

From Gut to Brain: Targeting Probiotics in Neurodegenerative Health

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ABSTRACT

Probiotics have evolved from a dynamic and living culture that enhances the composition of the GI tract microbiota to encompass more specific benefits, notably the immunomodulatory ability of well-defined strains. The most prevalent sources of beneficial strains, or potential probiotics, are commonly found within the *Bifidobacterium* and *Lactobacillus* genera, and certain strains among them possess remarkable capabilities in reducing inflammation, preventing ulcers, alleviating diarrhea, and even combating autism. Recent evidence further emphasizes the essential part of GI microbiome dysbiosis in neurodegenerative disorders. These conditions may manifest through the intricate network of interconnections amongst the microbiota, gut, and brain, facilitating bidirectional transmission *via* pathways involving neuroimmune responses, neuroendocrine signaling, and direct neural connections like the vagus nerve. The present focus of probiotic research aims to provide suitable and secure bacterial stimulation to counteract abnormal immune reactions linked to allergic inflammation and various neurodegenerative diseases. Nonetheless, additional careful scientific efforts are essential to completely clarify the immune-modulating potential of certain probiotic types regarding these particular goals.

Keywords: Autism, Gut microbiota, Immunomodulation, Neurodegenerative diseases, Probiotics.

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INTRODUCTION

The term “probiotics” comes from the Greek dialect and means “for life.” A group of experts designated by the World Health Organization (WHO) has defined probiotics as microorganisms that are active and, once provided in appropriate amounts, deliver health benefits to the host.¹ The term “probiotics” was initially developed based on studies examining how particular bacteria found in yogurt affect the makeup of the human gut. Initially, probiotics were used to alter intestinal microbiota in both animals and humans to promote better health outcomes. As of now, analysts are investigating the impact of particular live microbial nourishment fixing on human well-being, both in the context of food products as well as in individual or blended culture preparations.² In 1965, probiotics were defined by Lilly and Stillwell as microorganisms that stimulate the growth of other microorganisms. Probiotics are living microbes that promote and keep a favorable balance of the natural microbial population in the digestive tract, hence contributing to good health.³

The effectiveness of probiotics is determined by a strain’s capacity to provide health benefits to a host after being consumed orally in the form of live cells. Various types of *Lactobacilli* and *Bifidobacterium* strains and species have been utilized in commercial probiotic products (as shown in

Table 1).⁴ Probiotics containing *Bifidobacterium lactis Bb-12* and *Lactobacillus* strain *GG* have been proven to be safe for consumption at an early age, and these strains were chosen for the study.⁵ Lactic acid bacteria (LAB) strains are the primary types of microorganisms used in probiotics, found in both food and pharmaceutical products. These LAB strains thrive in a range of environments, especially those with high nutrient content.⁶ The primary way in which probiotics exert their good effects is by influencing the intestinal microbiota, which plays a basic part in defending against harmful pathogens, as well as fermenting non-digestible carbohydrates, which primarily takes place in the proximal colon. One of the key items of this process is SCFAs, counting acetic acid derivatives, propionate, and butyrate. Butyrate is especially critical because it serves as a noteworthy source of vitality for intestinal epithelial cells. It also impacts cell proliferation, differentiation, mucus secretion, and barrier function. Furthermore, butyrate has demonstrated anti-inflammatory and antioxidant properties.⁷

Probiotics work by directing the adjustment of the intestine microbiota, ruining the capacity of hurtful pathogens to colonize and taint the mucosa, adjusting local and systemic immune responses, stabilizing the gastrointestinal barrier function, inhibiting pro-carcinogenic enzymatic activity, and promoting enzymatic activity that enhances good nutrition.

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Table 1: Probiotic strain along with their setting, health benefits and respective producers

S No.	Probiotic strains	Setting	Health benefits	Producer	References
1.	Mixture of <i>L. acidophilus</i> , <i>B. bifidum</i> , <i>L. reuteri</i> , and <i>L. fermentum</i>	Male Wistar rats	Enhance behavior, cognition, and neural health.	Lactocare Zistakhmir Company	8
2.	Probiotic formulation <i>L. helveticus</i> and <i>B. longum</i>	Male Wistar rats	Lower TNF-a and IL1-b levels in LPS-induced rats.	Jamieson Laboratories, Toronto, Ontario, Canada	9
3.	Mixture of <i>L. rhamnosus</i> , <i>B. animalis lactis</i> , and <i>L. acidophilus</i>	C57BL/6 male mice	Reduces MAO B expression, decreases 1-MPP+ neurotoxin.	Chr. Hansen (Denmark)	10
4.	<i>L. acidophilus</i> extract	C57BL/6 male mice	LA may protect neurons via microbiota remodelling	Sine Pharmaceutical Corp. Ltd.	11
5.	Combination of <i>B. breve</i> , <i>L. casei</i> , <i>L. bulgaricus</i> and <i>L. acidophilus</i>	Male BLC57 mice	Powerful anti-inflammatory, antioxidant properties protect tissues.	Neurophysiology Research Centre of Shahid Behest, Tehran, Iran	12
6.	SLAB51	3xTg-AD mice	Activates SIRT1, reducing AD brain stress	Mendes S.A. (Lugano, Switzerland)	13
7.	Mixture of <i>L. plantarum</i> , <i>S. thermophilus</i> and <i>S. thermophilus</i>	C57BL/6 male mice	Reduced IL-6 and TNF-alpha; increased IL-10	CERELA Culture Collection (Tucuman, Argentina)	14
8.	<i>L. rhamnosus</i>	Male SD rats	Enhanced hippocampal cognition selectively targeted	Lallemand Health Solutions (Montreal, QC, Canada)	15
9.	<i>C. butyricum</i>	C57BL/6 male mice	It may enhance motor function and reduce neuron loss.	Wenzhou Medical University	16
10.	<i>L. rhamnosus</i>	Swiss Albino female mice	Curcumin with <i>L. rhamnosus</i> enhances memory and antioxidants	Unique Biotech Ltd., India	17

Each of these mechanisms can be categorized depending on their specific function.¹⁸ The larger part of probiotics is classified as corrosive microscopic organisms, simply, we can say that (LAB), are a group of microorganisms that have been extensively employed as probiotics to treat various intestinal conditions. These incorporate lactose bigotry, intense gastroenteritis caused by rotavirus and other enteric pathogens, antagonistic impact of pelvic radiotherapy, clogging of feces, inflammatory bowel syndrome (IBD), and nourishment sensitivities.¹⁹

In addition to LAB, newer probiotic formulations may also include other types of microorganisms, such as yeasts like *Saccharomyces boulardii*, as well as totally distinctive sorts of microbes such as *Clostridium* and *Bacillus subtilis*.²⁰ Ingestion of probiotics has been detailed to supply a wide run of benefits, including balancing the composition of the colonic microbiota, acting as a vaccine adjuvant, decreasing the action of fecal enzymes embroiled in cancer start, treating travel- and antibiotic-associated diarrhea, controlling rotavirus and clostridium difficile-induced colitis, and anticipating ulcers caused by *Helicobacter pylori*.²¹

MATERIAL AND METHODS

Extensive exploration of an extensive array of internet-based sources, inclusive of a multitude of reviews and research papers employing keywords like probiotics, microflora, neurodegeneration, and mental illnesses, is conducted. This

investigation delves into the regulation of probiotics and their prospective application in addressing cerebral disorders and gastrointestinal tract (GIT) ailments. For the purpose of the literature survey, an extensive volume of scholarly articles sourced from reputable websites, including Google Scholar, Springer, Taylor & Francis, Elsevier, and Bentham, are meticulously assessed.

Intestinal Microbiota-Brain Communication

It is well believed that the human gastrointestinal tract contains an abundance of microorganisms, estimated to be approximately 100 trillion, which are thought to have significant impacts on human physiology.²² The gut microbiota is considered to be a crucial "organ" for the regular functioning of the defense system, carbohydrate metabolism, and metabolic balance,²³ and it is noteworthy that various physiological processes depend on bacteria. For instance, the bacterial origin of cellular organelles such as mitochondria, which generate ATP, the energy domain of the body, and seem to be related to Proteobacteria is interesting.²⁴ The gut microbiome was discovered to alter the production of neurotransmitter syntheses like serotonin, GABA, and BDNF. These chemicals interact with the enteroendocrine cells' (EEC) and bile acid receptors like FXR and TGR5, leading to the production of growth factors like FGF19. FGF19 easily penetrates BBB and affects hypothalamic production of neuropeptide Y, which subsequently exerts an influence on glycolysis via the

ejection of peptide GLP-1 having activity like glucagon. This implies that the gut microbiota is important in learning and retention processes.²⁵

The gut microbiome is hypothesized to have a considerable impact on the growth of the nervous system and to operate as a fundamental regulator of the intricate link between the gastric system and the central nervous system (CNS). It acts as a go-between for the gut and brain. The GI microbiota demonstrated in mice to perform a role in the formation of the gastrointestinal and nervous systems at both the neonate and adult phases.²⁶ The brain and spinal cord receive information from the nervous system that controls the intestines (ENS) and contributes to the regulation of movement of the GI tract. Research involving GF mice discovered that the lack of gut microbiota led to a more irregular myenteric plexus in the intestines compared to animals with a standard microbiota. The irregularity in germ-free mice is detected as early as the third day of life and is characterized by a decrease in nerve density, an increase in inhibitory myenteric neurons, and a decrease in the total amount of neural cell bodies per ganglion.²⁷ Astroglia are also affected by GI bacteria. These cells are crucial in linking the stomach and the brain via the ENS.²⁸ The microbiota residing within the ileum has been discovered to perform a vital part in the initial establishment of homeostatic flux within the intestinal mucosa of mice.²⁹ Mice that are germ-free (GF) exhibit a significantly lower count and concentration of mucosal enteric glial cells in comparison to their non-GF counterparts. This phenomenon showcases the potential effects of microbiota, microbial products, and astroglia on gastrointestinal balance. The gut microbiota may also affect gastrointestinal movement and enteric neuron preservation through interactions with Toll-like receptors. Administration of antibiotics may exacerbate ENS issues, particularly if it results in the reduction of glial cell line-derived protein and neurotrophic agents.³⁰

The reciprocal linkage between the stomach and the brain encompasses a myriad of pathways. Notable among these conduits are the vagus nerve, hypothalamus, pituitary gland, and the production of SCFAs by gastrointestinal microorganisms, immune mediators, and enteroendocrine signalling.³¹ The vagus nerve is regarded as the fastest and most efficacious signaling route connecting the brain with the digestive system. In the past, vagal nerve ablation was used to treat peptic ulcers, but research studies from 1953 and 1961 have linked it to an increased prevalence of mental disorders.³² SCFAs produced by gut bacteria can indirectly communicate with the brain by influencing nerve activity, which can impact behaviour.³³ Butyrate, propionate, and acetate make up almost 95% of all SCFA molecules. SCFA levels are limited in germ-free and antibiotic-treated animals, supporting the hypothesis that gut microbe-mediated degradation of food fibers is the principal way to produce SCFAs.³¹ Propionic acid can increase the synthesis of the enzyme tryptophan hydroxylase, which in turn can decrease serotonin levels, potentially impacting serotonergic neurotransmission. The metabolism of tryptophan is modulated by gut bacteria, which is different from the metabolism of other metabolites.³⁴

Dysfunctional Gut-Brain Communication in Neurodegeneration

Neurodegenerative disorders, distinguished by gradual degeneration of the neurological systems. Approximately 1% of the populace is affected by PD, and 8% by AD, respectively.³⁵ AD is a common cause of dementia in elderly people, responsible for 60 to 70% of cases involving gradual cognitive decline³⁶ while PD causes motor issues and muscle rigidity. It results from the degeneration of dopaminergic neurons in the pars compacta, leading to the loss of dopaminergic terminals in the striatum.³⁷ Research suggests that dysbiosis of the microbiota may be a contributing factor in neurological diseases, including neurodegenerative disorders and mood disorders.³⁸ Emerging research indicates that the intricate interplay between the gut and the brain potentially participate in a pivotal role in the etiology of neurological ailments and affective disorders. Studies have found that microbes within the gut can produce neurotransmitters, such as serotonin, and promote its production by gut epithelial cells. Additionally, bioactive compounds and fermentation by-products can be produced by gut microbes, and metabolic by-products are liberated into the circulatory system, capable of permeating the BBB. “The profound importance of the gut microbiome is underscored by these discoveries, which may have a significant impact on brain function and mental health.³⁹ It has been observed that both elderly individuals and individuals with neurodegenerative diseases have a decrease in the diversity of their gut microbiota.⁴⁰

Research has revealed that the abundance of certain SCFA-producing genera, such as *Coprococcus*, *Blautia*, and *Roseburia*, *Prevotellaceae*, is decreased in individuals with PD.⁴¹ An increase in the prevalence of Enterobacteriaceae may be linked to the intensity of motor impairment in Parkinson’s disease.⁴² When examining the phylum classification, individuals afflicted with AD exhibited a decline in the abundance of *Firmicutes* and *Actinobacteria*, coupled with an elevation in *Bacteroidetes*.⁴³ There is also a positive correlation between *Helicobacter pylori* and AD. It is postulated that *H. pylori* may impair the BBB in AD by inducing elevated homocysteine levels within the bloodstream.⁴⁴ The dysregulation of gut microbiota and the process of aging are linked as a consequence of heightened intestinal permeability, which leads to the entry of certain microbes and products originating from the gut microbiota traversing the circulatory system, encompassing substances such as β -methylamino-L-alanine (BMAA), lipoglycans (LPS), and GMB-derived amyloids. These compounds possess the capability to penetrate the brain, thereby influencing the progression of AD and cognitive decline⁴⁵ and also. One of the neurotoxins generated by *Cyanobacteria* residing in the gut is BMAA.⁴⁶

Research indicates that individuals afflicted with IBD bear an elevated susceptibility to Parkinson’s disease (PD) in comparison to those devoid of these conditions.⁴⁷ Several wide-ranging antibiotics were demonstrated to induce a substantial reduction in the gut microbiota of mice, thereby impeding the neurogenesis process within the hippocampus.⁴⁸

The Potential of Probiotics in Managing Neurodegeneration

The use of probiotics has transformed the management of digestive disorders. Based on these discoveries, probiotics are now available as dietary supplements in capsules and probiotic beverages.⁴⁹ Modern probiotics are touted as beneficial for numerous health conditions, ranging from diarrhea to neurological disorders like depression and Alzheimer's, though their therapeutic effectiveness remains debated.⁵⁰ Research studies involving healthy individuals who consumed probiotics with *Bifidobacterium* and *Lactobacillus* showed a reduction in anxiety, depression, and stress-related behaviors.⁵¹ People diagnosed with PD received a probiotic supplement that included multiple bacterial strains, such as *L. fermentum*, *B. bifidum*, *L. reuteri*, and *L. acidophilus*.⁵² Individuals experiencing cognitive challenges were given kefir fermented milk that included various bacteria, such as *Acetobacter* species, *Enterococcus faecium*, *A. aceti*, *L. kefirianofaciens*, *L. delbrueckii*, *L. fermentum*, *L. fructivorans*, *Leuconostoc* species, *C. krusei*, and *Candida famata*.⁵³

Empirical investigations have revealed that probiotic therapy exhibits noteworthy efficacy in enhancing memory, augmenting visual-spatial and abstraction abilities, improving executive and language functions, as well as promoting nitric oxide bioavailability.⁵⁴ Concurrently, it effectively mitigates inflammation, attenuates redox imbalance, suppresses advanced oxidation protein products, mitigates mitochondrial malfunction, and alleviates indications of genetic impairment in individuals with AD. The probiotic mixture, De Simone formulation previously sold as VSL#3, was administered to mice in the study, and restored decline in neurogenesis induced by antibiotics.⁵⁵ CRP, an inflammatory cytokine, has emerged as a pivotal "precursor" in the development of PD, AD and cognitive impairment. The management of the previously mentioned probiotic supplement to individuals led to a significant decrease in hs-CRP, along with a decline in malondialdehyde levels and a rise in glutathione concentration.⁵⁶

An additional investigation unveiled that organisms with diminished gut microbiota exhibited compromised gastrointestinal maturation and a decline in nitrergic neurons, consequently impacting motility.⁵⁷ It is noteworthy that the gut microbiota possesses the capacity to impact BBB permeability in mice.⁵⁸ Administration of *Clostridium tyrobutyricum* and sodium butyrate in mice led to an upregulation in the articulation of occluding junctions, consequently leading to a reduction in the permeability of the BBB. In the same way, an upsurge in the synthesis of the occluding junctions was observed, coupled with a decrease in the presence of inflammatory interleukins, in a rat model subjected to a long-term water avoidance test and treated with rifaximin. These discoveries suggest that the gut microbiota is likely to impact the coherence of the BBB by modulating occluding junctions.⁵⁹ The beneficial effects of rifaximin on tight junction protein synthesis and inflammatory interleukin levels are linked to an

increase in the concentration of LAB in the intestine. Some species of *Lactobacillus*, like *Lacticaseibacillus casei*, are known to reduce inflammation in the gut mucosa.⁶⁰

An investigation revealed the prevalence of spore-forming bacteria in the gut microbiota of stimulate the production of serotonin in the colon, which is responsible for regulating intestinal motility and platelet function.⁶¹ Studies suggest that the microbiome may regulate the brain's serotonergic system, and one possible mechanism is through the synthesis of colonic serotonin by gut bacteria that create spores. Furthermore, phytoestrogens like equol, which are formed when specific gut microorganisms break down by isoflavones, may be an example of microbial metabolites that might connect gut-brain function.⁶² Equol-producing *Eubacterium* bacteria have been isolated from porcine faeces.⁶³ The administration of equol has been found to reduce histological damage in the brain and inhibit phospho-Src, which helps protect rats against cerebral ischemia or reperfusion injury,⁶⁴ although the mechanisms are not yet understood. The findings indicate that the presence of equol, synthesized in the stomach, may exert an effect on the functioning of the neurological system.⁶⁵

The Role of Probiotics in Alleviating Autism Symptoms

In 1943, researchers first reported autism as a developmental disability. It affects social interaction and communication, making it difficult for individuals with ASD to interact with others, show interest in others, and have social awareness. Autism exhibits a higher prevalence among males than females, with a projected ratio of 4:1.^{66,67} In the case of children diagnosed with ASD who experience GI disorders, conventional GI treatments often yield suboptimal responses.⁶⁸ Abundant scientific investigations have unveiled a correlation between GI complications and ASD, while an expanding body of evidence indicates that gut bacteria might exert influence on children with autism^{69,70} and alter the structure and functional processes of the gut microbiota seemed posited as a plausible underlying factor accord to GI disturbance in children with ASD, potentially fostering the proliferation of deleterious microbial species (as shown in Figure 1).⁷¹ Elevated levels a metabolite produced by various pathogenic *Candida* species, have been noticed in the urine of individuals with autism, indicating its potential association with the disorder.⁷²

Some studies have reported different gut microbiota compositions in people with ASD compared to neurotypical persons, with some revealing greater numbers of harmful *Clostridium* bacteria.⁷³ Research indicates that individuals with autism exhibit a distinct makeup of gut microbiome compared to those without the condition, who are referred to as neurotypical individuals, with higher levels of pathogenic *Clostridium* bacteria and a lower *Bacteroides/Firmicutes* ratio.^{74,75} Studies have demonstrated that Clostridiaceae, a bacterial family, has the capability to produce metabolites, including tyrosine derivative, which possess the potential to pose risks to human health.⁷⁶ Metabolites such as indole derivatives, which can be toxic to humans, are produced by Clostridiaceae. These metabolites were found in significantly

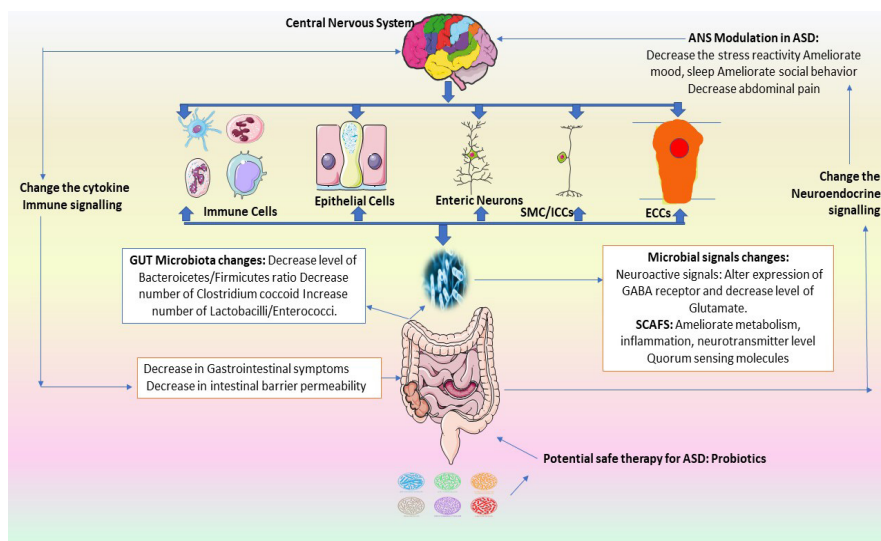


Figure 1: Illustration showing probiotics' potential as a safe ASD symptom treatment

higher concentrations in fecal samples obtained from children with autism compared to those without the condition.⁷⁷ Children diagnosed with autism commonly experience challenges related to feeding, gastric reflux, abdominal discomfort, diarrhea, fecal incontinence, constipation, as well as alternating episodes of diarrhea and constipation and have been observed in approximately one-third of children with autism.^{78,79} Autism has been associated with heightened activation of T cells, elevated levels of immunoglobulins and cytokines, as well as histological irregularities observed in intestinal biopsies. These abnormalities encompass the infiltration of WBCs that are usually composed of granulocytes and non-granulocytes.^{80,81}

“Gut-brain communication” proposes a sophisticated communication network between the stomach and the brain, in which these two organs interact in intricate ways. Within this framework, scientists believe that the GI microbiota, the bacteria residing in the gut, significantly influence the gut-brain axis. Disruptions or dysbiosis in the GI microbiota, along with imbalances, can have detrimental ramifications not only on the gastrointestinal system but also on psychiatric symptoms.⁸² “In recent years, researchers have concentrated their efforts on unraveling the interplay between the gut and brain in the context of ASD, which has been a subject of ongoing debate regarding the complex bidirectional connectivity between the central and enteric nervous systems. As a result, significant breakthroughs have been made, revealing compelling associations between gut bacteria and the development of ASD.³¹

Research has explored the use of dietary exclusions and supplements to manage symptoms of ASD.⁸³ Probiotics have been explored as a potential management strategy for ASD symptoms, with some anecdotal evidence suggesting that they may alleviate GI symptoms and improve behavioral issues in affected children.⁸⁴ A hypothesis has been put forth suggesting that the frequent utilization of oral antibiotics during the formative stages of early childhood, particularly within the

initial 3 years of life, among individuals with autism ASD, could disrupt the delicate equilibrium of gut microorganisms. Nonetheless, it is worth noting that specific antibiotics may offer potential benefits in certain cases.⁸⁵ A fermented dairy item that contains a combination of *L. bulgaricus*, *Bifidobacterium animalis* subsp *lactis*, *L. lactis*, and *S. thermophilus* have been shown to have an impact on brain centres that control emotions and sensations. Additionally, studies have found that *L. plantarum* PS128, among other probiotic species, may have positive effects specifically for children with ASD.

The efficacy of probiotics in restoring a harmonious gut microbiota, thereby alleviating gastrointestinal symptoms, has been substantiated. The efficacy of probiotics hinges on their capacity to withstand the physiological and biochemical milieu of the gastrointestinal tract, encompassing factors such as gastric acidity, competition with resident gut microbes, and the presence of bile secretions.⁸⁶ As per the study findings, aerobic probiotics do not constitute a significant component of the human GI tract microbiome and have a constrained lifespan within the predominantly anaerobic gut environment. Consequently, the effectiveness of orally administered aerobic probiotics is being subjected to scrutiny.⁸⁷ Extensive evidence has demonstrated the diverse array of favorable effects exerted by probiotics, encompassing the production of beneficial acids derivative, antagonistic at receptor sites within the gut, immunostimulatory, and the synthesis of antibacterial compounds possessing distinctive properties.⁸⁶ Oral administration of probiotics during pregnancy has demonstrated the ability to diminish the creation of proinflammatory interleukin in both mother's serum and fetal brains, thereby potentially mitigating autism-related behaviors in children. Moreover, the *L. rhamnosus* GG has been employed in *in-vivo* settings and exhibited anti-inflammatory advantages in children with allergies by elevating IL-10 levels in the bloodstream.⁸⁷ Over a duration of two months, children diagnosed with ASD adhered to a diet devoid of sugar while concurrently consuming probiotic capsules containing

L. acidophilus twice daily. Following an assessment of the behavioral alterations resulting from the probiotic intervention, substantial enhancements were observed in key areas such as concentration and the ability to follow instructions.⁸⁸

The probiotic strain *L. reuteri* has demonstrated the ability to ameliorate social behavioral abnormalities, albeit without significant effects on repetitive behaviors and anxiety in individuals with ASD. This underscores the variation in effects observed among different probiotic strains. Moreover, *L. reuteri* has been found to elevate oxytocin levels in the maternal body, which assumes a pivotal role in the mesolimbic dopamine reward pathway, believed to be dysregulated in individuals with ASD.^{89,90} An investigation conducted by Santocchi *et al.*, children detected with ASD were administered a multispecies probiotic blend comprising, three strains of *Bifidobacterium S. thermophilus DSM 24731*, and four strains of *Lactobacillus*. This study shed new light on clinical and neurophysiological patterns observed in ASD individuals following the administration of this mixture. It's noteworthy that the effects of various probiotic strains can differ significantly. For instance, *L. reuteri* has exhibited the ability to ameliorate while demonstrating limited impact on repetitive habits or anxiety, it has been observed that the intervention effectively addresses social behavioral challenges. Additionally, the intervention has been found to elevate oxytocin levels in the maternal physiology, which constitutes a vital element of the dysregulated mesolimbic dopamine reward pathway implicated in individuals with ASD.⁹¹

CONCLUSION

The human digestive system serves as a habitation to a varied spectrum of microorganisms that together create a distinct microbiome for every person. To assess emerging strains of probiotics, it is essential to establish a clear risk-to-reward ratio and develop fresh methodologies for risk evaluation. Presently, the evidence on modern probiotics is noteworthy for their remarkable safety records. Based on findings, the GI microbiota has emerged as a pivotal player in facilitating two-way communication between the gut and the brain. The multifaceted interplay of direct and indirect pathways, encompassing neuronal, immune-mediated, and neuroendocrine signaling, intricately connects in this scenario. The present review article underscores notable shifts in the microbial makeup within the autistic population, with one prevalent alteration observed in children with autism. ASD is a widespread decline in bacterial diversity. These factors have the potential to influence the entirety of the GI ecosystem and should be taken into account for generalizing the advantages of these “beneficial bugs” in neurodegenerative disorders.

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