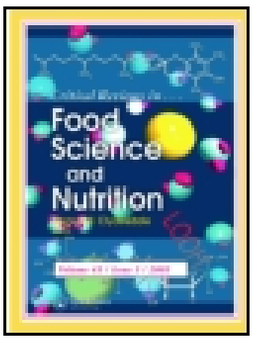

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Psychobiotics: A new approach for treating mental illness?

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ABSTRACT

Gut microbiomes may have a significant impact on mood and cognition, which is leading experts towards a new frontier in neuroscience. Studies have shown that increase in the amount of good bacteria in the gut can curb inflammation and cortisol level, reduces symptoms of depression and anxiety, lowers stress reactivity, improves memory and even lessens neuroticism and social anxiety. This shows that, probably the beneficial gut bacteria or probiotics function mechanistically as delivery vehicles for neuroactive compounds. Thus, a psychobiotic is a live organism, when ingested in adequate amounts, produces a health benefit in patients suffering from psychiatric illness. Study of these novel class of probiotics may open up the possibility of rearrangement of intestinal microbiota for effective management of various psychiatric disorders.

KEYWORDS

Gut microbes; psychobiotics; mental illness

Introduction

Major depressive disorder (MDD), mood disorders and stress are complex and multi-factorial disorders that involves marked disabilities in global functioning, anorexia, and severe medical comorbidities. MDD affects about 20% of the population at some point, during the lifetime of an individual (Yamanishi et al. 2015; Kessler et al. 2005). With emerging body of knowledge on human microbiomes and its relationship with mental health, it is becoming increasingly clear that there are some missing links between the resident microbes and other aspects of physiology. Reports from animal studies, suggest interactions of gut microbiota not only with the enteric nervous system but also with the central nervous system via neural, neuroendocrine, neuroimmune and humoral links. From recent evidences, scientists are suggesting that the neuroimmune system may have an impact on the composition of the microbiota. However, the modern day life style factors (diet, stress, physical activity), antibacterial products, environmental factors (contaminants in food), and antibiotics both in food and as medicine-may deplete such microbes which are beneficial for physical, mental, and emotional health. Insufficiency of such beneficial microbes, may lead to health consequences. Evidences from animal and human studies have shown that the administration of beneficial microbes can reduce depression, anxiety, stress and improve cognition, suggesting possibilities for a new class of probiotics known as "psychobiotics". Psychobiotics are a group of probiotics, capable of producing and delivering neuroactive substances such as gamma-aminobutyric acid and serotonin (the "happy" chemical) that act across the brain-gut axis. Particularly, it can also reduce the levels of cortisol (the "stress" hormone), and increase levels of oxytocin (the "cuddle" hormone) (Mayer 2011; Selhub et al. 2014; Akkasheh et al. 2016). Logan and Katzman first proposed the use of probiotics as adjunct therapy in the management of depression. According to Lyte (2011) probiotics function mechanistically as delivery vehicles for neuroactive compounds; and these probiotics have the potential to act as psychotropic agents. Hence, he hypothesizes that a broad range of bacteria manufacture and secrete neurochemicals. Certain strains of Lactobacillus and Bifidobacterium secrete gamma-aminobutyric acid (GABA). This is the main inhibitory neurotransmitter in the brain regulating many physiological and psychological processes, with dysfunction in the system implicated in anxiety and depression. This review discusses the various psychobiotic strains, mechanisms of action and its effect on neuropsychological disorders.

Gut microbes as psychobiotics

Psychobiotics are the most recent of those agents with hypothesized psychotropic properties. Dinan et al. defined psychobiotics as those living organisms, upon sufficient ingestion produces a health benefit to patients with psychiatric illnesses. Thus, the term "psychobiotics" designates this novel class of probiotics, which has wider applications in psychiatric medicine (Dinan et al. 2013). Numerous commensal gut microbes, traditionally known as probiotics (*Lactobacillus* spp, *Bifidobacterium* spp and *Saccharomyces* spp), exerts several beneficial health effects and used to treat intestinal dysbiosis. Table 1 presents examples of gut microbes with psychotropic properties

Interestingly, some of the intestinal microbes such as *Lactobacillus acidophilus, Lactobacillus casei, Bifidobacterium infantis, Bifidobacterium longum, Bifidobacterium bifidum, Escherichia, Bacillus, Saccharomyces, Candida, Streptococcus* and *Enterococcus* can produce neurotransmitters including serotonin,

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Table 1. Gut microbes having psychotropic properties.

Lactobacillus spp	*Bifidobacterium* spp	Other spp
L. acidophilus	*B. infantis*,	*Bacillus*
L. casei	*B. longum*,	*Candid*
L. rhamnosus	*B. bifidum*	*Enterococcus*
L. helveticus	*B. lactis*	*Escherichia*
L. plantarum	*B. breve*	*Streptococcus thermophilus*
L pentosus		Saccharomyces spp
L casei Shirota		
L. hilgardii,		

Table 2. Pyscobiotics used in different neurological conditions.

Neurological Condition	Gut microbes	Psychobiotic Strains
Anxiety	*Lactobacillus* spp	*L. fermentum* NS9,
		Lactobacillus casei Shirota,
		L. rhamnosus JB-1
		L. helveticus ROO52
	Bifidobacterium spp	*B. breve* 1205
		B. infantis
		B. longum 1714
		B. longum NCC3001
		B. longum R0175
Depression	*Lactobacillus* spp	*L. acidophilus*
		L. acidophilus W37
		L. brevis W63
		L. casei
		L. casei Shirota
		L. casei W56
		L. gasseri OLL2809
		L. helveticus NS8
	Lactococcus	*L. lactis* W19
		L.lactis W58
	Bifidobacterium spp	*B. infantis*
		B. bifidum
		B. bifidum W23
		B. lactis W52
		B. longum R0175
Stress	*Lactobacillus* spp	*L. casei Shirota*
		L. helveticus
		L. helveticus R0052
		L. plantarum PS128
		L. rhamnosus
	Bifidobacterium spp	*B. infantis*
		B. longum R0175

norepinephrine and gamma-aminobutyric acid. They also can modulate expression of neurochemical receptors like endocannabinoid receptors and act on the postulated brain-gut axis resulting in psychotropic effects (antidepressant and anxiolytic) (Barrett et al. 2012; Akkasheh et al. 2016; Selhub et al. 2014).

It has also been reported that an oral administration of a combination of probiotics, *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175 (Probio'Stick®) for a period of one month, improves depression, anger, anxiety, and lowers the level of the stress hormone cortisol (Messaoudi et al. 2011) (Table 2). A small placebo-controlled study involving functional magnetic resonance imaging (fMRI) has also demonstrated that a one-month consumption of a fermented food containing *Bifidobacterium animalis* subsp *lactis, Streptococcus thermophilus, Lactobacillus bulgaricus*, and *Lactococcus lactis* subsp *lactis* can influence brain activity as compared to baseline (Tillisch et al. 2013).

Prebiotics for psychobiotics

The relationship between fermented dairy products and the growth of beneficial intestinal microbes is well studied. However, recent reports have indicated that (non-dairy) fermented foods and herbs can also have a positive influence on the intestinal microbiota. These are equally important, as there may be an influence on longer-term gut-brain communication. Evidence also suggests that the health-promoting target of flavonoids directs towards the human gut bacterial metagenomes, whose benefits have an evolutionary origin.

Functional analysis using clusters of orthologous groups of bacteria target proteins suggests that, flavonoids regulate the metabolism of gut microbiota. Experimental research has shown that when common dietary polyphenols, subjected to fermentation, the newly formed biotransformation phytochemicals are more capable of causing a beneficial shift in microbial growth stimulation (Selhub et al. 2014). For example, isomalto-oligosaccharides are found in traditional foods (honey, sake, miso, and soy sauce), fermented cabbage (kimchi), and fermented fish oil, fiber-rich components of traditional diets (soy germ, wheat germ, rice bran, or breads). They have shown in animals and human beings to have a beneficial effect in promoting the growth of *Bifidobacteria* and *Lactobacillus* spp (Goffin et al. 2011; Han et al. 2012; Selhub et al. 2014).

Gut microbiota-brain axis in mental illness: Mechanism of action

Gut microbiota affects the brain too. It affects the brain not only through the nervous system (gut-brain's neuroanatomical pathway) but also through the endocrine system, immune system and metabolic system. Gut-brain axis is a bi-directional communication between the gut and the brain. Understanding the ability of the gut microbiota to communicate bi-directionally with the brain in the modulation of human health, is at the forefront of research examining the microbiome-gut-brain axis. Gut microbiota-brain axis mainly includes five possible communication routes. Although the exact mechanism of gut microbiota-brain axis has not yet been fully understood and clarified, yet, the evidence from animals and human studies have shown that gut microbiota or commonly referred to as Psychobiotics, can play an important role in brain behavior and cognitive development by producing hormones, immune factors, and metabolites. This also indicates that altering the gut microbiota may improve or even cure brain diseases (Cryan and Dinan 2012; Montiel-Castro et al. 2013; Saulnier et al. 2013; Foster and McVey Neufeld 2013; Luna and Foster 2014; Sherman et al. 2015). Possible communication routes between gut microbiota and brain as well as their mechanisms of actions are presented in Figures 1 and 2.

At a basic level, enteric nervous system and vagus nerves connect the intestine with the central nervous system. Microbe-derived neurotransmitters or neuroactive molecules from enterocytes under control of gut microbes influence the neural signaling of this gut-brain axis (Schmidt 2015). One of the ways probably could be, "mind-altering" probiotics likely act via their ability to produce various biologically active compounds, such as neurotransmitters. The gut bacteria (Table 3) can produce several molecules with neuroactive functions such as gamma – aminobutyric acid (GABA), serotonin, catecholamines, and acetylcholine. When concentration of neurotransmitters increases

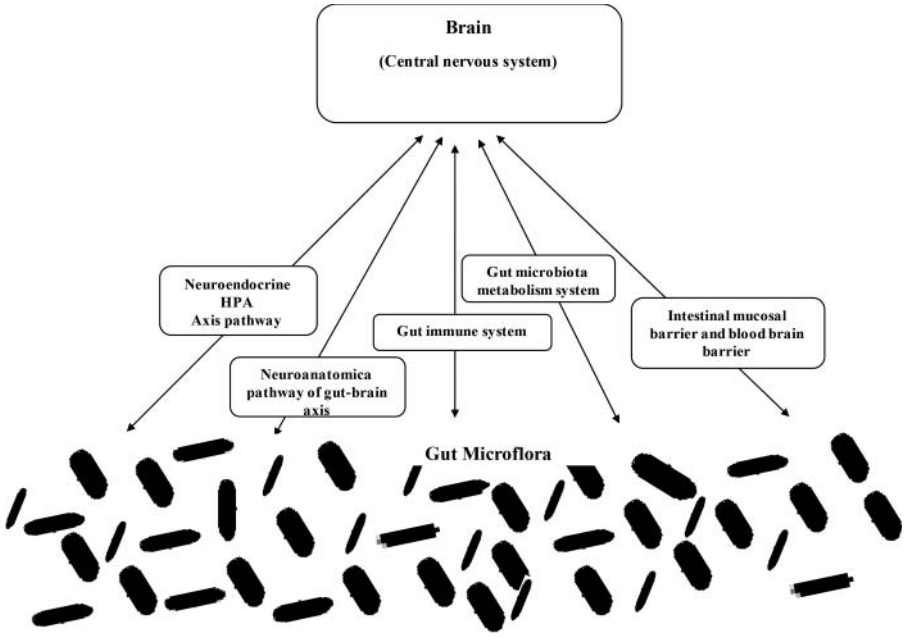

Figure 1. Possible communication routes in Gut - Brain axis.

within the gut, it can decrease the plasma tryptophan concentrations and triggers the cells within the gut's lining to release molecules to the brain thereby improving mental illness (Desbonnet et al. 2008; Lyte 2011; Akkasheh et al. 2016).

Short-chain fatty acids (SCFAs), such as butyrate, propionate, and acetate are essential metabolic products of gut microbial activity. Another possibility of the mode of functioning of Psychobiotics on the gut-brain axis may be through the SCFAs exerting central effects either through G-protein–coupled receptors, although such receptors are sparsely concentrated in the brain. It is more likely that they act as epigenetic modulators through histone deacetylases (Stilling et al. 2014). A third way that psychobiotics appear to act on the brain is by exerting effects on the body's stress response system, which involves the brain and the adrenal glands. This system, known as the hypothalamic-pituitary-adrenal (HPA) axis, becomes dysfunctional in the context of chronic stress or illness. When HPA-axis dysfunction occurs, there is a disruption of production and functions of stress-related hormones. This probably plays a central role in causing mood disorders and cognitive problems. The

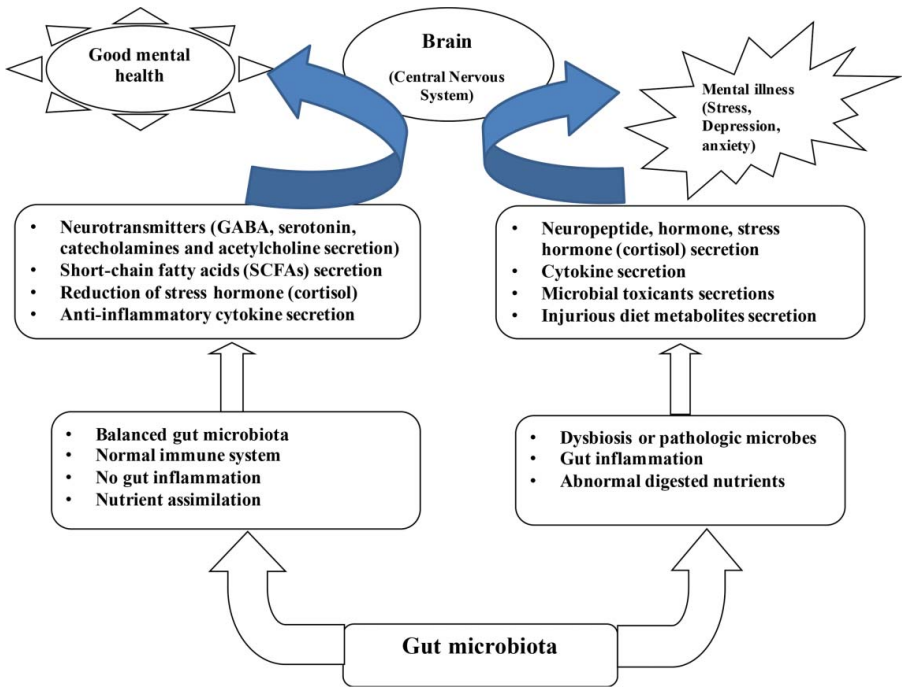

Figure 2. Possible mechanisms of actions of Psycobiotics in mental illness.

Table 3. Gut microbata as producers of neurotransmitters.

Serial No	Gut microbata	Neurotransmitter productions
1.	*Lactobacillus and Bifidobacterium* spp	Ý-aminobutyric acid (GABA)
2.	*Bifidobacterium Infantis, Candida, Streptococcus, Escherichia, and Enterococcus*	Serotonin (5-HT)
3.	*Escherichia, Bacillus*, and Saccharomyces	Norepinephrine
4.	*Bacillus* and *Lactobacillus* spp	Dopamine
5.	Escherichia, Bacillus, and Saccharomyces spp	Noradrenaline
6.	*Lactobacillus* spp	acetylcholine

gastrointestinal microbiota is a critical factor in the regulation of the HPA axis to reduce stress hormone, cortisol (Foster and McVey Neufeld, 2013 Luna and Foster 2014).

Several other reports have hypothesized that psychobiotics act on the brain in the capacity of anti-inflammatory actions. Chronic exposure to elevated inflammatory cytokines and persistent alterations in neurotransmitter systems can lead to neuropsychiatric disorders and depression. Furthermore, inflammatory cytokines may serve as mediators of both environmental (e.g. childhood trauma, obesity, stress, and poor sleep) and genetic (functional gene polymorphisms) factors that contribute to occurrence of depression. Psychobiotics are capable of regulating the body's response to inflammation by reducing the production of cytokines where as stimulate the release of an anti-inflammatory cytokine Interleukin 10 (IL-10) (Cryan and Dinan 2012; Montiel-Castro et al. 2013).

In addition, psychobiotics and the overall profile of the intestinal microbiota can influence tissue levels of mood-regulating minerals, such as magnesium and zinc (Pachikian et al. 2010). Beyond direct nutritional and glycemic effects, there are other intriguing ways in which psychobiotics and the intestinal microbiota connects to the brain. It demonstrates that supplementation with *Bifidobacterium* also provides systemic protection against lipid peroxidation and decreases brain monoamine oxidase activity, thereby potentially increasing inter-synaptic neurotransmitter levels (Ait-Belgnaoui et al. 2012; Cani et al. 2012; Shen et al. 2011).

Hence, the deficiency of healthy gut microbiota may also lead to a weakening of these relationships resulting in disease conditions. Indeed, a dysfunction in the gut–brain axis links to neuropsychological, metabolic, and GI disorders (Bercik et al. 2012; Foster and McVey Neufeld 2013).

In the ensuing years, many of the characteristics first proposed by Logan and colleagues (Table 4) (adapted from Logan et al 2005, 2003; Selhub et al. 2014) whereby beneficial microbes could influence mood or fatigue, have been examined experimentally.

Table 4. Characteristics of psychobiotics.

1. Direct, microbial-produced neurochemical production, for example, gamma-aminobutyric acid (GABA)
2. Direct activation of neural pathways between gut and brain
3. Indirect influence on neurotransmitter or neuropeptide production
4. Modulation of neurotrophic chemicals, including brain-derived neurotrophic factor
5. Influence on local and systemic antioxidant status, reduction in lipid peroxidation
6. Improvement of nutritional status, for example, omega-3 fatty acids, minerals, dietary phytochemicals
7. Limitation of small intestinal bacterial overgrowth
8. Inhibition of gastric or intestinal pathogens
9. Prevention of stress-induced alterations to overall intestinal microbiota
10. Reduction of amine or uremic toxin burden
11. Limitation of inflammatory cytokine production
12. Direct protection of the intestinal barrier
13. Limitation of carbohydrate malabsorption

Effect of psychobiotics in neuropsychological disorders

The emerging field of human microbiome research, though in its early stage, has indicated that gut microbiota may also play an important role in influencing brain development, behavior, and mood in humans (Mayer et al. 2014; Tillisch et al. 2013). Table 5 presents studies on the effects of psychobiotics (probiotics) on mood disorders and stress in animals and humans.

Animal studies

Probiotic studies supports a relationship between gut microbiota and brain and behavior. The impact of *Lactobacillus rhamnosus* on behavior and central GABA receptors in mice is studied. Animals fed with *L. rhamnosus* demonstrated reduced anxiety on a variety of behavioral measures and altered central expression of both $GABA_A$ and $GABA_B$ receptors. In order to determine the mechanism of action, animals underwent vagotomy or sham surgery and were treated either *L. rhamnosus* or inactive broth. Vagotomy prevented the emergence of an anxiolytic effect from the probiotic and prevented changes in GABA receptor expression. This study provides compelling evidence to indicate that the vagus mediates the behavioral and neurochemical effects of *L. rhamnosus* (Bravo et al. 2011).

A growing body of evidence is emerging using different models to support the contention that a variety of other potential probiotics can exert psychotropic potential. Specifically, *B. Infantis* has shown to reverse maternal-separation-induced increases in immobility in the forced swim test and increased plasma tryptophan levels. To evaluate the potential antidepressant properties of probiotics, rats were chronically treated with *Bifidobacteria infantis* in the forced swim test., Then, they were assessed on its effect on immune, neuroendocrine and central monoaminergic activity. Bifidobacteria treatment also resulted in a reduced 5-HIAA concentration in the frontal cortex and a decrease in DOPAC in the amygdaloid cortex. This study aimed to study the potential benefits of the probiotic *Bifidobacterium infantis* in the rat maternal separation (MS) model, a paradigm that has proven to be of value in the study of stress related GI and mood disorders. Cytokine concentrations in stimulated whole blood samples, monoamine levels in the brain, and central and peripheral hypothalamic-pituitary-adrenal (HPA) axis measures were also analysed. MS reduced swim behavior and increased immobility in the FST, decreased noradrenaline (NA) content in the brain, and enhanced peripheral interleukin (IL)-6 release and amygdala corticotrophin-releasing factor mRNA levels. Probiotic treatment resulted in normalization of the immune response, reversal of behavioral deficits, and restoration of basal NA concentrations in the brainstem (Desbonnet et al. 2010, 2008) *L. helveticus* prevents

Table 5. Details of human and animal studies on psychobiotics.

Authors	Study design	Microbiota	Duration of intervention	Results
Tillisch et al. (2013)	Human	A mixute of *Bifidobacterium animalis* subsp. *Lactis, Streptococcus thermophilus, Lactobacillus bulgaricus* and *Lactococcus lactis* subsp. *Lactis*	4 weeks	influenced brain activity in emotional centers
Benton et al. (2007)	Human	A mixute of *Lactobacillus casei* Shirota	3-week	improved mood
Messaoudi et al. (2011)	Human	A mixute of *L. helveticus* and *B. longum*	30 days	less psychological distress
Barrett et al. (2012)	Human	A mixute of *Bifidobacterium bifidum* W23, *Bifidobacterium lactis* W52, *Lactobacillus acidophilus* W37, *Lactobacillus brevis* W63, *Lactobacillus casei* W56, *Lactobacillus salivarius* W24, and *Lactococcus lactis* W19 and W58	4 weeks	reduced rumination and aggressive cognition
Savignac et al (2014)	BALB/c mice	*Bifidobacterium longum* (B.) 1714, *B. breve* 1205	6 weeks	reduced anxiety

diet-induced anxiety-like behavior and memory (Ohland et al. 2013) and *B. longum* NCC3001 reversed colitis-induced anxiety in the mouse via the vagus nerve (Bercik et al. 2013). Moreover, a cocktail of probiotics (*L. acidophilus, B. lactis* and *L. Fermentum*) reversed diabetes-induced cognitive and electrophysiologiocal changes (Davari et al. 2013) whereas a combination of *L. helveticus* and *B. longum* decreased anxiety (Messaoudiet al. 2011) and reversed post-myocardial infarction-induced depression in the rat (Arseneault-Breard et al. 2012). In a muse study, innately anxious BALB/c mice received daily *Bifidobacterium longum* (B.) 1714, *B. breve* 1205, and the antidepressant escitalopram or vehicle treatment for 6 weeks. Stress-induced hyperthermia test, marble burying, elevated plus maze, open field, tail suspension test, and forced swim test assessed their behavior. Also,physiological responses to acute stress is assessed too. This study data shows that these two Bifidobacteria strains reduced anxiety in an anxious mouse strain (Savignac et al. 2014).

Another study reported that, an anti-depressant effect of *L. helveticus* NS8 in rats subjected to chronic restraint stress depression could be due to the microbiota-gut-brain axis. It suggests that there is a therapeutic potential of *L. helveticus* NS8 in stress-related and possibly other kinds of depression too (Liang et al. 2015).

The psychotropic effects of a potential psychobiotic bacterium, *Lactobacillus plantarum* strain PS128 (PS128) on mice subjected to early life stress (ELS) and on naïve adult mice is studied. Results suggest that chronic ingestion of PS128 could ameliorate anxiety- and depression-like behaviors and modulate neurochemicals related to affective disorders. Thus, PS128 shows psychotropic properties and has great potential for improving stress-related symptoms (Liu et al. 2016).

The probiotic *Bifidobacterium longum* NCC3001 normalizes anxiety-like behavior and hippocampal brain derived neurotrophic factor (BDNF) in mice with infectious colitis (Bercik et al. 2012). In a pilot study, 39 CFS patients were randomized to receive either 24 billion colony-forming units of *Lactobacillus casei* strain *Shirota* (LcS) or a placebo daily for two months. Patients provided stool samples and completed the Beck Depression and Beck Anxiety Inventories before and after the intervention. We found a significant rise in both *Lactobacillus* spp and *Bifidobacteria* spp in those taking the LcS, and there was also a significant decrease in anxiety symptoms among those taking the probiotic vs controls ($p = 0.01$) (Rao et al. 2009).

Human studies

The use of probiotics and antibiotics isextensively studied in animals concerning neuropsychological disorders such as anxiety and depression; yet, research in human populations is limited. However, there is increasing evidence that probiotics may be beneficial by reducing depressive and anxiety-like symptoms (Zhou and Foster 2015). Certain strains with respect to its effects on neurological conditions is presented in Table 6 and 7.

A 4 weeks study, on healthy female volunteers, consuming a fermented milk product with a mixture of probiotics, (including *Bifidobacterium animalis* subsp. *Lactis, Streptococcus thermophilus, Lactobacillus bulgaricus* and *Lactococcus lactis* subsp. *Lactis)* showed that probiotic consumption influenced brain activity in emotional centers in healthy individuals (Tillisch et al. 2013). A 3-week consumption of a probiotic-containing milk drink that contained *Lactobacillus casei* Shirota, showed improved mood in healthy volunteers (Benton et al. 2007).

Table 6. Combination regimens for psychobiotic formulation.

1.	Lactobacillus curvatus and Lactobacillus plantarum
2.	Lactobacillus helveticus and Bifidobacterium longum
3.	Bifidobacterium animalis subsp. Lactis, Streptococcus thermophilus, Lactobacillus bulgaricus and Lactococcus lactis subsp. Lactis
4.	Bifidobacterium infantis and Lactobacillus salivarius
5.	L. acidophilus, B. lactis and L. Fermentum

Table 7. Psychobiotic strains with multiple effects.

Serial No.	Multiple neurolgical conditions	Psychobiotic Strains
1.	Depression and stress	*B. breve* 1205 *B. longum* 1714 *B. longum* NCC3001 *L. fermentum* NS9
2.	Depression and anxiety	*L. helveticus* *L. rhamnosus*
3.	Stress and anxiety	*B. bifidum* *B. bifidum* W23 *B. lactis* W52 *L. acidophilus* *L. acidophilus* W37 *L. brevis* W63 *L. casei* *L. casei* W56 *L. helveticus* NS8 *L. salivarius* W24 *L. lactis* W19 *L. lactis* W58

In another double-blind, randomized clinical trial, on healthy subjects who were given a mixture of probiotics, containing *L. helveticus* and *B. longum*, for 30 days demonstrated significantly less psychological distress, as measured by various instruments, as compared to their matched counterparts on placebo control (Messaoudi et al. 2011). Overall, these studies in healthy individuals provide clear evidence of a link between microbiota and emotional processing; however, to date, clinical studies focused on microbiota in psychiatric disorders have only considered depression, hepatic encephalopathy, autism spectrum disorder (ASD), and in some cases, anxiety-related symptoms associated with other medical conditions (Zhou and Foster 2015).

Healthy male and female participants (n = 40) were administered with, either a placebo product or a mixture of several probiotics (*Bifidobacterium bifidum* W23, *Bifidobacterium lactis* W52, *Lactobacillus acidophilus* W37, *Lactobacillus brevis* W63, *Lactobacillus casei* W56, *Lactobacillus salivarius* W24, and *Lactococcus lactis* W19 and W58) over a period of 4 weeks. As compared to the placebo group, probiotic treated participants exhibited substantially reduced reactivity to sad mood (assessed by the Leiden Index of Depression Sensitivity Scale); an effect that was specifically attributable to reduced rumination and aggressive cognition. Similarly, another double-blind, placebo-controlled trial, demonstrated that healthy subjects who scored in the lower third for depressed mood showed significant improvement, after being fed a probiotic-containing milk drink for 3 weeks, as compared to their counterparts on placebo control (Barrett et al. 2012).

Consumption of probiotic yogurt or a multispecies probiotic capsule for 6 weeks had beneficial effects on mental health parameters in petrochemical workers (Mohammadi et al. 2015). Similarly, consumption of probiotic containing yoghurt improved the mood of those whose mood was initially poor (Benton et al. 2007). It is assumed that the administration of probiotic bacteria to address changes in the microbiota may be able to reduce inflammation, restore epithelial barrier function, and potentially ameliorate behavioral symptoms among children with autism (Critchfield et al. 2011). Fermented milk containing *Lactobacillus casei* strain *Shirota* prevents the onset of physical symptoms in medical students under academic examination stress (Kato-Kataoka et al. 2016).

The above studies have thrown some light on the future prospects of psychobiotics. However, the evidence in human population is still limited. Further clinical studies are recommended to provide stronger evidence in favour of adopting psychobiotics as an affordable, adaptable and more compliant mode of treatment for mental illness.

Conclusions

Currently, the most effective treatment of mental illnesses is by administering antidepressants, antipsychotics and their likes. However, the possibility of treating a wide spectrum of these mental illnesses viz., anxiety, autism, disorders of mood, behavior, and cognition, with psychobiotics may be a promising solution. This solution would be cost effective and hence, can alleviate the quality of life of people with mental disorders. Psychobiotics proves to be well adapted to the intestinal environment and naturally modulate the gut-brain axis, reducing the chance of adverse reactions. These psychobiotics in the form of food supplements can be used as 'add-on' or adjunctive therapies to the current practice of treatment, for improving the response of the brain. Food supplements containing psychobiotics and probiotics are also gaining popularity. Hence, the emergence of non-conventional antidepressants in the form of psychobiotics is a promising move. Further research is recommended to affirm our assumptions on psychobiotics as an alternative remedy for mental illnesses.

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