk for cognitive decline. With additional clinical validation, these foods may serve as dietary adjuncts for managing mood disorders, chronic stress, and mild cognitive impairment, potentially reducing reliance on conventional medications.

CONCLUSION

As the global burden of cognitive decline and mental health disorders continues to rise, driven by an aging population and increased psychosocial stressors, the search for novel, non-invasive, and preventative therapeutic approaches becomes more urgent. This review has synthesized mounting evidence highlighting the gut-brain axis as a crucial mediator in neurological and psychological health, with psychobiotics emerging as a promising intervention. Specifically, psychobiotics derived from fermented foods offer a unique and accessible dietary strategy to support brain function, mood regulation, and resilience against stress.

The mechanisms by which psychobiotics influence the central nervous system are multifaceted, involving modulation of neurotransmitter pathways, reduction of neuroinflammation, preservation of gut barrier integrity, and the production of neuroactive compounds, including short-chain fatty acids, vitamins, and polyphenol metabolites. These mechanisms highlight the complexity of gut-brain communication and emphasize the therapeutic potential of targeting the microbiome to modulate brain health. Numerous psychobiotic strains have been repeatedly shown to positively affect stress, mood, memory, and cognition, particularly when delivered in functional fermented food matrices such as kefir, yogurt, kimchi, and fermented soy products.

However, despite promising findings from animal models and early human trials, several challenges remain, such as the limited scale of human clinical studies, inconsistent methodologies, lack of strain-specific standardization, and variability in dietary and genetic factors among participants. Additionally, the mechanisms underlying psychobiotic action in humans are still not fully understood, particularly regarding long-term effects and interactions with host-specific microbiota compositions. Future research must prioritize large-scale, double-blinded clinical trials with clearly defined psychobiotic strains, standardized dosages, and longitudinal assessments to better capture the dynamic nature of gut-brain interactions.

Another equally important factor to the success of psychobiotics is the development of robust, strain-specific biomarkers to evaluate psychobiotic efficacy and a better understanding of the host-microbe-environment triad that modulates mental health outcomes. Advances in metagenomics, metabolomics, and neuroimaging may help address these gaps by enabling researchers to draw clearer causal relationships between microbial composition, metabolite production, and neurological function.

Nonetheless, integrating psychobiotics into daily dietary practices represents a compelling frontier in preventive health care. Fermented foods enriched with targeted psychobiotic strains could eventually serve as adjuncts, or even alternatives, to conventional pharmacological treatments, particularly in cases of mild cognitive impairment, chronic stress, and mood disorders. The interdisciplinary nature of this field, encompassing microbiology, neuroscience, nutrition, and psychology, underscores the importance of collaborative research efforts to unlock the full therapeutic potential of psychobiotics.

In conclusion, while we are still at the early stages of fully understanding and harnessing the power of psychobiotics from fermented foods, current evidence strongly supports their role as a natural, sustainable, and accessible intervention to improve cognitive and mental health outcomes. With further validation and refinement, psychobiotics may become essential to personalized nutrition and mental health care in the 21st century.

Abbreviations: GBA: gut-brain axis; MDD: major depressive disorder; CGRP: calcitonin gene-related peptide; BDNF: brain-derived neurotrophic factor; ASD: autism spectrum disorder; VLMT: Verbal Learning Memory Test; SCFAs: short-chain fatty acids; HDAC: histone deacetylase

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REFERENCES

1. Doctrow B. Risk and future burden of dementia in the United States. National Institutes of Health (NIH). 2025. [cited 2025 May 23] Available from: https://www.nih.gov/news-events/nih-research-matters/risk-future-burden-dementia-united-states.
2. National Institute of Mental Health. Mental Illness [Internet]. National Institute of Mental Health; 2024. [cited 2025 May 23] Available from: https://www.nimh.nih.gov/health/statistics/mental-illness
3. Carabotti M, Scirocco A, Maselli MA, Severi C. The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. *Ann Gastroenterol.* 2015;28(2):203-209.
4. Casertano M, Fogliano V, Ercolini D. Psychobiotics, gut microbiota and fermented foods can help preserving mental health. *Food Res Int.* 2022;152:110892. DOI: https://doi.org/10.1016/j.foodres.2021.110892.
5. Passeri E, Elkhoury K, Morsink M, Broersen K, Linder M, Tamayol A, et al. Alzheimer's disease: treatment strategies and their limitations. *Int J Mol Sci.* 2022;23(22):13954. DOI: https://doi.org/10.3390/ijms232213954.
6. Lader M. Limitations of current medical treatments for depression: disturbed circadian rhythms as a possible therapeutic target. *Eur Neuropsychopharmacol.* 2007;17(12):743-755. DOI: https://doi.org/10.1016/j.euroneuro.2007.05.004.
7. Cichońska P, Kowalska E, Ziarno M. The survival of psychobiotics in fermented food and the gastrointestinal tract: a review. *Microorganisms.* 2023;11(4):996. DOI: https://doi.org/10.3390/microorganisms11040996.
8. Berding K, Bastiaanssen TFS, Moloney GM, Boscaini S, Strain CR, Anesi A, et al. Feed your microbes to deal with stress: a psychobiotic diet impacts microbial stability and perceived stress in a healthy adult population. *Mol Psychiatry.* 2023;28(2):601-610. DOI: https://doi.org/10.1038/s41380-022-01817-y.
9. Dinan TG, Butler MI, Cryan JF. Psychobiotics: evolution of novel antidepressants. *Mod Trends Psychiatry.* 2021; 32:134-143. DOI: https://doi.org/10.1159/000510424.
10. Socała K, Doboszewska U, Szopa A, Serefko A, Włodarczyk M, Zielińska A, et al. The role of the microbiota-gut-brain axis in neuropsychiatric and neurological disorders. *Pharmacol Res.* 2021;172:105840. DOI: https://doi.org/10.1016/j.phrs.2021.105840.
11. Wang Q, Yang Q, Liu X. The microbiota-gut-brain axis and neurodevelopmental disorders. *Protein Cell.* 2023; 14 (10): 762-775. DOI: https://doi.org/10.1093/procel/pwad026.
12. Mincic AM, Antal M, Filip L, Miere D. Modulation of gut microbiome in the treatment of neurodegenerative diseases: A systematic review. *Clin Nutr.* 2024;43(7):1832-1849. DOI: https://doi.org/10.1016/j.clnu.2024.05.036.
13. Oroojzadeh P, Bostanabad SY, Lotfi H. Psychobiotics: the influence of gut microbiota on the gut-brain axis in neurological disorders. *J Mol Neurosci.* 2022;72(9):1952-1964. DOI: https://doi.org/10.1007/s12031-022-02053-3.
14. McGovern PE, Zhang J, Tang J, Zhang Z, Hall GR, Moreau RA, et al. Fermented beverages of pre- and proto-historic China. *Proc Natl Acad Sci U S A.* 2004;101(51):17593-17598. DOI: https://doi.org/10.1073/pnas.0407921102.
15. Kindstedt P. Cheese and culture: a history of cheese and its place in western civilization. Chelsea Green Publishing; 2012. DOI: https://doi.org/10.1558/ppc.28580
16. Tamang JP, Cotter P, Endo A, et al. Fermented foods in a global age: East meets West. *Compr Rev Food Sci Food Saf.* 2020;19:184-217. DOI: https://doi.org/10.1111/1541-4337.12520.
17. Leroy F, De Vuyst L. Lactic acid bacteria as functional starter cultures for the food fermentation industry. *Trends Food Sci Technol.* 2004;15(2):67-78. DOI: https://doi.org/10.1016/j.tifs.2003.09.004.
18. Leeuwendaal NK, Stanton C, O'Toole PW, Beresford TP. Fermented foods, health and the gut microbiome. *Nutrients.* 2022;14(7):1527. DOI: https://doi.org/10.3390/nu14071527.
19. Cummings JH, Pomare EW, Branch WJ, Naylor CP, Macfarlane GT. Short chain fatty acids in human large intestine, portal, hepatic and venous blood. *Gut.* 1987;28(10):1221-1227. DOI: https://doi.org/10.1136/gut.28.10.1221.
20. Koh A, De Vadder F, Kovatcheva-Datchary P, Backhed F. From dietary fiber to host physiology: short-chain fatty acids as key bacterial metabolites. *Cell.* 2016;165(6):1332-1345. DOI: https://doi.org/10.1016/j.cell.2016.05.041.
21. Yang FY, Huang SF, Cheng IH. Behavioral alterations following blood-brain barrier disruption stimulated by

focused ultrasound. *Oncotarget.* 2016 May 10;7(19):27916-27925. DOI: https://doi.org/10.18632/oncotarget.8444.

22. Jameson KG, Olson CA, Kazmi SA, Hsiao EY. Toward understanding microbiome-neuronal signaling. *Mol Cell.* 2020 Apr;78(4). DOI: https://doi.org/10.1016/j.molcel.2020.03.006.
23. Chen Y, Xu J, Chen Y. Regulation of neurotransmitters by the gut microbiota and effects on cognition in neurological disorders. *Nutrients.* 2021 Jun 19;13(6):2099. DOI: https://doi.org/10.3390/nu13062099.
24. Tarracchini C, Lugli GA, Mancabelli L, van Sinderen D, Turroni F, Ventura M, Milani C. Exploring the vitamin biosynthesis landscape of the human gut microbiota. *mSystems.* 2024 Oct 22;9(10):e0092924. DOI: https://doi.org/10.1128/msystems.00929-24.
25. Li Z, Kanwal R, Yue X, Li M, Xie A. Polyphenols and intestinal microorganisms: a review of their interactions and effects on human health. *Food Biosci.* 2024 Sep 30;62:105220. DOI: https://doi.org/10.1016/j.fbio.2024.105220.
26. Kamal N, Saharan BS, Duhan JS, Kumar A, Chaudhary P, Goyal C, et al. Exploring the promise of psychobiotics: bridging gut microbiota and mental health for a flourishing society. *Med Microecol.* 2024 Nov 30;23:100118. DOI: https://doi.org/10.1016/j.medmic.2024.100118.
27. Camilleri M. Leaky gut: mechanisms, measurement and clinical implications in humans. *Gut.* 2019 Aug;68(8):1516-1526. DOI: https://doi.org/10.1136/gutjnl-2019-318427.
28. Kaylor A. Enhancing mental wellness with psychobiotics, the gut-brain connection [Internet]. Pharma Life Sci. TechTarget; 2023 [cited 2025 May 23]. Available from: https://www.techtarget.com/pharmalifesciences/feature/Enhancing-Mental-Wellness-with-Psychobiotics-the-GutBrain-Connection
29. Chelakkot C, Ghim J, Ryu SH. Mechanisms regulating intestinal barrier integrity and its pathological implications. *Exp Mol Med.* 2018 Aug;50(8). DOI: https://doi.org/10.1038/s12276-018-0126-x.
30. Anderson RC, Cookson AL, McNabb WC, Park Z, McCann MJ, Kelly WJ, et al. Lactobacillus plantarum MB452 enhances the function of the intestinal barrier by increasing the expression levels of genes involved in tight junction formation. *BMC Microbiol.* 2010;10(1):316. DOI: https://doi.org/10.1186/1471-2180-10-316.
31. Schneider E, Doll JPK, Schweinfurth N, Kettelhack C, Schaub AC, Yamanbaeva G, et al. Effect of short-term, high-dose probiotic supplementation on cognition, related brain functions and BDNF in patients with depression: a secondary analysis of a randomized controlled trial. *J Psychiatry Neurosci.* 2023 Jan 18;48(1):E23-33. DOI: https://doi.org/10.1503/jpn.220117.
32. Hwang YH, Park S, Paik JW, Chae SW, Kim DH, Jeong DG, et al. Efficacy and safety of Lactobacillus plantarum C29-fermented soybean (DW2009) in individuals with mild cognitive impairment: a 12-week, multi-center, randomized, double-blind, placebo-controlled clinical trial. *Nutrients.* 2019 Feb 1;11(2):305. DOI: https://doi.org/10.3390/nu11020305.
33. van de Wouw M, Walsh AM, Crispie F, van Leuven L, Lyte JM, Boehme M, et al. Distinct actions of the fermented beverage kefir on host behaviour, immunity and microbiome gut-brain modules in the mouse. *Microbiome.* 2020 May 18;8(1). DOI: https://doi.org/10.1186/s40168-020-00846-5.
34. Ko CY, Lin HTV, Tsai GJ. Gamma-aminobutyric acid production in black soybean milk by Lactobacillus brevis FPA 3709 and the antidepressant effect of the fermented product on a forced swimming rat model. *Process Biochem.* 2013 Apr;48(4):559-68. DOI: https://doi.org/10.1016/j.procbio.2013.02.021.
35. Kato-Kataoka A, Nishida K, Takada M, Suda K, Kawai M, Shimizu K, Kushiro A, Hoshi R, Watanabe O, Igarashi T, et al. Fermented milk containing Lactobacillus casei strain Shirota prevents the onset of physical symptoms in medical students under academic examination stress. *Benef Microbes.* 2016;7:153-156. DOI: https://doi.org/10.3920/BM2015.0100.
36. Pinto-Sanchez MI, Hall GB, Ghajar K, Nardelli A, Bolino C, Lau JT, Martin F-P, Cominetti O, Welsh C, Rieder A, et al. Probiotic Bifidobacterium longum NCC3001 reduces depression scores and alters brain activity: a pilot study in patients with irritable bowel syndrome. *Gastroenterology.* 2017;153:448-459.e8. DOI: https://doi.org/10.1053/j.gastro.2017.05.003.
37. Del Toro-Barbosa M, Hurtado-Romero A, Garcia-Amezquita LE, García-Cayuela T. Psychobiotics: mechanisms of action, evaluation methods and effectiveness in applications with food products. *Nutrients.* 2020;12(12). DOI: https://doi.org/10.3390/nu12123896.
38. Sarkar A, Lehto SM, Harty S, Dinan TG, Cryan JF, Burnet PWJ. Psychobiotics and the manipulation of bacteria-gut-brain signals. *Trends Neurosci.* 2016 Nov;39(11):763-781. DOI: https://doi.org/10.1016/j.tins.2016.09.002.
39. Johnson D, Letchumanan V, Thum CC, Thurairajasingam S, Lee LH. A microbial-based approach to mental health: the potential of probiotics in the treatment of

depression. *Nutrients.* 2023 Mar 13;15(6):1382. DOI: https://doi.org/10.3390/nu15061382.

40. Marco M, Heeney D, Binda S, Cifelli C, Cotter P, Foligne B. Health benefits of fermented foods: microbiota and beyond. *Curr Opin Biotechnol.* 2017 Apr;44:44. DOI: https://doi.org/10.1016/j.copbio.2016.11.010.
41. Martirosyan DM, Singh J. A new definition of functional food by FFC: what makes a new definition unique? *Functional Foods in Health and Disease.* 2015 Jul 1;5(6):209. DOI: https://doi.org/10.31989/ffhd.v5i6.183.
42. Shawky E, Surendran S, El-Khair RMA. Fermented Vegetables as a Source of Psychobiotics: A Review of the Evidence for Mental Health Benefits. *Probiotics and Antimicrobial Proteins.* 2025 May 22. DOI: https://doi.org/10.1007/s12602-025-10592-5.
43. Danielyan DV, Hovhannisyan HG, Baghdasaryan LG, Barseghyan AH. New generation of functional yogurts fermented with probiotic lactic acid bacteria isolated from human milk. *Functional Foods in Health and Disease.* 2024;14(4):232-247. DOI: https://doi.org/10.31989/ffhd.v14i4.1299.
44. Manshin D, Kuntsova M, Shilenko A, Andreeva A. Probiotic yeast Saccharomyces cerevisiae var. boulardii: properties and peculiarities of use in functional foods development. *Functional Foods in Health and Disease.* 2025;15(5):295-315. DOI: https://doi.org/10.31989/ffhd.v15i5.1482.
45. Karbownik MS, Mokros Ł, Dobielska M, Kowalczyk M, Kowalczyk E. Association Between Consumption of Fermented Food and Food-Derived Prebiotics with Cognitive Performance, Depressive, and Anxiety Symptoms in Psychiatrically Healthy Medical Students Under Psychological Stress: A Prospective Cohort Study. *Front Nutr.* 2022;9:850249. DOI: https://doi.org/10.3389/fnut.2022.850249.
46. Liu WH, Chuang HL, Huang YT, Wu CC, Chou GT, Wang S, et al. Alteration of behavior and monoamine levels attributable to Lactobacillus plantarum PS128 in germ-free mice. *Behav Brain Res.* 2016 Feb 1;298(Pt B):202-9. DOI: https://doi.org/10.1016/j.bbr.2015.10.046.
47. Wu SI, Wu CC, Tsai PJ, Cheng LH, Hsu CC, Shan IK, et al. Psychobiotic supplementation of PS128™ improves stress, anxiety, and insomnia in highly stressed information technology specialists: A pilot study. *Front Nutr.* 2021;8:614105. DOI: https://doi.org/10.3389/fnut.2021.614105.
48. Liu YW, Liu WH, Wu CC, Juan YC, Wu YC, Tsai HP, et al. Psychotropic effects of Lactobacillus plantarum PS128 in early life-stressed and naïve adult mice. *Brain Res.* 2016 Jan 15;1631:1-12. DOI: https://doi.org/10.1016/i.brainres.2015.11.018.
49. Patterson E, Tan HTT, Groeger D, Andrews M, Buckley M, Murphy EF, et al. Bifidobacterium longum 1714 improves sleep quality and aspects of well-being in healthy adults: a randomized, double-blind, placebo-controlled clinical trial. *Sci Rep.* 2024 Feb 14;14(1):3725. DOI: https://doi.org/10.1038/s41598-024-53810-w.
50. Ho YT, Tsai YC, Kuo TBJ, Yang CCH. Effects of Lactobacillus plantarum PS128 on Depressive Symptoms and Sleep Quality in Self-Reported Insomniacs: A Randomized, Double-Blind, Placebo-Controlled Pilot Trial. *Nutrients.* 2021 Aug 17;13(8):2820. DOI: https://doi.org/10.3390/nu13082820.
51. Meng X, Gao Y, Qi H, Ding Y, Sun Y. Clinical Application Value of Lactobacillus Plantarum PS128 in Patients with Anxiety Disorders. *Clin Psychopharmacol Neurosci.* 2022 Aug 31;20(3):560-566. DOI: https://doi.org/10.9758/cpn.2022.20.3.560.
52. Allen AP, Hutch W, Borre YE, Kennedy PJ, Temko A, Boylan G, et al. Bifidobacterium longum 1714 as a translational psychobiotic: modulation of stress, electrophysiology and neurocognition in healthy volunteers. *Transl Psychiatry.* 2016 Nov 1;6(11):e939. DOI: https://doi.org/10.1038/tp.2016.191.
53. Wang H, Braun C, Murphy EF, Enck P. Bifidobacterium longum 1714™ Strain Modulates Brain Activity of Healthy Volunteers During Social Stress. *Am J Gastroenterol.* 2019 Jul;114(7):1152-1162. DOI: https://doi.org/10.14309/ajg.0000000000000203.
54. Binda S, Tremblay A, Iqbal UH, Kassem O, Le Barz M, Thomas V, et al. Psychobiotics and the microbiota-gut-brain axis: where do we go from here? *Microorganisms.* 2024; 12(4):634. DOI: https://doi.org/10.3390/microorganisms12040634.
55. Ma Q, Xing C, Long W, Wang HY, Liu Q, Wang RF. Impact of microbiota on central nervous system and neurological diseases: the gut-brain axis. *J. Neuroinflammation.* 2019 16(1):53. DOI: https://doi.org/10.1186/s12974-019-1434-3.
56. Zhuang Z, Shen L, Li W, Fu X, Zeng F, Gui L, et al. Gut microbiota is altered in patients with Alzheimer's disease. *J Alzheimers Dis.* 2018;63(4):1337-1346. DOI: https://doi.org/10.3233/jad-180176.
57. Bhandage AK, Jin Z, Korol SV, Shen Q, Pei Y, Deng Q, et al. GABA regulates release of inflammatory cytokines from

peripheral blood mononuclear cells and CD4+ T cells and is immunosuppressive in type 1 diabetes. *EBioMedicine.* 2018;30:283-294.
DOI: https://doi.org/10.1016/j.ebiom.2018.03.019.

58. Gonzalez-Gonzalez C, Gibson GR, Jauregi P. Novel probiotic-fermented foods with potential to improve human health. *Nutrients.* 2019;11(8):1805.
DOI: https://doi.org/10.1016/j.ijfoodmicro.2013.09.002.

59. Mohajeri MH, Brummer RJ, Rastall RA, Weersma RK, Harmsen HJM, Faas M, et al. The role of the microbiome for human health: from basic science to clinical applications. *Eur J Nutr.* 2018;57(Suppl 1):1-14.
DOI: https://doi.org/10.1007/s00394-018-1703-4.

60. Li X, Zheng P, Cao W, Cao Y, She X, Yang H, et al. Lactobacillus rhamnosus GG ameliorates noise-induced cognitive deficits and systemic inflammation in rats by modulating the gut-brain axis. *Front Cell Infect Microbiol.* 2023;13:1067367.
DOI: https://doi.org/10.3389/fcimb.2023.1067367.

61. Zhu G, Guo M, Zhao J, Zhang H, Wang G, Chen W. Bifidobacterium breve intervention combined with environmental enrichment alleviates cognitive impairment by regulating the gut microbiota and microbial metabolites in Alzheimer's disease mice. *Front Immunol.* 2022; 13:1013664.
DOI: https://doi.org/10.3389/fimmu.2022.1013664.

62. Pérez-Rubio Á, Soluyanova P, Moro E, Quintás G, Rienda I, Periañez MD, et al. Gut Microbiota and Plasma Bile Acids Associated with Non-Alcoholic Fatty Liver Disease Resolution in Bariatric Surgery Patients. *Nutrients.* 2023; 15(14):3187. DOI: https://doi.org/10.3390/nu15143187.

63. Yu S, Zhang W, Wang X, Luo Q, Gu B, Zhao Y, et al. H2S improves hippocampal synaptic plasticity in SPS rats via PI3K/AKT signaling pathway. *Brain Res.* 2024 Dec 15; 1845:149286.
DOI: https://doi.org/10.1016/j.brainres.2024.149286.

64. Porras-Garcia E, Calderón IFE, Gavala-González J, Fernandez-Garcia JC. Potential neuroprotective effects of fermented foods and beverages in old age: A systematic review. *Front Nutr.* 2023;10:1170841.
DOI: https://doi.org/10.3389/fnut.2023.1170841.

65. Kumar MR, Nor FA, Yeap SK, Abdullah JO, Khalid M, Omar AR, et al. Clinical and preclinical studies of fermented foods and their effects on Alzheimer's disease. *Antioxidants.* 2022;11(5):883.
DOI: https://doi.org/10.3390/antiox11050883.