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Psychobiotics in daily food against psychiatric disorders

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Psychobiotics are probiotics microorganisms that affect the central nervous system neurological functions of a host. The gut-brain-axis via immune-metabolic pathways balances the gastrointestinal function and improves the quality of life of hosts with psychiatric disorders. Gut microorganisms have been found to participate in the balance of various psychiatric disorders, including "Anxiety and Depression", "Alzheimer's disease", "Parkinson's disease", "Autism Spectrum Disorder" and "Tourette syndrome". Scientific evidence points to an association between gut microbial imbalance and psychiatric disorders. The microbiome-gut-brain axis is a target for treating psychiatric disorders using nutritional strategies, such as through the intake of probiotics. Here, we report the main effects of psychobiotic therapy against psychiatric disorders. In conclusion, psychobiotics showed considerable neurological benefits, which opens avenues for new scientific research *in vivo* towards treating psychiatric disorders.

Key words: Probiotic food, microbiome-gut-brain axis, mental health.

INTRODUCTION

The microbiome-gut-brain axis is one of the most important advances in the field of neuroscience and gastroenterology in the last times (Gill et al., 2006; Cryan et al., 2019). The gut-brain-axis via immune-metabolic pathways balance the gastrointestinal function and improve the quality of life of hosts with psychiatric disorders. Gut microorganisms have been found to participate in the balance of various psychiatric disorders (Turnbaugh et al., 2006; Sarkar et al., 2016; Cryan et al., 2019; Magalhães-Guedes, 2020). The host microbiota

profile is controlled by factors such as diets, genetics, sex and age. The gut microbiome is responsible for important functions in hosts health. In particular, gut dysbiosis is correlated with various disorders of the central nervous system. For example, low number of *Bifidobacterium* species and/or *Lactobacillus* species results in individuals with a high level of depressive disorder (Aizawa et al., 2016; Wallace and Milev, 2017).

The microbiome-gut-brain axis is involved in the neuropathology of psychiatric disorders (Carabotti et al.,

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2015; Evrensel and Ceylan, 2015; Sucksdorff et al., 2015; Cenit et al., 2017; Magalhães-Guedes, 2020). The scientific evidence came from the animal and human studies which compared gut microbiome composition of neurodepressed and non-neurodepressed animals/humans (Foster et al., 2017; Inserra et al., 2018; Partrick et al., 2018; Papalini et al., 2019). Nutritional therapies have been made to re-establish the gut microbiome in neurodepressed patients to alleviate symptoms.

New strains of probiotic microorganisms are important focus of future studies to elucidate their psychobiotic potential, particularly in psychiatric disorders. In this review, we report the main effects of psychobiotic therapy against various psychiatric disorders, including "Anxiety and Depression", "Alzheimer's disease", "Parkinson's disease", "Autism Spectrum Disorder" and "Tourette syndrome".

METHODOLOGY

A bibliographic research study was conducted to collect data and information on psychobiotics against psychiatric disorders. The research sites accessed were: e-books, theses and the Scielo database, Google Scholar, Medline, Pubmed, Science Direct and CAPES periodical portal and the virtual health/food library. The index terms used for single searches were psychobiotics, probiotics, psychiatric disorders, anxiety and depression, Alzheimer's disease, Parkinson's disease, autism spectrum disorder, Tourette syndrome, microbiome-gut-brain axis and mental health. Papers that did not match the searched words were excluded. The exclusion criterion also applies to articles that after reading that did not refer to the main objective of the study. In total, 50 articles were recruited and 3 scientific articles published on government research website: <https://ClinicalTrials.gov>.

RESULTS

Psychobiotics

Psychobiotics is a term used in preliminary research to refer to live microorganisms that, when ingested in appropriate amounts, might confer a mental health benefit by affecting microbiota of the host organism (Dinan et al., 2013; Ross, 2017; Sucksdorff et al., 2015; Cenit et al., 2017; Magalhães-Guedes, 2020; Magalhães-Guedes et al., 2020). The scientific evidence came from the animal and human studies which compared gut microbiome composition of neurodepressed and non-neurodepressed animals/humans (Sarkar et al., 2016; Foster et al., 2017; Inserra et al., 2018; Partrick et al., 2018; Papalini et al., 2019). Psychobiotic microorganisms can regulate proteins brain-derived, influencing the cognitive functions and memory (Sudo et al., 2004; Lu et al., 2008; Martinowich and Lu, 2008; Silverman and Sternberg, 2012; Foster et al., 2017; Inserra et al., 2018; Partrick et al., 2018; Papalini et al., 2019).

In experimental probiotic psychobiotics, the bacteria

most commonly used are Gram-positive bacteria, such as *Bifidobacterium* and *Lactobacillus* families, as these do not contain lipopolysaccharide chains, reducing the likelihood of an immunological response (Silverman and Sternberg, 2012; O'Mahony et al., 2015; Roshchina, 2016).

The gut microbiota is modified and evolves from birth, moving from an immature state in newborns during childhood to a more complex and diverse ecosystem in adulthood. Gut microbial imbalance can have negative consequences on the health of the host, leading to gastrointestinal, immunological and neurological disorders. In this context, different strains of psychobiotics have been successfully used as food to improve the health of the host by modulating the gut microbial ecosystem and improving the hosts gut behavior (Hemarajata and Versalovic, 2013; Sucksdorff et al., 2015; Cenit et al., 2017; Ross, 2017; Magalhães-Guedes, 2020).

The combination of a diet probiotica and physical activity have been shown to affect behavior and mood, in part by modifying the functions of the microbiome-gut-brain axis, keeping the host health relatively stable (Magalhães-Guedes, 2020).

Gut-brain axis

According to previous studies, the interest in the connection between gut health and psychological well-being received the name "Axis of the Microbiome-Gut-Brain", which is a bidirectional regulatory system involving the brain, the central nervous system and the gut (Konturek et al., 2011; Hemarajata and Versalovic, 2013; Sucksdorff et al., 2015; Cenit et al., 2017; Ross, 2017; Magalhães-Guedes, 2020).

The gut and brain send and receive information through the enteric nervous system, through neural pathways such as the efferent sympathetic system and the afferent vagal nerve, as well as through the bloodstream (Bercik et al., 2012). The enteric nervous system also influences the functions of the gastrointestinal tract, pancreas, gallbladder, endocrine function and nervous system, as well in the regulation of the host health (Bercik et al., 2012).

Although the interactions of the gut-brain and microbiome are multifactorial and not well understood. The gut-brain axis system functions as a communication channel between the gut microbiome and the brain (Konturek et al., 2011). The gut-brain axis provides a pathway of bidirectional communication that can cause several pathophysiological consequences if there is deregulation. This axis is regulated at the neural, hormonal and immune levels. Modulation of the function of the gut-brain axis is associated with specific changes in the response to stress and behavior in general (Konturek et al., 2011). Figure 1 shows the

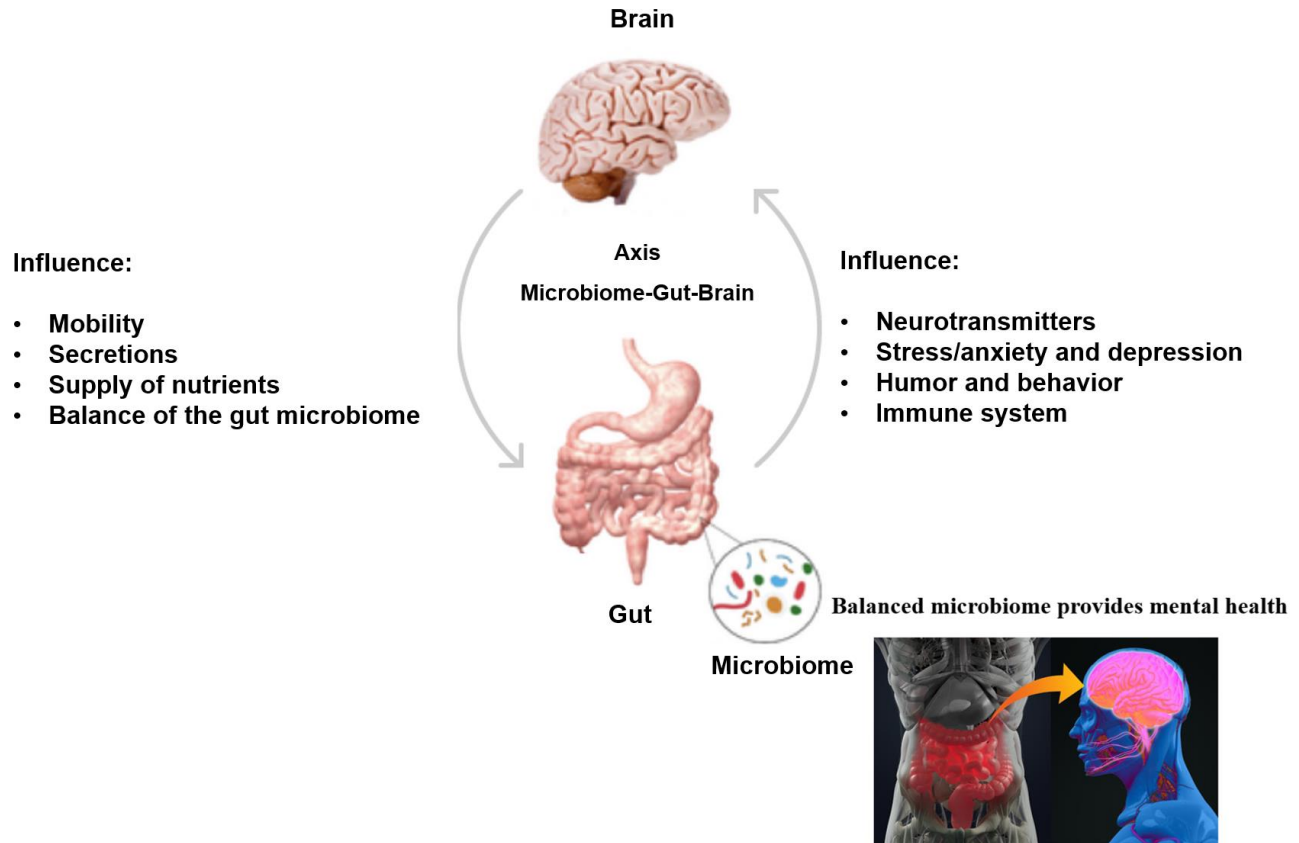


Figure 1. System “Microbiome-Gut-Brain Axis”.

“Microbiome-Gut-Brain Axis” mechanism.

Several afferent or efferent pathways are connected in the Microbiome-Gut-Brain axis. Antibiotics, environmental factors infectious agents, neurotransmitters, fibers and cytosines transmit information about the gut microbiome state to the central nervous system. Such interactions seem to influence the pathogenesis of a series of disorders in which inflammation is implicated as mood disorder, stress and depression (Petra et al., 2015; Cryan et al., 2019).

Psychobiotics action against psychiatric disorders

Anxiety and depression

A healthy mind represents a mental status of physical and neurological well-being (Dinan et al., 2013). They report that the ingestion of psychobiotics microorganisms may require a precision to address anxiety and depression symptoms. Scientific research has shown that psychobiotics have a promising effect on depression, anxiety and stress (Dinan et al., 2013). Several probiotic microorganisms strains have been reported as psychobiotics according to animal (mice) studies (Liu et

al., 2016). Regular consumption of strains of *Lactobacillus* reduced anxiety and depression symptoms in mice. *Lactobacillus* significantly decreased inflammation and corticosterone levels. Consumption of the *Lactobacillus* strains significantly increased the levels of dopamine and serotonin in the prefrontal and striated cortex of mice (Liu et al., 2016). Dairy *Lactobacillus* consumption reduced the anxiety, depression and intestinal dysbiosis in mice. In addition, *Lactobacillus* strains increased levels of serotonin and norepinephrine in the brain (Bravo et al., 2011; Liang et al., 2015). Using the *Bifidobacterium* strains daily, it was found that the stress, depression and anxiety symptoms have been reduced (Savignac et al., 2014). Regular consumption of the *Bifidobacterium longum* was effective in treating anxiety symptoms (Savignac et al., 2014).

In addition to studies with promising animals (mice), several studies have found positive effects of probiotics microorganisms on psychological health in humans. Healthy volunteers who were given *Bifidobacterium* strain for four weeks exhibited reduced anxiety and better mood (Allen et al., 2016).

Psychobiotics microorganisms were administered to a population of 10^9 CFU/mL in 16, 21 and 28 days, observing the reduction in levels of anxiety and

depression (Mohammadi et al., 2016). Petrochemical workers using both psychobiotics (probiotic capsules and yoghurts) exhibited better health parameters, assessing anxiety and depression (Mohammadi et al., 2016).

Some clinical studies have looked at the effects of some probiotic supplements (*Lactobacillus plantarum* PS128, *Lactobacillus plantarum* 299, *Lactobacillus rhamnosus* GG, Probio'Stick and Vivomixx®) in combating depression and anxiety (Mohammadi et al., 2016). These studies evaluated in humans the state of stress and mood. Approximately, 95% of the serotonin formed is derived from gut enterochromaffin cells and neurons, which is associated with the gut-brain axis regulation. In addition, serotonin brain pathways are involved in the regulation of mood (Savignac et al., 2014; Mohammadi et al., 2016; Cryan et al., 2019).

Alzheimer's disease

Alzheimer's disease is a chronic neurodegenerative disorder characterized by characterized by loss of cognitive movements and memory (Kumar et al., 2015). Studies investigated the effect of multiple microbial strains, such as *Lactobacillus* and *Bifidobacterium* strains on an animal model (mice) with Alzheimer's. The total counts of *Lactobacillus* and *Bifidobacterium* strains were increased and Coliform strain was decreased in the stool of mice after regular consumption of these probiotic strains. Furthermore, probiotic microorganisms supplementation improved learning deficits in Alzheimer's disease mice compared with control mice (Athari et al., 2018).

One randomized, double-blind, and controlled clinical trial found that consumption of probiotic-fermented milk improved the health of mice with Alzheimer's disease (Akbari et al., 2016). Based on the findings from mice studies, probiotics improved the cognitive movements and memory of the control mice (Musa et al., 2017; Athari et al., 2018).

There is scientific evidence that there is a direct biochemical link between the brain and the digestive system, but there is still no complete data on the subject. Alzheimer's acts directly on a neuroinflammation, in insulin resistance that can cause diabetic processes and also alter the metabolism of lipids. However, probiotics can reduce this influence by acting directly on these disorders (Musa et al., 2017; Agahi et al., 2018; Athari et al., 2018).

Parkinson's disease

Parkinson's disease is a neuropsychiatric disorder that reduces the neurological health of two percent of the elderly population (Barichella et al., 2009). Gut dysbiosis is a common symptom in elderly people with Parkinson's disease (Barichella et al., 2009).

The use of probiotics microorganismis in patients with Parkinson's disease diet has been previously studied. Studies have found that patients with Parkinson's disease who were using probiotic microorganisms exhibited improvement in gut dysbiosis (Barichella et al., 2016). The clinical studies of the probiotics microorganisms consumption by patients with Parkinson's disease have been focused on gut-brain axis function (Barichella et al., 2009, 2016; TPCPD, 2020). Only one recent study reported that probiotics microorganisms consumption improves the movement of the upper limb (arm) of patients with Parkinson's disease (Tamtaji et al., 2018).

Autism spectrum disorder

Autism spectrum disorder, a neurodevelopmental disorder, is characterized by deficits in social interactions across multiple contexts and levels, accompanied by behavior and repetitive patterns of interests, and/or activities (Wang et al., 2011; Li-Hao et al., 2019). Patients with autism spectrum disorder frequently experience gut dysbiosis (diarrhea or constipation) (Wang et al., 2011). Recent studies have shown that probiotics microorganisms could improve the gastrointestinal disorders and even the autism spectrum disorder-related symptoms in diagnosed patients (PQLASD, 2020). The effects of some multiple commercial strain/probiotic products on patients with autism spectrum disorder have been investigated. In 2016 and 2017, the effects of "Visbiome (product containing eight probiotic strains)" on gut dysbiosis symptoms in children with autism spectrum disorder were investigated (PQLASD, 2020). Satisfactory results have been achieved (PQLASD, 2020). Multiple microbial strains or single microbial strains of probiotics (mainly bacteria from the genera *Lactobacillus* and *Bifidobacterium*) were reported to exhibit healthy effects on children with autism spectrum disorder (Parracho et al., 2010; Shaaban et al., 2018).

Tourette syndrome

Tourette syndrome is a neurological disorder that are typically first observed in childhood (Rampello et al., 2006; Li-Hao et al., 2019). It is characterized by multiple movement (motor) tics and at least one vocal (phonic) tic. Common tics are blinking, coughing, throat clearing, sniffing, and facial movements. These are typically preceded by an unwanted urge or sensation in the affected muscles, can sometimes be suppressed temporarily, and characteristically change in location, strength, and frequency (Li-Hao et al., 2019).

Tourette syndrome is at the more severe end of a spectrum of "tic disorders". The clinical treatments of Tourette syndrome include behavioral treatments, antipsychotics, and deep brain stimulation (Murphy et al.,

2013; Weisman et al., 2013; Li-Hao et al., 2019). According to one recent study, consumption of probiotic microorganisms strains ameliorates Tourette syndrome in eight weeks after the treatment daily consumption (Zhao et al., 2017).

Randomized, double-blind, placebo-controlled clinical trial was conducted to elucidate the effect of strains of probiotic microorganisms as psychobiotics in Tourette's syndrome (TRPMD, 2020). The primary studies showed satisfactory results after two months of intervention of strains of probiotic microorganisms (TRPMD, 2020).

DISCUSSION

Scientific studies reported in this review provided evidence of the effects of psychobiotics (probiotic microorganisms) on psychiatric disorders, including "Anxiety and Depression" (Liu et al., 2016), "Alzheimer's disease" (Athari et al., 2018), "Parkinson's disease", "Autism Spectrum Disorder" (Shaaban et al., 2018) and "Tourette syndrome" (Zhao et al., 2017).

Scientific evidence points to an association between gut microbial imbalance and psychiatric disorders (Konturek et al., 2011; Hemarajata and Versalovic, 2013; Sucksdorff et al., 2015; Cenit et al., 2017; Ross, 2017; Magalhães-Guedes, 2020). Some of the single or multiple microbial strains can improve the functions of the central nervous system, including mood, anxiety, stress and depression (PQLASD, 2020). In addition, psychobiotic treatments have shown promising effects on the balance of the gut-brain axis (Konturek et al., 2011; Hemarajata and Versalovic, 2013; Sucksdorff et al., 2015; Cenit et al., 2017; Ross, 2017; Magalhães-Guedes, 2020). Thus, psychobiotic treatments can be a promising strategy to improve the quality of life of people with various mental imbalances.

Therefore, the use of probiotic microorganisms is recommended to maintain mental and emotional balance. Regardless of the diagnosis of physical or emotional disorders, we recommend daily consumption of probiotic microorganisms. The benefits to your health and well-being are immense.

Conclusion

In this review, the main effects of psychobiotic therapy against psychiatric disorders was reported. In conclusion, psychobiotics microorganisms showed considerable neurological benefits, which opens avenues for new scientific research towards treating psychiatric disorders, for example the elaboration and *in vivo* analysis of "psychobiotic foods" for insertion in the market.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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