Chapter 2

Influence of Probiotic Supplementation on Brain Function: Involvement of Gut Microbiome, Inflammation, and Stress Pathway

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Abstract

Probiotics were reported for several physical and psychological health benefits. Probiotics can positively alter the gut microbiome and nourish the commensal microbial load. Recent studies revealed that the cognitive functions (anxiety and depression) of human beings are meticulously associated with their genetic makeup, food habits, and gut microbiome. The gut microbiome may communicate with the brain through neural and humoral pathways, while involving several neurotransmitters and signaling molecules. The immune response, especially inflammatory system, plays a critical role in the microbiome and in mental health. Thus, many studies were conducted to explore the beneficial effect of probiotic, single and multistrain, formulations. Fruitful results were observed, but the underlying mechanism of probiotic-mediated improvement of mental health is not fully illustrated, even though some studies explained that the production of neurotransmitter-like metabolites by the probiotic strain could be the possible mediator of gut-brain axis. The present chapter summarizes the outcome of probiotic-based treatment for the improvement of stress and depression with respect to microbiome change, inflammation, and stress pathway.

Keywords: probiotics, stress, depression, anxiety, microbiome, inflammation

1. Introduction

According to FAO/WHO, probiotics are living bacteria that, which when administered in suitable amounts, confer a health benefit to the host. *Lactobacillus* (*Lactobacillus casei, L. paracasei,*

L. acidophilus, L. fermentum, L. rhamnosus, L. brevis, L. plantarum, L. johnsonii, and *L. delbrueckii* subsp. *bulgaricus*), *Bifidobacterium* (*Bifidobacterium bifidum, B. breve, B. longum, B. adolescentis, B. infantis, B. animalis* subsp. *animalis, B. animalis* subsp. *lactis*), *Enterococcus, Saccharomyces* (*Saccharomyces bayanus, S. boulardii*), *Streptococcus, Leuconostoc, Pediococcus,* and *Bacillus* are the common genera of probiotic strains [1]. Generally, probiotics are known for the improvement of digestion, nutrient absorption, immune modulatory property, maintaining the intestinal microbiota and supplement for metabolic disorders. But recent studies suggested that the supplementation of probiotic-containing traditional functional foods improved the mental health and cognitive function of the host [2, 3].

The brain is a vital organ involved in leading and coordinating the homeostasis of the body. The changes or defect in the brain functions are closely associated with the development of serious physiological and emotional impairment [4, 5]. The cognitive impairment is not only associated with a decline in brain function but also linked to the immune system and the changes in microbiome. The new finding and complexity of the network provide new perceptions into cognitive dysfunctions [6].

The microbes residing in the gastrointestinal tract of human have been referred as gut microbiota or gut microbiome. The commensal microbial population was closely associated with the host system, and they have a complex connective ecosystem, which influences the physical and functionality of the host. Bacteroides, Prevotella, and Ruminococcus families are three most abundant bacterial communities in the gastrointestinal tract. Recent studies demonstrated how the commensal microbes modify them according to the environment and the availability of nutrition [7].

Inflammation is one of the body processes of protecting against harmful stimuli or any antigens. Even though inflammation is a part of the immune system, the chronic inflammation may lead to the development of malignancy. The alteration in microbiome and release of endogenous microbial debris induce chronic inflammation. More significantly, the microbiome may play an imperative role in modulating behavior by linking the immune systems and neuroendocrine via cytokines and the nerve system [8].

The stress and immune-induced pathways, for example, kynurenine pathway (PK), are involved in several neurodegenerative diseases and psychiatric disorders. Manipulating the gut microbiome may diminish the effect of stress-induced neurological damages. Studies on the link between the gut microbiome and brain provide significant information about the role of the microbiome in brain function and development [9]. The metabolites of gut microbiome act as neurotransmitters, which regulate the brain function [10]. The role of the gut microbiome and probiotic supplementation on the improvement of memory has been reported [3]. The infection-mediated induction of cytokines altered the neuronal system and leads to the development of behavioral abnormalities [11].

Recently, probiotics were studied for their involvement in neurology, neurobehaviors, brain function, and cognition. Several preliminary studies revealed the importance of probiotics in neuroscience and cognition [12, 13]. The present chapter compiles the information about the probiotic-based improvement of brain health with respect to the cognitive function and discusses the microbiome changes upon probiotic supplementation.

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2. Gut microbiome, inflammation, and brain function

The microbial load in the human gastrointestinal tract is about 10^{14} cells; on the other hand, studies suggested that the ratio of microbial and human cells is 3:1. The diversity and richness of the microbial community are varied during the developmental stage of the host, and two-thirds of microbes are unique to every human being. This unique microbial community is responsible for the host individuality in terms of immunity, physical activity, and overall health status. The mislead in the symbiotic relationship between host and microbes cause some unwanted health conditions like diabetes, obesity, and inflammatory bowel diseases [14, 15].

The mutual communication between brain and gut is documented, and the information exchange has been carried out via several immunes, neuroendocrine pathways, and enteric nerve systems [16, 17]. About 500 million nerve endings, mostly enteric nerve system, and high concentrations of immune cells are present in the gastrointestinal tract (GI), so most of the bidirectional interaction between the gut and brain mainly occurs in the GI tract. The afferent neurons of the enteric nervous system communicate with the GI tract and brain through the vagus nerve [18].

Several biochemical and neuronal signaling pathways are established and involved in the GI tract and central nerve system (CNS), and the signaling network is known as gut-brain-axis. The malfunction of the gut-brain axis may cause pathophysiological events and is linked to inflammation, chronic abdominal pain, eating disorders, and stress [16, 17]. The vagus nerve system, cell wall components (pathogen-associated molecular patterns, e.g., lipopolysaccharide, peptidoglycan monomers, and lipoteichoic acids), fatty acids, metabolites, neurotransmitters and neuropeptides-like gamma-aminobutyric acid (GABA), serotonin, and brain-derived neurotrophic factors are the key players of the gut-brain axis [15].

The association of microbiome and immune system has been studied using germ-free mice. The supplementation of specific microbes, either pathogenic or commensal, to germ-free mice and the study of the changes in the behavior and immune system help to understand the role of particular microbes in host immune system and cognition. The results of studies using germ-free model revealed the importance of gut microbiome. The immune system of gut protects the system from pathogenic infection and supports the growth of commensal microbes [8]. The immune system of the antibiotic-treated mice was diminished during flu virus exposure compared to untreated mice, which revealed the importance of beneficial gut microbes, especially *Bifidobacterium* and *Lactobacillus* spp. [19].

A balanced communication between host immune system and gut microbiome is necessary to establish the homeostasis, which protects the system during adverse conditions. The weakening of gut-brain signaling is linked with the development of inflammation. If there is any alteration in the neuroendocrine system, for example, cortisol level, the barrier function of the gut is amended and the permeability increased, which in turn induces the release of cytokines by immune cells [16].

The lipopolysaccharide (LPS) injection is employed to induce a strong immune response, which increases the level of pro-inflammatory cytokines and glucocorticoids. The LPS challenging mimic as pathogenic infection and the elucidated immune response can weaken the development of the physiological system [20]. LPS can induce the release of pro-inflammatory cytokines, interferons, IL-1β, IL-2, IL-6, and TNF-α that can act on the brain, and initiates the

acute-phase responses like fever, reduced food intake, and boosted pain response [21, 22]. The responses, both physiological and behavioral, to pathogen-associated molecular pattern (like LPS, lipoteichoic acid, and flagellin) are comparable to the physiological and behavioral changes in neurological disorders like anxiety, depression, and autism. It is evidenced that gut-brain axis, microbiome, and immune system are related to each other [21–23].

3. Stress, microbiome, and immune system

Psychological disorders like anxiety and depression display consequences on the gastrointestinal function that links to the brain. The brain can communicate with the gut via the hypothalamic-pituitary-adrenal (HPA) axis, autonomic, and the enteric nervous system. Stress may be responsible for the dysregulation of gut-brain axis and cause gastrointestinal consequences [24]. The corticotrophin-releasing factor (CRF), a group of peptides of the central nervous system, is one of the regulators of immune, endocrine, and behavioral response to stress. The CRFs can alter the gut-brain interaction, which can alter the gastrointestinal motility, gastrointestinal secretion, intestinal permeability, intestinal microbiota, and visceral perception.

The pituitary gland releases the adrenocorticotropic hormone that stimulates the adrenal glands to produce cortisol, a stress hormone. All the processes were initiated by the release of CRF in the hypothalamus, which in turn activates the hypothalamic pituitary adrenal axis [25]. The crosstalk between gut-brain axis, the gut microbiome, and the immune system has a crucial role in the inflection of the stress response of the gut in terms of the development of gut disorders and diseases. The stress changes the microbial flora, which may have a reflective effect on the gut-brain axis and may alter the permeability, motility, and visceral sensitivity [26].

The microbiome of normal and depressed humans has been analyzed and the results revealed that there were no significant changes in the microbial group, but the amount of specific bacterial groups was altered (increase in Bacteroidetes species and decrease in Lachnospiraceae) among the depressed people. Especially, Oscillibacter (can produce GABA like neurotransmitter) and Alistipes were more abundant in depressed individuals. Alistipes was reported to be associated with stressed mice, chronic fatigue syndrome, and irritable bowel syndrome [27–30]. Jiang et al. reported that major depressive people have high amounts of Bacteroidetes, Actinobacteria, and Proteobacteria, while Firmicutes content was very low [31].

The stress brings the changes in inflammatory cytokines and neurotransmitter levels that could disturb the microbiota either directly or indirectly. The increase in norepinephrine alters the virulence of commensal bacteria like *Escherichia coli*. The sensitivity to pain can be altered in the gut microbiota, and stress-induced intestinal permeability has been suppressed by the probiotic supplementation [32]. For example, *E. coli* Nissle strain reduced the stress-mediated gastric lesions, and the effect was sensitive to capsaicin-mediated blockage of the sensory nerves. The probiotic effect of *E. coli* Nissle was restored by the addition of calcitonin gene-related peptide. The study proved the bidirectional talk between microbiota and the enteric nervous system [33]. The mast cells produced several vital mediators and acted as a receptor for CRF, thereby conveying the stress signal to the gut. The prolonged exposure to stress, chronic stress, may cause even permanent changes in the brain which affects the alertness of pain in the gut [32, 34].

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Stress can induce the tryptophan metabolic pathways, also known as kynurenine pathway (KP). KP is known to be involved in several neurological regulations and neurodegenerative diseases [35, 36]. The connections between kynurenine pathway, stress, microbiota, and gut-brain axis are not fully elucidated. The involvement of KP in stress and neuropsychiatric disorder has been reported [37].

4. Impact of probiotic supplementation on brain function, immunity, and microbiome

4.1. *In vivo* studies

The mice (germ-free and specific pathogen-free) were supplemented with *B. infantis* or enteropathogenic *Escherichia coli* (EPEC) and then the acute restraint stress response was analyzed. The adrenocorticotropic hormone and corticosterone levels were high in germ-free mice, while brain-derived neurotrophic factor was low compared to specific pathogen-free mice. *B. infantis* intervention reduced the stress response in germ-free mice, whereas the EPEC enhanced the stress response. The authors suggested that the boost in HPA response in germ-free mice was associated with reformation of gut microbiota with the faces of specific pathogen-free mice. The development of postnatal hypothalamic-pituitary-adrenal (HPA) stress response is greatly associated with commensal microbes, which were exposed during the early stage of development [38].

The female Wister rats were supplemented with *L. farciminis*, with the ability to release nitric oxide, and proved to have anti-inflammatory property, (10^{11} CFU/day) for 15 days and were subjected to partial restraint stress study and hemoglobin measurement. The results proved that *L. farciminis* intervention suppressed the stress, reduced the colonial permeability, and colonocyte myosin light chain phosphorylation compared to control [39].

Trichuris muris mediated gastric inflammation was induced in the mice and were supplemented with *Lactobacillus rhamnosus* NCC4007 or *Bifidobacterium longum* NCC3001 for 10 days. The supplementation of *B. longum* NCC3001 normalized the behavior and expression of a brain-derived neurotrophic factor, whereas kynurenine and cytokines levels were not affected. The study suggested that chronic gastrointestinal inflammation mediated anxiety-like behavior can be normalized by *B. longum* NCC3001 via either inflammation-dependent or independent mechanisms [40]. The anxiolytic effect of *B. longum* NCC3001, in DSS-induced colitis mice, was associated with vagal integrity without the involvement of immune modulation and brain-derived neurotrophic factor. The histopathological status and myeloperoxidase activity were not affected by the probiotic intervention [41].

The male BALB/c mice supplemented with *L. rhamnosus* (10^9 CFU) for 28 days showed differential expression of $GABA_{B1b}$ mRNA in various regions of the brain and also exhibited the region-specific expression of $GABA_{A\alpha2}$. The study also highlighted the involvement of vagus nerve system in the bidirectional communication between gut microbiome and brain. *L. rhamnosus* supplemented mice showed a reduction in anxiety and depression and stress-induced corticosterone levels [41].

The anxiolytic-like activity of probiotic preparation comprising of *L. helveticus* R0052 and *B. longum* R0175 (PP) has been reported in rats. The rats supplemented with PP for 14 days showed reduced anxiety-like behavior in conditioned defensive burying test [2].

The communication between gut-brain, inflammatory response, and function of probiotic were interconnected and also associated with diet and genetic makeup of individuals. *L. helveticus* ROO52 (10^9 CFU/d) was supplemented to wild-type and immune-deficient mice (IL-$10^{-/-}$) for 21 days, and the experimental animals were maintained with normal diet or high-fat Western-style diet (WSD) (33% of fat and 49% carbohydrates). The mice under the WSD increased body weight and showed altered cytokine expression, microbiome change, and anxiety-like behavior, irrespective of their genetic makeup. The intervention of *L. helveticus* ROO52 improved the anxiety-like behavior in wild-type mice with normal laboratory diet. The effect of *L. helveticus* ROO52 was negative in WSD mice. The microbiota analysis revealed that microbial clustering was associated with diet, immunity, and probiotic intervention. The study suggested that the diet and immune status of an individual greatly influence the functionality of an active probiotic supplement [42].

Due to the changes in brain function, inflammatory disease patients may have sickness behaviors. The supplementation of VSL#3 (a mixture of 1.7 billion cells of *Streptococcus salivarius* subsp., *thermophilis*, *B. longum, B. breve, B. infantis, L. casei, L. acidophilus, L. plantarum*, and L. *delbrueckii* subsp. *Bulgaricus*) for 10 days reduced the sickness behavior, which was associated with decrease in cerebral monocyte infiltration and microglial activation [43].

The rats were supplemented with 0.5–1.0% of *Lactobacillus* metabolites (LM) (containing lactate, organic and amino acids, enzymes, polypeptides, and microelements), and the animals were subjected to ratiometric Ca^{2+} imaging. The results suggested that the continuous supplementation of LM improved the release and absorption of Ca^{2+}, which in turn enhanced the psychological and cognitive functions and also stimulated the brain intracellular signaling [44].

L. rhamnosus (JB-1)™ was supplemented to C57BL/6 mice for 4 weeks and were exposed to chronic social defeat. The stress-mediated anxiety-like behavior was reduced and improved the social interaction in *L. rhamnosus* supplemented mice, without affecting the aggressor avoidance behavior. The intervention of *L. rhamnosus* weakened the dendritic cell activation while increasing the regulatory T cells. The social defeat exposure altered the fecal metabolites and gut microbiota. The study suggested that JB-1 can reduce the stress-induced behaviors, but failed to prevent dysbiosis [45].

4.2. Clinical trails

The mood and cognition of the healthy human volunteers were measured at baseline, during and after the intervention of *L. casei* strain Shirota (6.5×10^9 CFU) containing probiotic yogurt. The study results suggested that probiotic supplementation improved the stress, anxiety, and depression state of the subjects. Overall, probiotic yogurt enhanced the good mood [46].

The impact of probiotic supplementation on stress-induced gastrointestinal consequences was studied. The stressed people were treated with probiotic preparation, which contains 3×10^9 CFU of *L. acidophilus* Rosell-52 and *B. longum* Rosell-175, for 3 weeks. The probiotic supplementation significantly reduced the symptoms of stress-induced gastrointestinal problems

such as nausea and abdominal pain, while not affecting the social, emotional, mental, psychological, physical, and sleeping problems attributed to the stressful lifestyle [47].

The patients with chronic fatigue syndrome (CFS) were supplemented with *L. casei* strain Shirota (24 billion CFU/day) for 60 days. The Beck Anxiety and Beck Depression data were collected from the volunteers before and after the intervention. Anxiety was decreased and a load of Bifidobacteria and *Lactobacillus* spp. were increased after intervention compared to placebo control. The results suggested that single probiotic intervention could alter the gut microbiota and can improve the health status of CFS patients [48].

The intervention of probiotic preparation containing 3 billion CFU of *L. helveticus* R0052 and *B. longum* R0175 (PP) in human volunteers improved the psychological distress, measured by Hopkins Symptom Checklist, Hospital Anxiety and Depression Scale, and urinary free cortisol levels. There were no adverse effects recorded during the study period [2]. The supplementation of PP has not affected the learning and memory of human volunteers, and also not cause any addition [49].

The children with the autism spectrum disorder were supplemented with *L. acidophilus* strain Rosell-11 (5×10^9 CFU/g) for 2 months, and the urine D-arabinitol and the D-/L-arabinitol ratio at baseline and after the intervention period were measured. The level of D-arabinitol and the D-/L-arabinitol ratio was reduced after probiotic supplementation, and the results also suggested that probiotic intervention was an effective antifungal treatment. The study also reported that the supplementation of Rosell-11 significantly improved the concentration and response to the order among the autistic children [50].

The fermented milk with probiotics (FMP) consisting of 1.25×10^{10} CFU of *B. animalis* subsp. *Lacti*s and 1.2×10^9 CFU of *Streptococcus thermophiles*, *L. bulgaricus*, and *Lactococcus lactis* subsp. *Lactis* was supplemented to healthy women volunteers twice daily for 4 weeks, and they were subjected to functional magnetic resonance imaging. The results suggested that FMP intake reduced the task-related responses and altered the midbrain connectivity. The FMP intervention influences the central processing of emotion and consciousness in healthy volunteers [51].

Acute psychological stress is linked to the onset of flu/cold. The supplementation of *L. helveticus* R0052, *B. longum* ssp. infantis R0033, and *B. bifidum* R0071 to healthy, but academically stressed, students for 6 weeks significantly reduced the flu/cold symptoms. Especially, those who were supplemented with *Bifidobacterium* spp. showed better protective effects than other groups [52].

The healthy volunteers were consumed the multispecies probiotic preparation containing *Lactococcus lactis*, *L. brevis* W63, *L. salivarius* W24, *L. acidophilus* W37, *L. casei* W56, *B. lactis* W52, and *B. bifidum* W23 for 4 weeks, and cognitive response to sad mood was measured. The results suggested that probiotic intervention reduced the negative thoughts, depression, and improved the ability to manage the sad situation compared to placebo group [53].

Kato-Kataoka et al. conducted a double-blind, placebo-controlled study on the impact of probiotic supplementation (*L. casei* strain Shirota) on the physical, psychological, and stress response of the students, those who prepared for the medical entrance qualification examination. An 8-week probiotic supplementation and measurement of salivary cortisol, serotonin, L-tryptophan, and psychophysical state at different points of intervention revealed that the consumption of probiotic drink reduced the consequences of stress and improved the general health [54].

The healthy petrochemical workers were randomized and supplemented with probiotic yogurt containing *L. acidophilus* LA5 and *B. lactis* BB12 or probiotic capsule containing *L. casei, L. acidophilus, L. rhamnosus, L. bulgaricus, B. breve, B. longum, Streptococcus thermophilus*, or conventional yogurt or placebo for 6 weeks, and the mental health of the participants was measured by using depression anxiety and stress scale scores and general health questionnaire. The study results suggested that the supplementation of probiotic yogurt and multispecies capsule improved the psychological state of petrochemical workers while conventional yogurt does not have any health promoting role [55]. The 8-week supplementation of *L. casei* strain Shirota (10^9 CFU/day) significantly reduced the stress-induced upsurge of cortisol level and improved the stress management among the academically stressed students [56].

5. Conclusion

Depression and stress are associated with several inflammatory consequences and dysregulation of gut microbiota. The brain function, microbiome, and immune system were interconnected. The childhood experiences like diet habit, stress, and immune activation can affect the development of specific microbiome and cognition in the later age of life. The supplementation of probiotic, especially multispecies formulation, can positively regulate the gut microbiota, brain function, and helps to maintain the typical immune state of the host (**Table 1**). The beneficial effects of probiotic are closely associated with diet, genetic makeup, and commensal microbiota of the host. The secretion of neurotransmitters-like molecules and promoting the growth of beneficial commensal microbes are the possible ways by which probiotics confer the mental health benefits. How the microbiome is influencing the cognition and brain function and its mechanisms are scope for further investigation.

S. No.	Model	Intervention	Duration	Effects	Refs.
In vivo studies					
1	Male BALB/c mice	*Lactobacillus rhamnosus* (10^9 CFU)	28 days	Modulation of the GABAergic system. Reduced the depression and anxiety	[12]
2	Germfree, specific pathogen-free, and gnotobiotic BALB/c mice	*B. infantis*	—	Normalized the inflated stress response	[38]
3	Female Wistar rats	*L. farciminis* (10^{11} CFU/day)	15 days	Reduced the partial restraint stress	[39]
4	Male AKR mice	*Bifidobacterium longum* NCC3001	10 days	Normalized the anxiety behavior	[40]
5	Dextran sodium sulfate treated mice	*B. longum* NCC3001	7 days	Normalized the anxiety behavior, but not myeloperoxidase activity	[41]
6	Wistar rats	*L. helveticus* R0052, and *B. longum* R0175	14 days	Reduced the anxiety-like behavior	[2]
7	Mice	*L. helveticus* R0052 (10^9 CFU/day)	21 days	Decreased anxiety-like behavior	[42]

S. No.	Model	Intervention	Duration	Effects	Refs.
8	Mice	VSL#3 (*Streptococcus salivarius* subsp., *thermophilis, B. breve, B. infantis, B. longum, L. acidophilus, L. plantarum, L. casei,* and *L. delbrueckii* subsp. *Bulgaricus*) (1.7 billion cells)	10 days	Reduced the inflammation-associated sickness behavior	[43]
9	Rats	*Lactobacillus* spp. fermented product (metabolites of *Lactobacillus*)	—	Improved the brain intracellular signaling	[44]
10	Male C57BL/6 mice	*L. rhamnosus* (1.67×10^9 CFU)	28 days	Protected from stress-induced behaviors	[45]
Clinical trials with human subjects					
11	Healthy human	Probiotic yogurt containing *L. casei* Shirota (6.5×10^9 CFU)	21 days	Improved the mood	[46]
12	Stressed human volunteers	*L.s acidophilus* Rosell-52, and *B. longum* Rosell-175 (3×10^9 CFU)	21 days	Reduced the stress-induced gastrointestinal problems	[47]
13	Chronic fatigue syndrome patients	*L. casei* strain Shirota	60 days	Reduced the symptoms of anxiety	[48]
14	Healthy human	*L. helveticus* R0052, and *B. longum* R0175	30 days	Reduced the psychological distress	[2]
15	Healthy human	*L. helveticus* R0052, and *B. longum* R0175	—	Reduced the cortisol level and improved the anxiety and depression. Not affecting the learning and memory	[49]
16	Autism spectrum disorder patients	*L. acidophilus* strain Rosell-11 (10×10^9 CFU/day)	60 days	Reduced the level of D-arabinitol, and D-/L-arabinitol ratio. Improved the responsiveness to the orders	[50]
17	Healthy women	*B. animalis* subsp. *Lactis* (1.25×10^{10} CFU), *Streptococcus thermophiles*, *L. bulgaricus* (1.2×10^9 CFU), and *Lactococcus lactis* subsp. *Lactis* (1.2×10^9 CFU) in fermented milk	28 days	Modulate the sensitivity of brain network in healthy women	[51]
18	Academically stressed students	*L. helveticus* R0052, *B. longum* ssp. *infantis* R0033, *B. bifidum* R0071.	42 days	Prevented the onset of stress-related cold/flu	[52]
19	Healthy volunteers	*B. bifidum* W23, *B. lactis* W52, *L. acidophilus* W37, *L. brevis* W63, *L. casei* W56, *L. salivarius* W24, and *L. lactis*	28 days	Reduced the negative thoughts	[53]
20	Healthy medical students	*L. casei* strain Shirota	56 days	Prevent the stress-related physical symptoms	[54]
21	Healthy petrochemical workers	*L. acidophilus LA5*, and *B. lactis BB12* (10^7 CFU); Multispecies probiotic capsule.	42 days	Improved the general health, and reduce the stress and depression	[55]
22	Healthy medical students	Fermented milk with *L. casei* strain Shirota (10^9 CFU)	56 days	Reduced the cortisol level, and reduced the symptoms of stress	[56]

Table 1. The influence of probiotic supplementation on brain function of the host system.

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Conflict of interest

The authors declare that there is no conflict of interests.

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