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NARRATIVE REVIEW OF USING PSYCHOBIOTICS AND NUTRITIONALLY BALANCED DIETS TO PROMOTE MENTAL HEALTH AND WELLNESS

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SUMMARY

Introduction: *The gut microbiota is essential for digestion, nutrient absorption, and overall health, with the gut-brain axis linking it to mental and neurological function. Dysbiosis, an imbalance in gut bacteria, is associated with mental health disorders like anxiety and depression. Psychobiotics, a promising subgroup of probiotics, may help treat these conditions by reducing inflammation, stress, and improving cognitive function. Objectives were to analyse the gut-brain axis and its impact on mental health issues.*

Results: *Bidirectional communication between the brain and gastrointestinal tract regulates homeostasis and nervous, immune, and hormonal functions, with the vagus nerve linking the gut and brain. Psychobiotics, such as Bifidobacteria and Lactobacilli found in fermented foods, support cognitive and emotional health by influencing neurotransmitter synthesis and reducing inflammation. While promising, psychobiotics are most effective when used alongside conventional treatments for mental health conditions like depression and anxiety.*

Discussion and conclusion: *The brain-gut axis regulates homeostasis at neuronal, immunological, and hormonal levels, with psychobiotics like Bifidobacteria and Lactobacilli supporting both digestive and mental health. Found in fermented foods, psychobiotics show potential in improving neuropsychiatric conditions, reducing inflammation, and enhancing cognitive and emotional functions, particularly as part of synbiotics or complementary therapies.*

Key words: *probiotics; mental health; diet; supplement; mental disorders.*

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INTRODUCTION

The gastrointestinal tract (GIT) is colonised by a diverse range of micro-organisms collectively known as the gut microbiota. It is estimated by scientists that there are more bacterial cells in the body than there are genes in the entire genome. The microbiota plays a crucial role in maintaining overall health and wellbeing, facilitating the functioning of the gut and enabling the digestion and absorption of essential nutrients (Butler et al. 2019a). The gut microbiota represents a significant mechanism for the gut-brain axis (GBA), also known as the microbiota-gut-brain axis (MGB) (Butler et al. 2019b, Dziedzic et al. 2024). The GBA encompasses a range of interconnected systems, including the central nervous system, the neuroendocrine system, the neuroimmune system, the sympathetic and parasympathetic nervous systems (autonomic nervous system), the enteric nervous system and the gut microbiota (Bermúdez-Humarán et al. 2019). The concept of the bidirectional communication between the brain and the gut was first identified and acknowledged in the early 19th and 20th centuries. Research conducted during this period demonstrated that an individual's emotional state can exert an influence on the functioning of the gastrointestinal tract (Zhou & Foster 2015). The mechanism of action of bidirectional communication is complex and involves the communication of information between the gut microbiota and the brain, and vice versa (Dinan & Cryan 2017). A disruption in the gut microbiota can result in an imbalance, leading to the development of a disorder known as dysbiosis. Dysbiosis is defined as an instability of the microbial balance, characterised by alterations in functional composition and metabolic processes. Dysbiosis has been associated with a number of diseases, including anxiety, depression, autism and neurodegenerative disorders (Cocean & Vodnar 2024). Although a number of different approaches can be taken to treat mental health problems, there has recently been a significant increase in research activity in the area of psychobiotics and their impact on mental health (Adikari et al. 2019, Butler et al. 2019c).

Psychobiotics represent the latest class of agents that are believed to possess psychotropic properties. The term "psychobiotic" is used to describe living organisms that, when ingested in sufficient quantities, are believed to confer health benefits to patients with mental health disorders (Misra & Mohanty 2019, Mosquera et al.

2024b, Evrensel et al. 2019, Zawistowska-Rojek & Tyski 2022). They are classified in a subgroup of probiotics that have the potential to increase the number of beneficial bacteria in the gut, thereby reducing inflammation, lowering cortisol levels, relieving symptoms of depression and anxiety, reducing the body's stress response and improving cognitive function, including memory, learning and behaviour (Misra & Mohanty 2019, Mosquera et al. 2024b, Cheng et al. 2019, Sarkar et al. 2016, Zawistowska-Rojek & Tyski 2022). In addition to their role in maintaining overall health, they are also instrumental in regulating neurological function, as they synthesize psychoactive compounds and influence brain activity (Giri & Sharma 2022). The available evidence indicates that they play a crucial role in the synthesis of neurotransmitters, including dopamine, norepinephrine, GABA, serotonin, and acetylcholine. These neurotransmitters are vital for maintaining optimal brain and central nervous system (CNS) function (Mosquera et al. 2024a, Zawistowska-Rojek & Tyski 2022). The interaction between psychobiotics and the gut-brain axis represents a significant emerging field of research with important implications for mental health and general well-being (Sarkar et al. 2016).

The objective of this study is to conduct a comprehensive review of the existing literature on psychobiotics. This will entail defining the mechanisms of action of these bacteria, identifying the different types of psychobiotics and their sources, and examining their potential as supportive treatments for mental health problems. Our objectives were to analyse the gut-brain axis and its impact on mental health problems; to review and present the literature on psychobiotics and their role in the treatment of mental disorders.

RESULTS

The brain-gut axis, mental health and disorders

Bidirectional signalling between the brain and the gastrointestinal tract is of vital importance for the maintenance of self-regulating homeostasis, as well as for the regulation of processes at the nervous (central and enteric nervous system), immunological and hormonal levels (Margolis et al. 2021, Warren et al. 2024)

The enteric nervous system, also known as the "second brain", comprises networks of neurons that regulate gastrointestinal functions. It is comprised of the myenteric and submucosal plexuses, which are involved in information processing and function independently or in conjunction with the central nervous system. The principal component of the GBA, the nervus vagus, is also implicated at this level and directly connects the gut and the brain, thereby enabling signals to be transmitted in both directions. Sensory signals from the gut can influence brain functions via the vagus nerve and vice versa, including signals from gut bacteria (Chowdhury 2024, Cryan et al. 2019, Margolis et al. 2021, Radford-Smith & Anthony 2023, Zhu et al. 2017). Furthermore, there is an immunological connection between the gut and the brain. The microorganisms present in the gut have the potential to impact the immune system, which plays a crucial role in maintaining homeostasis and transmitting signals to the CNS. Consequently, an imbalance in the microbiota may result in inflammation that affects the brain's functionality, potentially leading to adverse outcomes (Sherman et al. 2015, Wang & Wang 2016, Warren et al. 2024). From a hormonal perspective, various hormones (cortisol, ghrelin) facilitate the transmission of signals between the gut and the brain, which in turn influence behaviour, stress responses and appetite. Additionally, neuroendocrine signals from the gastrointestinal (GI) tract exert influence over the smooth muscles, blood vessels, and glands within the digestive tract, thereby regulating digestive processes (Cussotto et al. 2018, Sun et al. 2020, Verma et al. 2024).

Psychobiotics are a subcategory of probiotics that frequently synthesize vital neurotransmitters, including gamma-aminobutyric acid (GABA) and serotonin. They also mitigate the hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis. Furthermore, they possess anti-inflammatory properties that are beneficial in the treatment of various neuropsychiatric conditions (Suravi 2016, Warren et al. 2024). Additionally, Sharma & Bajwa (2022) identify potential benefits associated with appropriate intake in individuals experiencing mental health challenges. Psychobiotics have the capacity to modulate specific neurotransmitters and proteins (glucagonate, serotonin, GABA) and exert a pivotal influence on the regulation of inhibitory and excitatory receptors, the memory process, and cognitive function.

Psychobiotics are a subcategory of probiotics and prebiotics. The most commonly cited effective psychobiotics are bifidobacteria, lactobacilli, Escherichia coli, enterococci, and streptococci (Choudhary et al. 2023, Zagórska et al. 2020). Probiotics are primarily sourced from fermented foods such as yoghurt, kefir, tempeh, kimchi, and others (Chowdhury 2024, Dimidi et al. 2019, Oroojzadeh et al. 2022). In order for a food or probiotic product to exert beneficial effects on the gut and brain, it is necessary for the product to contain a minimum of 107 colony-forming units (CFU) per gram or 107 CFU per dried viable probiotic cells (Homayouni-Rad et al. 2020, Oroojzadeh et al. 2022).

Bifidobacteria can produce and synthesize a range of vitamins, including riboflavin, thiamine, vitamin B6 and vitamin K. Additionally, they are able to synthesise other biologically active molecules, such as folic acid, niacin and pyridoxine. In comparison to lactic acid bacteria, bifidobacteria demonstrate a proclivity for the production of L(+)-lactic acid, which is more readily metabolised by humans and may prove to be a crucial factor for infants or individuals with metabolic acidosis (Sharma et al. 2021). The most prevalent Bifidobacterium species that

colonise the human gut and are employed as probiotics are B. animalis, B. adolescentis, B. bifidum, B. breve, B. infantis and B. longum. The majority of these bacteria have been demonstrated to possess both probiotic and postbiotic properties (O'Callaghan & van Sinderen 2016, Sharma et al. 2021).

Lactobacillus is a type of bacteria that is indigenous to the digestive, urinary, and genital tracts of humans without causing disease (Arshad et al. 2018). They are Gram-positive, non-spore-forming and facultatively anaerobic bacteria. Lactobacilli are classified as lactic acid bacteria on the basis of their capacity to ferment sugars into lactic acid, which creates an acidic environment and, as a consequence, inhibits the growth of other pathogenic microorganisms (Goldstein et al. 2015, Seddik et al. 2017, Zhang et al. 2018). In humans, Bacillus species are found in the digestive tract, where they facilitate digestion and maintain a healthy gut environment. They are also present in the urogenital tract, where they help maintain a proper pH and protect against various urinary tract infections. Finally, they can be found on the skin (Di Cerbo et al. 2016, Mu et al. 2018).

Lactobacillus helveticus is a bacterium that produces lactic acid (LAB) and has a variety of rods. It has been found to be able to relieve visceral pain caused by stress (Ait-Belgnaoui et al. 2018). Furthermore, the coadministration of Bifidobacterium longum has been demonstrated to alleviate feelings of anxiety and depression (Sharma & Bajwa 2022).

Lactobacillus rhamnosus is a facultatively anaerobic and gram-positive bacterium with probiotic properties (Sharma & Bajwa 2022). Rieder et al. (2017) posit that Lactobacillus rhamnosus modulates the central expression of GABA receptors, and its use is indicated in the treatment of depression and anxiety. Additionally, Slykerman et al. (2017) demonstrated in a randomised controlled trial that this strain of the bacterium significantly reduced feelings of anxiety and symptoms of depression in female children.

Bifidobacterium longum is a Gram-positive, catalase-negative, rod-shaped bacterium that inhabits the human gastrointestinal tract. Several strains within the Bifidobacterium genus have been identified as a valuable addition to a healthy lifestyle, offering benefits in the management of various health conditions. These include the regulation of neural function, the normalisation of the hypothalamic-pituitary-adrenal (HPA) axis, and the treatment of stress-induced visceral pain (Sharma et al. 2020).

Psychobiotics and treatment of mental health disorders

Sharma & Bajwa (2022) & Cocean & Vodnar (2024) define psychobiotics as all symbiotics (combinations of probiotics and prebiotics (Borrego-Ruiz & García 2024)) that contain a specific combination of bacteria that have a positive effect on neuropsychiatric diseases and mental health. It is hypothesised that psychobiotics may exert anxiolytic and antidepressant effects, in addition to improving neurological, emotional and cognitive functions (Cocean & Vodnar 2024, Radford-Smith & Anthony 2023, Sarkar et al. 2016). Sarkar et al. (2016) categorise the effects of psychobiotics into three groups: psychological effects on cognitive and emotional processes; systemic effects on the hypothalamus-pituitary-adrenal gland; and glucocorticoid stress response and inflammatory properties. The advantage of psychobiotics is that they have few side effects. However, it is challenging to achieve an immediate effect with psychobiotics. For this reason, they are recommended as a supportive therapy when the disease is under control (Zou et al. 2021). By influencing the gut microbiota and the brain-gut axis, psychobiotics provide a multifaceted approach that could be beneficial in the management of specific psychiatric disorders. Their capacity to regulate neurotransmitters such as tryptophan and serotonin, in addition to their anti-inflammatory effect, may markedly enhance psychiatric symptoms associated with brain inflammatory conditions (Mosquera et al. 2024b).

As the prevalence of depression and anxiety increases and psychological stress becomes a daily companion of human life, it is imperative that effective, easily accessible treatment options be developed to help overcome the burden of these conditions. The current treatments for mental illness are costly and have adverse side effects. In contrast, psychobiotics have been demonstrated to alleviate the symptoms of mental illness. In addition, the administration of psychobiotics has been demonstrated to result in a reduction in gastrointestinal disturbances, a decrease in inflammatory processes, and an enhancement of the immune response (Mosquera et al. 2024a, Smith et al. 2021, Warren et al. 2024). Given the association between depression and increased gut wall permeability, immunological and inflammatory activation, and gut disorders, probiotics may be employed as a supportive therapy for depressive symptoms (Dao et al. 2021, Romijn et al. 2017).

A beneficial effect on depressive symptoms was observed in a study by Schaub et al. (2022), where probiotics were administered concurrently with conventional therapy. The findings indicated that 55% of participants achieved remission, characterised by reduced depressive symptoms, when taking probiotics consistently, compared to a control group (40%). Additionally, the combination of SSRI antidepressants and probiotics demonstrated effective therapeutic action, with a notable reduction in depressive symptoms, and positive outcomes were observed in individuals with anxiety (Denysov et al. 2023a, Denysov et al. 2023b). Baião et al. 2023 additionally document an improvement in mild to moderate levels of depression with regular consumption of multiple probiotic strains. In cases of moderate to severe depression, however, a mixture of Lactobacillus

helveticus and Bifidobacterium longum did not demonstrate a statistically significant effect on depressive symptoms (Romijn et al. 2017). This finding suggests that psychobiotics may serve as a supportive therapy to conventional antidepressant treatment. Based on their impact on gut microbiota and the metabolism of neurotransmitters, including tryptophan (a vital precursor for serotonin synthesis), dopamine, noradrenaline and GABA, it can be postulated that these compounds influence the transmission of nerve signals within the enteric nervous system (Mosquera et al., 2024a, Zielińska et al. 2022).

People coping with schizophrenia are in a long process of different psychiatric problems, with around 20% of people dealing with chronic symptoms and disabilities. In addition, the illness results in a shorter life expectancy, which can be caused by suicide, co-morbid health problems and a high risk lifestyle - from unhealthy diet, addictions, lack of physical activity and the side effects of the medications used to treat schizophrenia, which can add to the incidence of metabolic syndrome. People affected by schizophrenia show changes in the composition of the gut microbiota that indicate the severity of the condition (Mosquera et al. 2024a, Warren et al. 2024). Gut microbiota has been found in several research studies to influence brain function, and has been associated with conditions such as schizophrenia through interactions with the immune system and the effects of neurotransmitters. Factors such as inflammation, stress and circadian rhythms can significantly modify the gut microbiota, reducing the number of beneficial bacteria and therefore increasing susceptibility to disease (Minichino et al. 2021, Mosquera et al. 2024b, Munawar et al. 2021, Warren et al. 2024). Substances with antipsychotic effects cause dysfunction within the gut barrier (Misera et al. 2023). Faecal microbiota transplantation (FMT) can be performed to improve the gut barrier and metabolic function. FMT is the transfer of faecal bacteria from a healthy donor to a recipient, which directly reduces metabolic function and the beneficial bacteria have a similar role to probiotics (Alagiakrishnan & Halverson 2021, Castro-Vidal et al. 2024, Mosquera et al. 2024a).

In some cases, antidepressants and antipsychotics have a positive effect on other pathologies, including irritable bowel syndrome, where the antidepressant is used in lower doses. Benefits are also claimed for premenstrual syndrome, but vulvovaginal candidiasis has been reported. From which they concluded that antidepressants have a negative impact on the growth of Candida albicans (Caldara & Marmiroli 2021). A study by Ait Chait (2021) demonstrates that psychotropic drugs have antimicrobial effects on the composition of the microbiota and, consequently, on the metabolism of the human gut, leading to the conclusion that probiotics or psychobiotics may alleviate gut dysbiosis.

DISCUSSION

In the interest of collecting relevant literature, we limited the time period to 10 years and searched in English. We reviewed articles summarizing the main findings of previous research on psychobiotics, specific brain-gut axis links and where the probiotics in interest are located.

The brain-gut axis is key to homeostasis and functions at three levels (Margolis et al. 2021, Arneth 2018, Zhou & Foster 2015). It operates at the neuronal level where the nervus vagus transmits bidirectional signals between the gut and the brain, including signals from the microbiota (Zhu et al. 2017, Mayer et al. 2015, Margolis et al. 2021). At the immunological level, where the microbiota affects the immune system and imbalances can lead to inflammation and brain dysfunction, and at the hormonal level, where hormones such as cortisol and ghrelin modulate stress, appetite, behaviour, and influence digestive processes (Cussotto et al. 2018, Wang & Wang 2016, Makris et al. 2021, Sherman et al. 2015, Hattori & Yamashiro 2021). Psychobiotics are considered a sub-type of probiotics and prebiotics and include bifidobacteria and lactobacilli. The main source is fermented food such as yoghurt, kefir, tempeh and kimchi. To have a beneficial effect on the gut and brain, a product should contain at least 10^7 CFU/g or 10^7 CFU/dried probiotic cells (Chowdhury 2024, Del Toro-Barbosa et al. 2020, Dimidi et al. 2019, Homayouni-Rad et al 2020, Oroojzadeh et al. 2022, Casertano et al. 2022). The main psychobiotics come from the strains of lactobacilli and bifidobacteria, both are beneficial bacteria that support both digestive tract health and brain health. Therefore, both types of bacteria play an extremely important role in improving and regulating mental and physical health (Sharma & Bajwa 2022, Sharma et al. 2021, Slykerman et al. 2017). Psychobiotics are classified in the group of symbiotics (combinations of both probiotics and prebiotics), which have proven benefits on mental health and neuropsychiatric diseases. They have both antianxiety and antidepressant effects and enhance neurological, emotional and cognitive functions (Abhari & Hosseini 2018, Aththanayaka 2024, Cheng et al. 2019, Cohen Kadosh et al. 2021, Smith et al. 2021, Warren et al. 2024). People with schizophrenia often experience chronic symptoms, a shorter life expectancy and alterations in the gut microbiota, which impacts the brain through the immune system and neurotransmitters (Kelly et al. 2021, Nguyen et al. 2019, Szeligowski et al. 2020). Faecal microbiota transplantation (FMT) can enhance gut balance and metabolic function by introducing beneficial bacteria (Alagiakrishnan & Halverson 2021, Castro-Vidal et al. 2024, Mosquera et al. 2024a). Medications with antidepressant and antipsychotic effects may be beneficial for irritable bowel syndrome and premenstrual syndrome, but increase the risk of Candida albicans (Caldara & Marmiroli 2021) and Clostridium difficile (Misera et al. 2023) infections, and affect microbiota and intestinal metabolism (Ait Chait,

2021). Psychobiotics are helpful in dysbiosis, and prebiotics are effective in reducing constipation due to antipsychotics such as clozapine (Munawar et al. 2021).

CONCLUSION

The bidirectional brain-gut communication axis is very important in mental health issues, where the use of antidepressant and antipsychotic drugs can lead to gut dysbiosis. The evidence suggests that psychobiotics are effective in relieving these problems where they are used as supporting therapy when taken alongside regular therapy. With psychobiotics, it should be remembered that the products must contain a sufficient amount of beneficial bacteria to have an effect on the microbiota (107 CFU/dried viable probiotic cells). We also need to be aware that psychobiotic products take longer to have a beneficial effect, so we need to be consistent in their use in the longer term. As registered nurses, we recommend and encourage all health technicians, nurses and doctors to promote the use of psychobiotics in practice, as they improve the gut microflora, reduce the side effects of medications, improve the functioning of the gastrointestinal system and have a beneficial effect on mental health with long-term use. Patients should be educated and made aware of the benefits of taking psychobiotics, both in the form of food and dietary supplements. Finally, we recommend that further studies be conducted in our region to investigate the effects of psychobiotics and that clinical trials be conducted to learn more about this important area of research.

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