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Effects of Probiotics on Cognitive Functions in Autism Spectrum Disorder

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ABSTRACT:
Autism spectrum disorder (ASD) is a multifaceted neurodevelopmental condition marked by restricted and repetitive behaviors, as well as challenges in social communication and engagement. The etiology of ASD is influenced by intricate interactions between genetic and environmental factors. The influence of gut microbiota on ASD and the potential benefits of probiotic supplements have attracted growing attention in recent years. The gut-brain axis is crucial in understanding the impact of gut microbiota on cognitive function. The gut microbiota comprises numerous elements that affect individual health and significantly impact the immune system, metabolism, and neurotransmitter synthesis. Probiotics may enhance cognitive performance and behavioral symptoms by increasing gut health. Research indicates that probiotic administration mitigates gastrointestinal symptoms and diminishes behavioral issues in individuals with ASD. Probiotics have the potential to reduce inflammation by supporting the production of neurotransmitters such as Gamma-Aminobutyric Acid (GABA), serotonin, and dopamine. Probiotics may enhance cognitive performance in persons with ASD by fortifying the intestinal barrier and diminishing intestinal inflammation. The impact of probiotics on cognitive function remains constrained, and the existing findings are preliminary. Consequently, extensive, longitudinal research is required to acquire more conclusive and thorough data in this area. Examining the possible advantages of probiotics in enhancing the quality of life for patients with ASD is essential for formulating treatment methods. The utilization of probiotics is emerging as a potential approach for addressing cognitive and behavioral problems.
Keywords: *Autism; cognitive dysfuncyion; microbiota; probiotics*

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INTRODUCTION

Autism spectrum disorder (ASD) is a multifaceted neurodevelopmental condition marked by impairments in social communication and interaction, alongside restricted and repetitive behaviors, interests, or activities (Critchfield et al., 2011). ASD was initially characterized by American child psychologist Leo Kanner, who proposed that it was an inherent characteristic that constrained the socializing capabilities of 11 children exhibiting distinct behavioral patterns. The disorder, previously known as “early infancy ASD” or “Kanner ASD,” is now categorized under the more inclusive label ASD, indicating the extensive range in symptom severity and presentation (Critchfield et al., 2011; Navarro et al., 2016). The US National Institute of Child Health and Human Development defines ASD as “a complex biological disorder that commences prior to the age of three and results in delays or challenges across various developmental domains” (Dlugosz et al., 2025). Data from the Centers for Disease Control and Prevention indicates that 1 in 36 children aged 8 currently has ASD (Maenner et al., 2023). The incidence of ASD has risen by 150% since 2000 (Baio et al., 2018). The World Health Organization indicated that one in every 160 children with ASD was diagnosed in 2023. A meta-analysis and various regional research has shown that ASD risk rates in

Turkey can vary between 0.8% and 1.0% (Kilicaslan and Tufan, 2022). The frequency of ASD in numerous low- and middle-income nations remains undetermined. The rise in the number of children identified in these nations is posited to contribute to the increased incidence of ASD (World Health Organization, 2024).

Autism affects individuals of all ages, contingent upon severity and cognitive capacity. Both genetic and non-genetic risk factors contribute to the etiology of autism. Factors including prenatal and postnatal exposure to environmental elements and pharmaceuticals, autoimmune disorders, microbial infections, dietary influences, gut dysbiosis, and immunological dysregulation contribute to the development of autism. Recent results indicate that the development and severity of autism are influenced by a complex interplay of genetic predisposition and environmental factors (Critchfield et al., 2011). ASD is a significant area of contemporary research due to its unclear cause and treatment, manifesting in early childhood; nonetheless, many psychotherapeutic and dietary interventions have been identified to alleviate its symptoms (Doenyas, 2018). Dietary intervention in individuals with ASD can have beneficial outcomes for overall health and behavior. In recent years, the significance of gut health in dietary interventions for ASD has garnered attention. In this context, probiotic supplementation has demonstrated beneficial effects in individuals with ASD. This review analyzes probiotic supplementation in autism spectrum disorder, the effects of probiotics on the microbiome, and the influence of probiotics on behavior and cognitive functioning.

Gut-Brain Axis and Gastrointestinal System in Autism Spectrum Disorder

Alterations in the composition and quantity of gut bacteria can result in disorders affecting not only the digestive system but also other body systems; research has demonstrated our current understanding of the influence of gut microbiota on digestive health. The gut microbiota is believed to actively contribute to the genesis of other diseases outside intestinal disorders. Research on neuropsychiatric disorders such as autism, dementia, depression, anxiety disorder, and schizophrenia, which remain incompletely understood, has examined the microbiota-gut-brain axis (Yitik et al., 2019). Autism Spectrum Disorder is defined by enduring challenges in social interaction and communication, accompanied by restricted and repetitive interests and behaviors. The etiopathogenesis of this intricate and diverse illness is linked to early alterations in structural and functional brain development, resulting from interactions among various genetic and environmental factors, many of which are still unexplained. Recent neuroscience research has concentrated on the involvement of the microbiota-brain-gut axis in the etiopathogenesis of neurodevelopmental disorders. The gut microbiota synthesizes neurotransmitters, short-chain fatty acids (SCFAs), vital dietary amino acids, and metabolites. Moreover, the gut microbiota can affect brain function both directly and indirectly by stimulating the immune system via inflammatory cytokines and chemokines, including IL-6 and TNF-α. The gut microbiota affects intestinal barrier permeability, consequently elevating circulating lipopolysaccharide levels. The gut microbiota influences the levels of brain-derived neurotrophic factors, hence altering the functioning of vagal afferents, the enteric nervous system, and neuroendocrine pathways such as the hypothalamic-pituitary-adrenal axis. The brain regulates intestine peristalsis, sensory, and secretory functions through the vagus nerve. Disruptions to the gut microbiota can result in modifications to these pathways, hence facilitating the emergence or phenotypic manifestation of neuropsychiatric and neurodevelopmental diseases (Fattorusso et al., 2019).

Multiple lines of evidence have conceptualized the potential function of gut microbiota in autism. The incidence of gastrointestinal (GI) symptoms is greater in individuals with ASD than in their counterparts. Children with ASD have a notable shift in the stability, variety, composition, and metabolism of the gut microbiota compared to others their age, accompanied by impaired intestinal permeability and systemic and intestinal inflammation (Fattorusso et al., 2019).

Gut and Oral Microbiota in Autism Spectrum Disorder

The microbiota consists of the aggregation of microbial cells within the human body. The gastrointestinal microbiota comprises around 1,000 species. Six bacterial clusters, predominantly Bacteroidetes and Firmicutes, exist within the gut microbiota. Significant bacterial types in the gut microbiota comprise obligate anaerobes, including Bacteroides, Ruminococcus, Eubacterium, Peptococcus, Clostridium, Peptostreptococcus, Bifidobacterium, and Fusobacterium, alongside facultative anaerobes (Tekin et al., 2019). The gut microbiota significantly influences human health, encompassing metabolic functions and immune system effects. Consequently, comprehending the interplay between gut microbiota and the gut-brain axis is believed to facilitate the identification of novel strategies for GI and central nervous system disorders (Fidan and Özkaya, 2024). Dysbiosis emerges when the healthy balance of microorganisms within the gut microbiota is disturbed, leading to a reduction in beneficial bacteria or an augmentation of pathogenic germs. Dysbiosis in the gut microbiota results in negative consequences, including gastrointestinal disorders like Crohn's disease and ulcerative colitis, metabolic abnormalities, and central nervous system disorders. Alongside neurological or mental disorders in individuals with ASD, autistic enterocolitis is linked to severe gastrointestinal distress, including constipation, diarrhea, and bloating. This syndrome is believed to result from microbiota imbalances that disrupt the microbiota-gut-brain axis, contributing to numerous neurological disorders (Shaaban et al., 2018).

Metagenomic investigation of the gut microbiota in patients with autism has revealed mucosal dysbiosis, characterized by reduced levels of Bacteroidetes and elevated Firmicutes. The fecal microbiota of autistic children exhibits elevated levels of Desulfovibrio species and Bacteroides vulgatus in comparison to healthy controls (Adams et al., 2011). A study of the gut microbiota in patients with late-onset autism revealed a significant presence of Clostridium and Ruminococcus species, particularly *Clostridium bolteae* (Song et al., 2004). Research indicates elevated amounts of *Clostridium hystolyticum* in children with autism in comparison to their healthy counterparts, irrespective of culture. The increasing number of neurotoxin-producing bacteria, contributes to autistic symptoms (Parrocho et al., 2005). A further investigation into the gut microbial composition of children with autism demonstrated diminished levels of Bifidobacterium and Enterococcus, alongside elevated levels of Lactobacillus species. Commensal bacteria, which are neither detrimental nor advantageous have been documented in autistic children (Adams et al., 2011). A pilot study conducted by Kang et al. indicated reduced numbers of carbohydrate-fermenting bacteria, including Prevotella, Coprococcus, and Veillonellaceae, in individuals with autism, an association between the gut microbiome and autism. Pyrosequencing results indicated modified gut microbial diversity in autistic children (Kang et al., 2013). Research indicates that the free amino acids and volatile organic chemicals in the feces of autistic children differ from those in non-autistic children (Yap et al., 2010).

In autism spectrum disorders, a complex interplay between dental health and microbiome, along with a significant association between microbial alterations and ASD clinical manifestations, is emphasized. Individuals with ASD have elevated incidences of self-injurious behaviors, sensory hypersensitivity, and dietary selectivity, which lead to the development of oral diseases such as traumatic lesions, gingivitis, enamel hypoplasia, and imbalances in oral microbiota. Dysbiosis of the oral and gut microbiota is believed to significantly influence the neuroinflammatory mechanisms and behavioral abnormalities associated with ASD. Alterations in SCFA levels, including acetate, propionate, and butyrate, may influence the clinical symptoms of ASD by impacting the gut-brain and oral-brain axes. Therapeutic strategies focused on modulating the microbiota, such as probiotic supplements, are believed to enhance dental health and certain behavioral facets of autism spectrum disorder. Nevertheless, further investigation is required to ascertain the enduring efficacy of these techniques. The findings underscore the significance of comprehensive therapy approaches,

encompassing oral health management, nutritional interventions, and microbiota-targeted medications, to enhance the quality of life for individuals with ASD (D'Angelo et al., 2025).

Autism Spectrum Disorder and Probiotics

Probiotics are non-pathogenic bacteria that, when consumed in sufficient quantities as food or supplements, positively influence the host's health. Probiotic products predominantly comprise lactic acid-producing bacteria, including lactobacilli, lactococci, and bifidobacteria, as well as yeasts like *Saccharomyces boulardii*. The health effects of probiotics varies among selected species and individual bacterial strains, influenced by genetic variations and the characteristics of bacterial-host interactions. Probiotics have been utilized safely in the fermentation of food products for decades (Liang et al., 2024). Studies on probiotics have shown the efficacy of probiotic bacteria across various health issues. Gastrointestinal disorders, including antibiotic-associated diarrhea, acute infectious diarrhea, inflammatory bowel disease (IBD), and irritable bowel syndrome (IBS), have demonstrated responsiveness to probiotics. Moreover, probiotics have exhibited efficacy in modulating the host's immune system. Given the growing studies on probiotics and their essential role in overall health, their incorporation as a complementary treatment may be advantageous for children with autism (Ng et al., 2019; Tiwari et al., 2025). Comprehending the complex connections between the gastrointestinal system and the brain in autism spectrum disorders, along with the therapeutic potential of probiotics, presents exciting opportunities for intervention. Enhancements in both behavioral and gastrointestinal symptoms have been noted in children with ASD subsequent to probiotic therapy. Addressing gastrointestinal disorders is essential for addressing behavioral difficulties associated with ASD to enhance the quality of life in children with ASD. In this context, probiotics may restore gut microbiota balance, mitigate gastrointestinal disorders, and enhance neurobehavioral outcomes (Khanna et al., 2025).

Probiotics increase the population of advantageous microorganisms in the gastrointestinal tract. Their advantages include the removal of acids, competition for nutrients and intestine receptor sites, immunomodulation, and the production of particular antibacterial agents. Probiotic supplements have demonstrated efficacy in reducing symptoms of IBS and gastrointestinal illnesses by modulating the gut microbiota. In this context, it is essential to incorporate probiotics into the therapy regimen for patients with ASD who also experience gastrointestinal disorders (Doenyas 2018). Probiotics have demonstrated the ability to stabilize the intestinal barrier, modulate the immune system, diminish intestinal inflammation, and alleviate gastrointestinal symptoms in models of IBD and pediatric IBD patients. Consequently, it is posited that probiotics may mitigate the inflammatory condition and modulate gastrointestinal and behavioral symptoms in autism. Probiotics diminish intestinal barrier permeability, hence alleviating intestinal inflammation as well as inflammation induced by cytokines and other immunomodulatory effects. Literature indicates that probiotics can stimulate the production of pro-inflammatory cytokines to mitigate intestinal inflammation linked to dysbiosis, as well as promote the production of anti-inflammatory cytokines to sustain homeostatic balance by curtailing excessive inflammatory responses (Abdellatif et al., 2020). Wang et al. demonstrated that the administration of oral probiotics during pregnancy mitigated autism-related symptoms in children by suppressing the synthesis of proinflammatory IL-6 and IL-17 in both maternal blood and fetal brains (Wang et al., 2019). Bidirectional connection has been established among the stomach, immune system, and brain. This communication may occur, for instance, via stress, which can induce alterations in the gut microbiota, or directly between the central nervous system and gut microbes. The infusion of propionic acid, a metabolite generated by gut bacteria, has been demonstrated to modify both brain function and behavior in a manner analogous to symptoms linked to autism. Moreover, the administration of specific probiotics may influence brain activity. A probiotic beverage with *Lactobacillus casei* shown beneficial benefits on mood and cognition in participants (Abdellatif et al., 2020). The beneficial effects of

probiotics as a prospective treatment for autism has been investigated in both animal and human model studies. Liu et al. demonstrated that four human-derived probiotic strains of *Lactobacillus reuteri* alleviated lipopolysaccharide-induced intestinal inflammation in newborn Sprague Dawley rats. Moreover, these strains exhibited advantageous effects on lipopolysaccharide-induced inflammation by diminishing intestinal levels of IL-8 and modulating the production of intestinal inflammatory cytokines and chemokines in neonatal rats (Liu et al., 2019). Lipopolysaccharides reduce intestinal barrier integrity and increase intestinal tight junction leakage. Probiotic supplementation mitigates intestinal histological damage induced by lipopolysaccharides, enhances intestinal permeability, and diminishes the translocation of endotoxins and inflammatory cytokines across the intestinal barrier (He et al., 2023). Probiotics, beneficial bacterial supplements, have surfaced as a possible therapeutic approach owing to their capacity to modulate the gut microbiota. Possible processes that contribute to their effects encompass the restoration of microbial balance, modulation of immunological responses, and synthesis of neuroactive chemicals. Probiotics may mitigate gastrointestinal symptoms and enhance behavioral signs in ASD by altering the composition of the gut flora.

Effect of Probiotic Supplementation on Cognitive Function and Behavior in Autism Spectrum Disorder

Probiotic strains include those recently classified as "psychobiotics." The term psychobiotics has been defined as “living organisms that, when taken in adequate doses, confer health benefits on individuals suffering from psychiatric illnesses.” Psychobiotics are characterized as probiotic supplements believed to exert beneficial benefits on mental health through the gut-brain axis. Probiotics are considered an effective therapeutic instrument for modifying brain function by restoring an optimal balance of gut bacteria and regulating tissue neurotransmitter levels. Probiotic bacteria, particularly Lactobacillus and Bifidobacterium species, facilitate the synthesis of neurotransmitters such as GABA, serotonin, and dopamine in the gastrointestinal tract and enhance the creation of SCFAs, so benefiting both gut health and cognitive function (Darwesh et al., 2024). Consequently, it establishes an adequate basis for the application of probiotics in autism, a topic lately explored by numerous preclinical and clinical investigations. Probiotic supplementation in children with autism may enhance gastrointestinal function and fecal microbiota while also mitigating the severity of autism symptoms. Some research have indicated that probiotics may reduce the severity of autistic symptoms as measured by various behavioral assessments (Abdellatif et al., 2020).

Multiple environmental influences, certain food and pharmacological habits, and antibiotic usage can induce detrimental changes in the gut-brain axis and gut microbiota composition, resulting in severe health conditions. Consequently, therapy modalities, including probiotic supplementation, may be regarded as possible interventions for neurobehavioral symptoms and gastrointestinal dysfunction in patients with ASD. Recent research indicates that probiotic intervention may serve as a successful alternative or complementary treatment for children with ASD (Soleimanpour et al., 2024). An essential component of therapeutic methodologies is the formulation and assessment of interventions aimed at enhancing patients of social competencies. Existing options are confined to social skills training methodologies and programs or the implementation of humanoid robotic technologies. Nonetheless, despite these measures, there are no established pharmacological interventions that can enhance the fundamental characteristics of ASD. Nevertheless, research indicates that therapies with sulforaphane, oxytocin, or arginine-vasopressin can enhance patients of general well-being (Canitone 2014). Research utilizing an animal model indicates that the homeostatic balance of the gut microbiota significantly influences social behavior. The probiotic mixture utilized in the study demonstrates the capacity to reinstate identical antisocial behavior in two distinct animal models, each established through separate ways. This study provides preliminary evidence that the gut microbiome, specifically certain bacterial species, may serve as an effective intervention for improving social conduct

and mitigating antisocial behavior associated with ASD (Mintal et al., 2022). Certain maladaptive behaviors may correlate with gastrointestinal issues in individuals with autism. Parrocho et al. conducted a study assessing children who received probiotics vs those who received a placebo, utilizing the Developmental Behavior Checklist to evaluate social issues, disruptive behavior, communication deficits, egocentrism, and anxiety levels. No differences were observed in the median scores for the five subdomains between children receiving placebo and those receiving probiotics; however, the probiotic group exhibited a significant reduction in scores for disruptive/antisocial behavior, communication, anxiety problems, and selfish behavior from baseline (Parrocho et al., 2010).

Recent research indicate that some gut bacteria may influence cognitive networks related to emotional and social domains. The microbiota-gut-brain axis is recognized for its role in modulating brain development, function, and behavior through numerous mechanisms, including immunological, endocrine, and neurological pathways (Roman et al., 2018). Individuals with autism spectrum disorders encounter numerous difficulties in cognitive functioning and behavior. Cognitive and behavioral deficits in ASD may be associated with disruptions in the gut-brain axis and gut dysbiosis. Recent studies on the gut-brain axis have explored the possible advantages of probiotic and prebiotic supplementation. The association between autism and cognitive deficits is elucidated by the disruption of the gut-brain axis, leading to diminished GABA levels, compromised serotonin signaling, and heightened inflammation. Probiotic supplements can directly influence neurotransmission by modulating the synthesis of neurotransmitters like GABA, dopamine, and serotonin, enhancing the intestinal barrier, and mitigating inflammation (Rodnyy et al., 2024). A randomized controlled research shown that a probiotic mixture positively influenced cognitive and linguistic development as well as brain function in children with ASD (Santocchi et al., 2016). Literature indicates that several strains of lactobacilli, including *Lactobacillus paracasei 37*, *Lactobacillus plantarum 128*, *Lactobacillus reuteri DSM 17938*, and *Bifidobacterium longum*, are efficacious in addressing neurodevelopmental disorders in children with ASD and attention deficit hyperactivity disorder (ADHD) (Khanna et al., 2022). In a pilot trial, children diagnosed with ASD and ADHD received supplements of *Lactiplantibacillus plantarum* and *Levilactobacillus brevis* or a placebo over a duration of 12 weeks. The research indicated that probiotics administered to children with ASD and/or ADHD may decrease hyperactivity-impulsivity and improve overall quality of life (Marticella et al., 2025). A separate study involving preschool children with ASD revealed significant enhancements in gastrointestinal symptoms, adaptive functions, and sensory profiles among those receiving probiotic supplementation (Santocchi et al., 2020). A study utilizing an animal model investigated the impact of oral probiotics on the progeny of pregnant mice. Oral probiotic supplementation diminished autism-like symptoms in the offspring. It was also observed to elevate IL-6 and IL-17A levels in both maternal serum and fetal brains, inhibit neuronal loss, and prevent the reduction of GABA levels in the prefrontal cortex of adult offspring. The findings indicate that prenatal probiotic treatment may diminish the risk of autism in offspring without affecting neurophysiology during fetal development (Quing et al., 2025). Probiotic supplementation has demonstrated potential advantages for gastrointestinal and certain behavioral symptoms in patients with ASD. Probiotic supplements may have a positive effect on ASD, especially on gastrointestinal and indirect behavioral symptoms. Although mechanisms are complex, neurotransmitter arrangement (GABA, serotonin levels), brain-induced neurotrophic factor levels, SCFA and metabolite effects, immune regulation, and decrease in neuro-inflammation. The impact of probiotics on cognitive function is yet constrained and reliant on initial findings. Consequently, more extensive research are required to yield more conclusive findings.

CONCLUSION

Probiotic supplementation has considerable advantages for enhancing the microbiota, facilitating the production of vital metabolites that positively influence intestinal permeability, immune response,

and cognitive function. Literature indicates the efficacy of probiotics in the management of ASD. Besides gastrointestinal problems and alterations in microbiota, probiotic treatment has demonstrated encouraging outcomes in cognitive performance and behavioral modifications. The research provided supports probiotic supplementation in alleviating gastrointestinal symptoms, enhancing cognitive performance, and influencing behavioral changes in children with autism. Despite advancements in comprehending and addressing the association between the gut microbiome and autistic symptoms, additional study is essential to endorse and utilize probiotics for the management of these symptoms. The ideal types, strains, and duration of probiotic supplementation must be identified, and more tailored therapies based on individual requirements should be investigated.

Conflict of Interest

The authors declare no conflict of interest.

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