JOURNAL OF EDUCATION, HEALTH AND SPORT
eISSN 2391-8306 · Open Access · Peer-reviewed
apcz.umk.pl/JEHS·Nicolaus Copernicus University in Toruń



SZCZĘSNY, Mikołaj, SZAREK, Rafał, KATRA, Małgorzata, STRZAŁKOWSKA, Bogumiła, SĘDEK, Łukasz, CZUBA, Zenon. Effects of probiotics in neurodegenerative disorders, *Journal of Education, Health and Sport*, 2026;95:73840. https://doi.org/10.12775/JEHS.2026.95.74001

ARTICLE TIMELINE
Received: 30/08/2026 Revised: 3/09/2026
Accepted: 1/09/2026 Published: 16/11/2026

INDEXING & EVALUATION
MEiN points: 40 Unique ID: 246387
Disciplines: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).

The journal has been awarded 40 points in the parametric evaluation by the Polish Ministry of Higher Education and Science (Annex to the announcement of 05.01.2024, No. 32318). Unique Journal Identifier: 201159. Scientific disciplines: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).

Punkty Ministerialne z 2019 – aktualny rok 40 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu). © The Authors 2026.

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SZCZĘSNY, Mikołaj, SZAREK, Rafał, KATRA, Małgorzata, STRZAŁKOWSKA, Bogumiła, SĘDEK, Łukasz, CZUBA, Zenon. Effects of probiotics in neurodegenerative disorders

1. Introduction

Probiotics are live microbes residing in the intestine, providing health benefits to the host. Probiotics may influence the nervous system through the so called gut-brain axis which is an anatomical and functional network linking enteric and central nervous systems. These interactions regulate important homeostatic and physiological functions, including food intake, regulation of immunological system and sleep [1].

Considering the human and microbiota coevolution, one would expect a significant role played by the microbiome in the development and functioning of all body systems. For example, the function of the nervous system can potentially be affected by changes in the composition of the human microbiota or introduction of probiotics and prebiotics. Probiotics are live microorganisms, mainly bacteria, that have health benefits when consumed or applied to the body, while prebiotics are food compounds that promote growth and activity of microbiota.

New generation of probiotics [2] and numerous new advanced studies on the influence of probiotics on neurodegenerative disorders hold significant promise on their usage in

neurodegenerative disorders treatment in the future. A great advantage of such approach would be low cost and broad availability.

In this review, we discuss the effects of probiotics usage in Alzheimer Disease (AD), Parkinson Disease (PD), Multiple Sclerosis (MS) and Amyotrophic Lateral Sclerosis (ALS).

2. Alzheimer Disease

AD is a major cause of dementia among the elderly . In 2021, only in the USA, about 6.2 million people suffered from AD. The occurrence of AD increases with age: approximately 5-8% and 25-50% of total population over 65 and over 85 is affected, respectively [3] . Due to the aging of developed countries population, AD will be a huge social problem in the near future, with predicted 152 million patients by 2050. Estimated worldwide cost of dementia will rise to US$2 trillion by 2030 [4] .

2.1 Pathogenesis

AD is caused by formation and deposition of amyloid β (Aβ) plaques in different regions of the brain. Aβ plaques are recognized as foreign material by the immune system, stimulating the microglia to produce and release pro-inflammatory cytokines which eventually lead to neurodegeneration. These pro-inflammatory cytokines can impair the function of dendritic spines of the cholinergic system that is involved in the process of cognition. Damages within these structures are considered causative of various dementias, including AD [3] .

2.2 AD and gut microbiome disruption

In normal conditions, the gut microbiota is responsible for the production of neuroprotective molecules such as fatty acids and antioxidants. Short-chain fatty acids (SCFAs) derived from the intestinal microflora strongly inhibit amyloid aggregation *in vitro* [5] and the antioxidants prevent reactive oxygen species (ROS) from damaging the neurons. Disruption in gut microbiota can weaken the protective effect and promote neuroinflammation followed by the production of pro-inflammatory cytokines and the loss of immune regulatory function [6] .

Synthesis and release of neurotransmitters from bacteria has also been reported: *Lactobacillus* and *Bifidobacterium* spp. can produce γ-aminobutyric acid (GABA); *Escherichia*, *Bacillus* and *Saccharomyces* spp. can produce noradrenaline; *Candida*, *Streptococcus*, *Escherichia*, and *Enterococcus* spp. can produce serotonin; *Bacillus* can produce

dopamine; and *Lactobacillus* can produce acetylcholine. These neurotransmitters can cross the mucosal layer of the intestines, however, they are incapable of crossing the blood-brain barrier. There is a possibility, that these neurotransmitters act indirectly on the nervous system [8] . Furthermore, gut microbes like *Bifidobacteria* and *Lactobacilli* convert nitrite and nitrate to nitric oxide (NO). NO is also secreted on activation of the N-methyl-D-aspartate (NMDA) receptors by glutamate and acts as a neurotransmitter of noradrenergic, noncholinergic and enteric nervous system. Alteration of the activity of these bacteria can lead to overproduction of NO and axonal degeneration [9]. *Enterobacter* spp. and some fungi species may produce amyloid fibers or peptides that are capable of forming seeds for aggregation of amyloid in the central nervous system (CNS) that can accelerate neurodegeneration and progression of AD [10] .

The clinical evidence suggest that the composition of the gut microbiota changes during aging process which specifically manifests with the increase of proteobacteria and reduction of probiotics such as *Bifidobacteria* or neuroprotective molecules, such as short-chain fatty acids (SCFAs).

2.3 Probiotics and AD

2.3.1 Animal Model Studies

Probiotics, due to their anti-inflammatory and antioxidative effects, dragged attention as a potentially useful tool to suppress neuroinflammation and thus slowing down the progression of AD. *Lactobacillus* and *Bifidobacterium* are the two most widely studied classes of gut microbes, also in the context of their usefulness in AD treatment. In a study conducted on an animal model, mice in the early stage of AD were given SLAB51 probiotic specimen which resulted in lower plasma concentration of inflammatory cytokines and reduced accumulation of Aβ aggregates [12] .

2.3.2 Clinical Studies in Humans

Randomized double-blind, placebo-controlled trial conducted on humans showed that after 16 weeks of probiotic *Bifidobacterium breve* A1 strain consumption, improvement in domain scores of immediate, visuospatial/constructional, and delayed memory types tests was achieved in adult patients suffering from mild cognitive impairment (MCI) [13]. Another study conducted among patients with AD, showed that probiotic and selenium co-supplementation resulted in significant increase in total antioxidant capacity, which is crucial in preventing neurodegeneration caused by ROS. Moreover, significant reduction of C-reactive protein

(CRP) levels were observed which indicated suppression of inflammation [14]. Other study revealed that sustained probiotics consumption for 24 weeks suppressed brain atrophy progression. In addition, improvement of results in some subscales was observed in the Alzheimer Disease Assessment Scale and mini-mental state examination (MMSE) test [15]. Another study revealed that probiotic-fermented milk supplementation in AD patients resulted in relative decrease in several cytokine markers of inflammation, as well as oxidative stress markers. In addition, participants of the study exhibited improvement in executive/language functions, visual-spatial/abstraction abilities and memory [16].

In an open-label, single-arm study, supplementation of *B. breve* strain A1 in adults with MCI resulted in increased score of MMSE, Profile Of Mood State Second Edition (POMS 2) and Gastrointestinal Symptom Rating Scale (GSRS), showing improved cognitive decline of MCI patients [17]. A study conducted by the same group revealed a significant improvement of immediate memory in MCI adults after *B. breve* strain A1 supplementation [18] .

In a randomized, double-blind, placebo-controlled trial supplementation of *Bifidobacterium longum* BB68S in patients with neurological disorders changed the composition of gut microbiota. The relative abundance of bacteria (i.e., *Bifidobacterium*, *Dorea* and *Lachnospira* spp.) that play a role in inhibiting the neurodegenerative diseases progression increased. *Bifidobacterium* plays beneficial roles in the body, including improvement of the immune function and regulation of the gut microbiota. *Dorea*, which produce acetate and lactate that serve as substrates for butyrate production, are positively related to the immune response and negatively related to depression. Butyrate treatment in animal model results in a considerable reduction in aberrant Paneth cells, which are specialized intestinal epithelial cells that govern host-bacterial interactions at the cellular level. *Lachnospira* is negatively related to anxiety, depression, Parkinson's disease, and psychiatric disorders. *Bifidobacterium longum* BB68S supplementation also reduced the relative abundance of bacteria associated with cognition impairment, i.e., *Tyzzerella* spp., *Bilophila* spp., and *Collinsella* spp. *Bilophila* is an obligatory anaerobic pathobiont that is harmful to the hippocampus and cognitive behaviors. Hippocampal IL-1β levels have shown a positive correlation with the relative abundance of *Tyzzerella*, indicating that its increase may lead to neuroinflammation to a certain extent. *Collinsella* is an inflammation-related bacterium. Many studies have reported the association between the increased abundance of *Collinsella* and inflammatory diseases [19,20]. Increase in the relative abundance of bacteria associated with inhibition of neurodegenerative diseases progression and decrease in the relative abundance of cognition impairment-related bacteria

resulted in significant improvement of cognitive functions, especially immediate memory, attention and delayed memory domains [21].

Table 1. The effect of selected probiotics on Alzheimer Disease in human and animal models

Type of probiotic	Observed effect
SLAB51	Attenuated neuroinflammation and a deceleration of AD progression
Bifidobacterium breve A1	Improvement in cognitive test scores among individuals with MCI and AD.
Probiotics combined with selenium supplementation	Augmentation of endogenous antioxidant system and reduction of inflammatory biomarkers in AD patients.
Bifidobacterium longum BB68S	Improvement in cognitive domains, particularly immediate memory and attention, in patients with neurological disorders.

3. Sclerosis Multiplex

Multiple sclerosis (MS) is an auto-immune, demyelinating and chronic disease of the central nervous system. It is highly heterogeneous, with clinical patterns characteristic for each individual patient and no single pathognomonic marker is known [22.

Based on pre-clinical animal models, a new conception of pro-inflammatory gut microbiota acting as a trigger of autoimmunity has recently arisen, and presumable relationship of dysbiosis demonstrated in MS with the disease development has been proposed [23].

Alterations in gut microbiota, gut-derived products, intestinal permeability and enteric nervous system functions play a role in pathophysiology of MS [24]. Probiotics, by changing the composition of the intestinal microbiota, can affect all these alterations.

3.1 Pathogenesis

The BBB plays a key role in protection of CNS and maintaining its homeostasis. In MS, the BBB is damaged by the secretion of inflammatory cytokines, soluble constituents, reactive oxygen species and matrix metalloproteinases. Breakdown of the BBB can be a herald of MS pathophysiology. Immune mediated dysregulation of the BBB allows for migration of activated inflammatory cells like cytotoxic T cells into the CNS, resulting in demyelination, axonal loss and tissue damage [25]. The activated cytotoxic T cells damage the myelin sheath by activation of microglia and macrophages. When the myelin gets continuously destroyed, nerves lose their ability of proper signal transmission, causing neurological problems [22].

3.2 MS and gut microbiome disruption

A comparison between individuals with MS and healthy controls showed impairment in microbiota composition in MS patients, which may suggest its causative role in development of the disease. This postulate is supported by dysbiosis found in many patients suffering from relapsing remitting multiple sclerosis (RRMS); increased levels of *Monoplane*, *Pseudomonas*, *Blautia*, *Haemophilus* or *Dorea* genera and decreased levels of *Parabacteroides*, *Adlercreutzia* and *Prevotella* were found as compared to healthy controls. Furthermore, a decrease in amount of *Bacteroides*, *Prevotella*, *Anaerostipes*, *Faecalibacterium* and *Clostridia* XIVa, as well as an increase in the proportions of *Actinobacteria*, *Bifdobacterium*, *Akkermansia muciniphila*, *Mycoplasma*, *Acinetobacter calcoaceticus* were observed in the gut microbiota of MS patients [26].

These intestinal microbiota composition changes could alter the immune system function by changing the cytokine production profile and synthesis or activity of immune system cells, promoting both local and systemic immune responses. Thus, neuroinflammatory processes in CNS and the progression of changes characteristic for MS could be induced via gut-brain axis [23].

3.3 Probiotics and MS

3.3.1 Effects on Peripheral Immune Response

Lactobacillus and *Bifidobacterium* are the two most studied genera of gut microbes in context of their usefulness in MS treatment. Many studies showed that probiotics could have a beneficial effect on many parameters affecting the development and the course of MS. For example administration of VSL3 probiotic, which is a mixture of *Lactobacillus* and *Bifidobacterium* strains, was associated with an anti-inflammatory peripheral immune response characterized by decreased frequency of intermediate monocytes and decreased level of CD80

on classical monocytes. Classical and intermediate monocytes produce effector molecules such as cytokines, myeloperoxidase, superoxide, and initiate inflammation processes in MS [27]. Administration of VSL3 was also associated with decreased level of HLA-DR on myeloid-derived dendritic cells in MS subjects [28].

3.3.2 Changes in Cytokine Gene Expression and Neurotrophins

In another randomized, double-blind, placebo-controlled study conducted among patients with MS, parameters such as serum levels of brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF) and IL-6 were measured, together with mental health assessment for 6 months of probiotic supplementation. The improvement as compared to the placebo group was noticed in general health questionnaire, Beck Depression Inventory-II, Fatigue Severity Scale and Pain Rating Index. Moreover, probiotic supplementation resulted in a significant increase in BDNF and a significant reduction in the IL-6 levels, with no significant difference in the NGF serum level [29].

Other study revealed that *Lactobacillus* and *Bifidobacterium* supplementation caused down-regulation of gene expression of pro-inflammatory interleukin-8 and tumor necrosis factor-alpha (TNF-α) in peripheral blood mononuclear cells of patients with MS [30]. In another study, five subjects with newly diagnosed, treatment-naive RRMS, were given 2500 ova of the non-pathogenic helminth *Trichuris suis* (TSO) every 2 weeks for 3 months. During the study, an increased level of IL-4 and IL-10 was detected, however the mean number of brain lesions detected by MR dropped from 6.6 at baseline to 2.0 at the end of *Trichuris suis* ova administration, and rose again to 5.8 two months after TSO discontinuation [31]. Maizels et al. suggested that the long co-evolution of helminths with humans made these organisms master regulators of host immune responses, and due to hygiene hypothesis, lower incidence of intestinal colonization by helminths in developed countries, may be one of the reasons for higher frequency of MS in these populations [32].

Table 2. The effect of selected probiotics on Multiple Sclerosis in human and animal models.

Type of probiotic	Observed effect
VSL3	Decreased inflammation markers and improvement of peripheral immune balance .

Mixed *Lactobacillus* and *Bifidobacterium* strains	Reduced inflammatory gene expression, supporting the role of probiotics in modulating systemic inflammation.

4. Amyotrophic Lateral Syndrome

Amyotrophic Lateral Sclerosis (ALS), is a progressive neurodegenerative disease affecting motor neurons, which are responsible for muscle movement control [33]. ALS is a complex disease with a multifactorial etiology, involving genetic, environmental, and age-related factors [34]. Most patients die from respiratory muscle failure and the average survival is 2 to 5 years [33,35]. Historically, only one drug, riluzole was known and used to slow down the progression of the disease, however, its effectiveness was limited, extending ALS patients survival by only a few months [33]. Recently, several alternatives have been invented, such as AMX0035 (combination of sodium phenylbutyrate and taurursodiol), edaravone, and tofersen in 2023 which have already been approved by the FDA [36].

4.1 Pathogenesis

In 90% of cases, ALS is sporadic while in 10% of cases, it has familial occurrence [37]. One of the best-known genetic mutations associated with ALS is a mutation in the Cu/Zn superoxide dismutase (SOD1) gene, which is responsible for encoding an antioxidant enzyme. This mutation leads to the acquisition of toxic functions but the pathophysiology remains unknown [38,39]. Other examples of mutations that can lead to ALS include: TAR DNA-binding protein (TARDBP), fused in sarcoma (FUS), valosin-containing protein (VCP) and many others [34,37]. On top of the genetic factors, environmental factors such as exposure to toxins and traumatic brain injury have also been implicated in the development of ALS [34]. The mechanisms underlying the selective degeneration of motor neurons in ALS are complex and not fully understood, but several molecular pathways have been identified, including oxidative stress, excitotoxicity, and protein misfolding [40].

4.2 Microbiome

High-throughput sequencing allows assessment of gut microbiota diversity. In a study by Fang et al., significant differences were found between the microbiota of healthy individuals and ALS patients. *Faecalibacterium*, *Anaerostipes*, and *Lachnospira* were more abundant in ALS, while harmful *Dorea* spp. increased and beneficial *Oscillibacter* spp. and *Anaerostipes* spp. decreased. ALS patients also showed a reduced *Firmicutes/Bacteroidetes* ratio at the genus level, suggesting that gut microbiota imbalance may be linked to ALS pathogenesis [43].

In a study of five ALS patients, gut infections, inflammation markers, and microbiome composition were analyzed. Compared to healthy controls, all ALS patients showed reduced gut microbiome diversity. Three of five patients had elevated or borderline levels of inflammatory markers such as fecal secretory IgA, calprotectin, and eosinophilic protein X. The dominant bacterial phyla were *Firmicutes* and *Bacteroidetes*; patients with low *Firmicutes/Bacteroidetes* ratios also had reduced *Ruminococcus* spp. Overall, intestinal inflammation was present in most individuals [44].

4.3 Probiotics and metabolites in ALS models

4.3.1 Effect of butyric acid and bacterial supplementation on the course of ALS

The studies performed on mice subjects also showed that gut dysfunction and dysbiosis might be actively contributing to the pathogenesis of ALS. In a study by Zhang et al., G93A transgenic mice were used as a model of human ALS. G93A ALS mice carry the human SOD1 mutant gene, introducing a Gly-93 to Ala (G93A) swap which results in the restoration of neurons and muscles occurring in ALS patients [45]. In addition, these mice have aberrant gut microbiota and disrupted cell-cell tight junctions that are depleted of ZO-1 and adherens junction protein E-cadherin [46]. The G93A mice were subsequently fed with a natural bacterial product, 2% butyrate dissolved in drinking water. As a result of butyrate intake, intestinal microbial equilibrium was restored, gut integrity was enhanced, and life span was prolonged, as compared to the control mice group. Butyrate treatment in ALS animals resulted in a considerable reduction in aberrant Paneth cells, which are specialized intestinal epithelial cells that govern host-bacterial interactions at the cellular level [47].

4.3.2 The role of *Akkermansia muciniphila* and other strains

In a study by Blacher et al., ALS-prone SOD1 transgenic mice were used to examine the link between commensal bacteria and ALS symptoms. Eleven bacterial species were identified; *Akkermansia muciniphila* (AM) reduced ALS symptoms, whereas *Ruminococcus torques* and *Parabacteroides distasonis* aggravated them. Systemic nicotinamide

supplementation improved motor symptoms and altered spinal cord gene expression in SOD1 mice. AM-treated mice also accumulated AM-associated nicotinamide in the central nervous system. The study demonstrated pre-symptomatic dysbiosis influenced by vivarium conditions and altered metabolite profiles, with more severe symptoms observed in germ-free or antibiotic-treated mice [48].

Table 3. Effects of selected probiotics, prebiotics and metabolites on ALS models

Probiotic / prebiotic	Function	Observed effect
Butyrate (butyric acid)	Restores gut microbiota balance and strengthens intestinal barrier.	Extended lifespan in ALS G93A mice and improved gut integrity.
Akkermansia muciniphila	Reduces ALS symptoms, produces nicotinamide.	Decreased disease symptoms and improved motor functions in SOD1 mice.
Nicotinamide	Influences gene expression and motor functions.	Improved symptoms in ALS mice.

5. Parkinson's disease

Parkinson's disease (PD) affects 2-3% of people over the age of 65. PD is a chronic and progressive neurodegenerative disorder that primarily affects the motor system [49]. The disease is characterized by the loss of dopaminergic neurons in the substantia nigra, a region of the brain responsible for the regulation of voluntary movement [50]. This area of the brain, along with other regions, also experiences aberrant intracellular deposits in the form of Lewy bodies, which are composed of aggregated α-synuclein [50]. The loss of these neurons leads to a reduction in dopamine levels, which results in the characteristic motor symptoms of PD, including tremors, rigidity, bradykinesia, and postural instability [51]. Current treatment of PD is directed at alleviating the symptoms and slowing the course of the disease. Currently, drugs such as levodopa, dopamine agonists, catechol-O-methyl transferase inhibitors, monoamine oxidase B inhibitors, amantadine and trihexyphenidyl are being used.

5.1 Pathogenesis

The pathogenesis of PD is multifactorial, involving genetic, environmental, and cellular factors. Several genetic factors have been suggested in the pathogenesis of Parkinson's disease. Mutations in specific genes, such as SNCA (α-synuclein), LRRK2 (leucine-rich repeat kinase 2), PARKIN, and PINK1, have been associated with familial forms of the disease, highlighting the genetic basis of Parkinson's pathology [54,55].

The aggregation of α-synuclein protein plays a central role in the pathogenesis of PD. α-synuclein forms insoluble aggregates within neurons, known as Lewy bodies. These aggregates are pathological hallmarks of PD [56].

5.2 Microbiome

Recent research has suggested a possible relationship between the microbiota and PD [58,59]. Several studies have shown that people with PD have a different composition of the gut microbiota compared to healthy individuals. PD patients have lower levels of some bacterial species such as *Prevotellaceae* and higher levels of others such as *Enterobacteriaceae* which correlates with increased postural instability and gait difficulties [58].

Animal studies have provided further evidence for a link between the gut microbiota and PD [61]. For example, mice with a disrupted gut microbiota have been found to display motor deficits and neuroinflammation similar to those seen in PD, while faecal microbiota transplantation from PD patients to mice has also been shown to induce motor deficits and α-synuclein pathology [62].

These findings suggest that modulating the gut microbiota could be a potential therapeutic target for PD. Strategies such as probiotics, prebiotics, and faecal microbiota transplantation [63] are currently being investigated as possible interventions to restore gut microbial balance and improve PD symptoms [64].

5.3 Probiotics in PD Treatment

5.3.1 Improvement of Non-Motor Symptoms (Constipation, Discomfort)

Probiotics may effectively modify microbiota composition related to PD, improve gastrointestinal health, and reduce gut leakiness, bacterial translocation, and neuroinflammation [64]. Cassani et al. studied the effects of the probiotic strain *Lactobacillus casei* Shirota on constipation in PD patients. Two randomized, controlled trials assessed the impact of

Lactobacillus casei Shirota on gastrointestinal symptoms in individuals meeting the Rome III criteria for functional gastrointestinal disorders, such as irritable bowel syndrome, functional dyspepsia, and chronic constipation [65]. The Rome III criteria define these conditions, their subtypes, and treatment guidelines [66]. Forty PD patients participated, with bowel function evaluated during two treatment periods: one week of diet therapy alone, followed by five weeks of daily intake of 65 ml of fermented milk containing 6.5×10^9 CFU of *Lactobacillus casei* Shirota. Patients kept a six-week diary documenting bowel function [65]. After probiotic intake, participants reported more days with normal stool consistency and fewer days with bloating, stomach discomfort, and incomplete bowel movements [65].

Another study examined the effect of probiotics on constipation in PD patients meeting the Rome III criteria. In a four-week randomized, double-blind, placebo-controlled trial with 120 participants, patients received either a placebo or fermented milk containing several probiotic strains and prebiotic fibre once daily in a 1:2 ratio. The primary goal was to increase weekly bowel movement frequency and the sensation of complete bowel emptying, which was achieved compared to the placebo group [67].

A subsequent study also confirmed the efficacy of probiotics. PD patients with Rome III-defined constipation were randomly assigned to receive either a placebo (fermented milk) or a multi-strain probiotic (*Lactobacillus* spp. and *Bifidobacterium* spp., 30×10^9 CFU) with fructooligosaccharide twice daily for eight weeks. Constipation symptoms, including bowel frequency (BOF), were assessed using the nine-item Garrigues Questionnaire (GQ). After eight weeks, the probiotic group showed a significantly higher mean weekly BOF than the placebo group [68].

In a 2020 double-blind, randomized, placebo-controlled trial, 72 patients were block-randomized (1:1) to receive either multistrain probiotic capsules (n = 34) or placebo (n = 38) for four weeks. The primary outcome was the change in average weekly spontaneous bowel movements (SBM) between the final two intervention weeks and the two preintervention weeks. Secondary outcomes included stool consistency, constipation severity, and constipation-related quality of life. Following probiotic treatment, SBM increased by 1.0 ± 1.2 per week in the probiotic group, while it decreased by 0.3 ± 1.0 in the placebo group, resulting in a mean difference of 1.3 SBM per week. Significant improvements were also observed in stool consistency and constipation-related quality of life [69].

Another randomized, controlled study enrolled 46 PD patients meeting the Rome III criteria for constipation. Pre- and post-intervention data were collected on weekly complete bowel movements (CBM), defecation effort, Bristol Stool Scale (BSS), Patient Assessment of

Constipation Symptoms (PAC-SYM), and Patient Assessment of Constipation Quality of Life (PAC-QOL). The treatment group showed increased weekly CBM and improvements across all scales, unlike the control group [70]. Additionally, after 12 weeks of probiotic treatment, fecal analysis revealed that *Christensenella* sp. Marseille-P2437 significantly increased, while *Eubacterium oxidoreducens* group, *Eubacterium hallii* group, and *Odoribacter* sp. N54.MGS-14 significantly decreased compared to controls [70].

In another study, it was shown that treatment with probiotics can help relieve such symptoms as abdominal pain or flatulence, and a similar effect can be achieved with the drug trimebutine, which had a better effect on constipation with incomplete evacuation. The study involved 40 patients treated with levodopa or dopamine agonists. They were investigated for symptoms such as abdominal pain, bloating and constipation. 20 patients consumed trimebutin 200 mg three times a day for 3 months and 20 patients received probiotics (60 mg per tablet of two lactic bacteria: *Lactobacillus acidophilus* and *Bifidobacterium infantis*) twice daily [71].

5.3.2 Effects on Motor Functions and Inflammation

Probiotics can also be used in PD to improve metabolic and motor parameters, which was shown in a study by Tamtaji and colleagues. Motor parameters were measured on The Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) before and after supplementation of probiotics. Compared to placebo, probiotic supplementation reduced MDS-UPDRS, lowered high-sensitivity C-reactive protein and malondialdehyde levels, and increased glutathione levels [72].

Table 4. Effects of probiotic supplementation on gastrointestinal and motor symptoms in Parkinson's disease (PD).

Type of probiotic	Observed effect
Lactobacillus spp. and *Bifidobacterium* spp. (including *L. casei* Shirota, *L. acidophilus*, *B. infantis*)	Increased weekly bowel movements, improved stool consistency, reduced bloating and discomfort, better quality of life, and modulation of gut microbiota
Multi-strain probiotics with prebiotic fibre (e.g., fructooligosaccharides)	Increased bowel movement frequency and sensation of complete evacuation after 4–8 weeks
Probiotic supplementation (various strains, unspecified)	Reduced MDS-UPDRS scores, lower CRP levels, increased glutathione levels — indicating improved oxidative balance and motor control.

6. Summary

Research has demonstrated that probiotic supplementation can decrease neuroinflammation, a key factor in the development of AD. The use of probiotics in AD has been shown to reduce inflammatory markers. In particular, the use of a probiotic with selenium resulted in decreased CRP levels [14]. Additionally, supplementation may impact the symptoms and progression of the disease. For instance, in adults with moderate cognitive impairment, the

Bifidobacterium breve A1 strain and *Bifidobacterium longum* BB68S have been shown to improve memory test scores and cognitive function [17,18,21]. Furthermore, research has demonstrated that probiotics have the potential to decelerate neurodegenerative processes and brain atrophy [15], as well as influence the gut microflora and, consequently, the mental state of the patient.

In the case of PD, probiotics are mainly tested for non-motor symptoms such as constipation, abdominal pain and problems with bowel movements [68–70]. Studies have shown that, after taking a probiotic, patients reported an increase in the number of days per week with stools of normal consistency and a significant decrease in the number of days per week with bloating, stomach discomfort and incomplete bowel movements [65]. The probiotics tested most commonly contained the bacterial strains *Lactobacillus* casei Shirota, *Lactobacillus* sp. *Bifidobacterium* or fermented milk [65,67,68]. Probiotics can also be used to improve a patient's motor function and reduce inflammatory markers, compared to placebo. Probiotic supplementation reduced The Movement Disorders Society-Unified Parkinson's Disease Rating Scale, lowered high-sensitivity C-reactive protein and malondialdehyde levels, and increased glutathione levels [72]. *In vitro* studies have shown that L. acidophilus and L. salivarius LS01, significantly lowered pro-inflammatory cytokines and elevated levels of anti-inflammatory cytokines [74] and that the bacteria can, among others, affect IL-1, IL-8, and TNF-α in the peripheral blood mononuclear [73].

In the case of MS administration of probiotics (*Lactobacillus* and *Bifidobacterium* strains) resulted in a reduction of inflammation in peripheral areas, as evidenced by the decrease in the frequency of intermediate monocytes. This suggests a potential modulation of the immune system. Additionally, the decrease in levels of classical monocytes indicates a potential reduction in immune activation within this subset. The reduction in levels of dendritic cells shows a possible attenuation of the immune response mediated by these cells [28,29]. In the peripheral blood, supplementation reduced the expression of pro-inflammatory genes such as interleukin-8, interleukin-6 and TNF-α and a significant increase in BDNF, which is important for brain function. This all indicates a reduction in inflammation in patients and could potentially affect the course of the disease [29,30]. Taken together, these findings suggest that the administration of the probiotic VSL3 [28] may have a modulating effect on the immune system in people with MS. This could lead to slowing disease progression and improving symptoms.

Research suggests a link between the microbiota and the development and symptoms of ALS [75]. Studies in mice predisposed to ALS showed that the bacterium *Akkermansia*

muciniphila reduced ALS symptoms and mice accumulated AM-bound nicotinamide in the central nervous system [47]. When mice were given 2% butyrate, the balance of the gut microbiota was restored, resulting in increased intestinal integrity and longer lifespan [48]. The study found that certain bacteria, including *Ruminococcus* torques and *Parabacteroides distasonis*, may exacerbate symptoms of ALS [47]. The results suggest that modifying the gut microbiota with probiotics could potentially alter the course of the disease, impacting both symptoms and life expectancy. However, further research is necessary to fully comprehend the mechanisms and potential therapeutic benefits of this interaction [48]. Although there are many studies, more research is needed to go beyond the identified association between probiotics and neurodegenerative disorders.

Disclosure:

Author's contribution:

Conceptualization: MS, RS

Methodology: MK, BS

Formal analysis: ŁS, ZC

Investigation: MS, MK

Resources: BS, RS

Data curation: RS

Writing – original draft: RS, MS

Writing – review & editing: ŁS, ZC

Visualization: BS, MK

Supervision: ŁS, ZC

Project administration: ŁS, ZC

Funding Statement: The study did not receive special funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgements: Not applicable.

Conflict of Interest Statement: The authors declare no conflicts of interest.

Declaration of the use of generative AI and AI-assisted technologies in the writing process: During the preparation of this work, the authors used ChatGPT for the purpose of language editing and stylistic refinement to improve clarity and readability of the manuscript. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the accuracy, integrity and conclusions of the publication.

8. References

[1] Mayer EA, Nance K, Chen S. The Gut-Brain Axis. Annu Rev Med 2022;73:439–53. https://doi.org/10.1146/ANNUREV-MED-042320-014032.

[2] Chang CJ, Lin TL, Tsai YL, Wu TR, Lai WF, Lu CC, et al. Next generation probiotics in disease amelioration. J Food Drug Anal 2019;27:615–22. https://doi.org/10.1016/J.JFDA.2018.12.011.

[3] Khan S, Barve KH, Kumar MS. Recent Advancements in Pathogenesis, Diagnostics and Treatment of Alzheimer's Disease. Curr Neuropharmacol 2020;18:1106–25. https://doi.org/10.2174/1570159X18666200528142429.

[4] Deng H, Dong X, Chen M, Zou Z. Efficacy of probiotics on cognition, and biomarkers of inflammation and oxidative stress in adults with Alzheimer's disease or mild cognitive impairment-A meta-analysis of randomized controlled trials. Aging 2020;12:4010–39. https://doi.org/10.18632/AGING.102810.

[5] Ho L, Ono K, Tsuji M, Mazzola P, Singh R, Pasinetti GM. Protective roles of intestinal microbiota derived short chain fatty acids in Alzheimer's disease-type beta-amyloid neuropathological mechanisms. Expert Rev Neurother 2018;18:83–90. https://doi.org/10.1080/14737175.2018.1400909.

[6] Angelucci F, Cechova K, Amlerova J, Hort J. Antibiotics, gut microbiota, and Alzheimer's disease. J Neuroinflammation 2019;16. https://doi.org/10.1186/S12974-019-1494-4.

[8] Dinan TG, Cryan JF. The Microbiome-Gut-Brain Axis in Health and Disease. Gastroenterol Clin North Am 2017;46:77–89. https://doi.org/10.1016/J.GTC.2016.09.007.

[9] Luca M, Mauro M Di, Mauro M Di, Luca A. Gut microbiota in Alzheimer's disease, depression, and type 2 diabetes mellitus: The role of oxidative stress. Oxid Med Cell Longev 2019;2019. https://doi.org/10.1155/2019/4730539.

[10] Lundmark K, Westermark GT, Olsén A, Westermark P. Protein fibrils in nature can enhance amyloid protein A amyloidosis in mice: Cross-seeding as a disease mechanism. Proc Natl Acad Sci U S A 2005;102:6098–102. https://doi.org/10.1073/PNAS.0501814102.

[12] Bonfili L, Cecarini V, Berardi S, Scarpona S, Suchodolski JS, Nasuti C, et al. Microbiota modulation counteracts Alzheimer's disease progression influencing neuronal proteolysis and gut hormones plasma levels. Sci Rep 2017;7. https://doi.org/10.1038/S41598-017-02587-2.

[13] Xiao J, Katsumata N, Bernier F, Ohno K, Yamauchi Y, Odamaki T, et al. Probiotic Bifidobacterium breve in Improving Cognitive Functions of Older Adults with Suspected Mild Cognitive Impairment: A Randomized, Double-Blind, Placebo-Controlled Trial. Journal of Alzheimer's Disease 2020;77:139–47. https://doi.org/10.3233/JAD-200488.

[14] Tamtaji OR, Heidari-soureshjani R, Mirhosseini N, Kouchaki E, Bahmani F, Aghadavod E, et al. Probiotic and selenium co-supplementation, and the effects on clinical, metabolic and genetic status in Alzheimer's disease: A randomized, double-blind, controlled trial. Clinical Nutrition 2019;38:2569–75. https://doi.org/10.1016/J.CLNU.2018.11.034.

[15] Asaoka D, Xiao J, Takeda T, Yanagisawa N, Yamazaki T, Matsubara Y, et al. Effect of Probiotic Bifidobacterium breve in Improving Cognitive Function and Preventing Brain Atrophy in Older Patients with Suspected Mild Cognitive Impairment: Results of a 24-Week Randomized, Double-Blind, Placebo-Controlled Trial. Journal of Alzheimer's Disease 2022;88:75–95. https://doi.org/10.3233/JAD-220148.

[16] Ton AMM, Campagnaro BP, Alves GA, Aires R, Côco LZ, Arpini CM, et al. Oxidative Stress and Dementia in Alzheimer's Patients: Effects of Synbiotic Supplementation. Oxid Med Cell Longev 2020;2020. https://doi.org/10.1155/2020/2638703.

[17] Kobayashi Y, Kinoshita T, Matsumoto A, Yoshino K, Saito I, Xiao JZ. Bifidobacterium Breve A1 Supplementation Improved Cognitive Decline in Older Adults with Mild Cognitive Impairment: An Open-Label, Single-Arm Study. J Prev Alzheimers Dis 2019;6:70–5. https://doi.org/10.14283/JPAD.2018.32.

[18] Kobayashi Y, Kuhara T, Oki M, Xiao JZ. Effects of bifidobacterium breve a1 on the cognitive function of older adults with memory complaints: A randomised, double-blind, placebo-controlled trial. Benef Microbes 2019;10:511–20. https://doi.org/10.3920/BM2018.0170.

[19] van Soest APM, Hermes GDA, Berendsen AAM, van de Rest O, Zoetendal EG, Fuentes S, et al. Associations between pro-and anti-inflammatory gastro-intestinal microbiota, diet, and cognitive functioning in dutch healthy older adults: The nu-age study. Nutrients 2020;12:1–19. https://doi.org/10.3390/NU12113471.

[20] Candela M, Biagi E, Soverini M, Consolandi C, Quercia S, Severgnini M, et al. Modulation of gut microbiota dysbioses in type 2 diabetic patients by macrobiotic Ma-Pi 2 diet. British Journal of Nutrition 2016;116:80–93. https://doi.org/10.1017/S0007114516001045.

[21] Shi S, Zhang Q, Sang Y, Ge S, Wang Q, Wang R, et al. Probiotic Bifidobacterium longum BB68S Improves Cognitive Functions in Healthy Older Adults: A Randomized, Double-Blind, Placebo-Controlled Trial. Nutrients 2023;15. https://doi.org/10.3390/NU15010051.

[22] Ravi AK, Muthukrishnan SK. Combination of Probiotics and Natural Compounds to Treat Multiple Sclerosis via Warburg Effect. Adv Pharm Bull 2022;12:515–23. https://doi.org/10.34172/APB.2022.057.

[23] Parodi B, Kerlero de Rosbo N. The Gut-Brain Axis in Multiple Sclerosis. Is Its Dysfunction a Pathological Trigger or a Consequence of the Disease? Front Immunol 2021;12. https://doi.org/10.3389/FIMMU.2021.718220.

[24] Ghezzi L, Cantoni C, Pinget G V., Zhou Y, Piccio L. Targeting the gut to treat multiple sclerosis. Journal of Clinical Investigation 2021;131. https://doi.org/10.1172/JCI143774.

[25] Camara-Lemarroy CR, Metz L, Meddings JB, Sharkey KA, Wee Yong V. The intestinal barrier in multiple sclerosis: Implications for pathophysiology and therapeutics. Brain 2018;141:1900–16. https://doi.org/10.1093/BRAIN/AWY131.

[26] Atabati H, Yazdanpanah E, Mortazavi H, bajestani SG, Raoofi A, Esmaeili SA, et al. Immunoregulatory Effects of Tolerogenic Probiotics in Multiple Sclerosis. Adv Exp Med Biol 2021;1286:87–105. https://doi.org/10.1007/978-3-030-55035-6_6.

[27] Yang J, Zhang L, Yu C, Yang XF, Wang H. Monocyte and macrophage differentiation: Circulation inflammatory monocyte as biomarker for inflammatory diseases. Biomark Res 2014;2. https://doi.org/10.1186/2050-7771-2-1.

[28] Tankou SK, Regev K, Healy BC, Cox LM, Tjon E, Kivisakk P, et al. Investigation of probiotics in multiple sclerosis. Multiple Sclerosis 2018;24:58–63. https://doi.org/10.1177/1352458517737390.

[29] Rahimlou M, Hosseini SA, Majdinasab N, Haghighizadeh MH, Husain D. Effects of long-term administration of Multi-Strain Probiotic on circulating levels of BDNF, NGF, IL-6 and mental health in patients with multiple sclerosis: a randomized, double-blind, placebo-controlled trial. Nutr Neurosci 2022;25:411–22. https://doi.org/10.1080/1028415X.2020.1758887.

[30] Tamtaji OR, Kouchaki E, Salami M, Aghadavod E, Akbari E, Tajabadi-Ebrahimi M, et al. The Effects of Probiotic Supplementation on Gene Expression Related to Inflammation, Insulin, and Lipids in Patients With Multiple Sclerosis: A Randomized, Double-Blind, Placebo-Controlled Trial. J Am Coll Nutr 2017;36:660–5. https://doi.org/10.1080/07315724.2017.1347074.

[31] Fleming JO, Isaak A, Lee JE, Luzzio CC, Carrithers MD, Cook TD, et al. Probiotic helminth administration in relapsing-remitting multiple sclerosis: A phase 1 study. Multiple Sclerosis Journal 2011;17:743–54. https://doi.org/10.1177/1352458511398054.

[32] Maizels RM, Balic A, Gomez-Escobar N, Nair M, Taylor MD, Allen JE. Helminth parasites - Masters of regulation. Immunol Rev 2004;201:89–116. https://doi.org/10.1111/J.0105-2896.2004.00191.X.

[33] Glicksman MA. The preclinical discovery of amyotrophic lateral sclerosis drugs. Https://DoiOrg/101517/174604412011628654 2011;6:1127–38. https://doi.org/10.1517/17460441.2011.628654.

[34] Al-Chalabi A, Hardiman O. The epidemiology of ALS: a conspiracy of genes, environment and time. Nat Rev Neurol 2013;9:617–28. https://doi.org/10.1038/NRNEUROL.2013.203.

[35] Mazzini L, Mogna L, De Marchi F, Amoruso A, Pane M, Aloisio I, et al. Potential Role of Gut Microbiota in ALS Pathogenesis and Possible Novel Therapeutic Strategies. J Clin Gastroenterol 2018;52:S68–70. https://doi.org/10.1097/MCG.0000000000001042.

[36] Rothstein JD. Bench to Bedside Edaravone: A New Drug Approved for ALS. Cell 2017;171. https://doi.org/10.1016/j.cell.2017.10.011.

[37] Renton AE, Chiò A, Traynor BJ. State of play in amyotrophic lateral sclerosis genetics. Nature Neuroscience 2013 17:1 2013;17:17–23. https://doi.org/10.1038/nn.3584.

[38] Kiernan MC, Vucic S, Cheah BC, Turner MR, Eisen A, Hardiman O, et al. Amyotrophic lateral sclerosis. Lancet 2011;377:942–55. https://doi.org/10.1016/S0140-6736(10)61156-7.

[39] Vetrie D. The gene involved in X-linked agammaglobulinaemia is a member of the src family of protein-tyrosine kinases. Nature 1993 364:6435 1993;364:362–362. https://doi.org/10.1038/364362a0.

[40] Ferraiuolo L, Kirby J, Grierson AJ, Sendtner M, Shaw PJ. Molecular pathways of motor neuron injury in amyotrophic lateral sclerosis. Nature Reviews Neurology 2011 7:11 2011;7:616–30. https://doi.org/10.1038/nrneurol.2011.152.

[41] Quigley EMM. Microbiota-Brain-Gut Axis and Neurodegenerative Diseases. Curr Neurol Neurosci Rep 2017;17:94. https://doi.org/10.1007/s11910-017-0802-6.

[42] Rowin J, Xia Y, Jung B, Sun J. Gut inflammation and dysbiosis in human motor neuron disease. Physiol Rep 2017;5:e13443. https://doi.org/10.14814/phy2.13443.

[43] Fang X, Wang X, Yang S, Meng F, Wang X, Wei H, et al. Evaluation of the Microbial Diversity in Amyotrophic Lateral Sclerosis Using High-Throughput Sequencing. Front Microbiol 2016;7. https://doi.org/10.3389/fmicb.2016.01479.

[44] Rowin J, Xia Y, Jung B, Sun J. Gut inflammation and dysbiosis in human motor neuron disease. Physiol Rep 2017;5. https://doi.org/10.14814/phy2.13443.

[45] Tu PH, Raju P, Robinson KA, Gurney ME, Trojanowski JQ, Lee VMY. Transgenic mice carrying a human mutant superoxide dismutase transgene develop neuronal cytoskeletal

pathology resembling human amyotrophic lateral sclerosis lesions. Proc Natl Acad Sci U S A 1996;93:3155–60. https://doi.org/10.1073/PNAS.93.7.3155.

[46] Wu S, Yi J, Zhang YG, Zhou J, Sun J. Leaky intestine and impaired microbiome in an amyotrophic lateral sclerosis mouse model. Physiol Rep 2015;3:e12356. https://doi.org/10.14814/PHY2.12356.

[47] Zhang Y guo, Wu S, Yi J, Xia Y, Jin D, Zhou J, et al. Target Intestinal Microbiota to Alleviate Disease Progression in Amyotrophic Lateral Sclerosis. Clin Ther 2017;39:322–36. https://doi.org/10.1016/j.clinthera.2016.12.014.

[48] Blacher E, Bashiardes S, Shapiro H, Rothschild D, Mor U, Dori-Bachash M, et al. Potential roles of gut microbiome and metabolites in modulating ALS in mice. Nature 2019 572:7770 2019;572:474–80. https://doi.org/10.1038/s41586-019-1443-5.

[49] Poewe W, Seppi K, Tanner CM, Halliday GM, Brundin P, Volkmann J, et al. Parkinson disease. Nature Reviews Disease Primers 2017 3:1 2017;3:1–21. https://doi.org/10.1038/nrdp.2017.13.

[50] Schapira AHV. Science, medicine, and the future: Parkinson's disease. BMJ : British Medical Journal 1999;318:311. https://doi.org/10.1136/BMJ.318.7179.311.

[51] Beitz JM. Parkinson's disease: a review. Front Biosci (Schol Ed) 2014;6:65–74. https://doi.org/10.2741/S415.

[52] Przedborski S. The two-century journey of Parkinson disease research. Nat Rev Neurosci 2017;18:251–9. https://doi.org/10.1038/NRN.2017.25.

[53] Reich SG, Savitt JM. Parkinson's Disease. Med Clin North Am 2019;103:337–50. https://doi.org/10.1016/J.MCNA.2018.10.014.

[54] Paisán-Ruíz C, Jain S, Evans EW, Gilks WP, Simón J, Van Der Brug M, et al. Cloning of the gene containing mutations that cause PARK8-linked Parkinson's disease. Neuron 2004;44:595–600. https://doi.org/10.1016/j.neuron.2004.10.023.

[55] Singleton AB, Farrer M, Johnson J, Singleton A, Hague S, Kachergus J, et al. alpha-Synuclein locus triplication causes Parkinson's disease. Science 2003;302:841. https://doi.org/10.1126/SCIENCE.1090278.

[56] Jenner P, Hunot, Olanow, Beal, Kordower, Tatton, et al. Oxidative stress in Parkinson's disease. Ann Neurol 2003;53:S26–38. https://doi.org/10.1002/ANA.10483.

[57] Hirsch EC, Vyas S, Hunot S. Neuroinflammation in Parkinson's disease. Parkinsonism Relat Disord 2012;18 Suppl 1. https://doi.org/10.1016/S1353-8020(11)70065-7.

[58] Scheperjans F, Aho V, Pereira PAB, Koskinen K, Paulin L, Pekkonen E, et al. Gut microbiota are related to Parkinson's disease and clinical phenotype. Mov Disord 2015;30:350–8. https://doi.org/10.1002/MDS.26069.

[59] Chandra S, Alam MdT, Dey J, Sasidharan BCP, Ray U, Srivastava AK, et al. Healthy Gut, Healthy Brain: The Gut Microbiome in Neurodegenerative Disorders. Curr Top Med Chem 2020;20:1142–53. https://doi.org/10.2174/1568026620666200413091101.

[60] Spielman LJ, Gibson DL, Klegeris A. Unhealthy gut, unhealthy brain: The role of the intestinal microbiota in neurodegenerative diseases. Neurochem Int 2018;120:149–63. https://doi.org/10.1016/j.neuint.2018.08.005.

[61] Sampson TR, Mazmanian SK. Control of brain development, function, and behavior by the microbiome. Cell Host Microbe 2015;17:565–76. https://doi.org/10.1016/J.CHOM.2015.04.011.

[62] Sampson TR, Debelius JW, Thron T, Janssen S, Shastri GG, Ilhan ZE, et al. Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson's Disease. Cell 2016;167:1469. https://doi.org/10.1016/J.CELL.2016.11.018.

[63] Fang X. Microbial treatment: the potential application for Parkinson's disease. Neurol Sci 2019;40:51–8. https://doi.org/10.1007/S10072-018-3641-6.

[64] Gazerani P. Probiotics for Parkinson's Disease. Int J Mol Sci 2019;20. https://doi.org/10.3390/IJMS20174121.

[65] Cassani E, Privitera G, Pezzoli G, Pusani C, Madio C, Iorio L, et al. Use of probiotics for the treatment of constipation in Parkinson's disease patients. Minerva Gastroenterol Dietol 2011;57:117–21.

[66] Shih DQ, Kwan LY. All Roads Lead to Rome: Update on Rome III Criteria and New Treatment Options. Gastroenterol Rep 2007;1:56.

[67] Barichella M, Pacchetti C, Bolliri C, Cassani E, Iorio L, Pusani C, et al. Probiotics and prebiotic fiber for constipation associated with Parkinson disease. Neurology 2016;87:1274–80. https://doi.org/10.1212/WNL.0000000000003127.

[68] Ibrahim A, Raja Ali RA, Abdul Manaf MR, Ahmad N, Tajurruddin FW, Qin WZ, et al. Multi-strain probiotics (Hexbio) containing MCP BCMC strains improved constipation and gut motility in Parkinson's disease: A randomised controlled trial. PLoS One 2020;15. https://doi.org/10.1371/journal.pone.0244680.

[69] Tan AH, Lim SY, Chong KK, A Manap MAA, Hor JW, Lim JL, et al. Probiotics for Constipation in Parkinson Disease: A Randomized Placebo-Controlled Study. Neurology 2021;96:e772–82. https://doi.org/10.1212/WNL.0000000000010998.

[70] Du Y, Li Y, Xu X, Li R, Zhang M, Cui Y, et al. Probiotics for constipation and gut microbiota in Parkinson's disease. Parkinsonism Relat Disord 2022;103:92–7. https://doi.org/10.1016/j.parkreldis.2022.08.022.

[71] Georgescu D, Ancusa OE, Georgescu LA, Ionita I, Reisz D. Nonmotor gastrointestinal disorders in older patients with Parkinson's disease: Is there hope? Clin Interv Aging 2016;11:1601–8. https://doi.org/10.2147/CIA.S106284.

[72] Tamtaji OR, Taghizadeh M, Daneshvar Kakhaki R, Kouchaki E, Bahmani F, Borzabadi S, et al. Clinical and metabolic response to probiotic administration in people with Parkinson's disease: A randomized, double-blind, placebo-controlled trial. Clinical Nutrition 2019;38:1031–5. https://doi.org/10.1016/j.clnu.2018.05.018.

[73] Borzabadi S, Oryan S, Eidi A, Aghadavod E, Kakhaki RD, Tamtaji OR, et al. The effects of probiotic supplementation on gene expression related to inflammation, insulin and lipid in patients with Parkinson's disease: A randomized, double-blind, placebo-controlled trial. Arch Iran Med 2018;21:289–95.

[74] Magistrelli L, Amoruso A, Mogna L, Graziano T, Cantello R, Pane M, et al. Probiotics May Have Beneficial Effects in Parkinson's Disease: In vitro Evidence. Front Immunol 2019;10. https://doi.org/10.3389/FIMMU.2019.00969.

[75] Calvo AC, Valledor-Martín I, Moreno-Martínez L, Toivonen JM, Osta R. Lessons to Learn from the Gut Microbiota: A Focus on Amyotrophic Lateral Sclerosis. Genes 2022, Vol 13, Page 865 2022;13:865. https://doi.org/10.3390/GENES13050865.