International Journal of Research in Medical Sciences
*Srinivas YR et al. Int J Res Med Sci. 2025 Sep;13(9):3921-3932*
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20252821

**Review Article**

# A review on probiotics and mental health: exploring the gut-brain axis and its therapeutic potential

**Yogish R. Srinivas[1], Tejashree M. Ramesh[1], Pavan K. C. Muddanna[2]*, Mahendra K. B. Jayappa[1]**

[1]Department of Pharmacy Practice, Sri Adichunchanagiri College of Pharmacy, Adichunchanagiri University, B.G. Nagara, Mandya, Karnataka, India
[2]Sri Adichunchanagiri College of Pharmacy, Adichunchanagiri University, B.G. Nagara, Mandya, Karnataka, India

**Received:** 16 July 2025
**Accepted:** 14 August 2025

***Correspondence:**
Pavan K. C. Muddanna,
E-mail: pavankumarcm15@gmail.com



## ABSTRACT

The relationship deemed with the axis of gut-brain has come to be a major area of interest in the pathophysiology of mental health disorders. At the centre of this interaction is the gut microbiota, which communicates with the brain through neural, endocrine, immune, and metabolic pathways. Probiotics, which has led to the term "psychobiotics" being coined. This article is meant to bring out the elements and mechanisms of the gut-brain axis concerning microbiota's role in neurodevelopment and behaviour, and its probiotics' therapeutic potential in psychopathologies such as depression, anxiety, stress response disorders, and other psychiatric disorders. Both preclinical and clinical studies have been reviewed for their evidence on the efficacy and safety of probiotics in strengthening mental health outcomes. Challenges such as strain and dosage variance, by understanding and possibly using the gut-brain-microbiota interaction via selective probiotic treatments could open up new ways of adjunctive treatment for mental health disorders.

**Keywords:** Psychobiotics, Probiotics, Gut-brain axis, Mental health, Microbiota, Neurotransmitters

## INTRODUCTION

Mental health ailments such as depression, anxiety, stress-related conditions, and neurodevelopmental disorders are increasingly being considered among the significant public health problems of the world. As per the World Health Organization (WHO), mental illness is supposed to have affected more than 970 million sufferers worldwide, which causes disability and hampers the quality of their lives. Pharmacotherapy and psychotherapy form the foundation for treatment, yet many patients refuse complete alleviation of symptoms, resist treatment, or suffer from side effects that interfere with their adherence to the treatment. Because of this, there is increasing interest in alternative and adjunctive procedures that could work alongside existing treatments and yield better outcomes in mental health.[1,2]

A complicated, two-way communication network between the central nervous system and the gastrointestinal tract makes up the gut-brain axis, which has attracted a lot of scientific attention lately. The gut microbiota, or the trillions of microorganisms that live in the gastrointestinal (GI) tract, and the brain can communicate continuously thanks to neural, hormonal, immunological, and metabolic pathways. Changes in the makeup of the gut microbiota seem to have the potential to impact behavior, stress reactions, brain development, and even psychiatric diseases, indicating that the gut microbiome may have a significant impact on the control of mental health.[3,4]

The term "probiotics" refers to live microorganisms that, when given in suitable amounts, bestow health benefits upon the host. These are thought to influence the gut-brain axis. A subgroup of probiotics, termed psychobiotics, is being studied for their capability to produce neuroactive

compounds, govern inflammation, sustain the gut barrier, and influence hormones linked to stress, such as cortisol. These activities may work to relieve symptoms associated with depression, anxiety, and other psychological conditions. Promising evidence is starting to come through the animal studies and emerging clinical trials that affirm these effects.

This review serves to thoroughly examine the linkage between probiotics and mental health by exploring the gut-brain axis pathway and the influence of gut microbiota on neuropsychiatric health. Additionally, it looks at the status of preclinical and clinical evidence regarding the use of probiotics as a treatment for various mental conditions, plus barriers, limitations, and recommendations for future studies in the field.[5]

## THE GUT BRAIN AXIS: A BIDIRECTIONAL COMMUNICATION PATHWAY; ANATOMY AND PHYSIOLOGY OF THE GUT-BRAIN AXIS

The gut-brain axis (GBA) describes a multidimensional communication network that establishes an interface between the gastrointestinal (GI) tract and the central nervous system (CNS). Amazingly, this axis regulates digestion, metabolism, and immunity and will even interfere with behaviour and cognition. As a matter of fact, this consists of the interrelated central and enteric nervous systems, the autonomic nervous system (chiefly the vagus nerve), the neuroendocrine system (through the hypothalamic-pituitary-adrenal axis), and the immune system. The gut microbiota, which is an immensely heterogeneous community of microorganisms, is perhaps the other key player in this axis. The brain sends signals via afferent and efferent pathways to the gut to control motility, secretion, and permeability, and the gut passes back information about its state to the brain. The feedback loop involves neurotransmitters (e.g., serotonin, dopamine), hormones (e.g., cortisol), and immune signals (e.g., cytokines). If this system is disturbed, it can give rise to a series of disorders such as irritable bowel syndrome (IBS), depression, anxiety, and neurodevelopmental disorders. Looking at the structure and function of the GBA serves as the basis for the exploration of how gut-directed interventions of probiotics might assist with improving mental health by intervening in this bidirectional communication.[6,7]

### *Role of the enteric nervous system*

The enteric nervous system (ENS) is a huge network of neurons that is embedded in the deep walls of the gastrointestinal system and is also called the "second brain." Made up of over100 million neurons, it can control important digestive processes such as blood flow, secretion, and peristalsis without the help of the brain or spinal cord. The ENS is anatomically divided into two main plexuses: the submucosal plexus, controlling secretions and blood flow, and the myenteric plexus, controlling gut motility. Besides regulating digestion, the ENS acts as a key player in the gut-brain axis. It synthesises and responds to a plethora of neurotransmitters, serotonin (nearly 90% of the body's supply is produced in the gut) to acetylcholine and GABA-which are equally active in mood and behaviour. The ENS communicates with the CNS via the vagus nerve and other autonomic pathways. Modifications in ENS signalling have been related to mood disorders, stress responses, and neurodegenerative diseases. Probiotic bacteria may encourage the functioning of the ENS by helping maintain the composition of gut microbiota and promoting the production of neuroactive substances, thereby significantly improving gut and mental health.[8,9]

### *Involvement of the vagus nerve*

The vagus nerve is the 10th cranial nerve and one of the crucial components of the gut-brain axis. It is the main parasympathetic highway providing a direct avenue for communication between the gut and the brain. Of the entire fibre population of the vagus nerve, approximately 80% are afferent, i.e., they transfer sensory signals from the gut to the brain. Hence, this nerve acts as the communication pathway between the microbial and immune signals and the central nervous system. Vagal afferent stimulation represents brain control in mood and stress responses, but also governs inflammation. Activation of vagal nerve afferents decreases the production of pro-inflammatory cytokines and increases inhibition of the hypothalamic-pituitary-adrenal axis. Some evidence thus suggests that vagal modulation is effective for improving depression and anxiety symptoms. Some probiotic strains, for instance, Lactobacillus rhamnosus, have been shown to alter behaviour in a vagus-dependent manner and reduce responses to stress. This implies that changes in the gut microbiota caused by probiotics may be affecting brain function through vagal pathways. Hence, knowledge about the vagus nerve pathway gives insight into whether gut-targeting therapies could benefit through non-invasive modulation of mental health conditions.[10,11]

### *Neuroendocrine signalling pathways (HPA axis)*

In humans, the HPA axis is the major mechanism acting on stress responses. When an organism perceives stress, the hypothalamus releases CRH into the anterior pituitary, which releases ACTH into the bloodstream. ACTH reaches the adrenal cortex and instructs it to produce cortisol, the main stress hormone. The cortisol hormone plays an important role in metabolism, immune reactions, and brain function. Nevertheless, a constant activation of the HPA axis would cause an imbalance and promote mood disorders such as depression and anxiety.

Gut bacteria can influence the HPA axis on both direct and indirect levels. HPA responses to stress in germ-free animals are exaggerated, but upon colonisation with certain bacterial strains, these responses can be brought down to normal levels. Probiotics may also act to reduce

HPA hyperactivity. *Bifidobacterium longum* and *Lactobacillus helveticus* supplementation leads to reduced cortisol and improved mood in stressed individuals. Gut bacteria modulate the HPA axis do it from neural, immune, and metabolic routes, thus reinforcing the thought that the gut and brain are inextricably linked. This neuroendocrine axis being influenced may revitalise the prospect of managing mental health through food and probiotic intervention.[12,13]

### *Immune system involvement in GBA communication*

The immune system acts as an important middleman in the gut-brain axis, signalling and modulating neurological health. The gut, technically, is considered to be the biggest immune organ of the human body, housing more than 70% of the immune cells sitting within gut-associated lymphoid tissue (GALT). This particular immune tissue is in contact with microbial antigens to uphold immune tolerance and mount defences against pathogens. Cytokines and other immune mediators are released in the interaction between the gut and brain to alter neuronal functions and behaviour. Altered gut microbiota or dysbiosis causes increased permeability of the intestinal thin wall ("leaky gut") and the passage of pro-inflammatory molecules into the full-toned profuse blood circulation. The subsequent inflammatory signals originate from below the blood-brain barrier to exert their neuroinflammatory properties, being commonly observed in psychiatric disorders such as depression, schizophrenia, and autism spectrum disorders. By restoring this microbial balance, probiotics promote immune modulation, improve mucosal barrier integrity, and encourage anti-inflammatory cytokine production such as IL-10. Therefore, the immune system acts not only as a protective system but also as one of the most important mechanisms in communication with the brain. The manipulation of immune responses through gut microbiota alterations opens novel views toward psychiatric treatments.[14,15]

### *Gut microbiota diversity and dominant bacterial species*

The human gut microbiota is an extremely diverse ecosystem, made up of trillions of microorganisms such as bacteria, viruses, fungi, and archaea. This microbial community assumes a vital role in the maintenance of health, interacting with the whole human body in different physiological processes. It is believed that there are more than 1,000 bacterial species in the human gut, and each person has a unique gut microbiota. Among the main bacterial phyla present in the human gut are Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria. Typically, Firmicutes and Bacteroidetes constitute the majority of the microbiota composition. The major bacterial genera associated with gut-brain signaling and mental health are summarized in Table 1.

**Table 1: Key bacterial genera involved in mental health.**

| Bacterial genus | Role in mental health |
|---|---|
| **Lactobacillus** | Known for generating the neurotransmitter GABA, which regulates anxiety and mood. Lactobacillus supplementation showed anxiolytic and antidepressant-like effects in animal models. |
| **Bifidobacterium** | It ferments fibres to produce SCFAs, which help in maintaining gut health and also modulate serotonin production. Dysbiosis of Bifidobacteria has been linked to depression and anxiety, while supplementing it can improve mood and reduce symptoms of such states. |
| **Firmicutes** | Includes genera like Clostridium and Ruminococcus, which are involved in SCFA production. SCFAs such as butyrate reduce inflammation and promote brain health. Imbalances in Firmicutes have been considered to correlate with neuropsychiatric disorders like depression and anxiety. |
| **Bacteroides** | Breaks down complex carbohydrates, producing SCFAs that modulate the immune response to reduce inflammation. Imbalance in Bacteroides populations is perhaps underlying depression and other mood disorders. |
| **Akkermansia** | Affects gut lining integrity, maintenance and immune function regulation. The presence of the organism is thought to lower inflammation; hence, it may be protective against depression and anxiety. |
| **Roseburia** | Roseburia validates the production of butyrate, a neuroprotective SCFA. Low Roseburia levels have been associated with depression and anxiety. The enhancement of butyrate production may help uplift mood and diminish mental health symptoms. |
| **Faecalibacterium** | Helps produce SCFAs, especially butyrate, which has anti-inflammatory action. Faecalibacterium levels drop upon depression, and promoting Faecalibacterium may curb inflammation and proceed toward mental health. |
| **Enterococcus** | Regulate the gut environment together with immune modulation. The overgrowth of or imbalance in Enterococcus could cause gut dysbiosis, which might affect mood and behaviour through the gut-brain axis.[3,24] |

Certain bacterial genera under these phyla have been regarded as being predominant in a healthy gut. In particular, these beneficial and abundant species from Bacteroidetes belong to Bacteroides, while Firmicutes include Clostridium, Lactobacillus, and Faecalibacterium. These bacteria perform a variety of functions, including fermenting dietary fibres into SCFAs, producing vitamins, and modulating the immune system. The microbial diversity and the relative abundance of these species may greatly differ from one person or population to another based on factors such as food intake, age, and residence. A disruption in microbial population balance (dysbiosis) can give rise to some health issues involving metabolic, immune, neurological, and other.[16,17]

## FACTORS INFLUENCING GUT MICROBIOTA COMPOSITION; DIET AND NUTRITIONAL FACTORS

The diet constitutes a main player behind shaping the microbiota of the gut. High fibre intake, preferably from fruits, vegetables, and whole grains, would encourage the growth of beneficial bacterial flora such as Bifidobacteria and Lactobacillus. These bacteria would ferment dietary fibre into short-chain fatty acids, which have beneficial properties for gut health and immune functions. Conversely, high-fat and low-fibre diets tend to reduce microbial diversity, favouring bad bacteria presumably involved in obesity and metabolic syndrome illnesses.[18]

### *Antibiotics and medications*

The most important factor influencing microbiota composition is antibiotic use. Broad-spectrum antibiotics can, while eradicating an infection, kill beneficial microbes to create an imbalance termed dysbiosis. This could give an environment conducive to the overgrowth of pathogenic bacteria such as *C. difficile*.

Excessive use of antibiotics, in particular during the early stages of life, can result in long-term alteration of gut microbiota and predispose an individual to chronic diseases. Other drugs, such as proton pump inhibitors and chemotherapeutic agents, can affect the gut microbiome by modifying stomach acidity or by directly influencing microbial growth.[19]

### *Mode of birth and early life factors*

The method of delivery largely determines the initial colonisation of the gut microbiota. Vaginal births contain bacterial flora from the mother's vagina and feces, thus favoring healthy microbiome development. C-section births, however, often carry a different set of microbial communities, setting the stage for the infant to develop asthma, eczema, and allergies later in life. Breast milk consists of prebiotics and beneficial bacteria that can establish a diverse microbiota, but formula feeding may favour harmful bacteria.[20]

### *Environmental factors*

Environmental factors, such as geographic location, urbanisation, and pollution, are also responsible for gut microbiota composition shown in Figure 1. The gut microbiota of people living in urban situations is less diverse in comparison with those residents in rural environments due to the differences in food habits and hygienic conditions related to being more or less close to nature after all. Environmental pollutants, such as air pollution or pesticides, adversely affect microbial equilibrium by favouring the growth of harmful microbes that would otherwise be suppressed by beneficial microbes. These environmental stressors may lead to dysbiosis and the consequent emergence of chronic health problems.[22]

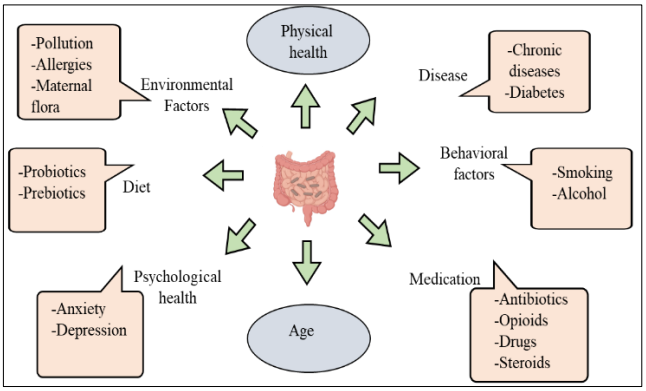


**Figure 1: Factors affecting the gut microbiota.**

### *Age and gender*

Age and gender are natural factors that influence the microbiota composition as in Figure 1. As the individual grows older, microbial biodiversity decreases, which can be associated with diseases of ageing, such as cognitive decline or frailty. Gender-based gut microbiota composition differences have also been found, with females tending to have more Firmicutes and Lactobacillus species, perhaps also depending on hormonal changes. Their knowledge will serve as a factors explaining how microbial composition changes with time and may influence health.[22]

### *Stress and mental health*

In psychological terms, stress, anxiety, and depression do affect the composition of gut microbiota. Chronic stress activates the hypothalamic-pituitary-adrenal (HPA) axis that releases stress hormones like cortisol that influence gut motility and microbial growth. This operates towards the imbalance of the gut microbiota, which in turn can be linked to gastrointestinal disorders and mental health ailments. Chronic stress activates the HPA axis that releases stress hormones like cortisol that influence gut motility and microbial growth. This operates towards the imbalance of the gut microbiota, which in turn can be

linked to gastrointestinal disorders and mental health ailments. There is a feedback loop between stress-induced changes in gut microbiota, with dysbiosis worsening both gut and mental health.[23]

### *Influence of microbiota on neurotransmitter production*

An important way the gut microbiota exerts its influence on brain function is through the setting or modulation of neurotransmitters determining mood, cognition, and mental health in general. Production of such bioactive compounds by gut microbes is how the gut-brain axis gets defined, a two-way street pathway in communication between the gut and brain.[9]

## MICROBIAL SYNTHESIS OF KEY NEUROTRANSMITTERS; SEROTONIN

Ninety percent of serotonin, a neurotransmitter responsible for mood regulation, appetite, and sleep, is formed in the gut. Other gut microbes, particularly Lactobacillus and Bifidobacterium, play a direct role in the manufacture of serotonin. The bacteria interact with gut enterochromaffin cells and determine the amount of serotonin the cells generate. This means a balanced microbiota will help maintain healthy serotonin levels, while dysbiosis could prevent it and, in turn, might contribute to different mood disturbances such as depression and anxiety.

### *Dopamine*

Dopamine is one of the most important neurotransmitters involved in pleasure, motivation, and reward. A few bacteria such as Lactobacillus and Enterococcus may also be capable of dopamine production. Dysbiosis, especially imbalance among Firmicutes and Bacteroides, will lower dopamine production, possibly leading to depression or lack of motivation.[25,26]

### *Gamma-aminobutyric acid*

GABA is the main inhibitory neurotransmitter in the brain and majorly contributes to the decrease of neuronal excitability and in producing a sense of relaxing effect. GABA production is associated with Lactobacillus and Bifidobacterium species, acting as a link for brain functions to be affected during stressful situations or anxiety levels. When GABA-producing microbes dwindle, agitation, anxiety, and other mental health pathologies may set in. GABA in the gut-brain axis affects the HPA axis, which governs the body's stress responses.

### *Acetylcholine*

Acetylcholine is one of the receptors involved with memory, attention, and learning. Furthermore, these areas can be aced by entry of Bacteroides and Bifidobacterium species in the gut that can produce acetylcholine. The imbalance in the gut microbiota can affect the production of acetylcholine, which may impair cognitive abilities and induce disorders such as Alzheimer's disease or cognitive decline.[27,28]

## MECHANISMS BEHIND MICROBIAL INFLUENCE ON NEUROTRANSMITTER PRODUCTION; DIRECT SYNTHESIS

Certain gut bacteria could directly synthesize neurotransmitters with the enzymatic possibility. These microbes metabolize dietary components or ferment fiber to metabolites, which could act as precursors for neurotransmitter synthesis.

### *Metabolic pathways involving short-chain fatty acids*

Dietary fibers are fermented by gut bacteria to produce SCFAs including acetate, propionate, and butyrate. These SCFAs modulate the gut-brain axis in various ways, such as affecting neurotransmitter production: butyrate elevates serotonin receptor expression and boosts serotonin levels in the brain, while acetate appears to affect GABA release.

### *Modulation of the blood-brain barrier*

The gut microbiota regulates the permeability of the blood-brain barrier, thereby allowing or preventing neurotransmitters from entering the brain. Beneficial microbes that produce SCFAs maintain the integrity of the BBB, whereas dysbiosis increases the permeability to allow neuroactive substances to alter cerebral function and behavior.

### *Immune system modulation*

From gut microbiota to the immune system and vice-versa, an enormous factor regulates the production of neurotransmitters. Through its modulation of immune mechanisms, the microbiota acts to reduce systemic inflammation, which results in neurochemical imbalances and the onset of psychopathologies. Cytokine-induced inflammatory conditions can inhibit the metabolism of tryptophan-a precursor to serotonin. Thus may give rise to lower serotonin levels and, ultimately, to mood disorders.[29,30]

## IMPACT OF DYSBIOSIS ON NEUROTRANSMITTER PRODUCTION

With dysbiosis and disturbance in the gut microbiota, the gut microflora loses its capacity to produce neurotransmitters, which changes brain chemistry and brings about various psychological and neurological disorders. The reduction in beneficial bacteria such as Lactobacillus and Bifidobacterium, which participate in serotonin and GABA production, can impair mood regulation, leading to increased incidences of depression, anxiety, and stress-related disorders. Moreover, the overgrowth of pathogenic bacteria can cause neuroinflammation, another harmful factor for the synthesis of neurotransmitters and brain function in

general. For example, decreased serotonin production in the gut due to a lack of serotonin-producing bacteria has been linked to depression and anxiety symptoms. Similarly, an imbalance in dopamine production in the gut, owing to dysbiosis, may lead to the onset of mood disorders, attention deficit, and impaired motivation.[31,32]

## THERAPEUTIC IMPLICATIONS: PROBIOTICS AND MICROBIOTA MODULATION

The capacity of the gut microbiota to influence the generation of neurotransmitters opens new therapeutic horizons. Probiotic administration, prebiotics in the diet, and antibiotic administration for the modulation of the gut microbiota constitute some of the approaches explored for treating mental disorders. The restoration of a normal microbial population may allow neurotransmitter levels to return to normal while decreasing neuroinflammation and psychological symptoms. Anxiety- and depression-relieving probiotics may, for example, be those increasing the population of GABA- and serotonin-producing bacteria.[33]

### *Probiotics*

The probiotics contain the living microflora, which, when given in adequate quantities, are advantageous to the health of the host by improving the environment of gut microbiota. The word "probiotic" has a Greek origin from "pro," meaning "for," and "bios," meaning "life"; thus, it means an organism "for life promotion." Various benefits of probiotics to human health have been claimed, such as improving digestive health, modulating some aspects of the immune system, and also affecting mental health via the gut-brain axis. These microorganisms usually reside in the gastrointestinal tract and promote the health of gut microbiota by possessing antagonistic abilities toward potential pathogens. Probiotics may be found in some fermented foods such as yoghurt, kefir, and kimchi, and in the form of dietary supplements. Common probiotic genera include Lactobacillus, Bifidobacterium, and Saccharomyces.[34]

Usually, probiotic preparations are therapeutic products that treat or prevent various gastrointestinal disorders such as irritable bowel syndrome (IBS), diarrhoea, and inflammatory bowel diseases (IBD). In recent times, more attention has been given to the beneficial effects of probiotic therapy in mental health, mainly through action on the gut-brain axis. It has been demonstrated that probiotics can improve mood and stress levels, which further attests to their general role in human health.

### *Classification of probiotics*

*Lactic acid bacteria (LAB)*

The most popular group of probiotics used and studied. LAB, such as Lactobacillus and Bifidobacterium species, are common in fermented dairy items. These bacteria work toward the maintenance of gut health by producing lactic acid, which lowers the pH in the gut and suppresses the growth of pathogenic organisms. LAB can even influence immune function and interact with the gut-brain axis.

*Bifidobacteria*

Bifidobacteria are considered a subgroup of lactic acid bacteria and are mainly found in the lower part of the intestinal tract. These bacteria are helpful for intestinal balance. They produce the short-chain fatty acids (SCFAs) that promote the integrity of the gut barrier system and quell inflammation. Certain species of Bifidobacteria are also believed to support mental well-being through the modulation of the gut-brain axis.

*Saccharomyces cerevisiae*

This probiotic yeast is conventionally used in dietary supplements and is beneficial in gastrointestinal disorders, predominantly diarrhoea. It also aids in immune modulation, which may have indirect repercussions on mental health.

*Streptococcus thermophiles*

There is another important bacterium that is part of the probiotics and often present in yoghurt, which helps in the fermentation process and in enhancing gut health by secreting some favourable metabolites.[35,36]

## MECHANISMS OF ACTION OF PROBIOTICS; MODULATION OF GUT MICROBIOTA COMPOSITION

Modifications in the central gut microbiota constitution are the most prominent mode of probiotics. Probiotics compete for the nutrients and sites of attachment with harmful microbes to avoid the proliferation of pathogenic bacteria. This microbial balance plays a very much in maintaining the health status within the gut and in the appearance of different kinds of gastrointestinal disorders such as diarrhoea, constipation, or IBD. By maintaining a healthy microbiome, probiotics promote good digestion, absorption of nutrients, and general immune function.[37]

### *Strengthening the gut barrier function*

The permeability of the intestinal epithelial barrier may be enhanced or stabilised by probiotics to avoid the entry of harmful substances into the bloodstream. This action is very essential in preventing phenomena such as "leaky gut syndrome," which is characterised by myriad diseases of autoimmune expression or mental health issues. Mucins are released because of probiotics, forming a protective mucus layer that guards the gut lining from toxins and pathogens. These probiotic strains release certain SCFAs, butyrate being one among them. It has proven to protect the intestinal barrier by maintaining the health of the epithelial cells. This mechanism thus allows prevention of

gut permeability and systemic inflammation, two conditions correlated with distinct mental health-related disorders.[38]

### *Immune system modulation*

Probiotics interact with the gut-associated lymphoid tissue, or GALT, which is where most of the immune cells of the body reside. These probiotics integrate the immune systems very well by increasing the release of beneficial cytokines, such as interleukin-10, while suppressing those pro-inflammatory cytokines, like TNF-α and IL-6. In that sense, immune modulation can also be useful against excessive inflammation, which is common in depression, anxiety, and neurodegenerative conditions. Otherwise, probiotics can alter the systemic immune system to reduce the risk of infections and autoimmune disorders. This is a crucial aspect since chronic inflammation has been implicated in the underlying pathology of several psychiatric disorders.[39]

### *Neurotransmitter and metabolite production*

Certain probiotics may influence brain function by producing various neurotransmitters or metabolites. Lactobacillus and Bifidobacterium species, in particular, have been implicated in modulating the production of serotonin, a neurotransmitter implicated in mood regulation. Since roughly 90% of serotonin production in the human body happens in the gut, probiotics have been hypothesised to improve mood and decrease the incidence of depression by modulating the gut microbiota. In addition to serotonin, probiotics also have an impact on dopamine and GABA, two neurotransmitters that regulate behaviour, stress response, and cognitive function. Additionally, probiotics release metabolites like SCFAs, which aid in regulating the HPA axis, which is the source of an organism's stress response.[40]

### *Vagus nerve activation*

The vagus nerve acts as an important communication link between the gut and the brain. It is thought that probiotics could activate the vagus nerve to send messages to influence brain functioning. Some studies indicated that such probiotic organisms could activate the vagus nerve, thus affecting mood, stress response, and mental well-being in general. This mechanism signifies the ability of probiotics to help with mental health through direct neural pathways.[41]

## IMPACT OF PROBIOTICS ON MENTAL HEALTH DISORDERS; PROBIOTICS AND DEPRESSION

This major depressive disorder (MDD) is a widely recognised psychiatric disorder and is characterised by a low mood, loss of interest, and impaired cognitive functions. Recent studies have suggested that gut dysbiosis and systemic inflammation eventually lead to its etiopathogenesis. The use of probiotics in the treatment of depression showed good preliminary evidence through a number of mechanisms, including amelioration of systemic inflammation, modification of the HPA axis, and enhancement of neurotransmitter synthesis. Several clinical trials investigating strains such as *Lactobacillus helveticus*, *Bifidobacterium longum*, and *Lactobacillus casei* have shown efficacy in improving mood, sleep, and emotional stability. The psychobiotics work by lowering cortisol and affecting serotonin pathways, thus providing an alternative, adjuvant treatment of depression.[42]

### *Probiotics and anxiety disorders*

Alterations in the gut microbiota have become more associated with anxiety disorders, including GAD, panic disorders, and social anxiety. Probiotics alleviate anxiety-like behaviours by promoting GABA production, reducing the HPA axis response, and mediating neuroinflammation. In animal models and human trials, Lactobacillus rhamnosus and Bifidobacterium breve strains have been known to lower the anxiety scores. Furthermore, probiotics have been found to promote stress resilience and cognitive performance during stress, suggesting that probiotics might be part of prevention and treatment approaches for anxiety-related conditions.[43] Table 2 highlights preclinical and clinical findings supporting the therapeutic effects of specific probiotics strains on mental health conditions.

### *Probiotics and stress management*

Psychological and physiological stress have the power to alter the constitution of the bacterial colonisation and also bring gastrointestinal symptoms, inflammation, and decline in mental health. It could be postulated that a probiotic may act against stress by reinforcing the gut barrier function, minimising cortisol levels, and balancing immune responses. The clinical studies about students and healthcare workers subjected to stress exerted by exams or occupations have evidenced the possibility of perceived stress diminishment and sleep enhancement through probiotic intake. The said benefits mostly owe to microbial balance restoration and increased communication across the gut-brain axis.[44]

### *Probiotics and cognitive function*

The literature strongly suggests an association between gut microbiota and memory, attention, and executive function. In neurodegenerative disorders such as Alzheimer's and MCI, gut dysbiosis has been observed along with systemic inflammation and oxidative stress. Probiotics might improve cognitive outcomes by regulating gut inflammation and amyloid accumulation and by promoting neurogenesis. Some isolated strains like *Lactobacillus plantarum* and *Bifidobacterium lactis* have managed preclinical studies to show some effects on memory and learning, in parallel with very early clinical trials noting improvements in cognitive scores among elderly

populations administered with multi-strain probiotic formulations.[45]

***Probiotics and autism spectrum disorders***

Children affected by autism spectrum disorders (ASD) often suffer from gastrointestinal disorders associated with an altered gut microbiota profile or composition. By the gut-brain axis, the disorders and manifestations of behaviour related to autism are considered in view of development. In this context, enough antibiotic potential may be awarded to stop degradation of microbial diversity, to decrease gut inflammation, and to prevent the induction of intestinal permeability. Considering this scenario, behavioural improvements in terms of hyperactivity, communication, and social interaction during probiotic administration have been reported by several clinical trials. *L. acidophilus*, *B. infantis*, and *S. thermophilus* have shown potential promise in this field, but larger studies still need to be conducted.[46]

***Psychobiotics: a subclass of probiotics for mental health***

Psychobiotics are an emerging subclass of probiotics that have shown the potential to improve psychiatric conditions by modifying GBA. Psychobiotics were first termed in 2013 by Dinan et al, who defined them as: "live organisms which when ingested in adequate amounts produce a health benefit in patients suffering from psychiatric illness". Most of these organisms are from the genus Lactobacillus and Bifidobacterium, with others being studied as research in this area continues.

Psychobiotics oppose effects in several ways, firstly by producing and modifying the key neurotransmitters serotonin, GABA, and dopamine. These neurotransmitters are essential for mood regulation, response to stress, and emotional behaviour. Few psychobiotics also interfere with the HPA axis that governs cortisol levels and the body's reaction to stress. These psychobiotics thus work by reducing inflammation all over the body and by strengthening the integrity of the intestinal barrier so that neuroinflammation may be avoided. It is becoming more and more accepted in the medical industry that such neuroinflammation is related to depression and anxiety.[47,48]

The preclinical and early phases of human studies seem to suggest that some or other beneficial effects in terms of alleviating stress and improving cognitive functioning could be imparted by Bifidobacterium longum, while anxiolytic effects have been observed to be exerted in animal experimentation on *L. rhamnosus* by vagus nerve signalling. Still rare, clinical trials seem to insinuate that such psychobiotic therapy could be given alongside conventional therapy for the treatment of depression, generalised anxiety disorder, and maybe even autism spectrum disorder shown in Figure 2.

Psychobiotics still show potential as an emerging concept. To mention a few, the issues at hand include strain specificity, the optimum dose, and perhaps just in terms of variability in the human gut microbiota. Beyond this, they represent a promising front in linking microbiome science and mental health, bearing in mind the possibility of a personalised, non-invasive approach toward psychological interventions.[49]

**Table 2: Preclinical and clinical evidence of probiotics in mental health.**

| Probiotic strain | Study type | Targeted condition | Citation | Conclusion |
|---|---|---|---|---|
| ***Lactobacillus rhamnosus* JB-1** | Preclinical (mouse model) | Anxiety and depression-like behaviour | Bravo et al | Targeted GABA modulation yielded reduced anxiety- and depression-like behaviours through vagus nerve signalling in mice.[50] |
| ***Lactobacillus rhamnosus* zz-1** | Preclinical (mouse model) | Depression induced by chronic stress | Xu et al | Reduction in depression-like behaviours as well as modulation of gut microbiota composition were observed in chronically stressed mice.[51] |
| ***Lactobacillus casei*** | Preclinical (rat model) | Depression-like behavior | Wang et al | Improvement of depressive behaviours and an increase in hippocampus BDNF levels in rats.[52] |
| ***Lactobacillus paracasei* CCFM1229 and *Lactobacillus rhamnosus* CCFM1228** | Preclinical (mouse model) | Depression and anxiety induced by chronic stress | Xu et al | Reducing depressive and anxiety-like behaviours and modulating the gut microbiota in stressed mice.[53] |
| ***Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175** | Clinical (randomised, double-blind, placebo-controlled trial) | Depression and anxiety in healthy volunteers | Messaoudi et al | Reduction of psychological distress and cortisol levels in healthy adults after 30 days of supplementation.[54] |

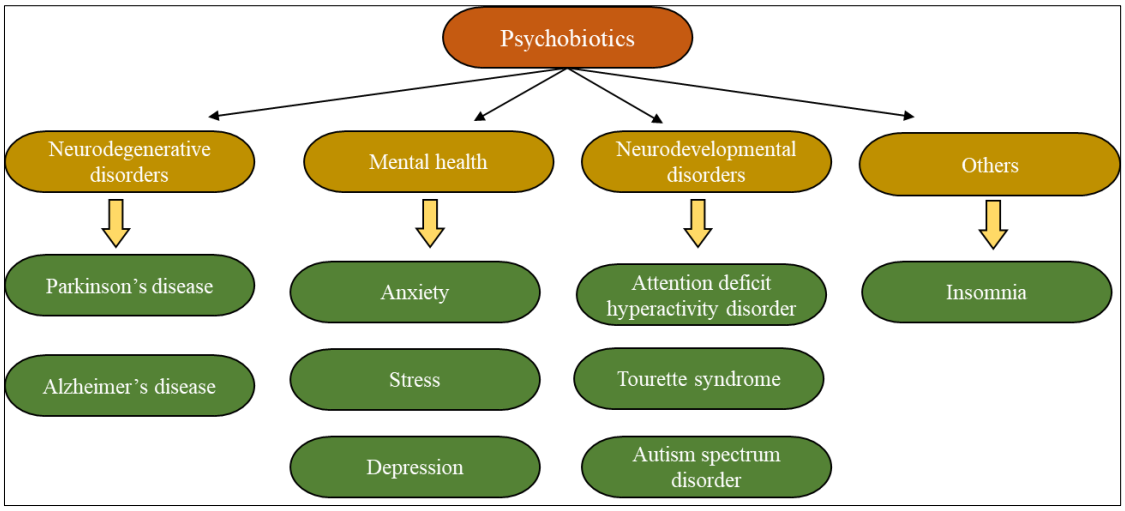


**Figure 2: Class of psychobiotics on mental health disorders.**

## SAFETY CONSIDERATIONS

Concerning their use, the safety aspects of psychobiotics hold a pivotal role, especially once such medications are to be used in any form of treatment for mental health. While probiotics work well, are safe, and in general are harmless for a healthy individual, it must be ensured that psychobiotics would not have adverse effects on those who are immune-compromised, infants, or suffer from serious gastrointestinal diseases. While in the clinical trials, side effects should be recorded for otherwise healthy individuals, such as gastrointestinal distress (bloating, gas), infections (in immunocompromised patients), and interactions with other medications. Also important would be long-term safety profiles to locate any risks in prolonged use, especially regarding assigning this to the delicate equilibrium of gut microbiota. Because of how complicated the gut-brain axis is, the possibility of psychobiotics having effects on psychological states themselves has to be examined, to preclude any adverse effect neuropsychologically, such as mood swings or even the deterioration of mental health conditions.[55]

## FUTURE PERSPECTIVES AND RESEARCH DIRECTIONS

As the research into gut-brain communication and the effect of probiotics on the mind is being expanded, future perspectives hold very promising possibilities of more personalised, effective, and integrative therapies. Among other paramount topics for future research would be precision psychobiotics, which would imply working toward developing customised probiotic strains designed with respect to one's particular gut microbiota pattern, genetic background, and mental health condition. Such an approach may indeed serve as a bridge toward targeted therapies for psychiatric disorders such as depression, anxiety, and autism spectrum disorders.[56]

Furthermore, to strengthen the current evidence base, more major longitudinal human trials are required. These should emphasise standardised probiotic strains, dosage, treatment durations, and validated psychiatric outcome measures. Employing multi-omics techniques of metagenomics, metabolomics, and proteomics in the research can unravel in-depth mechanisms linking gut microbes to mental functions. Artificial intelligence and machine learning could then be married together to track and analyse these complex datasets and predict outcome scenarios of treatment based on the profile of their microbiota.[57]

Ethical considerations, regulatory clarity, and consumer education will face more emphasis during the entry of psychobiotics into the mainstream clinical practice scenario. Gut-brain axis may soon take the centre stage in personalised mental healthcare through further interdisciplinary collaboration among microbiology, psychiatry, and neuroscience.[49]

## CONCLUSION

The exciting new field of the gut-brain axis has helped to yield a whole new appreciation of the complex relationship between gut microbiota and mental health. There is increasing evidence for gut microbes as modulators of brain function, mood, and behaviour via different neural, hormonal, and immune mechanisms. Dysbiosis, - imbalanced microbial populations of the gut- has been associated with many psychiatric disorders, such as depression, anxiety, and stress-related conditions. A great promise that probiotics and psychobiotics might offer is a natural therapeutic pathway to control the gut microbiota towards beneficial mental health outcomes. On the basis of promising preclinical and clinical studies so far, more standardised, larger human trials now need to be carried out to establish efficacy, safety, and usage parameters. As the research develops, it may soon be possible to integrate probiotics into the psychiatric practice as an emerging

complementary treatment of established therapies that is least invasive to the patients and follows the principles of holism.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: Not required*

## REFERENCES

1. Kirkbride JB, Anglin DM, Colman I, Dykxhoorn J, Jones PB, Patalay P, et al. The social determinants of mental health and disorder: evidence, prevention and recommendations. World Psychiatry. 2024;23(1):58.
2. Kuwahara A, Matsuda K, Kuwahara Y, Asano S, Inui T, Marunaka Y. Microbiota-gut-brain axis: Enteroendocrine cells and the enteric nervous system form an interface between the microbiota and the central nervous system. Biomed Res (Japan). 2020;41(5):199-216.
3. Zhu X, Han Y, Du J, Liu R, Jin K, Yi W. Microbiota-gut-brain axis and the central nervous system. Oncotarget. 2017;8(32):53829-38.
4. Butler MI, Mörkl S, Sandhu KV, Cryan JF, Dinan TG. The Gut Microbiome and Mental Health: What Should We Tell Our Patients?: Le microbiote Intestinal et la Santé Mentale : que Devrions-Nous dire à nos Patients? Canad J Psychiatr. 2019;64(11):747-60.
5. Jiang S, Hu JY, Cheng HW. The Impact of Probiotic Bacillus subtilis on Injurious Behavior in Laying Hens. Animals. 2022;12(7):870.
6. Rhee SH, Pothoulakis C, Mayer EA. Principles and clinical implications of the brain-gut-enteric microbiota axis. Nat Rev Gastroenterol Hepatol. 2009;6(5):306-14.
7. Zheng Y, Bonfili L, Wei T, Eleuteri AM. Understanding the Gut–Brain Axis and Its Therapeutic Implications for Neurodegenerative Disorders. Nutrients. 2023;15(21):4631.
8. Sharkey KA, Mawe GM. The enteric nervous system. Physiol Rev. 2023;103(2):1487-564.
9. Chen Y, Xu J, Chen Y. Regulation of neurotransmitters by the gut microbiota and effects on cognition in neurological disorders. Nutrients. 2021;13(6):2099.
10. Breit S, Kupferberg A, Rogler G, Hasler G. Vagus nerve as modulator of the brain-gut axis in psychiatric and inflammatory disorders. Front Psychiatry. 2018;9:3.
11. Bonaz B, Sinniger V, Pellissier S. Vagus nerve stimulation: a new promising therapeutic tool in inflammatory bowel disease. J Intern Med. 2017;282(1):46-63.
12. Rusch JA, Layden BT, Dugas LR. Signalling cognition: the gut microbiota and hypothalamic-pituitary-adrenal axis. Front Endocrinol (Lausanne). 2023;5:14.
13. Herman JP, McKlveen JM, Ghosal S, Kopp B, Wulsin A, Makinson R, et al. Regulation of the hypothalamic-pituitary- adrenocortical stress response. Compr Physiol. 2016;6(2):603-21.
14. O'Riordan KJ, Moloney GM, Keane L, Clarke G, Cryan JF. The gut microbiota-immune-brain axis: Therapeutic implications. Cell Rep Med. 2025;6(3):101982.
15. Rosendo-Silva D, Viana S, Carvalho E, Reis F, Matafome P. Are gut dysbiosis, barrier disruption, and endotoxemia related to adipose tissue dysfunction in metabolic disorders? Overview of the mechanisms involved. Intern Emerg Med. 2023;18(5):1287-302.
16. Ogunrinola GA, Oyewale JO, Oshamika OO, Olasehinde GI. The Human Microbiome and Its Impacts on Health. Int J Microbiol. 2020;2020:8045646.
17. Rinninella E, Raoul P, Cintoni M, Franceschi F, Miggiano GAD, Gasbarrini A, et al. What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. Microorganisms. 2019;7(1):14.
18. Hasan N, Yang H. Factors affecting the composition of the gut microbiota, and its modulation. Peer J. 2019;7:e7502.
19. Dahiya D, Nigam PS. Antibiotic-Therapy-Induced Gut Dysbiosis Affecting Gut Microbiota—Brain Axis and Cognition: Restoration by Intake of Probiotics and Synbiotics. Int J Mol Sci. 2023;24(4):3074.
20. Zhang C, Li L, Jin B, Xu X, Zuo X, Li Y, et al. The Effects of Delivery Mode on the Gut Microbiota and Health: State of Art. Front Microbiol. 2021;12:724449.
21. Vinogradova E, Mukhanbetzhanov N, Nurgaziyev M, Jarmukhanov Z, Aipova R, Sailybayeva A, et al. Impact of urbanization on gut microbiome mosaics across geographic and dietary contexts. mSystems. 2024;9(10):e0058524.
22. Li H, Ni J, Qing H. Gut Microbiota: Critical Controller and Intervention Target in Brain Aging and Cognitive Impairment. Front Aging Neurosci. 2021;5:13.
23. Wang HX, Wang YP. Gut microbiota-brain axis. Chin Med J (Engl). 2016;129(19):2373-80.
24. Nakhal MM, Yassin LK, Alyaqoubi R, Saeed S, Alderei A, Alhammadi A, et al. The Microbiota–Gut–Brain Axis and Neurological Disorders: A Comprehensive Review. Life. 2024;14(10):1234.
25. Terry N, Margolis KG. Serotonergic mechanisms regulating the GI tract: Experimental evidence and therapeutic relevance. Handb Exp Pharmacol. 2017;239:319-42.
26. Hamamah S, Aghazarian A, Nazaryan A, Hajnal A, Covasa M. Role of Microbiota-Gut-Brain Axis in Regulating Dopaminergic Signaling. Biomedicines. 2022;10(2):436.
27. Linseman D, Marini HR, Almutairi S, Sivadas A, Kwakowsky A. The Effect of Oral GABA on the Nervous System: Potential for Therapeutic Intervention. Nutraceuticals. 2024;4(2):241-59.
28. Dicks LMT. Gut Bacteria and Neurotransmitters. Microorganisms. 2022;10(9):1838.

29. Averina O V., Zorkina YA, Yunes RA, Kovtun AS, Ushakova VM, Morozova AY, et al. Bacterial metabolites of human gut microbiota correlating with depression. Int J Mol Sci. 2020;21(23):1-40.
30. Fusco W, Lorenzo MB, Cintoni M, Porcari S, Rinninella E, Kaitsas F, et al. Short-Chain Fatty-Acid-Producing Bacteria: Key Components of the Human Gut Microbiota. Nutrients. 2023;15(9):2211.
31. Mitrea L, Nemeş SA, Szabo K, Teleky BE, Vodnar DC. Guts Imbalance Imbalances the Brain: A Review of Gut Microbiota Association With Neurological and Psychiatric Disorders. Front Med (Lausanne). 2022;9:813204.
32. Bamicha V, Pergantis P, Drigas A. The Effect of Gut Microbiome, Neurotransmitters, and Digital Insights in Autism. Appl Microbiol. 2024;4(4):1677-701.
33. Ansari F, Neshat M, Pourjafar H, Jafari SM, Samakkhah SA, Mirzakhani E. The role of probiotics and prebiotics in modulating of the gut-brain axis. Front Nutr. 2023;10:1173660.
34. Mörkl S, Butler MI, Holl A, Cryan JF, Dinan TG. Probiotics and the Microbiota-Gut-Brain Axis: Focus on Psychiatry. Curr Nutr Rep. 2020;9(3):171-82.
35. Tabrizi A, Khalili L, Homayouni-Rad A, Pourjafar H, Dehghan P, Ansari F. Prebiotics, as promising functional food to patients with psychological disorders: A review on mood disorders, sleep, and cognition. NeuroQuantology. 2019;17(6):1-9.
36. Pandey KR, Naik SR, Vakil B V. Probiotics, prebiotics and synbiotics- a review. J Food Sci Technol. 2015;52(12):7577-87.
37. Plaza-Diaz J, Ruiz-Ojeda FJ, Gil-Campos M, Gil A. Mechanisms of Action of Probiotics. Adv Nutr. 2019;10(1):S49-66.
38. Azad MAK, Sarker M, Li T, Yin J. Probiotic Species in the Modulation of Gut Microbiota: An Overview. Biomed Res Int. 2018;2018:9478630.
39. Mazziotta C, Tognon M, Martini F, Torreggiani E, Rotondo JC. Probiotics Mechanism of Action on Immune Cells and Beneficial Effects on Human Health. Cells. 2023;12(1):184.
40. Akram N, Faisal Z, Irfan R, Shah YA, Batool SA, Zahid T, et al. Exploring the serotonin-probiotics-gut health axis: A review of current evidence and potential mechanisms. Food Sci Nutr. 2024;12(2):694-706.
41. Tan C, Yan Q, Ma Y, Fang J, Yang Y. Recognizing the role of the vagus nerve in depression from microbiota-gut brain axis. Front Neurol. 2022;13:1015175.
42. Gao J, Zhao L, Cheng Y, Lei W, Wang Y, Liu X, et al. Probiotics for the treatment of depression and its comorbidities: A systemic review. Front Cell Infect Microbiol. 2023;13:1167116.
43. Merkouris E, Mavroudi T, Miliotas D, Tsiptsios D, Serdari A, Christidi F, et al. Probiotics' Effects in the Treatment of Anxiety and Depression: A Comprehensive Review of 2014–2023 Clinical Trials. Microorganisms. 2024;12(2):411.
44. Madison A, Kiecolt-Glaser JK. Stress, depression, diet, and the gut microbiota: human–bacteria interactions at the core of psychoneuroimmunology and nutrition. Curr Opin Behav Sci. 2019;28:105-10.
45. Białecka-Dębek A, Granda D, Szmidt MK, Zielińska D. Gut microbiota, probiotic interventions, and cognitive function in the elderly: A review of current knowledge. Nutrients. 2021;13(8):2514.
46. Saurman V, Margolis KG, Luna RA. Autism Spectrum Disorder as a Brain-Gut-Microbiome Axis Disorder. Dig Dis Sci. 2020;65(3):818-28.
47. Dinan TG, Stanton C, Cryan JF. Psychobiotics: A novel class of psychotropic. Biol Psychiatry. 2013;74(10):720-6.
48. 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):1-31.
49. Sarkar A, Lehto SM, Harty S, Dinan TG, Cryan JF, Burnet PWJ. Psychobiotics and the Manipulation of Bacteria–Gut–Brain Signals. Trends Neurosci. 2016;39(11):763-81.
50. Bravo JA, Forsythe P, Chew MV, Escaravage E, Savignac HM, Dinan TG, et al. Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. Proc Natl Acad Sci U S A. 2011;108(38):16050-5.
51. Xu J, Tang M, Wu X, Kong X, Liu Y, Xu X. Lactobacillus rhamnosus zz-1 exerts preventive effects on chronic unpredictable mild stress-induced depression in mice via regulating the intestinal microenvironment. Food Funct. 2022;13(8):4331-43.
52. Gu F, Wu Y, Liu Y, Dou M, Jiang Y, Liang H. Lactobacillus casei improves depression-like behavior in chronic unpredictable mild stress-induced rats by the BDNF-TrkB signal pathway and the intestinal microbiota. Food Funct. 2020;11(7):6148-57.
53. Xu M, Tian P, Zhu H, Zou R, Zhao J, Zhang H, et al. Lactobacillus paracasei CCFM1229 and Lactobacillus rhamnosus CCFM1228 Alleviated Depression- and Anxiety-Related Symptoms of Chronic Stress-Induced Depression in Mice by Regulating Xanthine Oxidase Activity in the Brain. Nutrients. 2022;14(6):1294.
54. Messaoudi M, Violle N, Bisson JF, Desor D, Javelot H, Rougeot C. Beneficial psychological effects of a probiotic formulation (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) in healthy human volunteers. Gut Microbes. 2011;2(4):256-61.
55. 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.
56. Franco CD, Sagar RS, Bokhari SFH. From Microbes to Memories: Challenges and Future Perspectives Regarding the Gut-Brain Axis for Improved Cognitive Health in Alzheimer's. Cureus. 2024;16(1):e52795.

57. Cho M-Y, Eom J-H, Choi E-M, Yang S-J, Lee D, Kim YY, et al. Recent advances in therapeutic probiotics: insights from human trials. Clin Microbiol Rev. 2025;38(2):e0024024.

**Cite this article as:** Srinivas YR, Ramesh TM, Muddanna PKC, Jayappa MKB. A review on probiotics and mental health: exploring the gut-brain axis and its therapeutic potential. Int J Res Med Sci 2025;13:3921-32.