Effect of Probiotics on Gut Microbiota and Brain Interactions in the Context of Neurodegenerative and Neurodevelopmental Disorders

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Abstract

The bidirectional communication between the gut and the brain links emotional and cognitive centers of the brain with peripheral intestinal functions. This interaction between the gut microbiota and the gut-brain axis (GBA) involves signaling from the gut microbiota to the brain and from the brain to the gut microbiota through neural, endocrine, immune, and humoral links as evidenced by germ-free animal models and association of dysbiosis with central nervous system (CNS) disorders (i.e., autism, anxiety-depressive behaviors) and functional gastrointestinal disorders. Probiotics have been reported to influence this interaction by facilitating the colonization of beneficial microorganisms and suppressing the growth of harmful microorganisms, thus improving the gut-brain interactions. Psychobiotics being a novel class of probiotics hold special significance as these affect the central nervous system-related functions and behaviors mediated by the gut-brain axis (GBA) via immune, humoral, neural, and metabolic pathways to improve not only the gastrointestinal (GI) function but also the antidepressant and anxiolytic capacity. In the past few years, some of the psychobiotic strains have been proven scientifically beneficial in suppressing inflammation and reducing cortisol levels, thus improving anxiety and depression. In addition to that, psychobiotics have shown promising results in neurodegenerative and neurodevelopmental disorders, such as Alzheimer's disease (AD), Parkinson's disease (PD), and autism spectrum disorder (ASD). Initial clinical studies have shown that psychobiotics can improve overall GI function, improve symptoms of ASD, and regulate motor

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functions of PD patients and cognition behavior in AD patients. This chapter primarily focuses on the effect of psychobiotics on interactions between the gut microbiota and the brain in the context of neurodegenerative and neurodevelopmental disorders.

Keywords

Anxiety · Central nervous system · Depression · Probiotics · Psychobiotics

19.1 Introduction

Human body is home to trillions of bacteria, fungi, parasites, and viruses (collectively named microbiota) that mostly reside on our skin and gut mucosa and do not cause any adverse health issues. Indeed, some of these bacteria are extremely useful to maintain a healthy life. In fact, the human gut contains one of the most complex ecosystems composed of approximately 10^{13}–10^{14} microorganisms belonging to 500–1000 different species. The number of these microbes is one to ten times greater than the number of eukaryotic cells in the body (Qin et al. 2010). The mutual symbiosis between the host and the gut microbiome can be partially attributed to the nutrients present in gut that favor microbiota selection and colonization (Leung and Thuret 2015). The selection and colonization of gut microbiota that begins at birth and establishes within the first 3 years of life is crucial for regulating the development of intestinal physiology, maturation of the nervous and immune system (Palmer et al. 2007), and modulation of the angiogenesis (Andriessen et al. 2016). In addition to that, these microorganisms provide natural biocontrol against the pathogenic microorganisms by their antimicrobial activities which play an important role in maintaining the stability of the gut ecosystem (Bercik et al. 2012). Studies have shown that changes in the microbial colonization of the human gut during early life increase the risk of disease and have a significant impact on the host neurophysiology, behavior, and function of the nervous system (Kamada et al. 2013; Collins and Bercik 2009; Moustafa et al. 2018). Furthermore, these gut microorganisms possess immunomodulatory properties that mediate brain functions and behavior and contribute to etiopathogenesis in various neurodegenerative and behavioral disorders such as anxiety, depression, autism spectrum disorders (ASD), Alzheimer's disease (AD), and Parkinson's disease (PD) (Collins et al. 2012; Fung et al. 2017).

As mentioned above, the gut microbiota starts to colonize the gut during development and continues later on in life. At first, it is mostly composed of *Lactobacillus* sp. and *Bifidobacterium*; however, at later stages in life the microbiome becomes densely populated by the Bacteroidetes and Firmicutes phyla, and in small proportion of Proteobacteria, Verrucomicrobia, Actinobacteria, and Cyanobacteria phyla. In addition, the *Fusobacterium* genus can also be found in gut microbiota (Xu et al. 2019). There are several factors that affect the composition of gut microbiota such as genetic diversity, diet, environment, season, and overall health status, and it is extremely difficult to define a "normal" microbiome for the average human

population (Gibson and Roberfroid 1995; Wen and Duffy 2017). In addition to that, the microbial communities in the gut are shaped by the bacteriophages that inhabit this niche (Naureen et al. 2020) and are independent of environmental components such as age, body mass index, gender, and geographic location (Huttenhower et al. 2012; Bajinka et al. 2020).

In addition to these bacteria that colonize our gut by the passage of time, millions of bacteria transit through our gut every day. These bacteria are mostly present in our food and upon entering the gut interact with the gut microbiota in either a healthy or a pathological context. These live microorganisms that provide health benefit to us are termed as probiotics (Hill et al. 2014). Probiotics are the biotic organisms that can alter the gut microbiota composition while having a beneficial effect on the host's health and well-being. These probiotics naturally occur in food items such as olives and dark chocolates and in fermented foods such as sauerkraut, yogurt, cheeses, etc. These microorganisms not only improve the gut microbiota but also help in eliminating the harmful pathogenic microorganisms and improve the overall health (Hemarajata and Versalovic 2013).

19.2 History of Probiotics

The word "probiotic" is derived from the Latin words "pro," meaning to promote, and "biotic," meaning life. In 1907, Élie Metchnikoff observed that the regular consumption of lactic acid bacteria (LAB) in fermented dairy products, such as yogurt, led to enhanced health and relatively longer life in people living in Bulgarian villages (Metchnikoff and Mitchell 1907). However, the evidence on the beneficial effects of microbes was provided by Tissier (1899) when he compared the stool of children suffering from diarrhea with that of the healthy children. Tissier (1899) observed that the concentration of bacteria responsible for diarrhea was low in the stool of healthy children, and this gave him the idea of giving the infected children *Bifidobacteria*, which he had successfully isolated in 1988 from the feces of infants fed on breast milk, in order to rehabilitate the normal gut flora. The distinguishable work done by Henry Tissier led to the modern definition of probiotics by Havenaar and Huis In't Veld (1992) who describe probiotics as "an applicable bacterial culture that grant positive effects to the humans or animals by enhancing the native floral properties, when administered." However, to term a certain bacteria as probiotic, lots of scientific evidence proving its safety for consumption is required. This is extremely important as these live microorganisms have a direct impact on human health. It is worth mentioning here that when probiotics gained popularity, many food and drug companies started to designate bacterial species as probiotics without providing any scientific evidence, thus ending up in banning the word probiotics in the European Union by the European Food Safety Authority (EFSA) (Katan 2012).

However, now there is a huge repertoire of scientific evidence that shows the potential benefits of living microorganisms that are safe for human consumption,

e.g., *Lactobacillus* and *Bifidobacterium*, and are beneficial in certain medical conditions, such as irritable bowel syndrome (IBS), dermatitis, high cholesterol levels, eczema, and liver disease. In the past two decades, probiotics have gained much attention with respect to brain health and cognitive function and its effects on the central nervous system (CNS) and mood (Cryan and Dinan 2012). Additionally, probiotics have an important role in improving memory abilities (spatial and non-spatial memory rodents) of rodents and the human beings. Also, probiotics have a dynamic effect on relieving stress, anxiety, and depression. However, to understand this further, we need to first understand the gut-brain microbial axis (Crumeyrolle-Arias et al. 2014).

19.3 Gut-Brain Microbial Axis: Connection of the Gut and the Brain

Probiotics are widely being studied for their role in improving brain health and mental behavior. However to understand that how the microbes living inside the gut influence the brain activity we need to cosider the connection between the gut and the brain. The brain, communicates with the gut through a complex system comprising of the enteric nervous system (division of the peripheral nervous system controlling the gastrointestinal behavior independent of the CNS), the vagus (a large nerve of the central nervous system responsible for sending signals between the brain and the intestine), and the hypothalamus-pituitary axis. All of these components make immunological, neurological, and endocrine bridges allowing the information relay between the brain and the gut (Chandran et al. 2019). The microbes in the gut produce molecules that include neurotransmitters, short-chain fatty acids, and amino acids which travel through this complex system and a communication between the brain and the gut takes place (Fig. 19.1). Moreover, the presence of the gut-brain microbial axis (GBMA) links the emotional and cognitive centers of the brain with peripheral functions of the intestine and also provides communication between the enteric nervous system and the central nervous system. The gut bacteria will influence the brain and the central nervous system by regulating the inflammation and hormone production (Sommer and Bäckhed 2013; Bermúdez-Humarán et al. 2019).

19.4 Role of Microbiota in the Gut-Brain Microbial Axis

There are plenty of clinical and experimental evidences suggesting the importance of gut microbiome interactions with intestinal cells and the enteric nervous system (ENS) and direct involvement with the CNS through neuroendocrine and metabolic pathways (Fig. 19.2). Perhaps the most compelling evidence of GBM interactions comes from the dramatic improvement of patients suffering from hepatic encephalopathy (Bercik et al. 2012). This indicated the involvement of gut microbiota in

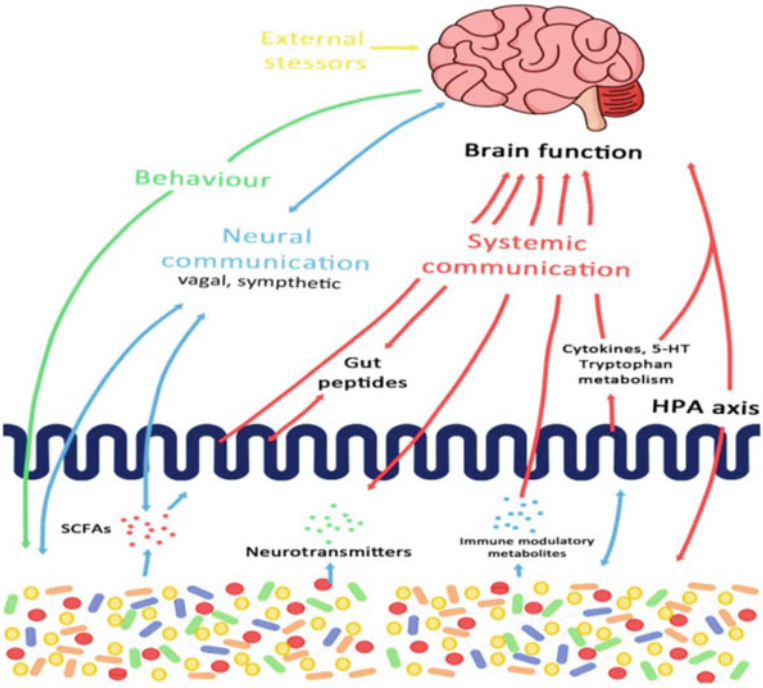

Fig. 19.1 Gut-brain-microbial axis revealing the regulatory interactions established between the gut microbiota, the intestine, and the brain. It includes the communication through vagus and sympathetic nerves; SCFAs, short-chain fatty acids; activation of hypothalamic-pituitary-adrenal (HPA) axis and release of gut peptides (Rogers et al. 2016)

maintaining the health and well-being and highlighted that the gut dysbiosis results in disease. Recent studies have shown that these microorganisms play a role in anxiety and depression (Collins and Bercik 2009; Kamada et al. 2013) and an imbalance in the gut microbiota results in several diseases, specifically autism (Kamada et al. 2013; Collins and Bercik 2009; Moustafa et al. 2018; Fung et al. 2017).

19.5 Gut Dysbiosis and Human Health

Gut dysbiosis refers to a condition in which the physiology of gut microbiome is altered owing to changes in diet, stress, or administration of antibiotics (Clemente et al. 2012). As a result, the intestinal permeability increases and results in leakage of bacteria, bacterial metabolites, and molecules through the mucosa into the systemic circulation, a condition termed as leaky gut syndrome. This in turn has a detrimental impact on the host immune system as demonstrated in diseases such as diabetes, asthma, inflammatory bowel disease (IBD), and psychiatric disorders including depression, anxiety, and autism (Sarkar et al. 2016; Shaaban et al. 2018a, b).

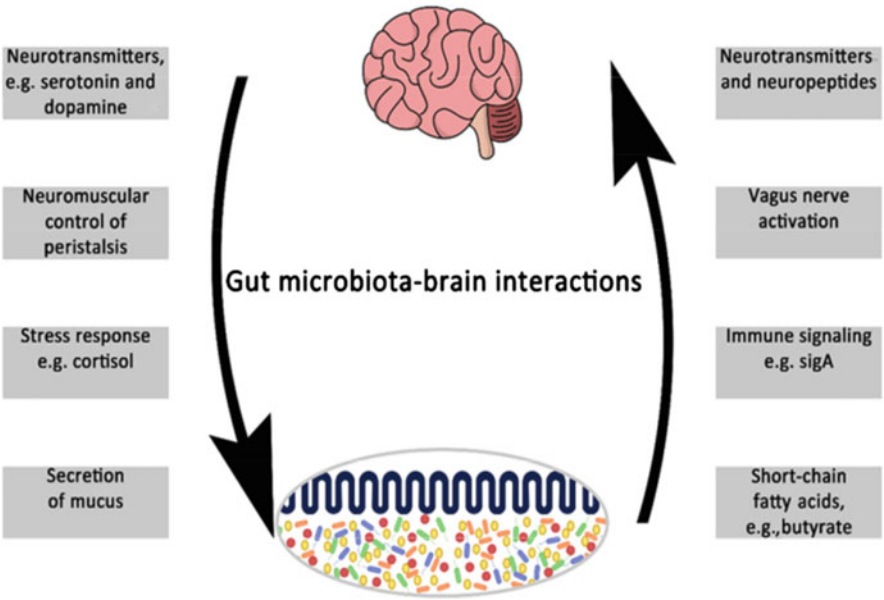

Fig. 19.2 The two-dimensional interactions between the gut microbiota and the brain

Although a huge repertoire of such studies has been focused on bacteria residing in the gut, some studies have emphasized the significance of other microbes such as yeast. For instance, it has been observed that the gut colonization with *Candida* species results in a decrease in carbohydrate and mineral absorption and excessive buildup of toxins that might contribute to development of autism spectrum disorder (Shaaban et al. 2018a, b). Dysbiosis also occurs in functional gastrointestinal disorders (FGID) that are linked to a disruption of the gut-brain axis and leading to mood disorders (Enck and Mazurak 2018). Similarly, in IBS, both brain-gut and gut-brain dysfunctions occur that eventually result in changes in intestinal motility and secretion, causing visceral hypersensitivity and cellular alterations of the enteroendocrine and immune system (Padhy et al. 2015). Recent studies report that probiotics are helpful in restoring microbiota to a healthy state and also in reducing various disease symptoms (Carabotti et al. 2015). The gut and the brain are interrelated in which the gut bacteria produce metabolites and have a major effect on the brain. Probiotics have a beneficial role in the brain and mental health and are called as psychobiotics (Dinan et al. 2013).

19.6 Psychobiotics and Their Role in Mental Health

Psychobiotics are novel types of probiotics used for the treatment of psychiatric distress (Dinan et al. 2013). Psychobiotic researches are conducted on the model organisms for behavioral assessments such as anxiety, depression, motivation, etc.

(Sarkar et al. 2016). This kind of probiotics can regulate neurotransmitters and proteins (GABA, serotonin, glutamate, and BDNF) and are helpful to regulate the neural excitatory-inhibitory balance, mood, cognitive functions, and learning and memory processes (Lu et al. 2008; Heldt et al. 2007; Martinowich and Lu 2008). The gut microbiota has a major role in stimulating the activity of the hypothalamic-pituitary-adrenal (HPA) axis (Sudo et al. 2004). Studies with the germ-free (GF) mice have shown that they release excess of corticosterone and adrenocorticotropic hormone as compared to specific pathogen-free (SPF) mice upon administration with psychobiotics (Sudo et al. 2004). The activation of the HPA axis by pro-inflammatory cytokines increases the blood barrier permeability which leads to reduction in serotonin level resulting in psychiatric distresses such as depression (Hammitt et al. 2019; Dowlati et al. 2010). *Lactobacillus brevis*, *Lactobacillus plantarum*, and *Bifidobacterium dentium* are able to secrete GABA and serotonin inside the gut (O'Mahony et al. 2015; Schousboe and Waagepetersen 2007; Barrett et al. 2012). The acetylcholine is secreted in the gut by the *Lactobacillus* spp. such as *L. plantarum* and *Lactobacillus odontolyticus* (Roshchina 2016). A recent study reports that microbes can regulate the serotonin synthesis in the gut. In additon the spore-forming bacteria present in gut microbiota can produce serotonin in enterochromaffin cells (Yano et al. 2015). The studies indicate the psychobiotic potential of pseudobiotics in improving the psychiatric conditions by secretion of neurotransmitters that can in turn alleviate stress.

Psychobiotics have been reported to exert psychotropic effects on various mental and psychological disorders, depression, anxiety, and stress; however, their application to improve mental health requires precision strategy. Animal studies have shown that many probiotics in fact act as psychobiotics. For instance, the administration of *Lactobacillus plantarum* PS128 supplements reduces anxiety and stress in mice as well as inflammation and the levels of corticosterone. As compared to the control mice, PS128 supplements can enhance the dopamine and serotonin levels in the prefrontal cortex and striatum (Liu et al. 2016, 2015). Similarly, the administration of *Lactobacillus helveticus* NS8 supplements is beneficial for the reduction of anxiety, cognitive dysfunction, and depression. These *L. helveticus* NS8 supplements can enhance the levels of serotonin, norepinephrine (NE), and brain-derived neurotrophic factor (BDNF) in the hippocampus (Liang et al. 2015). Furthermore, *Bifidobacterium longum* 1714, *B. longum* NCC3001, *Bacterium infantis* 35624, and *Lactobacillus rhamnosus* (JB-1) administration can reduce stress, depression, and anxiety (Savignac et al. 2014; Bravo et al. 2011; Bercik et al. 2010; Desbonnet et al. 2010). The intake of the JB-1 supplements can cause region-dependent modifications in the expression of GABA receptors resulting in the reduction of plasma corticosterone level (Bravo et al. 2011). The administration of *B. longum* NCC3001 upregulates the BDNF expression in the hippocampus (Bercik et al. 2010). The 4-week-long treatment of *B. longum* 1714 was effective in improving memory and reducing stress (Allen et al. 2016). Recipients who were administered with both probiotic yogurt (*Lactobacillus acidophilus* LA5 and *Bifidobacterium lactis* BB12) and probiotic capsules (*Lactobacillus casei*, *L. acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus bulgaricus*, *Bifidobacterium*

breve, *Bifidobacterium longum*, and *Streptococcus thermophilus*) have shown an improvement in mental health (Mohammadi et al. 2016). The combination of *L. helveticus* R0052 and *B. longum* R0175 can reduce stress and depression. Along with that, these combinations can decrease the levels of urinary free cortisol (Messaoudi et al. 2011). The effects of probiotic supplements such as *L. plantarum* PS128, *L. plantarum* 299v, *L. rhamnosus* GG, Bifihappy, Vivomixx®, Probio'Stick, etc. on depression and anxiety is under investigation (Cheng et al. 2019; Rucklidge 2013).

The brain-gut interaction involves immunoregulatory, neuroendocrine, and vagus pathways (Li et al. 2018). These interactions are mediated by secretion of many metabolites by the microorganism in the gut which in turn depends upon the diversity of microbes residing in the gut. Probiotics can help improve these interactions by maintaining a healthy microbiota which ultimately results in overall health improvement. For instance, the levels of inflammatory cytokines can be reduced by the treatment with the probiotic strains of *Lactobacillus*, *Bifidobacterium*, and *Enterococcus* (Vanuytsel et al. 2014). The probiotic anti-immunoregulatory effects can trigger T regulatory cells which lead to the secretion of IL-10 (Dinan et al. 2013). Moreover, the interaction of probiotics with gut epithelium enteroendocrine cells (EECs) results in secretion of neuropeptides and neurotransmitters such as peptide YY (PYY), neuropeptide Y (NPY), substance P, serotonin, glucagon-like peptide-1 and peptide-2 (GLP-1 and GLP-2), and cholecystokinin (Cani and Knauf 2016; Foster et al. 2017). About 95% of the serotonin is secreted from the gut enterochromaffin cells and ENS neurons along with the control of GI secretion and motility (Costedio et al. 2007). The effective brain serotonin pathways regulates the cognition and mood while the ineffective brain serotonin pathways leads to disorders in GI and mood (Wrase et al. 2006).

19.7 Psychobiotics in Neurodegenerative and Neurodevelopmental Disorders

19.7.1 Alzheimer's Disease (AD)

Although there is scarce evidence regarding the effectivity of probiotics in neurodegenerative disorders like AD and it has been reported that patients having severe AD are insensitive to probiotics; yet, one study using multiple strains of *L. casei* W56, *Lactococcus lactis* W19, *L. acidophilus* W22, *B. lactis* W52, *L. paracasei* W20, *L. plantarum* W62, *B. lactis* W51, *B. bifidum* W23, and *L. salivarius* W24, on subjects with AD reported that the composition of gut microbiota and tryptophan metabolism were affected by the administration of probiotics (Kumar and Singh 2015; Agahi et al. 2018; Leblhuber et al. 2018). Another study reported significant probiotic-mediated reduction in oxidative stress by induction of SIRT-1-dependent mechanisms in transgenic AD mouse models (Bonfili et al. 2018). Administration of probiotics comprising of *L. acidophilus*, *Lactobacillus fermentum*, *B. lactis*, and *B. longum* significantly decreased the coliform and increased *Bifidobacterium* spp.

and *Lactobacillus* spp. in the stool of AD animal models suggesting the efficacy of probiotics in maintaining healthy gut microbiota. Additionally, probiotics have been reported to improve learning and memory deficits in AD rats as compared to control rats probably because of the reduction in the number of amyloid plaques, inflammation, and oxidative stress (Athari Nik Azm et al. 2018). Furthermore, supplementing AD mice with cow's milk fermented with *L. fermentum* or *L. casei* enhanced learning, memory behavior, and antioxidant levels while reducing pro-inflammatory cytokines, malondialdehyde (MDA), and AChE as compared to the control (Musa et al. 2017). In addition to that, certain probiotic strains such as *L. plantarum* MTCC1325 prove beneficial in improving the cognitive and gross behavioral activities and restoration of acetylcholine (ACh) levels in D-galactose-induced AD rats (Nimgampalle and Kuna 2017). In yet another randomized, double-blind, and controlled clinical trial, consumption of probiotic-treated milk (*L. acidophilus*, *L. casei*, *B. bifidum*, and *L. fermentum*) led to decreased plasma MDA and serum high-sensitivity C-reactive protein (hs-CRP) levels while changing the insulin resistance, beta-cell function, and insulin sensitivity. Remarkably, the mini-mental state examination (MMSE) score in AD group was significantly improved after probiotic treatment (Akbari et al. 2016).

Based on the abovementioned findings, it can be stated that probiotics, specifically psychobiotics, can help improve the cognitive behavior, memory deficit, and overall mental health in AD animal models while reducing inflammation, possibly through SIRT-1 pathways, and thus hold promise in the treatment of AD in humans; however, this needs further confirmation by carefully designed, double-blind clinical trials considering other factors such as age and severity of AD to better elucidate the role of psychobiotics.

19.7.2 Parkinson's Disease (PD)

Another important neurodegenerative and neuropsychiatric disorder that affects nearly 2% of the elderly population is PD (De Rijk et al. 1997). Besides other problems, one of the major symptoms in these PD patients is constipation (Barichella et al. 2009; Fasano et al. 2015; Berg et al. 2015). Hence, most of the clinical studies related to probiotic administration in PD patients focus on gastrointestinal function (Barichella et al. 2016; Georgescu et al. 2016; Cassani et al. 2011). For instance, three studies have reported that probiotics containing *L. acidophilus* and *B. infantis* improved gastrointestinal function, regulate bowel movement, improve stool consistency, reduce abdominal pain and recipients with PD who were using probiotics exhibited improved gastrointestinal functions. Furthermore, PD patients exhibited improved bowel habits after 5 weeks of administration of milk fermented with *L. casei* Shirota (Cassani et al. 2011).

Results obtained from a randomized, double-blind, placebo-controlled clinical trial suggest that probiotic supplementation of PD patients with *L. acidophilus*, *B. bifidum*, *Lactobacillus reuteri*, and *L. fermentum* for 12 weeks decreases the overall score on the Unified Parkinson's Disease Rating Scale (UPDRS) as

compared to the placebo group. Besides that, probiotic supplementation increased the glutathione (GSH) levels, remarkably decreased the hs-CRP and MDA levels, and significantly improved the insulin function in contrast to the placebo (Tamtaji et al. 2019).

Patients suffering from PD have increased oxidative stress and inflammations that increase with the severity of disease (Taylor et al. 2013). Psychobiotics have shown promising results in reducing oxidative stress and the inflammations in patients with PD. For instance, probiotic interventions in PD patients for 12 weeks significantly upregulated the expression of transforming growth factor beta (TGF-β) and peroxisome proliferator-activated receptor gamma (PPAR-γ) while downregulating the expression of interleukin-1 (IL-1), IL-8, and tumor necrosis factor alpha (TNF-α) as compared to the placebo control in a randomized controlled study focusing on the effect of probiotic administration on inflammation, insulin, and lipid-related genes in peripheral blood mononuclear cells (PBMCs). However, no effect of probiotic administration was observed on the expression of markers of inflammation and oxidative stress, vascular endothelial growth factor (VEGF), and low-density lipoprotein receptor (LDLR) in the same study (Tamtaji et al. 2017). These studies depict the importance of probiotic administration in improving the overall health of PD patients; however, as with the case of AD, more studies are required to emphasize the role of psychobiotics in alleviating symptoms of PD. For instance, probiotics might prove useful in folding of α-synuclein produced in enteroendocrine cells eventually reducing the Lewy bodies formation of dopaminergic (Shults 2006; Liddle 2018; Chandra et al. 2017); however, this needs to be unrevealed by further research.

19.7.3 Autism Spectrum Disorder (ASD)

Although quite rare, ASD is a neurodevelopmental disorder characterized by inability to communicate socially, restrictive behavioral pattern, and limited activities and interest. ASD is prevalent in 0.1–1.8% of the population, and these patients frequently complain of gastrointestinal problems (American Psychiatric Association 2013; Wang et al. 2011) with interesting correlations between severity of behavioral and gastrointestinal symptoms. Evidence indicates that patients with ASD have varying levels of alteration in gut microbiota and this implicates the importance of considering the gut-brain axis in its treatment. Several species of bacteria are being evaluated as probiotics in improving the gastrointestinal and behavioral problems in ASD patients such as *L. acidophilus* DSM24735™, *L. plantarum* DSM24730™, *Lactobacillus paracasei* DSM24733™, *L. helveticus* DSM24734™, *Streptococcus thermophilus* DSM24731™, *B. lactis* DSM24736™, *B. breve* DSM24732™, and *Lactobacillus delbrueckii* subsp. *bulgaricus* DSM 24734 and *B. lactis* DSM24737™ (Arnold 2019; Cheng et al. 2019; Shaaban et al. 2018a, b)

A recent trial conducted in Egypt reports that administering probiotics for 3 months improved the severity of autism and GI symptoms as compared to control

(Shaaban et al. 2018a, b). Different trials using different bacterial strains as psychobiotic formulations are being investigated, and their results are still awaited.

A previous placebo-controlled trial conducted in the UK in 2012 evaluated the efficacy of the single probiotic strain *L. plantarum* WCFS1 in an ASD (Cheng et al. 2019). In this study, ASD patients reporting GI problems were given *L. plantarum* WCFS1 as compared to placebo for 6 weeks; however, the results of this study are not available. This study recruited patients with ASD presenting with GI problems for a 6-week intervention with either probiotics or placebo. Another trial conducted in the UK in 2010 *reports* that the administration of *L. plantarum* WCFS1 in ASD patients for 3 weeks altered the gut microbiota (Parracho et al. 2010). Currently, limited data are available that reveal the effects of probiotics on patients with ASD. However, numerous trials are under progress for which results are awaited to provide scientific evidence for the efficacy of these probiotics in the management of ASD-related GI and behavioral symptoms.

19.7.4 Attention Deficit Hyperactivity Disorder (ADHD)

ADHD is a neurological illness categorized on the hyperactivity, inattention, and impulsivity. The infants administrated with *L. rhamnosus* GG during the first 6 months after birth may have a reduced risk for ADHD (Pärtty et al. 2015). The Truehope GreenBAC capsules are administered to the ADHD patients to improve energy level and the mood (Rucklidge 2013). Moreover, *L. acidophilus* food supplements can recover the ADHD children with the self-control and the attention (Harding et al. 2003).

19.7.5 Tourette Syndrome (TS)

Tourette syndrome (TS) is a neurological disorder that is initially observed in childhood (Rampello et al. 2006). There are various TS clinical treatments such as behavioral treatments, α2-adrenergic agonists, antipsychotics, and deep brain stimulation (DBS) (Murphy et al. 2013; Weisman et al. 2013). The fecal microbiota transplantation (FMT) improves the TS after 8 weeks of treatment (Zhao et al. 2017).

19.7.6 Insomnia

Insomnia refers to the sleep disorder which causes illness such as depression, memory loss, and allergy (Kaneita et al. 2006; Grundgeiger et al. 2014; Cohen et al. 2009). Recent reports show that the usage of fermented products can improve sleep (Kitaoka et al. 2009). The studies suggest that the heat-killed *L. brevis* SBC8803 (SBL88™) improves sleep in mice and humans. Also, it improves walking sleep journal scores in healthy males (Nakakita et al. 2016) and increases delta power values in adults aged 40 years as compared with placebo control. Similarly,

the heat-killed *L. brevis* SBC8803 can increase the duration of wakefulness and nighttime wheel-running activity (Miyazaki et al. 2014). The administration of probiotics leads to the reduction in non-rapid eye movement (NREM) sleep during the active phase and improves NREM sleep during resting phase (Miyazaki et al. 2014). However, no significant effect can be found in the heat-killed *L. brevis* SBC8803 treatment in the sleep quality according to the electroencephalograms (EEG) and the Athens Insomnia Scale (AIS) (Nakakita et al. 2016). Based on the study reports, the consumption of *L. helveticus* CM4 containing fermented milk can improve the efficiency of sleep and wakening episodes in aged individuals (Yamamura et al. 2009).

19.8 Conclusion

In the past few years, the human gut microbiota and effect of probiotics on it have received considerable attention in the context of the relation between microbiota and health or disease. Association of gut dysbiosis with many health conditions has revealed the importance of healthy gut flora on overall human health. Animal studies have revealed that the gut-brain interaction is a two-way traffic with signals coming from the brain to the gut microbes and similarly response and feedback from the gut microbiota to the brain. These interactions are particularly important in maintaining brain health and that ultimately requires a balance of microbial structural and functional diversity in the gut. Probiotics, specifically psychobiotics, hold special significance in the sense that they can maintain a healthy gut microbiota, thus maintaining general brain health and alleviation of anxiety, stress, and behavioral problems. In addition to that, preliminary studies have revealed that these psychobiotics can prove beneficial in improving the symptoms of neurodegenerative and neurodevelopmental disorders.

Thus, psychobiotic treatments might be used as a promising strategy to improve the quality of life for people suffering from neurodegenerative and neurodevelopmental disorders; however, further studies in this arena are required to evaluate the effectiveness of psychobiotics as an alternative therapeutic regimen for alleviating stress, anxiety, cognitive function, and brain health.

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