Vol. 4 No. 4 (2025)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Noorulain et al., 2025

Interactions between the Intestinal Microenvironment and Neurodevelopment in Children: Current Evidence and Future Directions

Noorulain Hyder*
Department of Pharmacology, Faculty of Pharmacy, Hamdard University, Karachi-74600, Pakistan. Corresponding Author Email: dr.noorulain@hamdard.edu.pk
ORCID: https://orcid.org/0000-0002-7919-7859
Ale Zehra
Department of Pharmacy Practice, Faculty of Pharmaceutical sciences, Dow college of Pharmacy, DUHS, Karachi-74200, Pakistan. Email: ale.zehra@duhs.edu.pk
Syed Shaukat Ali Muttaqi Shah
College of Pharmacy, Al-Farahidi University, Baghdad, Iraq.
Email: syedshaukatali@uoalfarhidi.edu.iq
Israr Ali Soomro
Department of Pharmacology, Faculty of Pharmacy, Hamdard University, Karachi-74600, Pakistan. Email: israr3424@gmail.com
Kiran Rano Khan Solangi
Department of Pharmacology, Faculty of Pharmacy, Hamdard University, Karachi-74600, Pakistan. Email: kirankhan9122@gmail.com

Author Details

Received on 12 Nov, 2025
Accepted on 06 Dec, 2025
Published on 08Dec, 2025

Corresponding E-mail & Authors*:
Noorulain Hyder
dr.noorulain@hamdard.edu.pk

Abstract

Neurodevelopmental disorders in children are increasing as a public health issue in the world. Over the past few years, the contribution of intestinal microenvironment to neurodevelopment outcomes has become the focus of growing interest. Recent findings point to the fact that the gut and the nervous system are bidirectionally communicating at an early age, and this is the genesis of the microbiota-gut-brain axis. This review is a summary of the existing information on the role of changes in the intestinal microenvironment in the pathogenesis of neurodevelopmental disorders in children and the underlying biological

mechanisms of immune regulation, microbial metabolite signaling, neuroinflammation, and neural pathway interaction. It also addresses the progress in clinical assessment tools, diagnostic signs, and specific intervention techniques- such as dietary adjustment, microbiota-based therapy, and combined behavioral therapies. Lastly, the review provides future research priorities, including the necessity to explore further the mechanistic aspects of childhood neurodevelopmental disorders, develop therapeutic tools with a lot of precision, and increase collaborative efforts among multidisciplinary teams to facilitate innovative approaches to preventive and therapeutic interventions in the medical field.

Keywords: Gut Microbiota; Children; Neurodevelopmental Disorders; Fecal Microbiota Transplantation; Microbiota-Gut-Brain Axis; Probiotics; Immune Dysregulation; Dysbiosis.

Introduction

Neurodevelopmental disorders are a group of chronic developmental brain dysfunction caused by a variety of genetic or acquired causes, usually seen in early childhood or adolescence, including autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD) and tic disorder (TD). These diseases seriously affect the physical and mental health and future development of children, and bring heavy burden to families and society. With the continuous deepening of medical research, the role of the intestinal microenvironment in children's neurodevelopment has received increasing attention. A large number of studies have shown that there is a close relationship between the imbalance of the intestinal microenvironment and the neurodevelopmental disorders in children. Understanding the mechanism of this association is of great significance for elucidating the etiology and developing early diagnostic methods and intervention measures. However, research in this field is still in the exploratory stage,

and many key issues remain to be clarified. This article reviews the complex relationship between the intestinal microenvironment and neurodevelopmental disorders, analyzes the shortcomings of current research, and looks forward to the future research direction, in order to provide reference for promoting the development of this field and the prevention and treatment of neurodevelopmental disorders in children.

1. The Concept of the Microbiome-Gut-Brain Axis (MGBA)

Although the concept of MGBA is relatively new, the idea that there is a connection between the brain and the gut has been around for a long time. As early as the ancient Greek period, philosophers such as Hippocrates had already proposed the importance of the intestine in health. In the 1840s, William Beaumont proved thru experiments that emotions can affect the digestive process, providing early evidence for later research on the brain-gut relationship. However, due to technical limitations, early research on the interaction between intestinal physiology and psychological function progressed slowly. In the mid-20th century, the development of Pavlov's pouch associated intestinal physiological changes with emotional changes, laying an important foundation for understanding the key role of the gut-brain axis. Since the advent of brain imaging technology in 1980, scholars have gradually realized the bidirectional nature of the gut-brain axis. As research continues to deepen, the key influence of the intestinal microbiota on the gut-brain axis is becoming increasingly prominent. In recent years, with the development of second-generation sequencing technology and big data research, scholars have deepened their understanding of microbial communities, and the intestinal microbial community has been identified as an important participant in the gut-brain communication, thus formally proposing the concept of MGBA. The gut

microbiota communicates with the brain *via* the vagus nerve, immune system, and metabolites **(Figure 1)**.

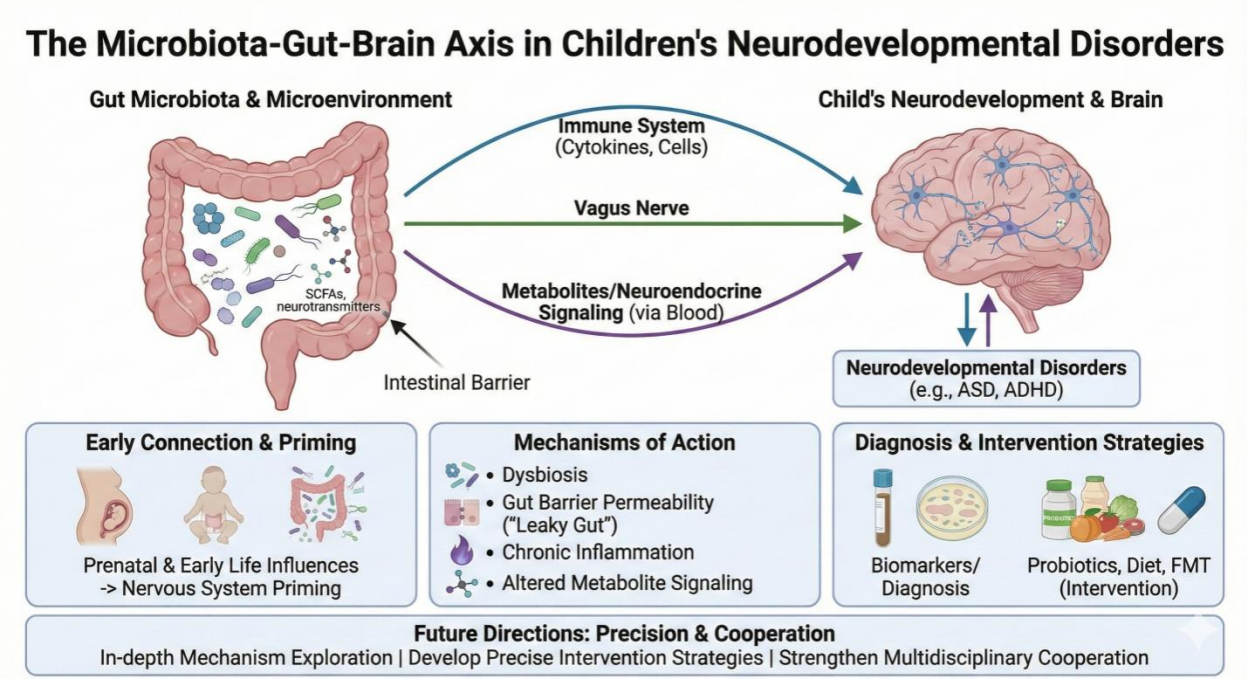

Figure 1 illustrates the bidirectional relationship between the intestinal microenvironment and children's neurodevelopmental disorders, highlighting the key pathways of the microbiota-gut-brain axis including immune, neural, and metabolic signaling.

2 . Early Connection between Intestinal Microenvironment and Nervous System

2.1 Establishment of nervous system More and more evidence shows that there is a two-way communication between the intestinal microbiome and the central nervous system, which is called MGBA. Studies have found that germ-free (GF) mice exposed to the gut microbiome early in life and specific pathogen-free (SPF) mice with normal gut microbiota exhibit similar characteristics, such as reduced expression of PSD-95 and synapsin in the striatum, indicating that the microbial colonization process initiates

signaling mechanisms that affect neuronal circuits involved in motor control and anxiety behavior. Emotional states can influence the signals produced by the gut and its microbiota, which in turn can feed back to the brain, further exacerbating and prolonging the emotional state. Preclinical studies have demonstrated that the gut microbiome plays a complex role in social behavior, depression-like behavior, physical performance, and motivation regulation. However, these studies are mainly based on simplified animal models, which are not sufficient to clarify the potential mechanism of action. Therefore, research in this field is still in its infancy. **Table 1** gives details gut brain axis and the role of neurodevelopment.

2.2 Development of the Gut Microbiota

The existence of a fetal gut microbiome has been a matter of debate. Studies on human and mouse models have not yet provided sufficient evidence that the fetal intestine contains flora. The fetal intestine is relatively sterile in utero, but it is rapidly colonized after birth. The initial colonization of microorganisms, most of which come from the maternal skin, oral cavity and vaginal microbial community. The composition of the microbiota in the feces of the mother and the infant overlaps by as much as 72% within 2 to 5 days after the infant is born, and most of the non-maternal-derived microorganisms in the infant's intestinal microbiota gradually disappear when the infant is 4 months old]. Studies have shown that strains derived from the maternal gut are more likely to be persistent colonizers of the infant gut microbiome than strains derived from the environment. Human milk oligosaccharides (HMOs) are the third most abundant component of human milk after lactose and lipids, and are not absorbed in the upper digestive tract of infants due to the lack of glycoside hydrolases and intestinal membrane transporters. Different microbial taxa in the gut microbiota have a wide

range of HMO digestive enzymes, and among the first colonizers of the infant gut, *Bifidobacterium* (especially *Bifidobacterium bifidum*, *Bifidobacterium breve*, and *Bifidobacterium longum* strains) can secrete corresponding hydrolases and intestinal membrane transporters. It is speculated that the mother may transmit microorganisms to the infant's intestine thru breast milk. **Table 1** gives details mechanisms involved in intestinal brain axis and the implications in neurodevelopment disorders.

Table 1: *Mechanisms Linking Gut Microenvironment to Neurodevelopmental Disorders*

Mechanism	Evidence Summary	Implications in Disorders
Microbial Dysbiosis	Altered diversity seen in ASD, ADHD	Affects neurotransmitter balance and metabolism
Metabolite Production (SCFAs, tryptophan metabolites)	SCFAs influence microglia maturation	Imbalances associated with behavioral changes
Neuroinflammation	Elevated pro-inflammatory cytokines in affected children	Contributes to altered synaptic pruning and connectivity
Vagus Nerve Signaling	Microbial metabolites modulate vagal tone	Impacts social behavior and stress regulation
HPA Axis Dysregulation	Stress increases intestinal permeability	Linked to anxiety-like and hyperactive behaviors

2.3 Establishment of the Immune System

The presence of intestinal microorganisms activates the fetal immune system, which has a profound impact on the health of the newborn [1]. MCGOVERN N et al. believe that the maternal microbiome begins to shape the fetal immune system in early pregnancy

and may have long-term effects on immune homeostasis. RACKAITYTE E et al. [12] pointed out that the growth of fetal immune cells and nerve cells began in the uterus and was affected by the maternal microbiome. In addition, recent studies [3] have shown that, in addition to nutrients, microbial metabolites can also cross the placenta and trigger immunogenic reactions. It is speculated that the maternal intestinal flora may indirectly promote fetal immune development thru its derived metabolites across the placenta.

2.4 Nutritional Support

Nutritional support is essential for early neurodevelopment and has a lasting and irreversible impact on an individual's cognitive development and mental health. As infants transition from exclusive breastfeeding or formula feeding to complementary solid foods, their gut microenvironment is gradually established and matured, and the composition of the gut microbiota presents a more stable adult-like phenotype by the age of 3 years [15]. After the microorganisms colonize in the infant's gastrointestinal tract, they can synthesize some amino acids and vitamins. In addition, the intestine absorbs a large number of nutrients in the early stage, such as minerals and fatty acids. These nutrients are essential for the development of the nervous system, and their sufficient supply can directly affect the growth, differentiation and formation of neuronal synapses of nerve cells [4].

3. The role of Intestinal Microenvironment in Children's Neurodevelopmental Disorders

3.1 Immune Regulation Imbalance: In neurodevelopmental disorders, one of the key factors affecting the dynamics of the microbiota and the integrity of the nervous system is the abnormal activity of the immune system and the local or systemic inflammation it causes. Gastrointestinal microorganisms can regulate the immune system and intestinal

epithelial cells, and transmit inflammatory or anti-inflammatory signals to the intestinal nervous system, thereby affecting the central nervous system [1]. AHRENS AP et al. [17] believe that the inflammatory process mediated by intestinal bacteria may increase the risk of neurodevelopmental disorders in early life, and there is a close relationship between neurodevelopment, intestinal barrier function and the immune system. Under physiological symbiotic conditions, immune cells in the gut-associated lymphoid tissue differentiate into anti-inflammatory regulatory T cells, producing anti-inflammatory cytokines such as interleukin (IL)-10 and transforming growth factor (TGF)-ß. During dysbiosis, lymphocytes differentiate into Th1/Th17 subtypes, promoting the production of pro-inflammatory cytokines such as IL-2, IL-12 and tumor necrosis factor (TF)-α [18]. In addition, lipopolysaccharide (LPS) can induce inflammatory cascade reactions thru the Toll-like receptor 4 (TLR4) signaling pathway, activate factor kB (NF-kB), promote the release of pro-inflammatory cytokines (such as TNF-α, IL-1ß and IL-6), and then directly affect brain function thru changes in the permeability of the blood-brain barrier or the transmission of pathogenic signals of the vagus nerve. The inflammatory process caused by this will damage oligodendrocytes, which is crucial for early brain development. The negative impact of intestinal inflammation on neurodevelopment has been confirmed during pregnancy and postpartum. A prospective follow-up study of 422 mother-infant pairs in Bangladesh found that serum inflammatory biomarkers C-reactive protein (CRP), soluble leukocyte differentiation antigen 14 (sCD14), IL-1ß and IL-6 were negatively correlated with neurodevelopmental outcomes.

Therefore, the immune imbalance mediated by intestinal microorganisms plays a key role in children's neurodevelopmental disorders, which may interfere with the normal development process of the nervous system, and then affect the development of

children's cognitive, social, behavioral and other aspects of ability. **Table 2** gives details gut brain axis component and the role in neurodevelopment.

Table 2: *Key Components of the Microbiota–Gut–Brain Axis in Children*

Component	Description	Role in Neurodevelopment
Intestinal Microbiota	Bacteria, viruses, fungi inhabiting the gut	Modulate immune response, produce neurotransmitters and metabolites
Gut Barrier	Intestinal epithelial lining and tight junctions	Maintains barrier integrity; dysfunction may lead to systemic inflammation
Immune System	Gut-associated lymphoid tissue (GALT)	Influences brain development *via* cytokine signaling
Neuroendocrine System	HPA axis, enteroendocrine cells	Regulates stress response; impacts neuronal maturation
Neural Pathways	Vagus nerve, ENS	Bidirectional communication between gut and brain

3.2 Impaired Intestinal Barrier Function: The intestinal barrier is composed of intestinal flora, mucosal layer, intestinal epithelial cells, blood vessels and lymphatic system [20]. By maintaining the dynamic balance between the charge of intestinal antigen and the complex structure of intestinal mucosa, it becomes the first line of defense for the human body to resist harmful substances, immunogenicity and pro-inflammatory substances. Its impaired function may promote the abnormal transport of bacteria and antigens, thus inducing diseases. Propionic acid, as a short-chain fatty acid, is an important intermediate product of cell metabolism and a metabolite of human intestinal flora, which plays an important role in organisms. MACFABE D F et al. [21] conducted an intra-cerebroventricular infusion of propionic acid in 15 adult rats, of which 14 rats

showed a series of abnormal behavioral responses, including repetitive dystonia behavior, hyperactivity, turning behavior, and marginal seizures, and other ASD-related symptoms. MARUNGRUANG N et al. [22] found that the intestinal barrier function of newborn rats was prematurely matured after food induction, leading to systemic inflammation and changing the utilization of short-chain fatty acids in the brain. It is speculated that such a mechanism may also exist in the neonatal intestinal barrier-blood-brain barrier dysfunction. To clarify the relationship between intestinal permeability and developmental behavior, TES-KEY G et al. [23] used intestinal fatty acid binding protein as a marker of intestinal permeability in children with ASD. The level of the protein, a biomarker of intestinal epithelial damage in children's plasma, was found to be positively correlated with the severity of communication barriers, social interaction defects and maladaptive behaviors. Therefore, maintaining an intact intestinal barrier helps to reduce neuroinflammatory responses and avoid adverse neurodevelopmental outcomes.

3.3 Dysbiosis

Dysbiosis of the gut microbiota is common in early life, which may interfere with the synthesis, release or metabolism of neurotransmitters, thus affecting the normal function of the nervous system and having adverse effects on children's cognition, emotion and behavior. Animal studies24 have shown that early use of broad-spectrum antibiotics can have long-term negative effects on the structure and function of the gut microbiome, especially during weaning (12-18 days after birth). Antibiotic exposure can lead to changes in the morphology of microglia and the expression of myelin-related genes in adolescent mice, accompanied by anxiety-like and compulsive behaviors. Notably, among neurons and glial cells, microglia are the most susceptible to changes in

the gut microbiome. Another study [25] found that the depletion of umbilical cord serum triglycerides (TG) in infants who would later develop ASD was associated with a decrease in the abundance of Bifidobacterium at 1 year of age.

3.4 Abnormal Metabolites

The gut microbiota produces a variety of metabolites thru bacterial metabolism and modifies host-derived molecules, such as short-chain fatty acids (including butyrate, acetate and propionate), tryptophan metabolites (such as indole) and bile acids. Short-chain fatty acids are associated with human physiological processes, including immune homeostasis, intestinal homeostasis, cholesterol metabolism, glucose metabolism, and energy balance, and help maintain and regulate the integrity of the intestine and the blood-brain barrier [2]. Short-chain fatty acids can directly affect the brain, change the permeability of the blood-brain barrier, or bind to local receptors to induce epigenetic modifications, thereby regulating brain homeostasis and neuroinflammation [26]. For example, butyrate has a direct anti-inflammatory effect on oligodendrocytes, which are essential for early brain development. Indole, a tryptophan derivative, has positive effects on neuroinflammation, neural signaling, and gut and blood-brain barrier integrity. Bile acids, on the other hand, can act on the brain and the pituitary-hypothalamic-adrenal axis thru specific local receptors [28]. In addition, peptidoglycan (PGN) produced by microorganisms also plays an important role. An animal study [2] found that the increase in PGN levels in the brain was synchronized with the increase in bacterial colonization after birth, further confirming the role of the microbiome in early neurodevelopment.

3.5. Diet and Nutrition

Disruption of the intestinal microenvironment may affect the absorption of nutrients that are essential for neurodevelopment (including vitamins, minerals, essential fatty acids, and amino acids), which in turn affects the growth, differentiation, and synapse formation of nerve cells, leading to delayed neurodevelopment. YAP C X et al. [30] conducted a large-scale metagenomic study of ASD feces and found that Now, the dietary diversity of ASD subjects is reduced, suggesting that their food quality is low, which may be related to the reduction of meat intake. This dietary imbalance, especially during childhood development, can significantly affect the quality and quantity of nutrient intake. For example, reduced lipid intake can lead to reduced production of bioactive lipid molecules, which are important mediators of brain signaling pathways3]. THAPA S et al. [32] found that the increase in solid food intake increased the diversity of intestinal bacteria in Rett syndrome (RETT) subjects compared with formula feeding alone. The functional link between diet and microbiome needs further exploration, which can provide scientific basis for the formulation of nutritional intervention strategies based on the microbiome-gut ecosystem.

3.6. Epigenetic Modification

Epigenetic modification enables mammalian cells to regulate gene expression without changing the genetic code, and is one of the important mechanisms for mammalian cells to adapt to environmental changes [33]. Gut microbes and their metabolites may affect the host's epigenetic modifications, such as DNA methylation, histone modification and non-coding RNA regulation, to change the expression of genes related to neural development, and then affect the process of neural development. DNA methylation can regulate gene expression, histone modification can change chromatin structure and

regulate gene transcription, and non-coding RNA plays an important role in chromatin remodeling, transcription and post-transcriptional regulation of gene expression. The gut microbiota interacts with epigenetic modifications to jointly affect important gene expression regions, including immune response, metabolic activity and nervous system development [4]. For example, short-chain fatty acids, as by-products of bacterial fermentation of dietary fiber, interact with the host by regulating epigenetic states (such as acetylation-modified histones and adjusting DNA methylation patterns), ultimately leading to changes in gene expression phenotypes. In addition, metabolic activity can also regulate the chromatin structure in the host brain, promote neuronal transcription and subsequent behavioral changes. The gut microbiota can affect the expression of small interfering RNAs (siRNAs) in the gut and brain, influencing host transcriptional reprogramming and increasing the likelihood of RNA or by-products of microbial origin communicating with somatic cells [36]. A study [37] showed that the microbiota affects the transcription of microRNAs (miRNAs) in the amygdala and prefrontal cortex of mice, especially miR-183-5p and miR-182-5p, because they are involved in stress and fear-related responses. Therefore, gut microbiota-mediated epigenetic modifications may have a profound impact on host neurodevelopment.

4. Clinical Diagnosis and Intervention Strategies

4.1. Diagnostic Methods based on the Intestinal MICROENVIRONMENT

4.1.1 Microbial community analysis: A large number of previous animal studies have focused on microbial populations in healthy and diseased states, aiming to explore possible intervention pathways. A large-scale prospective longitudinal study of infants and young children [17] found that by analyzing a single flora and a the same core flora can distinguish children who may suffer from neurodevelopmental disorders in the

future, suggesting that the infant gut flora is strongly correlated with the diagnosis of early neurodevelopmental disorders. In addition, the association between specific flora changes and diseases can be clarified by comparing the composition and diversity of intestinal microbial communities in children with neurodevelopmental delay and normal children thru gene sequencing and other technologies of fecal samples. Most microbiome studies use 16S ribosomal RNA (rRNA) gene amplicon sequencing technology, which can describe the characteristics of microbial communities in detail [38]. In recent years, shotgun metagenomic sequencing (sequencing of all DNA in a sample) has been increasingly used in human microbiome studies because it can provide in-depth and high-resolution genomic characteristics of microbial populations [39]. Table 3 gives details of Clinical Diagnosis and Intervention Strategies

Table 3: *Clinical Diagnosis and Intervention Strategies*

Domain	Approaches	Clinical Notes
Diagnostic Tools	Stool microbiome sequencing, inflammatory markers, behavioral assessments	Useful for early identification of dysbiosis-related patterns
Dietary Interventions	Probiotics, prebiotics, high-fiber diets, elimination diets	Show promise; effectiveness varies among individuals
Pharmacological Approaches	Anti-inflammatory agents, metabolic modulators	Experimental; still under research
Behavioral / Psychosocial Therapies	ABA therapy, parent training, cognitive training	More effective when combined with gut-targeted strategies

Future Strategies	Microbiota-based therapies (FMT), personalized nutrition	Require large-scale trials for pediatric populations

4.1.2 Metabolite Detection

The levels of short-chain fatty acids, bile acids and other intestinal microbial metabolites in children's stool samples and blood samples were analyzed to assess their correlation with neurodevelopmental indicators. For example, in children with ASD, the redox balance between reduced glutathione and oxidized glutathione is disrupted [4]. In addition, some metabolites have similar structures to neurotransmitters, and their abnormal proportions may directly affect the function of the nervous system. For example, an increase in the ratio of glutamate to y-aminobutyric acid (GABA) is one of the characteristics of sensory processing-related neuroinflammation. It has been reported that the ratio of these two key neurotransmitters in blood samples of children with ASD is different from that of children with TD [40]. When intestinal inflammation occurs, immune cells release inflammatory factors, which destroy the mucosal barrier, leading to increased intestinal permeability, making it easier for bacterial toxins to enter the body, and activating microglia to cause neuroinflammation, which in turn damages neurons and affects neurotransmitters, interfering with nerve signal transduction. In addition, the detection of the ratio of lactulose to mannitol and the level of tight junction protein helps to understand the relationship between the intestinal barrier and nerve development. Under normal circumstances, mannitol is easily absorbed, while lactulose is absorbed less. When the intestinal barrier is damaged, the absorption of lactulose increases, and the ratio increases, indicating that the intestinal permeability increases and the barrier function is damaged. Tight junction proteins play a key role in

maintaining the tight junctions of intestinal epithelial cells, and their decreased expression can lead to weakened barrier function and increased permeability.

4.2. Interventions

4.2.1. Early Intervention: According to statistics, about 20% of developmental delays originate in the fetal period, so interventions after leaving the mother may not be sufficient to avoid some adverse developmental events. A study42) showed that factors that may have a negative impact on the gut microbiota include cesarean section, short duration of breastfeeding or no breastfeeding (tending to formula feeding), early introduction of solid foods (3 months or earlier after birth), use of antibiotics during pregnancy and unhealthy lifestyle habits (including excessive consumption of ultra-processed foods, high antibiotic use, smoking toxins, smoking, alcohol consumption, and sedentary behavior). It is worth noting that the early infancy is an important colonization period of the intestinal microbiota. It is crucial to avoid dysbiosis during the fetal period and within 3 years after birth, which is closely related to the occurrence of intestinal diseases (such as neurological diseases). For children with the above high-risk factors, early monitoring of intestinal microenvironment indicators and appropriate preventive interventions may help reduce the risk of neurodevelopmental delay.

4.2.2. Dietary Adjustment: Linear growth retardation related to malnutrition in children is basically irreversible after 2 years of age. Therefore, preventing or reversing the factors that cause developmental delay (maternal nutritional status, epigenetic modification, environmental pathogen exposure, and feeding methods, etc.) can provide the best opportunity to improve the outcome [42]. Given the key role of the gut microbiome, a new therapeutic intervention approach, microbiome-directed complementary foods (MDCFs), has gradually attracted attention, which can regulate the microbial

communities closely related to the healthy development of early life. MDCFs are complementary foods designed to influence and modulate the gut microbiota of infants and young children, and are designed to change the target abundance of gut bacteria in children with moderate malnutrition, promote growth, bone formation, neurodevelopment and immune function [43]. These supplements often contain ingredients that can be used by specific gut microbes, such as dietary fiber, to support the growth of beneficial bacteria such as *Bifidobacterium*. In addition, MDCFs contain ingredients that are beneficial to gut health and the development of the immune system, which helps the overall health and normal development of infants and young children. In infants aged 12–18 months with moderate acute malnutrition, the use of MDCFs significantly increased weight-for-length Z-score and weight-for-age Z-score compared with the control group given ready-to-use supplementary food, and these changes were related to bone growth and neurodevelopment. Complex probiotic alliances and fermented foods may help restore environmental enteric dysfunction and the gut microbiome during pregnancy, and are therefore worth further exploration.

4.2.3. Supplementing Probiotics and Prebiotics

Supplementing probiotics, such as bifidobacteria and lactobacilli, helps restore the balance of the intestinal microbiota. A study on the impact of intestinal microbiota on the function of the nervous system [45] found that the supplementation of probiotics in early life can significantly reduce the incidence of neuropsychiatric problems in infancy. Animal experiments [46] have shown that the introduction of Lactobacillus reuteri can rescue synaptic plasticity thru the vagus nerve, thereby reversing social defects in the ASD model. These probiotics have been extensively studied in preclinical models of gut-brain axis abnormalities, including anxiety, depression, and stress-induced visceral pain

[47]. Research in this area may provide new perspectives for exploring the biological mechanisms between gut microbiota and neurodevelopment, and provide potential new strategies for early intervention of neurodevelopmental disorders.

4.2.4. Fecal Microbiota Transplantation (FMT) Individualized treatment plans based on the characteristics of the intestinal microenvironment, genetic background and clinical symptoms of children can improve the therapeutic effect and safety. FMT has been shown to alleviate behavioral symptoms of a variety of neuropsychiatric disorders, including ASD. Compared with gut microbiota transplantation (GMT) using the original donor gut microbiota, GMT of in vitro cultured microbiota can improve behavioral abnormalities and chemokine disorders in ASD mouse models [48]. Vaginal microbiota transfer (VMT) may also be a safe intervention to partially restore neurodevelopment and fecal microbiome in infants delivered by cesarean section [4]. Another study50 transplanted the feces of 6-month-old infants into sterile mice and found that the mice transplanted with the feces of infants had higher cognitive scores than the median, better memory function, and their intestinal flora was rich in microorganisms of the genus *Phocaeicola*, *Bacteroides* and *Bifidobacterium*.[50]

5. Summary and Outlook

The intestinal microenvironment is closely related to neurodevelopmental disorders in children, and affects social and emotional behaviors thru multi-system pathways. The protection of the intestinal microenvironment during the fetal period and early childhood is particularly important, and probiotics have a positive effect on children. Future research directions include: prioritizing the exploration of the interaction between the maternal prenatal microbiome-gut-brain system and the fetus, and clarifying the role of maternal factors; comprehensively using multi-omics methods to

analyze the interaction between the gut microbiome and the host and environmental factors; elucidating neural circuits and mechanisms, understanding the specific role of MGBA, laying the foundation for the discovery of early biomarkers and microbial therapy, and identifying different subgroups to promote the development of individualized treatment. Therefore, researchers need to continue to conduct large-scale clinical trials, combine emerging technologies, and strengthen interdisciplinary cooperation to solve the complex health problem of children's neurodevelopmental disorders, promote the development and progress of related fields, and bring more hope and possibilities for the rehabilitation of children.

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