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Psychobiotics: An emerging alternative to ensure mental health amid the COVID-19 outbreak?

To the editor:

COVID-19 is a highly infectious disease caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which is responsible for the development of serious and even fatal respiratory complications, resulting from the failure of the response adaptive immunology in the early stage of the disease (incubation period) (Shi et al., 2020; Zhang et al., 2020). In addition to respiratory complications and the potential threat of death, COVID-19 outbreak can also threaten the mental health of the general public and health professionals, causing problems such as stress, panic, depression, anxiety, sleep disorders, lower mental well-being, and even suicide (Rajkumar, 2020; Roy et al., 2020).

Social isolation associated with the occurrence of infections and deaths of family and friends and the lack of a possible vaccine for COVID-19 can be considered stressful factors, which lead to the development of feelings such as loneliness and anger, and cause short-term post-traumatic stress (Ahmed et al., 2020). In addition, the advance of the pandemic has overburdened health systems, reducing the availability of beds and personal protective equipment, causing health professionals to experience a great deal of anxiety and emotional stress. Likewise, the increase in the number of deaths, fears of infection, the lack of adequate supplies and inadequate information, as well as factors such as frustration, boredom, financial loss and a longer quarantine duration, can cause psychiatric problems in the general population (Brooks et al., 2020; Röhr et al., 2020; Roy et al., 2020). In view of this, there is a clear need for the urgent development of methods that aim to take care of the population's mental health. Thus, the utilization of psychotropic drugs to control potential problems related to emotional and behavioral responses during this pandemic is almost inevitable.

The use of psychotropic drugs as treatment options for maintaining mental health is often associated with endocrine and metabolic side effects, which involve changes in the composition of the gut microbiota and gastrointestinal function, hyperprolactinemia, hyponatremia, diabetes, hypothyroidism, hyperparathyroidism, sexual dysfunction, weight loss, weight gain, metabolic syndrome, dyslipidemia and hypertension (Bhuvanewar, Baldessarini, Harsh, & Alpert, 2009; Cusotto et al., 2019). Thus, the adoption of less aggressive therapies to the human body are important and need to be considered. Within this context, the use of microorganisms with psychobiotic properties has gained increasing attention in the scientific community in recent years.

Psychobiotics are considered a class of probiotic bacteria with great therapeutic potential for the treatment of psychiatric diseases (Dinan et al., 2013). Many microorganisms have been proposed as potential psychotropic agents, including *Streptococcus thermophiles*, *Bifidobacterium animalis*, *Bifidobacterium bifidum*, *Bifidobacterium longum*, *Streptococcus thermophiles*, *Lactobacillus bulgaricus*, *Lactococcus lactis*, *Lactobacillus acidophilus*, *Lactobacillus plantarum*, *Lactobacillus reuteri*, *Lactobacillus paracasei*, *Lactobacillus helveticus*, *Lactobacillus rhamnosus*,

Bacillus coagulans, *Clostridium butyricum*, and others (Cheng et al., 2019; Gualtieri et al., 2020; Vaghef-Mehrabany et al., 2020).

Ingestion of adequate amounts of these bacteria can assist in the production of neuroactive substances, such as gamma-aminobutyric acid (GABA), norepinephrine, dopamine, acetylcholine, cholecystokinin, serotonin, substance P, glutamate, glucagon-like peptide-1, glucagon-like peptide-2, peptide YY (PYY), neuropeptide Y (NPY), and may regulate proteins such as brain-derived neurotrophic factor (BDNF), which are important in the regulation of functions and behaviors related to the central nervous system (CNS) and also in gut-brain communication, through immunological, humoral, neural and metabolic pathways (Cheng et al., 2019; Dinan et al., 2015, 2013; Lyte, 2013). Several studies have suggested that the administration of psychobiotics can be effective in treating depression (Hao et al., 2019; Tian et al., 2020; Wei et al., 2019), stress (Allen et al., 2016; Savignac et al., 2014), and anxiety (Liang et al., 2015; Messaoudi et al., 2011).

A clinical study conducted on 22 healthy volunteers showed that ingesting strains of *Bifidobacterium longum* 1714 (1×10^9 colony-forming units per stick) for four weeks improved cortisol production and hippocampal-dependent visuospatial memory, in addition to reducing subjective anxiety and daily stress (Allen et al., 2016). In another randomized, placebo-controlled clinical trial involving 150 Italian subjects, it has been shown that consumption of 3g/day of probiotic oral suspension (containing 9 strains belonging to the genera *Streptococcus*, *Bifidobacterium*, *Lactobacillus*, and *Lactococcus* - 1.5×10^{10} colony-forming unit) for 12 weeks significantly reduced anxiety symptoms in carriers of allele A of interleukin-1 β gene (risk factor) (Gualtieri et al., 2020). The daily intake of *Lactobacillus gasseri* CP2305 (1×10^{10} bacterial cells) during 12 weeks it was effective in recovering from fatigue and in relieving anxiety and depressed mood in 49 male university students aged between 18 and 22 years old during a period of vigorous training (Sawada et al., 2019). Likewise, long-term use of tablets containing *Lactobacillus gasseri* CP2305 (1×10^{10} bacterial cells per 2 tablets) improved mental status and sleep quality in young students (n = 60) exposed to chronic stress (Nishida et al., 2019). Furthermore, psychobiotic microorganisms can improve energy metabolism and gastrointestinal function, reduce inflammation, stimulate the immune response, besides improving symptoms of autism, motor functions and cognition in patients with Parkinson's and Alzheimer's diseases (Cheng et al., 2019).

The main advantages of using psychobiotics in maintaining mental health during crises such as COVID-19 is that, because they are microorganisms that belong to microbial genera naturally found in the intestinal tract, they may present a lower risk of allergies, and less dependence compared to psychotropic drugs.

In light of the above, could these microorganisms be a "green" alternative for maintaining mental health in the face of a population that

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is already fragile? Certainly, supplementation of strains with psychobiotic properties will bring benefits to the host, but future clinical approaches are needed to ascertain their effectiveness in improving emotional and behavioral disorders resulting from the evolution of COVID-19 outbreak. Approaches are also needed to ensure delivery of these microorganisms. Some potential strategies include microencapsulation, elaboration of edible bars and functional beverages supplemented with psychobiotic microorganisms, development of suitable excipients, etc.

Declaration of competing interest

The authors declare no conflict of interest.

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