Medicinski podmladak

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Review article

THE ROLE OF GUT MICROBIOME MODULATION IN THE MANAGEMENT OF NEURODEVELOPMENTAL DISORDERS: CURRENT EVIDENCE AND FUTURE DIRECTIONS

ULOGA MODULACIJE CREVNOG MIKROBIOMA U LEČENJU NEURORAZVOJNIH POREMEĆAJA: TRENUTNI DOKAZI I PRAVCI BUDUĆIH ISTRAŽIVANJA

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Abstract

Neurodevelopmental disorders (NDDs), including autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), and other cognitive and behavioral impairments, are increasing globally, placing significant burdens on individuals and healthcare systems. Traditional therapeutic strategies, primarily pharmacologic and behavioral, offer limited efficacy and often fail to address the multifactorial etiology of these conditions. Recent advances in microbiome research highlight the gut microbiota as a potential modulator of brain function via the microbiota-gut-brain axis (MGBA). This bidirectional network influences neurodevelopment through neural, immune, endocrine, and metabolic pathways. Dysbiosis, or microbial imbalance, has been consistently reported in individuals with NDDs, particularly in ASD and ADHD, correlating with symptom severity and gastrointestinal comorbidities. Emerging interventions aimed at restoring microbial balance, such as probiotics, prebiotics, synbiotics, faecal microbiota transplantation (FMT), and dietary modifications – demonstrate potential in modulating behaviour and cognition. However, the current evidence is limited by small sample sizes, heterogeneous methodologies, and a lack of long-term follow-up. This mini-review synthesizes current findings on the role of gut microbiome modulation in NDDs, evaluates the therapeutic efficacy of microbiome-based interventions, and discusses future directions, including personalized microbiome-targeted strategies and the need for robust randomized controlled trials.

Keywords:
neurodevelopmental disorders,
gut microbiome,
dysbiosis,
probiotics,
prebiotics

doi:10.5937/mp76-60614
Editorial board: podmladak.med.bg@gmail.com

Sažetak

Neurorazvojni poremećaji (NRP), uključujući poremećaje iz autističnog spektra (PAS), poremećaj pažnje sa hiperaktivnošću (ADHD) i druge kognitivne i bihevioralne poremećaje, beleže sve veću učestalost širom sveta, predstavljajući značajan teret za porodice i zdravstveni sistem. Tradicionalne terapijske strategije, pretežno farmakološke i bihevioralne, imaju ograničenu efikasnost i često ne rešavaju multifaktorsku etiologiju ovih stanja. Najnovija istraživanja mikrobioma ističu crevnu mikrobiotu kao potencijalni modulator moždane funkcije putem „mikrobiota-creva-mozak" osovine (MCMO). Ova dvosmerna mreža utiče na neurorazvoj kroz neuronske, imunske, endokrine i metaboličke puteve. Disbioza – narušena ravnoteža crevne mikrobiote, primećena je kod osoba sa NRP, naročito kod PAS i ADHD i povezana je sa težinom simptoma i gastrointestinalnim komorbiditetima. Novi terapijski pristupi koji imaju za cilj obnavljanje mikrobiotske ravnoteže, kao što su probiotici, prebiotici, sinbiotici, fekalna transplantacija (FT) i dijetetske modifikacije, pokazuju potencijal u promeni ponašanja i kognicije. Ipak, trenutno raspoloživi dokazi ograničeni su malim uzorcima studija, heterogenim metodologijama i nedostatkom dugoročnog praćenja. Ovaj mini pregled sažima aktuelna saznanja o ulozi modulacije crevnog mikrobioma u NRP, procenjuje terapijsku efikasnost mikrobiomskih intervencija i diskutuje buduće pravce, uključujući personalizovane pristupe zasnovane na mikrobiotskom profilu i potrebu za snažno dizajniranim randomizovanim kontrolisanim studijama.

Ključne reči:
neurorazvojni poremećaji,
crevni mikrobiom,
disbioza,
probiotici,
prebiotici

Introduction

Neurodevelopmental disorders (NDDs) are a group of conditions characterized by impairments in brain development that result in difficulties in personal, academic, or social functioning (1). The most recent edition of the "Diagnostic and Statistical Manual of Mental Disorders" (Fifth Edition, DSM-5) classifies neurodevelopmental disorders NDDs as including autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), intellectual development disorder (ID), specific learning disabilities (e.g., dyslexia, dyscalculia), communication and language disorders, conduct disorders, and motor disorders such as tic disorders (including Tourette syndrome) (1-3). Additionally, conditions like cerebral palsy – categorized under congenital or traumatic brain injury – and Fetal Alcohol Spectrum Disorder (FASD) are recognized within this framework (1-3). Neurogenetic disorders, including Rett syndrome, Down syndrome (Trisomy 21), and fragile X syndrome (FXS), are also considered part of the expanded group of neurodevelopmental disabilities (1-3). The global prevalence of NDDs has increased in recent decades, with ASD now affecting approximately 1 in 36 children aged 8 years in the United States (4). This marks a substantial rise compared to two decades ago. According to the Autism and Developmental Disabilities Monitoring (ADDM) Network, the estimated prevalence of ASD was approximately 1 in 150 in 2000 and approximately 1 in 44 in 2018 (4).

Recent estimates indicate that attention-deficit/hyperactivity disorder (ADHD) affects approximately 2% to 11% of individuals (5,6), tic disorders (TD) range from 0.3% to 1% (7), and autism spectrum disorder (ASD) from 0.7% to 4.3% worldwide (6,8). Beyond their clinical impact, NDDs often necessitate long-term care and support, resulting in substantial individual, familial, and societal burdens, including increased healthcare costs and a reduced quality of life (1,9).

Individuals with NDDs often experience impairments in personal, academic, and social spheres of life (1,9). Core brain functions, including emotional regulation, self-control, learning capacity, memory, intelligence, and social interaction skills, are frequently affected (1,9). While initial symptoms and behavioural challenges typically emerge in early childhood, the full clinical spectrum of NDDs often becomes more evident as the individual develops (10). These developmental deficits are generally persistent and tend to continue across the lifespan (10). Current management of NDDs primarily involves behavioural interventions and pharmacological treatments targeting symptoms such as hyperactivity, distraction, or social communication deficits (11,12). However, these approaches are often insufficient, with many patients experiencing suboptimal responses or adverse effects (12).

The gut microbiome contains 10 - 100 trillion microorganisms – including bacteria, archaea, fungi, and viruses – residing in the gastrointestinal (GI) tract, collectively encoding over 100 times more genes than the human genome (13,14). These microorganisms establish symbiotic relationships with their hosts and are crucial for nutrient metabolism, immune system maturation, and maintenance of gut barrier integrity (15). Of particular interest is the microbiota-gut-brain axis (MGBA), a bidirectional communication network linking the gut microbiome with the central nervous system (CNS) through neural, immune, and endocrine pathways (16).

The MGBA allows the gut microbiota to influence brain development and function through several mechanisms. Microbial metabolites such as short-chain fatty acids (SCFAs), including butyrate and propionate, regulate blood-brain barrier permeability, modulate microglial activation, and affect synaptic plasticity (17,18). Additionally, gut microbes synthesize neurotransmitters

or their precursors (e.g., serotonin, gamma-aminobutyric acid) that can act locally or indirectly influence CNS function via vagal nerve signalling (19,20). Dysbiosis, an imbalance in the composition or function of gut microbiota, has been implicated in the pathogenesis of NDDs by promoting neuroinflammation, altering neurotransmitter systems, and impairing neurodevelopmental processes (20,21).

In humans, several studies have reported different gut microbial profiles in children with NDDs, particularly ASD and ADHD, compared to neurotypical controls (22,23). For example, children with ASD often show decreased microbial diversity and an overrepresentation of particular *Clostridioides*, along with gastrointestinal symptoms such as constipation or diarrhoea (24,25).

These findings have raised interest in microbiome-targeted therapies as potential interventions for NDDs. Probiotics (live microorganisms), prebiotics (nondigestible fibers promoting beneficial bacteria), synbiotics (a combination of probiotics and prebiotics), dietary modifications, and fecal microbiota transplantation (FMT) are being actively investigated (26,27). However, the application of microbiome-based therapies, particularly FMT, in pediatric populations raises important ethical and safety considerations. Potential risks include the transmission of infectious agents, unpredictable immune responses, and alterations in gut microbiota composition with unknown long-term effects. Therefore, strict donor screening procedures, standardized protocols, and close clinical monitoring are essential to ensure safety and minimize adverse outcomes in children undergoing such interventions (21).

Taken together, these studies suggest that the gut microbiome may play an important role in neurodevelopmental health and disease (16-28).

Given the rising prevalence of NDDs and the limitations of existing therapies, gut microbiome modulation represents a promising but still experimental approach. This mini-review aims to gather the current evidence on the role of the gut microbiome in the management of NDDs.

Methods

This mini-review was prepared through a comprehensive literature search using the PubMed, MEDLINE, and Google Scholar databases. The search focused on articles published over the past two decades, with particular emphasis on studies from the last five years, using the keywords: neurodevelopmental disorders (NDDs), autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), gut microbiome, microbiota-gut-brain axis (MGBA), probiotics, and prebiotics. Additional references were identified through manual screening of bibliographies from key articles. Studies were selected based on their relevance to the role of the gut microbiome in the pathophysiology, symptomatology, and potential therapeutic interventions for NDDs.

The gut microbiome and neurodevelopment

The human gut microbiome, a complex community of bacteria, viruses, fungi, and archaea, plays a critical role in neurodevelopment through its influence on the MGBA. This bidirectional communication system connects the gastrointestinal tract with the CNS, integrating neural, endocrine, immune, and metabolic pathways (20,28). Dysregulation of this system during critical periods of brain development has been increasingly implicated in the pathogenesis of NDDs (1).

Colonization of the gut microbiome begins at birth and evolves rapidly during the first three years of life. Factors such as mode of delivery, breastfeeding, antibiotic exposure, and maternal stress significantly influence this process (1,28). Early-life microbial colonization influences the maturation of the immune system, gut barrier integrity, and neurodevelopmental processes, including neurogenesis and myelination (1).

Evidence from germ-free (GF) animal models has shown that the absence of microbiota leads to impaired synaptic formation, hypermyelination, and altered microglial activity, all of which are crucial for normal brain development (1,20). Recolonization of GF animals can partially restore these deficits.

The MGBA operates through three principal pathways:

- **Immune Pathways:** Microbial metabolites, such as short-chain fatty acids (SCFAs), modulate microglial maturation and anti-inflammatory responses in the CNS (20,28). Dysbiosis can promote neuroinflammation through the translocation of bacterial endotoxins, such as lipopolysaccharides (LPS), leading to aberrant microglial activation and cytokine production (3).
- **Neuronal Pathways:** The vagus nerve acts as a direct conduit for gut-derived signals. Animal studies have shown that certain probiotics, such as *Lactobacillus rhamnosus*, can modulate emotional behaviour and GABA receptor expression in a vagus-dependent manner (3,29).
- **Endocrine/Metabolic Pathways:** Gut microbiota influences the hypothalamic-pituitary-adrenal (HPA) axis and produces neuromodulators, including serotonin, dopamine, and GABA. Approximately 90% of peripheral serotonin is synthesized in the gut, and microbial regulation of tryptophan metabolism affects CNS serotonergic signalling (1,20).

Gut dysbiosis in NDDs

Fecal microbiota transplantation from individuals with ADHD into mice has been shown to induce changes in microbial composition accompanied by behavioural and neural alterations, suggesting a possible causal relationship between gut dysbiosis and neurodevelopmental outcomes (3). In children with ASD and ADHD, gut dysbiosis is characterized by decreased microbial diversity and alterations in taxa such as reduced *Bifidobacterium* and increased *Clostridioides* (1,28).

Studies have reported distinct changes in GM composition in ASD. Finegold et al. observed increased GM diversity in children with ASD, with a higher abundance of the Bacteroidota phylum and lower levels of Bacillota (30), whereas Strati et al. reported an elevated Bacillota/Bacteroidota ratio due to reduced Bacteroidota (31). Genera found in increased numbers in ASD fecal samples include *Lactobacillus*, *Desulfovibrio*, *Fusobacterium*, *Faecalibacterium*, *Collinsella*, *Corynebacterium*, and *Oscillospira*, among others. Decreased abundance has been reported for genera such as *Bifidobacterium*, *Akkermansia*, *Roseburia*, *Veillonella*, and *Blautia* (28,32-37). For some genera (*Bacteroides*, *Prevotella*, *Sutterella*), findings have been inconsistent across studies (28). Several taxa, including *Faecalibacterium* and *Oscillospira*, have also been correlated with ASD symptom severity (35,37).

The changes in GM composition are often associated with gastrointestinal symptoms and correlate with neurobehavioral impairments. Furthermore, studies have demonstrated that metabolites produced by gut microbes, including SCFAs and indole derivatives, can influence synaptic plasticity, blood-brain barrier (BBB) integrity, and neuronal development (1,28). In human studies, contrasting findings have been reported regarding SCFA levels, with some studies noting elevated propionate and acetate, and reduced butyrate, while others report lower acetate and butyrate, and higher valerate levels (38,39).

Microbial production of neurotransmitters such as GABA, serotonin, and dopamine has also been implicated in ASD. Altered levels of *Clostridioides* producing neurotoxins have been associated with impaired serotonin signalling, potentially contributing to repetitive behaviours and impaired social interaction (40). Additionally, elevated glutamate and altered p-cresol metabolism have been linked to behavioural and cognitive impairments in ASD (28,41).

Comparative analyses of gut microbiota profiles between children with ADHD and healthy controls reveal distinct dysbiosis patterns, including reduced abundances of *Faecalibacterium* and *Veillonellaceae*, as well as increased levels of *Enterococcus* and *Odoribacter* (42). *Faecalibacterium*, known for its anti-inflammatory properties, is often reduced in inflammatory conditions and may play a protective role in the pathophysiology of ADHD (43). Szopinska-Tokov et al. observed increased *Ruminococcaceae_UGC_004* and reduced beta diversity in adolescents and young adults with ADHD, correlating particularly with inattention symptoms. *Ruminococcaceae_UGC_004* shares genetic sequences with species capable of degrading gamma-aminobutyric acid (GABA), a key inhibitory neurotransmitter (44). Prehn-Kristensen et al. further reported significantly reduced alpha diversity in ADHD patients, which inversely correlated with hyperactivity severity (45). These findings highlight the potential for microbiome modulation as an additional therapeutic strategy in ASD and ADHD (46). The summary of altered gut microbiota is presented in **table 1**. However, confounding variables including diet composition, gastrointestinal symptoms (e.g., constipation), medication use (stimulants, proton-pump inhibitors, or antibiotics), and socioeconomic status likely contribute to these inconsistencies and must be considered when interpreting microbiome–behaviour associations (47,48).

Current evidence for gut microbiome modulation in NDDs

Recent studies highlight the therapeutic potential of targeting the gut microbiome in NDDs through interventions such as probiotics, prebiotics, dietary modifications, and FMT. These approaches aim to restore microbial balance and modulate the MGBA, thereby influencing neurobehavioral outcomes in conditions such as ASD and ADHD (1).

Probiotics, primarily consisting of *Lactobacillus* and *Bifidobacterium* species, support gut health by enhancing microbial diversity and suppressing pathogens (1). Preclinical studies in ASD models demonstrated improved social behaviour following administration of *Lactobacillus reuteri*, potentially via oxytocin-mediated pathways (20). In the case of ADHD probiotics, primarily *Lactobacillus* and *Bifidobacterium* species, health benefits may be observed when administered in adequate amounts (49,50).

A systematic review of randomized controlled trials (RCTs) evaluating probiotics in children and adolescents found limited evidence, with only one study reporting significant reductions in ADHD and ASD risk (51). In this Finnish RCT, Pärtty et al. evaluated perinatal supplementation with *Lactobacillus rhamnosus* GG. The study included 159 infants, whose mothers were recruited from antenatal clinics and randomized to receive *Lactobacillus rhamnosus* GG or placebo, starting four weeks before delivery and continuing for six months postpartum (52). At 13-year

Table 1. Altered gut microbial taxa in neurodevelopmental disorders

Condition	Increased	Decreased
ASD	Bacteroidota phylum, *Lactobacillus*, *Desulfovibrio*, *Fusobacterium*, *Fecalibacterium*, *Collinsella*, *Corynebacterium*, *Oscillospira*, *Clostridioides* (*C. clostridioforme, C. neonatale, C.difficile, C. bolteae*), *Entrrococcus*, *Odoribacter*, *Ruminococcaceae*, *Bacteroides plebeius*	Bacillota phylum, *Bifidobacterium spp.* (*B. breve, B. bifidum, B. longum*), *Akkermansia*, *Roseburia*, *Blautia*
ADHD	*Enterococcus*, *Bacteroides caccae*, *Odoribacter splanchnicus*, *Paraprevotella xylaniphila*, *Veillonella parvula*	*Faecalibacterium* (*F. prausnitzii*), *Lachnospiraceae bacterium*, *Ruminococcus*

Data summarized in this table are synthesized from previously published studies (31-36,42)

follow-up, none of the children in the probiotic group developed ADHD or ASD, compared with 17.1% in the placebo group (p = 0.008). Lower *Bifidobacterium* levels were observed in children later diagnosed with NDDs, showing significantly lower median numbers of *Bifidobacterium longum* at three months, and reduced total *Bifidobacterium* counts at six months. However, high dropout rates and lack of data on maternal diet and other risk factors limit these findings (52).

Other trials in children and adolescents with ADHD showed mixed results. Kumperscak et al. reported an improvement in self-reported quality of life after three months of *Lactobacillus rhamnosus* supplementation but no consistent changes in ADHD symptoms or cytokine profiles (54). Similarly, Skott et al. evaluated a synbiotic (probiotics + prebiotics) over nine weeks and observed no significant effects on ADHD symptoms, with only a trend towards reduced autistic symptoms in specific subgroups (54).

An observational study in 2,467 very low birth weight infants receiving *Bifidobacterium infantis* and *Lactobacillus acidophilus* found no association between neonatal probiotic use and neurocognitive outcomes at 5 - 6 years. However, prolonged breastfeeding for at least three months correlated with a lower risk for inattention/hyperactivity and conduct disorders (55).

Prebiotics, such as galactooligosaccharides, also show potential. A six-week intervention in 30 children with ASD demonstrated improvements in anxiety and social behaviour (20). However, larger, placebo-controlled trials are needed to confirm these findings.

Fecal microbiota transplantation could also have influenced the severity of NDDs (56). In an open-label clinical trial, Kang et al. administered daily FMT to 18 young patients with ASD over two months. Improvements were observed in both GI and behavioural symptoms, with these benefits persisting for up to 24 months post-treatment (57). However, the absence of a placebo group limits the interpretation of these findings.

Dietary patterns are among the most potent environmental factors shaping gut microbiota composition and function. Nutritional interventions, such as high-fiber and plant-based diets, promote beneficial bacterial populations and increase SCFA production (58). Physical activity has also been shown to enhance microbial diversity, improve the Bacillota/Bacteroidota ratio, and increase SCFA production (59). Western diets, characterized by high levels of saturated fats, refined sugars, and low fiber content, have been consistently associated with reduced microbial diversity, diminished populations of beneficial bacteria, and an increased prevalence of pro-inflammatory groups (26, 29).

Gluten-Free and Casein-Free (GFCF) diets are widely adopted among families of children with ASD, largely due to reports of improved behavioural and gastrointestinal symptoms. Several small-scale studies suggest potential benefits in reducing social withdrawal, improving language skills, and alleviating GI disturbances (26). These effects are hypothesized to result from reduced gut inflammation and changes in microbial composition, as gluten and casein-derived peptides may influence gut-brain signalling. However, methodological weaknesses – such as small sample sizes, lack of placebo controls, and variability in study duration – limit the strength of evidence. Additionally, concerns about possible nutritional deficiencies and the reduction of microbiota-accessible carbohydrates highlight the need for careful monitoring when implementing long-term GFCF diets (59).

Ketogenic diets (high-fat, very low-carbohydrate), developed initially as a treatment for refractory epilepsy, have shown potential in modulating behavioural symptoms in ASD and other NDDs. Preclinical studies indicate that ketogenic diets may alter the gut microbiota by increasing the abundance of anti-inflammatory taxa, reducing oxidative stress, and enhancing mitochondrial function (26). These changes could support neuroprotection and modulate MGBA signalling. Despite these potential benefits, adverse effects such as constipation, nutrient deficiencies, and metabolic disturbances limit their widespread use, particularly in paediatric populations (26). More controlled trials are needed to assess their efficacy and safety in the context of NDDs.

Mediterranean and fiber-rich diets, rich in fruits, vegetables, legumes, whole grains, olive oil, and polyphenol-rich foods, promote a diverse and stable gut microbiome. It has been associated with increased levels of SCFA-producing bacteria such as *Roseburia* and *Faecalibacterium*, which support gut barrier integrity and modulate systemic inflammation (14, 29). Preliminary evidence from studies in neuropsychiatric populations suggests cognitive and emotional benefits, likely mediated through MGBA pathways. Fiber-rich diets provide substrates for microbial fermentation, resulting in the production of SCFAs and the regulation of microglial activity. Although promising, clinical studies specifically targeting NDD populations are limited, and further research is necessary to establish clear dietary recommendations (29).

While broad-spectrum antibiotics are widely used to suppress pathogenic bacteria, they often have harmful effects on the gut microbiota, including reduced SCFA-producing bacteria and increased potential pathogens. These changes have been associated with negative health outcomes, such as *Clostridioides difficile* infections and links to neurodegenerative and neurodevelopmental disorders (60). Early-life antibiotic exposure can have lasting effects on neurodevelopment and behaviour by disrupting the gut microbiota (61). In mice, targeted microbiota depletion during postnatal, pre-weaning, or weaning periods induced enduring changes, particularly during weaning, in caecal microbiome composition, circulating immune cells, and neurophysiology, including myelin-related gene expression in the prefrontal cortex and microglial morphology in the amygdala (61). These disruptions also produced sex- and time-dependent effects on anxiety-like behaviour, while social behaviour, depressive-like behaviour, and memory remained largely unaffected, underscoring the long-term impact of microbiota perturbations during

critical developmental windows (61). However, certain antibiotics may support microbiome health. For example, nitrofurantoin has been shown to increase beneficial genera like *Bifidobacterium* and *Faecalibacterium* (62). Rifaximin modulates gut inflammation, improves barrier integrity, and improves microbial diversity by increasing *Bifidobacterium*, *Lactobacillus*, and *Faecalibacterium* (63). Initially used for traveller's diarrhoea, Rifaximin is now the treatment of choice for small intestinal bacterial overgrowth (SIBO) and has shown benefits in inflammatory bowel diseases and preliminary studies in PD and AD models (64, 65). Vancomycin, a narrow-spectrum antibiotic targeting Gram-positive bacteria, has also demonstrated effects on the gut microbiota, increasing *Akkermansia* and improving metabolic outcomes in animal models. In ASD, vancomycin temporarily improved symptoms (29).

Despite the valuable insights provided by existing studies, several limitations should be acknowledged. Many studies have used relatively small sample sizes, heterogeneous populations, and short intervention durations, which may compromise the robustness and generalizability of the findings. These limitations may affect data interpretation and the formulation of future research directions. In future research, the standardization of study protocols and outcome measures will be essential to ensure comparability and reproducibility across studies. Moreover, long-term clinical follow-up is needed to provide reliable evidence that can inform clinical practice and improve patient outcomes.

Future directions

Clinical implementation of microbiome-based therapies requires well-designed, randomized controlled trials (RCTs) to evaluate the efficacy, effectiveness, and safety of interventions such as probiotics, prebiotics, synbiotics, FMT, and others. Given the heterogeneity of NDDs and inter-individual variability in microbiota composition, larger patient cohorts and stratification of study participants based on microbial profiles are needed to improve the accuracy and generalizability of findings. Future research should prioritize personalized treatment approaches tailored to individual microbiota profiles. Mechanistic studies are needed to clarify how specific microbial taxa and metabolites influence brain development, neuroinflammation, and behavior, thereby establishing causal links. Moreover, long-term follow-up is essential to assess the sustainability of therapeutic effects and monitor for potential adverse outcomes. Finally, these combined efforts should culminate in the development of evidence-based guidelines for a gut microbiome modulation therapy.

Conclusion

The gut microbiome has emerged as an important factor in the pathophysiology and potential treatment of neurodevelopmental disorders. Through complex interactions within the microbiota-gut-brain axis, alterations in microbial composition and function can influence neurodevelopmental processes, immune regulation, and neurotransmitter systems. Current evidence from preclinical and clinical studies suggests that interventions targeting the gut microbiota – such as probiotics, prebiotics, synbiotics, dietary modifications, and fecal microbiota transplantation – may offer promising strategies for managing conditions like ASD and ADHD. However, the field remains in its early stages, and causal relationships have not yet been established. The heterogeneity of study populations, methodological inconsistencies, and limited long-term data underscore the need for well-designed, large-scale randomized controlled trials. With a growing understanding of the gut–brain connection, microbiome modulation may become an integral part of neurodevelopmental care.

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