

Psychobiotics: Next Generation Treatment for Mental Disorders

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Editorial

Depression is a common disease worldwide. WHO (2017) has estimated more than 300 million people in the world suffer from depression. It is estimated that 20% of the world population have experienced major depressive disorder in their life that is associated with low mood, mood fluctuation, loss of interest, hopelessness, changes in appetite and sleep. Depression also can occurred sub clinically and affect daily performance. Now, a treatment for depression is based on pharmacological agent that has many side effects such as headaches, nausea, agitation and sedation [1-4].

In the last decade, studies exhibited that gut microbiota may play an important role in normal physiology and thereby influences brain development, behavior and mood. It is well documented that disturbance of gut microbiota balance has been associated to many metabolic disorders such as obesity, diabetes and neuropsychiatric conditions including anxiety and depression. Studies revealed that disruption of the gut bacteria balance or dysbiosis may occur as the result of antibiotics usage, medical treatments, poor hygiene food and water, synthetic preservatives, gluten, herbicides and stress. Stress also increases intestinal permeability, which permits bacteria to cross from the gut into the bloodstream and lead to an immune response. Several cross-sectional studies confirmed there is a correlation between gut microbiota and mental health, but the newest and possibly most interesting way of microbiome manipulation, is supplementation with psychobiotics. Based on the latest research psychobiotics are live microorganisms that if ingested in sufficient amounts can positively affect the brain and benefit anyone suffering from chronic stress, poor mood, or anxiety-like signs. Before this definition psychobiotics were used as an alternative treatment just in "Patients" with psychiatric disorders who dislike to use chemical treatments [5,6]. There are three suggested mechanisms for probiotics effects on mental health: The first way is referred to the probiotics ability in secretion of neurotransmitters such as gamma-aminobutyric acid (GABA), serotonin, catecholamines, and acetylcholine in the gut and notice brain function and affect behavior. Studies indicated that a considerable portion of brain chemicals like serotonin,

GABA, dopamine, and acetylcholine produces in the intestines by gut microbiota [2,3,7-9].

The second way of psychobiotics to battle with stress is by altering adrenal glands. A structure is in human body called hypothalamic-pituitary-adrenal (HPA) axis that becomes dysfunctional in situation of chronic stress or disease. When body faces an abnormal and stressful situation, production of cortisol and other stress-related hormones, started following the HPA-axis disorder [2]. The third approach of psychobiotics is through their anti-inflammatory actions. When an inflammation occurs, inflammatory transmitters elevated throughout the body and brain and causes depression and other mood and cognitive disorders. Psychobiotics may have their effects in the brain by lowering inflammation.

The important issues about using probiotics in mental disorders are the strain and their dosage. *Lactobacillus* and *Bifidobacterium* are the most popular probiotics respect to mental health.

Earlier research suggested that administration of *Lactobacillus rhamnosus* (strain GG) in diet can reduce anxiety in humans through shifting the expression of GABA receptors. Studies showed that *Lactobacillus plantarum* (strain PS128) can cause positive changes in emotional behaviors and significantly reduce anxiety-like behaviors through increasing dopamine and serotonin, lowering stress hormone levels, and reducing inflammation [7].

Researchers also have determined that *Bifidobacterium longum* (strain R0175) and *Lactobacillus helveticus* (R0052) can reduce cortisol and alleviate psychological distress in humans (including obsessions, compulsions, paranoia, anxiety) via reducing cortisol [8]. Animal research also displays that *Bifidobacterium longum* (strain 1714) potentially reduce anxiety-like behavior. *Lactobacillus reuteri* (strain 23272) also displayed the ability to reduce anxiety-like behaviors in animals by reducing stress hormone levels and exchanging the expression of GABA receptors [9]. In one double-blind, placebo-controlled trial, has been reported that administration of *Lactobacillus casei* (strain Shirota) in patients with chronic fatigue syndrome and digestive problems decreased the anxiety symptoms after two months [9]. In another

randomized clinical trial in patients with major depressive disorder [2], consumption of probiotic pills consisted of *Lactobacillus acidophilus*, *Lactobacillus casei*, and *Bifidobacterium bifidum* (2 billion CFUs each) significantly decreased total scores of depression. In an investigation changes in the brain activity in regions that are responsible in control and processing of emotion and sensation following consumption of fermented milk product with a mixture of probiotics, including *Bifidobacterium animalis*, *Streptococcus thermophilus*, *Lactobacillus bulgaricus*, and *Lactococcus lactis* for 4 weeks was observed [10].

It is obvious that many factors can influence the results of these studies. Method, sample size, probiotic strain, length of intervention and dosage are factors that vary in the trials [11-13].

Despite these preclinical data, still there are many unclear issues in preferring or choosing probiotics as alternative agents in treating mental disorders. Another question is their ability in alleviating daily stress. Further research with focus on strain, dosage, duration of treatment and nature of mental disorder are warranted to determine probiotics' efficacy for improving mental health. At the end the golden key to answer these questions is to study and compare the composition of gut microbiota using molecular methods in healthy and patient individuals and also before and after probiotic interventions.

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