

## UNVEILING THE MIND-GUT CONNECTION: A MINI-REVIEW ON PSYCHBIOTICS

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### ABSTRACT

The emerging domain of psychobiotics introduces an innovative framework in mental health treatments by leveraging the reciprocal interaction between the gut bacteria and the brain. The therapeutic benefits of psychobiotics, which include probiotics and prebiotics, on mental well-being are mediated through complex interactions with the gut microbiota and numerous neuroactive pathways. This brief analysis delves into the present comprehension of psychobiotics and their prospective uses in mental health. The available body of research indicates that psychobiotics exhibit potential in mitigating symptoms associated with anxiety, sadness, and stress-related pathologies. Mechanistic insights demonstrate their capacity to regulate the generation of neurotransmitters, control stress response systems, and improve the integrity of the gut barrier. Even with the encouraging results, additional investigation is necessary to clarify the most effective formulations and tailored interventions. The utilization of psychobiotics in mental health therapy holds great potential since it presents a natural and productive approach to enhancing mental well-being and supplementing conventional treatments.

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## 1. INTRODUCTION

The complex interplay between the gastrointestinal tract and the central nervous system has received considerable scholarly interest recently, as new investigations have provided insights into the impact of gut bacteria on mental well-being. Psychobiotics have emerged as a viable route among the different therapies addressing the gut-brain axis. When consumed in sufficient quantities, these living microbes provide mental health advantages by interacting with the gut microbiota. This brief review delves into the present comprehension of psychobiotics and their prospective utilization in mental health.

## 2. PSYCHBIOTICS AND MENTAL HEALTH

Emerging research indicates that the gut microbiota significantly influences brain function and behavior regulation via multiple mechanisms, such as the gut-brain axis, the immune system, and neurotransmitter synthesis. Psychobiotics are a class of drugs that essentially comprise probiotics, which are live beneficial bacteria, and prebiotics, which are substances that facilitate the growth of beneficial bacteria. These substances can regulate the makeup and activity of the gut microbiota, thereby influencing mental well-being.

Scientific research has shown that psychobiotics are effective in reducing symptoms of anxiety, sadness, and stress-related ailments. In preclinical models and clinical trials, it has been demonstrated that specific strains of *Lactobacillus* and *Bifidobacterium* can mitigate anxiety-like behavior and alleviate symptoms associated with

depression. In addition, prebiotics such as inulin and oligofructose have been linked to mood and cognitive function enhancements.

### 3. MECHANISM OF ACTION

The psychobiotic effects are attributable to a complex interplay between the gut bacteria and the host, involving multiple mechanisms. The administration of psychobiotics has the potential to regulate the synthesis of neurotransmitters, including serotonin and gamma-aminobutyric acid (GABA), which are crucial for regulating mood. Moreover, they can impact the synthesis of short-chain fatty acids (SCFAs), which are microbial byproducts that possess anti-inflammatory and neuroprotective characteristics.

Table 1. Mechanism of action of psychobiotics

Bacteria	Model	dose	findings	Possible Mechanism
Bacillus coagulans MTCC 5856	Clinical trial 2	billion spores	Robust efficacy for the treatment of patients experiencing IBS symptoms with major depressive disorder	Production of SCFAs and antimicrobial and anti-inflammatory substances.
Bifidobacterium longum 1714	Clinical trial	1 × 10 <sup>9</sup> CFU/day	Reduced stress and improved memory	Brain-Derived Neurotrophic Factor (BDNF) synthesis through vagal activity
Bifidobacterium longum NCC300	Clinical trial	1 × 10 <sup>10</sup> CFU/g	Reduction in depression scores on Hospital Anxiety and Depression Scale and reduced responses to negative emotional stimuli in multiple brain areas	Release of neuroactive compounds through vagal signaling as well as BDNF regulation.
Clostridium butyricum MIYAIRI 588	Clinical trial	60 mg/day	In combination with antidepressants, is effective in the treatment of treatment-resistant major depressive disorder.	Regulation of proinflammatory agents.
Lactobacillus casei Shirota	Clinical trial	1 × 10 <sup>9</sup> over 8 weeks	Decrease in the cognitive state anxiety scores, somatic state, and perceived stress scale.	
Lactobacillus casei Shirota	Clinical trial	100 mL of a fermented beverage containing more than 1 × 10 <sup>9</sup> CFU/mL/day	Salivary cortisol and plasma L-tryptophan levels were increased in the placebo group, while the experimental group had higher fecal serotonin levels. Lower rate of subjects experiencing common abdominal and cold symptoms, and total number of days experiencing these physical symptoms	Hypothalamic-pituitary-adrenal (HPA) axis modulation and promotion of serotonin synthesis
Lactobacillus gasseri CP2305	Clinical trial	1 × 10 <sup>10</sup> CFU	Stress-associated behaviors were improved, as well as the sleeping quality. The parabiotic	Regulation of inflammation mechanisms.

			administration also prevented increases in basal salivary cortisol release and expression of stress-responsive microRNAs	
Lactobacillus casei Shirota	Clinical trial and in vivo murine model	Milk fermented with $1 \times 10^9$ CFU/mL	Increases in salivary cortisol levels and incidence rate of physical symptoms were significantly suppressed. In rats, water avoidance stress-induced increases in plasma corticosterone were suppressed, and the number of corticotrophin-releasing factor-expressing cells in the paraventricular nucleus was reduced.	HPA axis regulation
Bifidobacterium breve 1205	In vivo murine model	$1 \times 10^9$ CFU/mL	Reduced anxiety in the marble-burying test and induced lower anxiety in the elevated plus maze	Immune system regulation and gut hormones secretion.
Bifidobacterium breve CCFM1025	In vivo murine model	0.1 mL/10 g body weight daily at $1 \times 10^9$ CFU/mL	Reduced depression and anxiety behaviors. The hyperactive HPA response and inflammation were also alleviated. Expression of the brain-derived neurotrophic factor was increased, while chronic stress was restored.	Capacity of SCFAs to improve serotonin levels, and regulation of the HPA axis and BDNF synthesis.
Bifidobacterium infantis 35624	In vivo murine model	$1 \times 10^{10}$ live bacterial cells/100 mL drinking/day	Normalization of the immune response, reversal of behavioral deficits, and restoration of basal noradrenaline concentrations in the brain.	Anti-inflammatory properties.
Bifidobacterium longum 1714	In vivo murine model	$1 \times 10^9$ CFU/mL	Reduced anxiety in the marble-burying test; decreased stress-induced hyperthermia, lower anxiety in the elevated plus maze, and antidepressant-like behavior in the tail suspension test.	Immune system regulation and gut hormones secretion.
Faecalibacterium prausnitzii ATCC 27766	In vivo murine model	$1 \times 10^9$ CFU by oral gavage	Preventive and therapeutic effects on depression and anxiety behavior, higher levels of SCFAs in the cecum, and higher levels of	SCFAs synthesis, immune system stimulation, and HPA axis regulation.

			cytokines interleukin-10 in the plasma. Corticosterone, C-reaction protein, and Interleukin-6 levels were normalized.	
Lactobacillus helveticus NS8	In vivo murine model	1 × 10 <sup>9</sup> CFU/mL in drinking water	The anxiolytic effect in hyperammonia-treated rats was associated with a reduction in hippocampal serotonin 5-HTP levels.	Downregulation of inflammation and serotonin metabolism
Lactobacillus plantarum ATCC 8014	In vivo murine model	Bacterial suspensions at 1 × 10 <sup>7</sup> CFU/mL	Favorable effects on oxidative markers of the blood and amygdala, as well as on concentrations of amygdala serotonin and brain-derived neurotrophic factor (BDNF). Beneficial effects were observed on the elevated plus maze and forced swimming tests.	HPA axis downregulation due to oxidative stress reduction.

Moreover, it has been demonstrated that psychobiotics can modulate the hypothalamic-pituitary-adrenal (HPA) axis, which serves as the principal stress response mechanism. Consequently, they can alleviate the adverse consequences of prolonged stress on mental well-being. Furthermore, these substances have the potential to improve the structural integrity of the gastrointestinal barrier and reduce systemic inflammation, both of which have been linked to the development of mood disorders.

#### 4. FUTURE DIRECTIONS

Although the initial results of psychobiotics show promise, there are still some unresolved inquiries. Subsequent investigations ought to prioritise the clarification of the most effective strains, doses, and duration of psychobiotic therapies for diverse mental health disorders. Furthermore, there is significant promise in optimising therapeutic outcomes through the advancement of personalised psychobiotic therapies that are tailored to individual gut microbiota patterns.

#### 5. CONCLUSION

Psychobiotics offer a new and encouraging method for enhancing mental well-being by specifically targeting the connection between the gut and the brain. By modulating the gut microbiota and activating multiple neuroactive pathways, psychobiotics can alleviate symptoms of anxiety, depression, and stress-related diseases. With the ongoing advancement of research in this area, psychobiotics have the potential to become effective supplements to traditional treatments for mental health disorders, providing optimism for a more promising future in psychobiotic-based therapies.

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#### COMPETING INTEREST

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## REFERENCES

- [1]. Sarkar A, Lehto SM, Harty S, Dinan TG, Cryan JF, Burnet PW. Psychobiotics and the manipulation of bacteria–gut–brain signals. *Trends in neurosciences*. 2016 Nov 1;39(11):763-81.
- [2]. Barrio C, Arias-Sánchez S, Martín-Monzón I. The gut microbiota-brain axis, psychobiotics and its influence on brain and behaviour: A systematic review. *Psychoneuroendocrinology*. 2022 Mar 1;137:105640.
- [3]. Kavvadia M, Santis GL, Cascapera S, Lorenzo AD. Psychobiotics as integrative therapy for neuropsychiatric disorders with special emphasis on the microbiota-gut-brain axis. *Biomed. Prev*. 2017;2(8).
- [4]. Cheng LH, Liu YW, Wu CC, Wang S, Tsai YC. Psychobiotics in mental health, neurodegenerative and neurodevelopmental disorders. *Journal of food and drug analysis*. 2019 Jul 1;27(3):632-48.
- [5]. Casertano M, Fogliano V, Ercolini D. Psychobiotics, gut microbiota and fermented foods can help preserving mental health. *Food Research International*. 2022 Feb 1;152:110892.
- [6]. Bermúdez-Humarán LG, Salinas E, Ortiz GG, Ramirez-Jirano LJ, Morales JA, Bitzer-Quintero OK. From probiotics to psychobiotics: live beneficial bacteria which act on the brain-gut axis. *Nutrients*. 2019 Apr 20;11(4):890.
- [7]. Sharma R, Gupta D, Mehrotra R, Mago P. Psychobiotics: The next-generation probiotics for the brain. *Current microbiology*. 2021 Feb;78:449-63.
- [8]. Wasilewski A, Zielińska M, Storr M, Fichna J. Beneficial effects of probiotics, prebiotics, synbiotics, and psychobiotics in inflammatory bowel disease. *Inflammatory bowel diseases*. 2015 Jul 1;21(7):1674-82.
- [9]. Strandwitz P. Neurotransmitter modulation by the gut microbiota. *Brain research*. 2018 Aug 15;1693:128-33.
- [10]. Cheng LH, Liu YW, Wu CC, Wang S, Tsai YC. Psychobiotics in mental health, neurodegenerative and neurodevelopmental disorders. *Journal of food and drug analysis*. 2019 Jul 1;27(3):632-48.
- [11]. Xing B, Li YC, Gao WJ. Norepinephrine versus dopamine and their interaction in modulating synaptic function in the prefrontal cortex. *Brain research*. 2016 Jun 15;1641:217-33.
- [12]. Ross SM. Microbiota in neuropsychiatry, part 3: psychobiotics as modulators of mood disorders. *Holistic Nursing Practice*. 2017 Jul 1;31(4):270-3.
- [13]. Kerage D, Sloan EK, Mattarollo SR, McCombe PA. Interaction of neurotransmitters and neurochemicals with lymphocytes. *Journal of neuroimmunology*. 2019 Jul 15;332:99-111.
- [14]. Oroojzadeh P, Bostanabad SY, Lotfi H. Psychobiotics: the influence of gut microbiota on the gut-brain axis in neurological disorders. *Journal of Molecular Neuroscience*. 2022 Sep;72(9):1952-64.
- [15]. Sarkar A, Lehto SM, Harty S, Dinan TG, Cryan JF, Burnet PW. Psychobiotics and the manipulation of bacteria–gut–brain signals. *Trends in neurosciences*. 2016 Nov 1;39(11):763-81.
- [16]. Yano JM, Yu K, Donaldson GP, Shastri GG, Ann P, Ma L, Nagler CR, Ismagilov RF, Mazmanian SK, Hsiao EY. Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis. *Cell*. 2015 Apr 9;161(2):264-76.
- [17]. Magalhães-Guedes KT. Psychobiotic therapy: method to reinforce the immune system. *Clinical Psychopharmacology and Neuroscience*. 2022 Feb 2;20(1):17.
- [18]. Parracho HM, Gibson GR, Knott F, Bosscher D, Kleerebezem M, McCartney AL. A double-blind, placebo-controlled, crossover-designed probiotic feeding study in children diagnosed with autistic spectrum disorders. *International Journal of Probiotics & Prebiotics*. 2010 May 1;5(2):69.
- [19]. Messaoudi M, Lalonde R, Violle N, Javelot H, Desor D, Nejdí A, Bisson JF, Rougeot C, Pichelin M, Cazaubiel M, Cazaubiel JM. Assessment of psychotropic-like properties of a probiotic formulation (*Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175) in rats and human subjects. *British Journal of Nutrition*. 2011 Mar;105(5):755-64.
- [20]. Barichella M, Cereda E, Pezzoli G. Major nutritional issues in the management of Parkinson's disease. *Movement disorders*. 2009 Oct 15;24(13):1881-92.
- [21]. Bravo JA, Forsythe P, Chew MV, Escaravage E, Savignac HM, Dinan TG, Bienenstock J, Cryan JF. Ingestion of *Lactobacillus* strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. *Proceedings of the National Academy of Sciences*. 2011 Sep 20;108(38):16050-5.
- [22]. Huang R, Wang K, Hu J. Effect of probiotics on depression: a systematic review and meta-analysis of randomized controlled trials. *Nutrients*. 2016 Aug 6;8(8):483.

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- [23]. Liang S, Wang T, Hu X, Luo J, Li W, Wu X, Duan Y, Jin F. Administration of *Lactobacillus helveticus* NS8 improves behavioral, cognitive, and biochemical aberrations caused by chronic restraint stress. *Neuroscience*. 2015 Dec 3;310:561-77.
- [24]. Silverman MN, Sternberg EM. Glucocorticoid regulation of inflammation and its functional correlates: from HPA axis to glucocorticoid receptor dysfunction. *Annals of the New York Academy of Sciences*. 2012 Jul;1261(1):55-63.
- [25]. Liang S, Wang T, Hu X, Luo J, Li W, Wu X, Duan Y, Jin F. Administration of *Lactobacillus helveticus* NS8 improves behavioral, cognitive, and biochemical aberrations caused by chronic restraint stress. *Neuroscience*. 2015 Dec 3;310:561-77.
- [26]. Parracho HM, Gibson GR, Knott F, Bosscher D, Kleerebezem M, McCartney AL. A double-blind, placebo-controlled, crossover-designed probiotic feeding study in children diagnosed with autistic spectrum disorders. *International Journal of Probiotics & Prebiotics*. 2010 May 1;5(2):69.
- [27]. Zhang L, Xu Y, Li H, Li B, Duan G, Zhu C. The role of probiotics in children with autism spectrum disorders: A study protocol for a randomised controlled trial. *PLoS One*. 2022 Feb 24;17(2):e0263109.
- [28]. Liu YW, Liu WH, Wu CC, Juan YC, Wu YC, Tsai HP, Wang S, Tsai YC. Psychotropic effects of *Lactobacillus plantarum* PS128 in early life-stressed and naïve adult mice. *Brain research*. 2016 Jan 15;1631:1-2.
- [29]. Liu YW, Liang MT, Chung YC, Huang HY, Peng WS, Cheng YF, Lin YS, Wu YY, Tsai YC. Effects of *Lactobacillus plantarum* PS128 on children with autism spectrum disorder in Taiwan: a randomized, double-blind, placebo-controlled trial. *Nutrients*. 2019 Apr 11;11(4):820.
- [30]. Carabotti M, Scirocco A, Maselli MA, Severi C. The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. *Annals of Gastroenterology: quarterly publication of the Hellenic Society of Gastroenterology*. 2015 Apr;28(2):203.
- [31]. Rucklidge JJ. Could yeast infections impair recovery from mental illness? A case study using micronutrients and olive leaf extract for the treatment of ADHD and depression. *Adv Mind Body Med*. 2013 Jun 1;27(3):14-8.
- [32]. Aizawa E, Tsuji H, Asahara T, Takahashi T, Teraishi T, Yoshida S, Ota M, Koga N, Hattori K, Kunugi H. Possible association of *Bifidobacterium* and *Lactobacillus* in the gut microbiota of patients with major depressive disorder. *Journal of Affective Disorders*. 2016 Sep 15;202:254-7.
- [33]. Musa NH, Mani V, Lim SM, Vidyadaran S, Majeed AB, Ramasamy K. *Lactobacilli*-fermented cow's milk attenuated lipopolysaccharide-induced neuroinflammation and memory impairment in vitro and in vivo. *Journal of Dairy Research*. 2017 Nov;84(4):488-95.
- [34]. Musa NH, Mani V, Lim SM, Vidyadaran S, Majeed AB, Ramasamy K. *Lactobacilli*-fermented cow's milk attenuated lipopolysaccharide-induced neuroinflammation and memory impairment in vitro and in vivo. *Journal of Dairy Research*. 2017 Nov;84(4):488-95.
- [35]. Saravanan KM, Kannan M, Meera P, Bharathkumar N, Anand T. E3 ligases: a potential multi-drug target for different types of cancers and neurological disorders. *Future Medicinal Chemistry*. 2022 Feb;14(3):187-201.
- [36]. Taylor JM, Main BS, Crack PJ. Neuroinflammation and oxidative stress: co-conspirators in the pathology of Parkinson's disease. *Neurochemistry international*. 2013 Apr 1;62(5):803-19.
- [37]. Akbari E, Asemi Z, Daneshvar Kakhaki R, Bahmani F, Kouchaki E, Tamtaji OR, Hamidi GA, Salami M. Effect of probiotic supplementation on cognitive function and metabolic status in Alzheimer's disease: a randomized, double-blind and controlled trial. *Frontiers in aging neuroscience*. 2016 Nov 10;8:256.
- [38]. Sharma R, Gupta D, Mehrotra R, Mago P. Psychobiotics: The next-generation probiotics for the brain. *Current microbiology*. 2021 Feb;78:449-63.