Review

Psikiyatride Güncel Yaklaşımlar-Current Approaches in Psychiatry 2022; 14(4):469-476

DOI: 10.18863/pgy.1033628

# Psychobiotics and Elderly Health

## *Psikobiyotikler ve Yaşlı Sağlığı*

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**ABSTRACT**

While aging with physiological dimensions refers to the changes seen with chronological age, on the other hand, aging with psychological dimensions refers to the change of humans' capacity to adaptively. Such as learning, psychomotor, problem-solving and personality traits. With the improvement of life quality in recent years, the average life expectancy and therefore the incidence of neurodegenerative diseases among the elderly have also increased. Although the aging process is universal, progressive, gradual and unstoppable, human gut microbiota-targeted aging management is a new approach to health and anti-aging. Nutrition plays a big factor in the elderly population with providing adequate cognitive and physical functions and when taking the right nutrition it also reduces the risk of chronic diseases. When adding functional foods into the diet, it can play a significant role to reduce the risk of diet-related diseases. Such as probiotics and prebiotics. In recent years, a new subclass of probiotics called 'psychobiotics' has emerged. These psychobiotics are defined as probiotics that, when taken in appropriate amounts, it creates positive psychiatric effects in human psychopathology. Examination of this new class of probiotics provides a glimmer of hope for the effective management of neurodegenerative diseases and various psychiatric disorders, especially with increasing life expectancy. Also, recommending the use of probiotics in old age will contribute to the treatment of some health problems related to aging.

**Keywords:** Probiotics, elderly, diet, food, nutrition

**ÖZ**

Fizyolojik boyutuyla yaşlanma kronolojik yaşla birlikte görülen değişiklikleri ifade ederken, psikolojik boyutuyla yaşlanma; kronolojik yaş ilerledikçe görülen öğrenme, psikomotor aktivite,problem çözme ve kişilik özellikleri açısından insanın uyum kapasitesindeki değişimi ifade eder.Son yıllarda yaşam kalitesinin yükselmesiyle ortalama yaşam süresi, dolayısıyla yaşlılar arasında nörodejeneratif hastalıkların görülme sıklığı artmıştır. Yaşlanma süreci evrensel, ilerleyici, kademeli ve engellenemez olmasına rağmen, insan bağırsağı mikrobiyota hedefli yaşlanma yönetimi, sağlığı ve yaşlanmayı önlemede yeni bir yaklaşımdır. Yaşlı popülasyonda yeterli bilişsel ve fiziksel fonksiyonların sağlanması ve kronik hastalık riskinin azaltılması için beslenme büyük önem taşımaktadır. Sağlıklı ve dengeli beslenme adına, fonksiyonel besinlerin diyete sokularak, diyetle ilişkili hastalık riskinin azaltılması hedeflenmiştir. Bu fonksiyonel besinlerden bir kaçı da probiyotikler ve prebiyotiklerdir. Son yıllarda, 'psikobiyotikler' adı verilen yeni bir probiyotik alt sınıfı ortaya çıkmıştır. Bu psikobiyotikler ilk olarak uygun miktarlarda alındığında psikopatolojide olumlu psikiyatrik etkiler yaratan probiyotikler olarak tanımlanır. Bu yeni probiyotik sınıfının incelenmesi, özellikle yaşam süresinin uzamasıyla artan nörodejeneratif hastalıkların ve çeşitli psikiyatrik bozuklukların etkin yönetimi için umut ışığı oluşturmaktadır.

Yaşlılıkta probiyotik kullanımının tavsiye edilmesinin, yaşlılıkla ilgili bazı sağlık problemlerinin tedavisine katkı sağlayacağı unutulmamalıdır.

**Anahtar sözcükler:** Probiyotikler, yaşlı, diyet, besin, beslenme

## Introduction

The rate of the elderly population in the world is increasing every year. As the World Health Organization (WHO) accepts, it is accepted as early old age between the ages of 65-75, middle age between the ages of 75-85, and advanced old age after 85 years of age (WHO 2011). The elderly population in our country shows an increase at a higher rate than populations in other age groups. Although Turkey seems to have a relatively young population compared to countries with an elderly population structure, the absolute number of elderly people is quite high. Whereas the rate of population aged 65 and over was 9.5% in 2020, it is expected to increase to 11.0% in 2025. The rate of the elderly population exceeding 10% of the total population is an indicator of the aging of the population (TUİK 2021). Aging is characterized by a decrease in the functional efficiency of tissues and organs (Öksüzokyar et al. 2016). It is a situation which creates social challenges and is a public health priority. Today, the decrease in cognitive function associated with aging due to the increase in the elderly population has become an important public health problem. In recent years, with the increase in the quality of life, the average life expectancy and so the incidence of neurodegenerative diseases among the

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elderly have increased. Neurodegenerative diseases are defined as a group of diseases which occur with the progressive loss of nerve cells and cause loss of nervous system functions due to this loss (Prince et al. 2015). The worldwide dementia's prevalence is around 50 million. According to the 2015 World Alzheimer's Report, the probability of developing some form of dementia in an older adult rises from 2-4% at age 65 to 15% at age 80. As the population gets old, current estimates project more than 130 million cases by 2050 (Patterson 2018). According to Turkey's death and cause of death statistics, while the number of elderly people who lost their lives from Alzheimer's disease was 12 thousand 59 in 2015, it increased to 13 thousand 498 in 2019. Whereas the rate of elderly people who died from Alzheimer's disease was 4.3% in 2015, this rate increased in number in 2019, but no proportional change was determined (TUIK 2021).

New methods are being developed so as to investigate aging mechanisms and retard aging. The main purpose of these methods is to improve the life expectancy and quality of life of the aging population (Li et al. 2018). Preventing aging-related diseases, improving elderly functions, maintaining health status and prolonging healthy life span cause people to create new demands (Ling et al.2020). Pathophysiological changes in the human intestinal microbiota during aging may lead to immune aging and increased infection, this can precipitate aging-related neurodegenerative diseases, metabolic syndrome, susceptibility to infection, and other conditions that ultimately affect the quality of life of the aging population (Kim and Jazwinski 2018). Although the aging process is universal, progressive, gradual and unstoppable, human intestinal microbiota-targeted aging management is a new approach to health and anti-aging (Lee et al.2012).

Nutrition plays a very important role in the prevention, retardation and treatment of aging-related diseases. Nutrition is of great importance in order to provide adequate cognitive and physical functions and to reduce the risk of chronic diseases in the elderly population (Öğüt et al. 2008). In behalf of healthy and balanced nutrition, it is aimed to reduce the risk of diet-related diseases by introducing functional foods into the diet. A few of these functional foods are probiotics and prebiotics. In recent years, there has been increased interest in the relationship between intestinal microbiota and mental health (Sakin and Tanoğlu 2016).

Scientific evidence over the past decade has demonstrated the vital roles of the human intestinal microbiota in human health, general well-being, and brain function through the intestinal-brain axis. Beneficial microorganisms in the intestinal are defined as 'probiotics'. They are live bacteria that, when administered in adequate amounts, provide a health benefit to the host (Karatay 2019).Since 2013, a new subclass of probiotics named 'psychobiotics' has emerged. These psychobiotics are defined as probiotics that, when taken in appropriate amounts, create positive psychiatric effects in psychopathology (Luang-In et al.2020). A psychobiotic is a living organism that, when taken in sufficient quantity, positively affects the health of patients with psychiatric illness (Misra and Mohanty 2019).Examination of this new class of probiotics provides a glimmer of hope for the effective management of neurodegenerative diseases and various psychiatric disorders, especially with increasing life expectancy. This review study aims to examine the relationship of psychobiotics on microbiota-intestinal brain axis and neurodegenerative diseases in elderly nutrition.

## Intestinal Microbiota and Aging

The human gastrointestinal system (GI) has a surface area of approximately (250-400 m2) and in an average lifetime, approximately 60 tons of food pass through the human GI tract. The human body contains 1013 human cells and 1014 common microbiota, and the integrity of this super microorganism is crucial for health. In humans, the intestinal microbiota is dynamic over a lifetime (Mateos et al. 2018). The formation of the intestinal microbiota continues to be shaped by various factors related to age, which are determined by both internal host characteristics and external factors. Intestinal microbiota formation begins with the presence of microorganisms in the endometrial lining, fetal membranes, amniotic fluid, placenta, cord blood, meconium and urogenital regions, and the pattern of nutrients consumed by the mother in the prenatal period (Akçakaya and Tengiz 2020). Intestinal microbial population begins to become different from birth and changes rapidly, especially during the weaning period and before 3 years of age. Stable microbiota occurs in adults and changes with aging (Ling ve ark. 2020). The intestinal microbiota consists of various types of microorganisms such as bacteria, yeast and viruses. While microorganisms belonging to 6 bacterial classes, *Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria, Fusobacteria and Verrucomicrobia*, colonize in the intestinal microbiota of healthy people, *Bacteroidetes and Firmicutes* constitute approximately 90% of the intestinal microbiota (Kumari et al. 2020). Many studies show that age-related changes in intestinal microbiota composition include decreased species diversity, increased interindividual variation, higher levels of *Proteobacteria*, and lower levels of beneficial bacteria such as *Bifidobacterium*. It has been stated that these changes may be associated with increased susceptibility to pathogens (Claesson et al.2012).

Aging is an important intrinsic factor that affects the structure and activity of the intestinal microbiota. Lower fiber intake, long-term home care, use of non-steroidal anti-inflammatory drugs and antibiotics are preparer factors for these changes (O'Toole and Jeffery 2015).Age-related changes in the intestinal microbiota appear to affect the onset and progression of enteric and extra enteric diseases, including sarcopenia and physical frailty, neurodegenerative diseases, non-alcoholic fatty liver disease, *Clostridium difficile* infection, colorectal cancer, and coronary heart (DeJong et al.2020). Before the emergence of these age-related diseases, the bidirectional interactions between the intestinal and extra enteric tissue will first change. Therefore, elucidating the possible pathophysiological roles of the aged intestinal microbiota in these diseases may lead to the development of new anti aging interventions (Ling et al.2020).

**Table 1. Psychobiotics and their effects in common neurological conditions in the elderly**

| Elderly Common Neurological Conditions | Miroorganism | Psychobiotic Strains | Effect |
|---|---|---|---|
| Alzheimer Disease | *Lactobacillus* ve *Bifidobacterium* | *L. acidophilus* , *L.fermentum* , *B.lactis* , *B. Longum* | It has cured learning deficiencies. |
| | | *L. acidophilus,* *L. casei,* *B.bifidum* , *L.fermentum* | It positively affected cognitive function and some metabolic states. |
| Parkinson Disease | *Lactobacillus* ve *Bifidobacterium* | *L. acidophilus,* *B. bifidum* , *L. reuteri* , *L. fermentum* | It decreased the level of inflammation and peroxidation and increased the levels of the powerful antioxidant glutathione. |
| | | *L. acidophilus* , *B. infantis* | It has significantly improved the complaints of abdominal pain and bloating. |
| | | *L. casei shirota* *L. plantarum* | Improvement in feces consistency and intestinal function was noted. It has been reported to improve quality of life. |
| Insomnia | *Lactobacillus* | L. fermentum , *L. brevis* , *L. helveticus* | Promising effect in the treatment of insomnia has been noted. |
| | | L. fermentum | It has been found to significantly reduce sleep latency and increase sleep duration. |
| | | *L. brevis* *L. helveticus* | It has been stated that it can regulate circadian movement and sleep rhythms. It has been noted to significantly improve sleep efficiency. |

## Aging in the Intestinal-Brain Relationship

The interplay of the gastrointestinal tract on brain function has been known since the 19th century. It is currently believed that the microbiota-intestinal-brain axis has an association on brain function of the GI tract and forms a bidirectional homeostatic communication pathway (Pinto-Sanchez et al. 2017). The intestinal-brain axis explains the functional relationship between intestinal and brain, which is controlled by intestinal microbiota, intestinal hormones, enteric nervous system, central nervous system, and nutrients. These components interact bidirectional through neurohumoral pathways and direct connections between the vagus nerve and the brain stem, and between the spinal nerves and the spinal cord (Cryan et al.2019). Understanding the ability of the intestinal microbiota to communicate bidirectional with the brain in the modulation of human health is at the forefront of research examining the microbiome-intestinal-brain axis. It is now accepted that the intestinal microbiota is a key modulator of brain and behavior (Ma et al. 2019). In the elderly, conditions such as Alzheimer's disease (AD) and Parkinson's disease (PD) are associated with intestinal microbiota changes (Sun et al. 2019). Although the precise mechanism of the intestinal microbiota-brain axis has not been fully understood and clarified yet, evidence from animal and human studies, micro-ecological regulators of the intestinal microbiota, commonly probiotics, prebiotics, synbiotics, postbiotics, and psychobiotics become increasingly important in preventing and/or reversing age-related imbalances in the intestinal microbiota and providing healthy anti-aging benefits (Mörkl et al. 2020). Psychobiotics can play an important role in brain behavior and cognitive development by producing hormones, immune factors, and metabolites. This also shows that it can alter the intestinal microbiota and heal brain diseases (Ling et al. 2020).

## Psychobiotics

Dinan et al. (2013) defined the term "psychobiotics" as a new class of probiotics, suggesting potential applications in the treatment of psychiatric diseases. Psychobiotics, when taken

in adequate amounts, should provide health benefit in patients suffering from a psychiatric illness. The microbiota-gut-brain axis, called "psychobiota", plays an important role in host physiology by regulating neuro inflammation and affecting as neuro endocrines. The psychobiotics involved here; It has been stated that they can regulate neurotransmitters and proteins, including gamma-aminobutyric acid (GABA), serotonin, glutamate and brain-derived neurotrophic factor (BDNF), which play an important role in neural excitatory-inhibitory balance, mood, cognitive functions, learning and control (Lu et al. 2008).

It has been reported that some intestinal microorganisms such as *Lactobacillus acidophilus, Lactobacillus casei, Bifidobacterium infantis, Bifidobacterium longum, Bifidobacterium bifidum, Escherichia, Bacillus, Saccharomyces, Candida, Streptococcus and Enterococcus*can produce serotonin, gamma-aminobituric acid and *Lactobacillus plantarum, Lactobacillus odontolyticus* acetylcholine, and these microorganisms are accepted as psychobiotics in studies (Roshchina 2016). In addition, it has been stated that psychobiotics can regulate the expression of neurochemical receptors such as endocannabinoid receptors and may cause psychotropic effects (antidepressant and anxiolytic) by acting on the putative brain-intestinal axis (Barrett et al. 2012). It has been stated that giving a probiotic combination *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175 (Probio'Stick®) in oral way for one month treats depression, anger, anxiety and lowers stress hormone levels (Messaoudi et al. 2011). Psychobiotics enhances the intestinal mucosal barrier by reducing age-related inflammation, immune aging, oxidative stress and intestinal dysbiosis and has positive effects on health with increased neurotransmitter production (Ling et al. 2020).

## Psychobiotics in Mental Health

In addition to the physical difficulties experienced with advancing age, psychological, social and economic difficulties also cause the elderly to experience depression problems. In other words, the physical problems of the elderly and the fact that these problems become chronic cause the elderly individuals to experience more dependent and depressive problems (Göktaş ve Özkan 2006).In the elderly, increased morbidity, mortality, hospitalization, and loss of functional status related to common mental disorders happen. The prevalence of depression and anxiety in the elderly is very common, and about half of the elderly individuals report significant depressive problems and anxiety symptoms (Parkar 2015).When mental problems in elderly individuals are detected in the early period, the affecting factors are determined and treated appropriately, the quality of life of the elderly increases and contributes to a healthier life of the individual (Özden et al. 2010).Good mental health encourages good conscious functions and psychological state.Recent studies have shown that psychobiotics have psychotropic effects on depression, anxiety and stress (Dinan et al. 2013). In animal studies, several probiotic strains have been considered psychobiotic. *L. plantarum* (PS128) has reduced mice's depression-like behavior and anxiety. The PS128 strain significantly has reduced inflammation and corticosterone levels.In particular, administration of the PS12 strain significantly increased dopamine and serotonin levels in the prefrontal cortex and striatum compared to control mice.In particular, administration of the PS12 strain has significantly increased dopamine and serotonin levels in the prefrontal cortex and striatum compared to control mice (Liu et al. 2016). Administration of a single strain *Lactobacillus helveticus* NS8 has reduced anxiety, depression, and cognitive dysfunction. In addition, *L. helveticus* NS8 has increased serotonin, norepinephrine, and brain-derived neurotrophic factor (BDNF) levels in the hippocampus (Liang et al. 2015). Healthy volunteers administered *Bifidobacterium longum* 1714 for 4 weeks have exhibited less stress and improved memory (Allen et al. 2016).In a randomized study of petrochemical workers, probiotic yogurt (*Lactobacillus acidophilus LA5 and Bifidobacterium lactis BB12*) and probiotic capsules (*Lactobacillus casei, L. acidophilus, , Lactobacillus rhamnosus, Lactobacillus bulgaricus, Bifidobacterium lactis BB12*) and probiotic capsules were assayed on workers.As a result; When individuals using both probiotic yogurt and probiotic capsules were evaluated with the stress scale and general health questionnaire, positive data were obtained regarding depression anxiety (Messaoudi et al. 2011).

## Psychobiotics in Neurodegenerative Disorders

Neurodegenerative changes are one of the main risk factors for many diseases, especially aging.In addition, age-related changes in the brain's structure, connectivity, and intrinsic metabolic pathways are thought to contribute to increased susceptibility to neurodegenerative diseases such as various types of dementia, Alzheimer's disease, and Parkinson's (Mattson and Arumugam 2018).The relationship between psychobiotics and neurodegenerative disorders and insomnia is discussed below.

### Alzheimer's Disease (AD)

Considered a progressive multifaceted neurodegenerative disorder, Alzheimer's disease is the leading cause of dementia in late adulthood. Pathologically, it is characterized by intracellular neurofibrillary tangles and extracellular amyloidal protein deposits which contribute to senile plaques (Kumar and Singh 2015).AD is characterized by progressive memory loss, cognitive impairment, and severe behavioral abnormalities. The main pathological features of AD are extracellular aggregation of amyloid β peptide (Aβ), which forms senile plaques (SP), and accumulation of intracellular neurofibrillary tangles (NFTs). Although there are extensive studies on the pathogenesis of AD, the exact mechanism of AD is still unknown due to its complex pathophysiological features (Wan et al.2020). Various mechanisms have been proposed to explain the pathogenesis of the disease, including the amyloid β (Aβ) cascade, hyperphosphory Tau protein, oxidative stress, central cholinergic neurotransmitter deficiency, inflammation, and toxic metal ions (Liu et al.2017).

The effects of multiple microbial strains, such as *Lactobacillus and Bifidobacterium* strains, were investigated in an animal model of Alzheimer's (mice). After regular consumption of these probiotic strains, the total numbers of *Lactobacillus and Bifidobacterium* strains increased and *Coliform* strain

decreased in the feces of mice. Furthermore, supplementation of probiotic microorganisms improved learning deficits in mice with Alzheimer's disease compared to control mice (Athari et al.2018). One randomized, double-blind, and controlled clinical trial found that consumption of fermented milk with probiotics (*Lactobacillus acidophilus, Lactobacillus casei, Bifidobacterium bifidum, and Lactobacillus fermentum*) improved the health of mice with Alzheimer's disease (Akbari et al. 2016). Postbiotics such as acetate, propionate and butyrate, which are formed by the synbiotic effect of psychobiotics with prebiotics, reduce neuro inflammation and amyloid formation by providing homeostasis, composition and functionality of the intestinal microbiota ecosystem. In addition to their effects, including neuro immune and control and regulation of the brain-intestinal axis, psychobiotics also play an active role in emotional disorders and neurological disorders with their key role in the immune system (Cohen Kadosh et al. 2021).In a study on rats, as a result of *B. Infantis* psychobiotic administration, the concentrations of tryptophan, a precursor of plasma serotonin, increased, resulting in improvement in immunological and neuro-endocrine functions (Clarke et al. 2013).

### Parkinson Disease

Parkinson disease (PD) is a neurodegenerative disease associated with motor and non-motor symptoms. The prevalence of PH increases with age (Elfil et al. 2020). Parkinson disease is pathologically characterized by degeneration of the pars compacta of the substantia nigra in the midbrain and diffuse neuro inflammation. Neurologically, Parkinson patients exhibit a range of motor-related disorders, including brady kinesia, resting tremors, muscle stiffness, and postural disturbances. Before the development of motor symptoms, Parkinson patients often report prodromal non-motor symptoms suggestive of gastrointestinal dysfunction, such as depression, sleep disturbances, and constipation (Poirier et al.2016).These findings also suggest possible uses of food-based therapies for Ph, including probiotics.

In view of the gastrointestinal disturbances reported in Parkinson disease, it is possible that the microbiota-intestinal-brain axis is affected in this neurodegenerative disease. It has been stated that probiotic bacteria *Prevotella* species decreased in fences samples taken from Parkinson's patients (Scheperjans et al. 2015). Considering the *Prevotella* species, it produces mucin that serve to increase the integrity of the intestinal barrier, decreased numbers of this bacterial strain may lead to increased intestinal permeability and subsequent bacterial translocation in Parkinson patients. An increase was detected in *Akkermansia muciniphilia* microorganism in Parkinson disease (Bedarf et al. 2017). In a randomized, double-blind, placebo-controlled clinical trial, subjects with PH were administered a probiotic supplement containing *L. acidophilus, B. bifidum, Lactobacillusreuteri, and L. Fermentum* for 12 weeks. The group that consumed the probiotic scored lower on the Unified Parkinson Disease Rating Scale (BPHRS) compared to the placebo group. In addition, probiotic consumption not only significantly reduced the levels of hs-CRP, an indicator of inflammation, and malondialdehyde, a lipid peroxidation product, but also increased the levels of the potent antioxidant glutathione. In particular, consumption of probiotics significantly improved insulin function compared to placebo (Tamtaji et al. 2019). In PD patients, 8×109 CFU/day probiotic supplementation for 12 weeks significantly improved IL-1, IL-8, TNF-Î±, TGF-Î² and PPAR-Î³ gene expression (Borzabadi et al. 2018). Constipation is an important complication in Parkinson disease. Treatment with a combination of L. acidophilus and *B. infantis* probiotics in the elderly with PH with a mean age of 76.05 years resulted in significant improvement in complaints of abdominal pain and bloating (Georgescu et al.2016). After 5 weeks of application of fermented milk containing *L. casei shirota* to patients with PH, improvement in stool consistency and intestinal function was determined (Cassani et al.2011). *Lactobacillus plantarum* (PS128) is a specific probiotic known as psychobiotic that can alleviate motor defects and inhibit neurodegenerative processes in model mice with Parkinson disease. In a pilot study, patients aged 52-72 years with Parkinson disease have been given continuous anti-Parkinson drugs and PS128 supplementation for 12 weeks. It has shown to improve the quality of life of PD patients (Lu et al.2021).

Most clinical studies of probiotics in Parkinson patients have focused on gastrointestinal function. It has been found that oxidative stress and inflammations increase in the severity of PH. Studies have shown promising effects of psychobiotics by reducing oxidative stress and inflammation in patients with PD (Taylor et al.2013).

## Insomnia

Insomnia is a common disorder characterized by difficulty falling asleep and staying asleep or waking up too early. About 20-30% of adults have chronic insomnia problems (lasting at least 1 month), which is the most common sleep disorder in the general population (Morin ve Benca2012).

Sleep patterns can change with aging. In particular, babies sleep between 10 and 14 hours a day, while the recommended sleep time for older adults is 7-8 hours a day. Many older adults experience dissatisfaction with the quantity and quality of sleep even when they have adequate sleep opportunities and when accompanied by daytime disturbances for a period of time, they may meet the criteria for sleep disturbance (Patel et al. 2018). Compared with young adults, the prevalence of insomnia is higher in middle and older adults. Up to 50% of older adults report symptoms of insomnia, which does not mean that insomnia is a normal part of aging. Older adults have more difficulty maintaining sleep than younger adults, and this causes a decrease in total sleep time and sleep efficiency. Life events such as retirement, hospitalizations, and new-onset illness can precipitate situational insomnia (Brewster et al. 2018). Insomnia also increases the risk of chronic diseases (for example, hypertension, diabetes, stroke, and coronary artery disease) and health care costs (Parekh et al. 2018).

Even if different medications are used to treat insomnia, most of them are not recommended for long-term use because of their

potential side effects. Hence, there is a need to seek alternative ways to treat insomnia. It has been reported that insomnia and gastrointestinal dysfunction affect each other, and that there is a dynamic bidirectional relationship between sleep and gastrointestinal health (Orr and Chen 2005).

In recent years, it has been shown that gut microorganisms interact indirectly with the host's central nervous system (CNS) through the intestinal-brain axis, a bidirectional communication system that combines neural, hormonal, and immunological signals between the intestinal and the intestinals. In addition, some probiotics identified as "psychobiotics" (*Lactobacillus fermentum PS150 TM, L. brevis SBC8803, L. helveticus CM4*) may provide health benefits to hosts with psychiatric or neurological diseases, with promising treatment for insomnia (Dinan and Cryan 2017). A study using a pentobarbital-derived sleep rat model investigated the effects of a psychobiotic strain (*Lactobacillus fermentum PS150 TM*) on sleep improvement. Oral using of PS150 TM was found to significantly reduce sleep latency and increase sleep duration of mice. The obtained results suggested the sleep-improving effects of the PS150 TM strain (Lin et al. 2019). In another study, mice were administered *L. brevis* SBC8803 (SBL88™) capsule/day for 10 days. As a result, it has been concluded that psychobiotics can regulate circadian movement and sleep rhythms, which may benefit individuals with impaired circadian rhythms due to stress or aging (Miyazaki et al. 2014). Healthy elderly subjects focusing on sleep were administered fermented milk containing *L. helveticus* CM4. Fermented milk intake has been found to significantly improve sleep efficiency and waking episodes (Yamamura et al. 2009).

## Conclusion

In recent years, studies on the effects of psychobiotics on neurodegenerative disorders tend to increase. By modulating inflammation, HPA (hypothalamic-pituitary-adrenal axis) and neurotransmitters, psychobiotics with positive health effects can affect central nervous system functions, including mood, anxiety, depression and stress response. Moreover, psychobiotic treatments have shown promising effects on neurodegenerative and neurodevelopmental disorders by altering the fecal microbiota, inflammation, oxidative status and insulin function. Probiotics may play a crucial role in regulating α-synuclein aggregation in enteroendocrine cells, production of microbial metabolites, and activation of the vagus nerve in neurodegenerative and neurodevelopmental disorders. For this reason, psychobiotic treatments may be a promising strategy in improving quality of life for older individuals suffering from neurodegenerative and neurodevelopmental disorders. In order for psychobiotics to be accepted as an alternative treatment in neurodegenerative disorders, further studies are needed in this area to determine the effectiveness and mechanisms of psychobiotics.

Diet and nutritional status are the most critical modifiable factors that regulate the intestinal microbiota at different time points and in various health conditions throughout the lifespan. Therefore, advances in our understanding of the mechanisms underlying the effects of macro- and micronutrients on the brain and microbiota-intestinal-brain axis will facilitate the development of nutritional interventions aimed at optimizing brain function and preventing or treating neurodegenerative disorders and other age-related disorders. Considering all these, improving the intestinal ecosystem should be an important goal in the development of strategies to improve health, especially in the elderly.

**Authors Contributions:** *The authors attest that they have made an important scientific contribution to the study and has assisted with the drafting or revising of the manuscript.*

**Peer-review:** *Externally peer-reviewed.*

**Conflict of Interest:** *No conflict of interest was declared by the authors.*

**Financial Disclosure:** *The authors declared that this study has received no financial support.*

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