



PROBIOTICS AND PREBIOTICS ON MENTAL HEALTH: A BRIEF REVIEW

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ABSTRACT

Nutrition have demonstrated an important role in preventing and treating mental health illness. Research on probiotics and prebiotics have shown that they may have a special part in mental wellbeing. Particularly, probiotics may have an essential role in the treatment of mental disorders, such as depression, anxiety, and stress within others. This brief literature review aimed to evaluate studies of the use of probiotic and prebiotic interventions in mental health. The more recent high-quality evidence suggests positive effects of probiotics on individuals with preexisting depressive symptoms, whereas the effect on mood symptoms was less significant, suggesting that probiotics have antidepressant effects. Besides depression, research suggested that prebiotics and probiotics have beneficial effects on anxiety, Alzheimer, and autism spectrum disorders. Research agrees that correcting intestinal dysbiosis, including restoring healthy microbiota, has shown improvement in physiological and psychological diseases. Methods of recovering microbiota have been found successful by utilizing probiotics, prebiotics, and a healthy diet high in fiber. Most important probiotics, according to literature, are *Lactobacilli* (e.g., *L. acidophilus*, *L. rhamnosus* and *L. helveticus*) and *Bifidobacteria* (e.g., *B. longum*, *B. bifidum*, *B. infantis*). In conclusion, it is becoming more evident that the modulation of the gut microbiota offers a novel approach for the prevention and treatment of mental health disorders.

KEYWORDS: Probiotics, prebiotics, mental health, nutrition, wellbeing.

INTRODUCTION

More than 16.1 persons in the USA suffer from depression and approximately 40 million from anxiety (ADAA, 2021). Mental and physical health are equally important components of overall health. Mental illness, especially depression, increases the risk for many types of physical health problems, particularly long-lasting conditions like stroke, type 2 diabetes, and heart disease (Centers for Disease Control and Prevention [CDC], 2018). Similarly, the presence of chronic conditions can increase the risk for mental illness (CDC, 2018). Even beyond diagnosed conditions, subclinical symptoms of depression and anxiety affect the wellbeing and functioning of a large proportion of the population (Besteher et al., 2020). In fact, it is estimated that 18.1% (43.6 million) of U.S. adult ages 18 years or older suffered from any mental illness and 4.2% (9.8 million) suffered from a seriously debilitating mental illness (Center for Behavioral Health Statistics and Quality, 2015). Therefore, new approaches to managing both, clinically and subclinical depression and anxiety, are needed to prevent more serious consequences. Even

among patients receiving psychopharmacological traditional treatment there exist serious failures and side effects. For instance, among those patients taking antidepressant medications it is reported that 30 to 50 percent in treatment fail to remit their initial symptoms, and approximately two-thirds reported at least one side effect (Mayo Clinic, 2021; Alboni, et al., 2016).

There are many different factors that can affect mental health, including diet (Medline Plus, 2021). Poor nutrition may be a causal factor in the experience of low mood and other signs and symptoms that limited patients' well-being, thus, improving diet may help to protect, not only the physical but also their mental health (Firth et al., 2020). Healthy eating patterns, such as certain diets, such as Mediterranean diet, are associated with better mental health than "unhealthy" eating patterns (i.e., rich in bad fats and sugars, lower consumption of fiber and vitamins and inadequate hydration) usually found in Western diets. Furthermore, the effects of certain foods or dietary patterns on glycaemia, immune activation, and the gut microbiome may play a role in the relationship between food and

mood (Firth *et al.*, 2020). Particularly, research on probiotics and prebiotics have shown a special interest in mental wellbeing (Ansari *et al.*, 2020; Desai *et al.*, 2021; Firth *et al.*, 2020; Liu *et al.*, 2019).

According to the World Health Organization (WHO), the accurate definition of probiotics is, “live microorganisms which when administered in adequate amounts confer a health benefit on the host” (WHO, 2001). The most important probiotics are *Lactobacilli* (e.g., *L. acidophilus*, *L. rhamnosus*, *L. helveticus*) and *Bifidobacteria* (e.g., *B. bifidum*, *B. infantis*, *B. longum*) (Ansari *et al.*, 2020). Foods containing such microorganisms fall within the “functional foods” class, and these foods should contain at least 10^7 CFU g⁻¹ or ml/day to have supportive effects on healthiness (Ansari *et al.*, 2020). Yogurt, sauerkraut, miso soup, soft cheeses (e.g., Gouda), kefir, sourdough bread, acidophilus milk, sour pickles and tempeh are some examples of foods with probiotics (Mikstas, 2020). Moreover, in order to optimize the pro mental health effect (i.e., diminish depression and anxiety) the addition of saffron extract in a 80% ethanolic extract, that have been standardized to 11 percent crocin and 2 percent of safranal found to promote maximum antidepressant and anxiolytic effects (Akhondzadeh, Tahamacebi-Pour and Noorbala *et al.*, 2005; Karimi, Hosseinzadeh and Khalegh, 2001).

On the other hand, prebiotics are described as, “a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improve host health” (Gibson & Roberfroid, 1995). Main prebiotics include resistant starch, beta-glucan, inulin, stachyose, raftilin, xylan, and fiber gums (Ansari *et al.*, 2020). One of the most important characteristics of these ingredients, mostly from carbohydrates and the family of Fructooligosaccharides (FOS), Galactooligosaccharides (GOS), and Xylooligosaccharides (XOS) is that they are resistant to enzymes and other secretions of the gastrointestinal tract (Ansani *et al.*, 2020). One of these compounds reach the colon, they are fermented by the gut microflora promoting the benefit of fermentation (Ansani *et al.*, 2020). The prebiotics act as the nutrient sources for probiotics living in the colon, and this cooperation can adjust the activity and composition of the GI system. Specific pro- and prebiotics work together to confront infections and to decrease the risk of general diseases including mental disorders (Ansani *et al.*, 2020; McEwen & Fénasse, 2019). It is important to remember that approximately 60% of patients with depression and anxiety have at least one intestinal disturbance and the use of probiotics affect favorably the reduction of stress symptomatology (Diop, L. Guillou, S. & Durand, H., 2008). Follow main findings related to the effects of pro- and prebiotics on mental health disorders and the potential mechanisms of action and application in clinical practice.

Effects of Probiotics and Prebiotics on Mental Health

Probiotics are said to have a bidirectional communication influence on the gut-brain axis and may have an essential role in the treatment of mental disorders, such as depression (Ansari *et al.*, 2020; Desai *et al.*, 2021; Liu *et al.*, 2019; McEwen & Fénasse, 2019; Probiotics alone or combined with prebiotics may help ease depression; 2020, July 20). Probiotics that influence the gut-brain axis have been labeled “psychobiotics”, highlighting their ability to improve the aspects of mental and emotional behaviours (Ansari *et al.*, 2020; McEwen & Fénasse, 2019). Clinical and animal studies have indicated success in the ability of psychobiotics to supplement reduction of depressive symptoms, showing similarities to traditional antidepressant treatments (McEwen & Fénasse, 2019). Psychobiotics have been found to relate mostly to the lactic acid bacteria family with specific strains *Lactobacillus casei*, *Lactobacillus helveticus*, and *Bifidobacterium bifidum* (McEwen & Fénasse, 2019).

Mechanisms of action

Several mechanisms have been suggested for the effects of probiotics and gut microbiota on depression and anxiety. The possible etio-pathological mechanisms of depression involving inflammation, neurotransmitters, the hypothalamic–pituitary–adrenal (HPA) axis and epigenetic mechanisms potentially benefit from probiotic intervention. The bidirectional communication between the gut and the brain is mediated by trillions of microbes residing in the human gut through several mechanisms encompassing neural, immunologic and humoral pathways (Johnson *et al.* 2021). It has been demonstrated that it happens through anatomical changes and alterations in the release of metabolites and neurotransmitters (Ansari *et al.*, 2020; McEwen & Fénasse, 2019). Several probiotic bacteria such as *Lactobacillus*, *Bifidobacterium*, and *Escherichia* produce neurotransmitters and neuropeptides including GABA, serotonin, and BDNF (Ansari *et al.*, 2020). Furthermore, *Lactobacillus acidophilus*, *Bifidobacterium infantis*, and *Bifidobacterium longum* have been found to improve mental health through secreting neurotransmitters, such as GABA, 5-HTP, glycine, and catecholamine, or regulating endocannabinoid expression (McEwen & Fénasse, 2019). Live cultures (probiotics) present in fermented food can synthesize GABA and improve depressive and anxiety-like behaviors (Aslam *et al.*, 2020). Thus, pro- and prebiotics are potential substitutes for current antidepressant drugs (Ansari *et al.*, 2020). One human study reported a 50 percent in depression scores and another study reported a 55 percent improvement in anxiety, all without side effects (Messaudi, Lalonde & Violle, 2011; Messaudi, Violle, & Bisson, 2011).

Summary of Clinical Trials

The idea of using probiotics to control mental health disorders, such as depression and anxiety has been examined in some clinical trials (Ansari *et al.*, 2020).

Wallace and Milev (2017) suggest a positive effect of probiotics with the most significant effects on symptoms of anxiety. Similarly, Galland (2014) showed that supplementation with *Bacteroides fragilis* also decreased anxiety levels while improving excessive gut permeability. Pirbaglou and collaborators (2016) also shows that probiotic supplementation had a positive impact on anxiety and depressive symptoms. Wang and collaborators (2016) concluded that *B. longum*, *B. breve*, *B. infantis*, *L. helveticus*, *L. rhamnosus*, and *L. casei* were more effective in improving symptoms. Ansari and collaborators (2020) suggested that prebiotics and probiotics not only improve mental health, but they have beneficial effects on depression, anxiety, Alzheimer, and autism spectrum disorders. Particularly, anxiety, depression, autism spectrum disorder, obsessive compulsive disorder (OCD), and memory abilities were improved in several studies where *Bifidobacterium* and *Lactobacillus* were used (Dolan et al., 2016).

Regarding schizophrenia, clinical trials are still limited and have focused on diet and probiotics, always in combination with antipsychotics (Balanza-Martinez, 2017). A clinical trial with probiotics in psychotic disorders showed that supplementation during 14 weeks of one tablet with a combination of *Lactobacillus Rhamnosus* GG and *Bifidobacterium animalis lactis* Bb12 (n=33) was not more effective than the placebo (n=32) to reduce the clinical severity when evaluated with the PANSS scale (Balanza-Martinez, 2017). However, the administration of the probiotic was well tolerated and was associated to a significant reduction in the incidence of severe gastrointestinal discomfort, which is a relatively frequent comorbidity in this population (Balanza-Martinez, 2017).

Other research concluded that probiotic supplements either alone or in combination with prebiotics may be linked to measurable reductions in depression (Probiotics alone or combined with prebiotics may help ease depression; 2020, July 20). This study also showed a significant improvement in anxiety symptoms and/or clinically relevant changes in biochemical measures of anxiety and/or depression with probiotic or combined pre-probiotic use (Probiotics alone or combined with prebiotics may help ease depression; 2020, July 20).

In infants, researchers found that *Lactobacillus rhamnosus* GG reduces the risk of neuropsychiatric disorder developmental later in childhood (Dolan et al., 2016). Furthermore, Desai and collaborators (2021) have shown the effectiveness of probiotics during pregnancy to reduce anxiety and depression symptoms. Liu and collaborators (2019) also have found antidepressant and anxiolytic effects of probiotics. They conducted a meta-analysis that suggested that probiotic effects were larger for clinical than community samples for depression (Liu et al., 2019). In conclusion, the more recent high-quality evidence base research, suggests positive effects of probiotics on individuals with preexisting depressive

symptoms, whereas the effect on mood symptoms is less significant in healthier populations.

Intestinal microbiota differences

Studies indicate that the intestinal microbiota of depressed patients is significantly different from that of healthy controls (Aizawa et al., 2016; Aslam et al., 2020; McEwen & Fénasse, 2019). Intestinal microbiota differences might be related to dysbiosis, which is a condition where the host microbiota are disturbed compared to healthy subjects, and can be categorized by a loss of beneficial microbes, expansion of pathobionts and loss of diversity (Aslam et al., 2020). Compositional differences have been noted between those with depression and healthy controls (Aslam et al., 2020; McEwen & Fénasse, 2019). *Bifidobacterium* levels have been found to be significantly lower in patients with depression than in healthy controls. (McEwen & Fénasse, 2019). Both microbiota diversity and richness declined in depressed patients. Also notable in the depressed patients was that the richness of *Lactobacillus* and *Bifidobacterium* was lower (McEwen & Fénasse, 2019). Similarly, it has been found in a six-week randomized, double-blind, placebo-controlled trial, *Bifidobacterium longum* was found to reduce depression scores and increase the quality of life in patients with irritable bowel syndrome (Wallace & Milev, 2017). The current evidence suggest that gastrointestinal (GI) disorders are often comorbid with depressive and anxiety symptoms and associated with increased level of inflammation (Aslam et al., 2020). Fermented foods are postulated to modify inflammation by reducing pro-circulating inflammatory cytokines, producing short-chain fatty acids (SCFA), and improving the gut barrier functions that are relevant to both GI and mental disorders (Aslam et al., 2020). In conclusion, research indicates that problems in the gut may directly lead to mental health disorders, such as anxiety and depression (Dolan et al., 2016).

CONCLUSIONS

Probiotics and prebiotics have demonstrated their positive effect on mental health. Fermented foods hold promises as a dietary intervention due to their theoretical potential to modify the gut microbiota and improve the integrity of the intestinal barrier. Correcting intestinal dysbiosis, including restoring microbiota, has seen improvement in physiological and psychological diseases. Methods of recovering microbiota have been found successful by utilizing probiotics, prebiotics, and a healthy diet.

Optimum nutrition plays a fundamental role in the management of mental health. The prescribing of probiotics for mental health, especially depression, is a novel treatment with numerous other health benefits. It is becoming more evident that the modulation of the gut microbiota offers a novel approach for the treatment and prevention of mood and anxiety disorders. Since probiotics may affect depression in strain-specific and

dosage-specific manner, more research is required to investigate the relationship between probiotics, the microbiome-gut-brain axis, and depression.

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