The prospect of using natural psychobiotics in dairy products to stabilize the diet

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Abstract. The spread of coronavirus infection has caused a disturbance in the structure of the diet, including the priority consumption of convenience foods and fast food. It is known, that inappropriate nutrition contributes both to the disruption of metabolic processes in the body and creates the prerequisites for the aggravation of nervous disorders. The development of functional products based on synbiotics, the components of which ensure the normalization of the intestinal microbiome composition, can become a promising direction for the prevention of malnutrition. The basis for developments in this area is a review of research data confirming the importance of the human intestinal microflora in the regulation of vital functions and psychosomatic reactions of the body, in particular, mood and behavior. The prospect of using fermented milk products with pre- and probiotic microorganisms and preparations based on them instead of chemical antidepressants is shown. The mechanism of action of psychobiotics, consisting in the formation of most of the nervous and immune systems due to microorganisms of targeted action and dietary fibers in food, in particular dairy, has been analyzed.

1. Introduction
The rapid spread of the coronavirus infection COVID-19 brings into our lives more and more stressful situations associated with the need for self-isolation, reports of the growth and spread of infection, lack of communication, and disruption of the usual way of life. This includes eating disorders associated with excessive consumption of various food groups, primarily semi-finished products and fast food to the detriment of, in particular, fermented milk products [1]. Despite the fact that the full picture of eating disorders in the future is quite difficult to track, due to the relatively short time frame since the start of the COVID-19 pandemic, nevertheless, certain statistics indicate the relationship between eating disorders and the psycho-emotional state of a person. This entails a deterioration in the state of the gut microbiota, which is directly related to human mental health. In this regard, the most promising approach seems to be an approach to reducing stress effects on the human body by including natural psychobiotic supplements (consortia of microorganisms) in the diet that improve the functioning of the gastrointestinal tract, which will allow avoiding the use of drugs with a wide range of side effects (allergic reactions, asthenia, impaired concentration and memory, constant drowsiness, internal anxiety) [2,3].

2. Materials and methods
The objects of research in the work were modern domestic and foreign scientific and statistical data devoted to the study of the influence of intestinal microbiota on the mental state of a person, the role of...
natural psychobiotics in maintaining the nervous system. The method of the study was a direct substantiated analysis of the data obtained.

3. Results
According to experts from the School of Public Health of Boston University, in the first half of 2020, during the spread of coronavirus infection COVID-19, the prevalence of symptoms of depression among various segments of the population increased many times compared to the pre-pandemic period [4,5]. Specialists of the Department of Psychiatry at the University Hospital of Belvitge (Barcelona, Spain) directly linked these psychoemotional pathologies with eating disorders. More than 38% of patients showed increased anxiety associated with overeating and unbalanced nutrition [6]. For the formation of adequate nutrition, nutritionists note the need for daily monitoring of the consumption of certain components, which ensure the full functioning of the immune and nervous systems. Such components can be milk proteins and probiotic cultures contained in fermented milk products, for example, a consortium of microorganisms consisting of L. rhamnosus tr, L. reuteri lr1 and L. acidophilus h-9, developed by scientists from the All-Russian Dairy Research Institute [7,8].

The foregoing necessitates the search for modern biotechnological solutions to the problem of relieving stress conditions by correcting food rations.

The purpose of this analytical study is to prove the prospects of using bacterial drugs, fermented milk products of psychobiotic orientation for the prevention of nervous disorders and concomitant pathologies against the background of the spread of COVID-19.

Most researchers in the field of biochemistry, medicine and biotechnology associate the functioning of the human nervous system with the state of the intestinal microbiota. The gut microbiome includes all microorganisms and their genomes found in the intestinal tract. Despite the fact that the foundations for the study of the relationship between the gut microbiota and the brain were laid by scientists who worked at the turn of the 19th and 20th centuries, the view of intestinal functionality as the main health determinant, including mental health, has been actively developed only now [9,10]. It has been established that microbial metabolites act according to the principle of two-way signal exchange in the “microbiota-host” system. They modify functions of the nervous system through epigenetic, metabolic and neuroendocrine mechanisms. For example, the brain system, dependent on the neurotransmitter serotonin, is responsible for many aspects of emotional behavior. The intestinal microbiota directly affects the activity of brain immune cells, the permeability of the barrier between blood flow and the brain, synthesis and release of neurotransmitters, etc. Equally important is the reverse effect of the brain and nervous system on the state of intestinal microflora. As shown by numerous studies, cerebral stroke also entails a change in the intestinal microflora composition, which is especially indicative of bacteria of the Peptococcaceae and Prevotellaceae families [11]. Various probiotic cultures can act as a powerful regulator of the composition of the microbiota, strains with scientifically proven beneficial properties, characterized in detail by their taxonomic, molecular genetics, toxicological, technological and probiotic properties [7,12,13]. Consumption in foodstuffs will allow maintaining microbial balance and ensuring greater body resistance to external environmental factors, including stress factors during the pandemic and post-pandemic period [14,15,16,17].

Good mental health is a state of mental, psychological well-being. Attention to the probiotic cultures ability by regulating the composition of the intestinal microflora to improve the nervous system functioning has attracted researchers since the beginning of the 20th century. However, the concept of "psychobiotics", under which was designated "living organisms that have a positive effect on the mental health of patients with mental disorders," Timothy Dinan, specialist at the Center for Food Pharmabiotics, (Cork, Ireland), was introduced only in 2013 [18].

Psychobiotics have anxiolytic and antidepressant effects, characterized by changes in emotional, cognitive, systemic and nervous parameters. The communication channels between bacteria and the brain through which psychobiotics act include the intestinal nervous system and the immune system.

The influence of psychobiotics on the human body is traditionally considered in three directions:
• psychological impact on emotional and cognitive processes;
• systemic effect on the hypothalamic-pituitary-adrenal system, which provides support for the body's homeostasis, recovery after prolonged aerobic exercise, the concentration of pro-inflammatory cytokines that cause depressive disorders;
• neuronal effects on the neurotransmitters production in the body [19].

Neurotransmitters control major bodily functions, including movement, emotional responses, and the physical ability to experience pleasure and pain. The best-known inhibitory neurotransmitters that affect mood regulation are serotonin, norepinephrine, dopamine, acetylcholine, and GABA (GABA). GABA is a monocarboxylic alpha amino acid that is involved in the regulation of the mammalian central nervous system. Under its influence, the energy processes of the brain are activated, the respiratory activity of tissues increases, the utilization of glucose by the brain improves, and the blood supply is activated. GABA has a hypotensive, sedative, diuretic effect, relieves pain and inflammation. Due to such a positive effect on the functioning of living organisms, γ-aminobutyric acid can be considered one of the main markers of psychobiotic activity [20].

Systematized data on the assessment of the psychobiotic microorganisms’ effect on the laboratory animals’ organism (rats, mice) under conditions of induced stress are shown in table 1. When testing psychobiotics on animal models of somatic, infectious and neurodegenerative diseases, conditions are created to predict the assessment of their possible positive effects in similar human diseases.

The presented in table 1 data indicate that various probiotic cultures, to one degree or another, have a certain therapeutic effect that is adequate to the induced load. Moreover, both individual types of crops and their consortia are capable of regulating both one and several functions of the animal body.

**Table 1.** Effects of psychobiotics *in vitro* in experiments on laboratory animals under artificial pathological conditions.

| Probiotic culture type | Therapeutic effect |
|------------------------|--------------------|
| **Induced colitis**    |                    |
| Consortium: *L. rhamnosus* и *L. helveticus* R0052 | Reduced mortality |
| *L. reuteri*           | Reducing tendency towards weight loss |
| Consortium: *L. acidophilus*, *B. lactis* и *L. fermentum* | Reducing the pathogens translocation from the intestine to the spleen |
| *L. brevis* DPC6108    | Overall reduction in colitis clinical symptoms |
| *L. helveticus* NS8    | Induced diabetes |
| *L. rhamnosus* JB-1    | Improving cognitive function |
| *B. infantis*          | Reflexes and attention initiation |
| *L. reuteri*           | Vegetative reactions regulation |
| *L. brevis* DPC6108    | Decreased blood glucose concentration |
| *L. helveticus* NS8    | General suppression of hyperglycemia symptoms |
| *B. infantis*          | Artificial hyperammononemia |
| *L. rhamnosus* JB-1    | Improving the emotional background |
| *L. helveticus* NS8    | Improving cognitive function |
| Generally healthy animals prone to stress and anxiety |
| *L. rhamnosus* JB-1    | Decreased activity of the hypothalamic-pituitary-adrenal axis by regulating corticosterone levels |
| *B. infantis*          | Increased plasma tryptophan |
| *L. rhamnosus* JB-1    | Decreased 5-hydroxyindoleacetic acid (a serotonin metabolite) in the brain |
Improving the serotonergic system of the brain functioning
Reducing systemic inflammation (decreasing tumor necrosis factor, interleukin-6 and γ-interferon)
Stress, anxiety

Relief of post-stress anxiety

**L. helveticus NS8**
Improving post-stress memory of object recognition
Decreased levels of adrenocorticotropic hormone and cortisol
Increased levels of interleukin-10, noradrenaline and serotonin

Researches of changes in central neurotransmitters

**L. rhamnosus JB-1**
Increased glutamate and glutamine content
Increased amount of N-acetylaspartylglutamic acid and γ-aminobutyric acid

Chinese experts from the Institute of Physiology of the Chinese Academy of Sciences found that, in general, the effect of the probiotic *Lactobacillus helveticus NS8* use is comparable to the effect of the antidepressant citalopram use [21].

Certain subspecies of *Lactobacillus*, as well as *Bifidobacterium*, are also capable to forming the neurotransmitter acetylcholine; other bacterial strains synthesize dopamine and noradrenaline. There is also data of the relationship between the microbiota state and the serotonin level in the blood. *In vitro* studies have shown that plasma serotonin levels in normal mice without pathologies were significantly higher than in artificially deprived microbiota. In experiments on rats, it was shown that oral administration of *Bifidobacterium infantis* increased the tryptophan level in blood plasma, a serotonin precursor, which indicates a certain psychotropic effect of the strain [22].

At the Department of Psychiatry and Behavioral Neurosciences, McMaster University (Canada), the ability of the gut microbiota to influence the function of the central nervous system has been proven and various probiotic cultures have been studied. In rats receiving a fermented milk drink fermented with *Lactobacillus reuteri* for 9 days, the activity of antihypertensive neurons in the muscular membrane of the intestine increased for 9 days, which indicates the direct effect of *Lactobacillus reuteri* on intestinal motility. In experiments on mice, it was proved that in animals whose diet was a drink containing *Bifidobacterium longum*, the excitability of neurons of the central nervous system decreased [23].

European experts have suggested that the use of psychobiotics requires a precise strategy to successfully combat anxiety and depressive behavior. They registered several strains of probiotics as psychobiotics, in particular *Lactobacillus plantarum PS128*. In animal researches, it was shown that administration of *Lactobacillus plantarum PS128 (PS128)* reduced anxiety and depressive behavior in mice, significantly reduced inflammation and corticosterone levels. It is also significant that PS128 administration significantly increased dopamine and serotonin levels in the prefrontal cortex and striatum compared to control mice (standard diet). They researched other strains as well, for example, administration of the *Lactobacillus helveticus NS8* strain reduced anxiety, depression and cognitive dysfunction, increased the levels of serotonin, norepinephrine and brain neurotrophic factor in the hippocampus. The use of *B. longum 1714* and *Lactobacillus rhamnosus JB-1* strains reduced stress, depression, and anxiety behavior. In particular, the consumption of JB-1 by animals led to region-dependent changes in the expression of the GABA receptor in the brain and decreased the level of corticosterone in the blood plasma [10].

Interesting studies were presented by specialists from Taiwan, for which mice were used that were raised in a sterile environment and, therefore, devoid of native bacteria. These animals had increased physiological responses to stress compared to controls. But the abnormal reactions were reversible due to probiotic-induced bacterial recolonization, predominantly by lactobacilli strains. This discovery once again confirmed the involvement of the microbiome in the development of the hypothalamus-pituitary-adrenal gland axis and the regulation of important physiological processes, including...
immunomodulation, obesity and energy balance, as well as the electrophysiological activity of the intestinal nervous system.

4. Conclusion
The conducted literary analysis confirmed the connection between the state of the intestinal microbiota and the emotional well-being of a person, the ability to withstand stressful situations.

A growing body of evidence shows that psychobiotics have a psychotropic effect on depression, anxiety and stress, especially bacteria of the Lactobacillus and Bifidobacterium families, replenishing the full composition of the gut microbiota, which is especially important during the pandemic and post-pandemic period. The widespread use of psychobiotic probiotics will help reduce the consumption of pharmacopoeial antidepressants, which have a number of dangerous side effects.

From all of the above, it can be concluded that it is advisable to use psychobiotics in dairy products in order to prevent mental disorders, which will have a beneficial effect on the living standards of the population.

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