

# Application of Microbial Intestinal Brain Axis Theory in the Nursing of Autism Spectrum Disorder

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**Abstract.** Autism spectrum disorder (ASD) is a neurodevelopmental disorder centered around social disorders and stereotyped behavior, with its global prevalence increasing year by year.

Traditional behavior and medication interventions have limited effectiveness. In recent years, the progress of the microbiota gut brain (MGB) axis theory has provided new directions for the etiology research and clinical nursing of ASD. The imbalance of gut microbiota in children with ASD can exacerbate neuroinflammation through neuroimmune mechanisms, further affecting central nervous system development. The nursing intervention strategy based on MGB axis can improve gastrointestinal symptoms and behavioral abnormalities in children with ASD. However, microbial intervention still faces multiple challenges. This review systematically integrates the clinical application and mechanism exploration of MGB axis in ASD, and constructs a nursing practice framework based on the existing research results of MGB axis, providing multidimensional theoretical support and practical path for optimizing ASD clinical nursing strategies.

**Keywords:** Autism Spectrum Disorder; Microbial gut brain axis; Nursing practice; fecal microbiota transplantation.

## Background

The global prevalence of autism spectrum disorder (ASD) as a neurodevelopmental disorder has risen from 0.67% in 2000 to 2.78% in 2020. Its core symptoms, social communication disorders, and repetitive stereotyped behaviors pose persistent challenges to children's development [1,2]. At present, the clinical practice of behavioral intervention combined with drug therapy faces a dual dilemma: on the one hand, 40% -65% of ASD children with gastrointestinal symptoms (such as chronic constipation and diarrhea) exhibit worsening behavioral problems; On the other hand, research on the etiology of ASD is mostly limited to the theory of genetic environmental interaction, lacking interventions targeting the source of symptoms [3,4]. In recent years, the breakthrough progress of the microbiota gut brain axis (MGB) theory has provided a new perspective for this dilemma [5]. Reeves et al.

[6] found that the gut microbiota of children with ASD showed an increasing trend in the level of rumen bacteria compared to normal developing children. Animal models further revealed that when mice bind with *Vibrio ruminatus* ATCC 29149, they degrade mucus and produce various neuroactive compounds. This finding is related to the reduction of granulos cells in the dentate gyrus and changes in animal behavior, providing a molecular biology basis for explaining the impact of gut microbiota on the gut brain axis [7]. Under this theoretical framework, clinical nursing interventions targeting the gut microbiota have demonstrated unique advantages. A randomized controlled study found that probiotics (*Bifidobacterium*, *Lactobacillus acidophilus*, *Enterococcus faecalis*) combined with behavioral analysis can effectively correct gut microbiota dysbiosis and improve related clinical symptoms in children with ASD [8]. This marks a potential shift in the paradigm of clinical nursing practice - from symptom management to pathogen intervention based on microbiome regulation. However, existing nursing guidelines have not yet systematically integrated evidence related to the MGB axis, and there are still significant gaps in the construction of nursing practice frameworks and the development of personalized nursing plans. This review aims to construct a transformation pathway connecting basic research and nursing practice, providing theoretical basis and practical framework for promoting precise health management of children with ASD.

## **1. Evidence of the correlation between MGB axis regulation mechanism and ASD pathology**

The MGB axis establishes a close communication network with the central nervous system through neural, endocrine, and immune signals, which can connect the bidirectional signal communication between the brain and the intestine, thereby affecting the physiological state of the body [9]. In recent years, many studies have gradually revealed the core mechanism of MGB axis in ASD. From the perspective of gut microbiota diversity, the alpha diversity (especially Shannon diversity index) of the gut microbiota in children with ASD is significantly lower than that in normally developing children, and the imbalance in the proportion of Bacteroidetes, Clostridium, and Firmicutes may lead to a decrease in the synthesis of short chain fatty acids (SCFAs). SCFAs, as key regulatory factors of blood-brain barrier permeability, can affect the immune function, epigenetics, and neuroplasticity of the central nervous system. A decrease in their concentration may exacerbate neuroinflammatory responses, thereby exacerbating symptoms of ASD [10, 11]. From the perspective of neuroimmune interaction mechanisms, dysbiosis of gut microbiota can activate peripheral immune cells, promote the transmission of pro-inflammatory cytokine IL-6 through the vagus nerve to the central nervous system, induce abnormal activation of microglia, lead to synaptic pruning dysfunction, and cause neurodevelopmental disorders [12, 13].

Observable biological markers in nursing practice provide entry points for clinical translation. The Bristol Fecal Profile Scale and Gastrointestinal Symptom Assessment Scale have been used in multiple studies to assess gastrointestinal symptoms in children with ASD, suggesting that intestinal function assessment can serve as an early warning indicator for nursing interventions [14, 15]. In addition, the elevated levels of lipopolysaccharide binding protein (LBP) in peripheral blood of children with ASD are directly correlated with increased intestinal permeability, indicating the disruption of intestinal barrier function and immune dysfunction, providing reliable laboratory evidence for nursing monitoring [16].

## **2. Current nursing practice of gut microbiota intervention in children with ASD**

### **2.1 Application of Probiotics/Prebiotics**

In the field of probiotic supplementation, a double-blind randomized controlled study showed that after 4 weeks of intervention with a formulation containing *Lactobacillus plantarum* PS128 (each containing  $3 \times 10^{10}$  CFU of PS128), the physical and object use scores as well as the Social Response Scale (SRS) scores in the Autistic Children's Behavior Scale Modified Version (ABC-T) were reduced in children with ASD, and the mechanism was related to the regulation of neurotransmitter levels in the brain by PS128 [17]. In addition, animal studies have found that Probio-M8, a subspecies of *Bifidobacterium lactis*, can regulate the structure of the gut microbiota by increasing the abundance of beneficial bacteria such as *Bifidobacterium bulgaricus* and *Actinobacteria mucilaginosus*. It also regulates metabolic activity by increasing choline levels, effectively reducing abnormal behavior in autistic mice [18]. In nursing practice, attention should be paid to individualized dosage of probiotics/prebiotics, while also paying attention to the medication time window to achieve the best therapeutic effect.

### **2.2 Fecal microbiota transplantation**

Fecal microbiota transplantation (FMT) has shown a more comprehensive improvement effect in open clinical trials. After 4 weeks of FMT treatment, gastrointestinal symptoms and abnormal behaviors in children with ASD were significantly improved. In addition, FMT can promote the colonization of donor microorganisms and transform the bacterial community of ASD children into that of normally developing children [19]. When performing FMT, attention should be paid to adjusting the freezing temperature to control microbial activity.

During nursing implementation, it is necessary to educate and follow up with fecal microbiota recipients, informing them not to use antibiotics 12-48 hours before fecal infusion, standard bowel preparation before surgery, and follow-up for postoperative adverse reactions (abdominal discomfort, diarrhea, constipation, low-grade fever, etc.) [20, 21].

### **2.3 Dietary interventions**

Children with ASD have more serious dietary behavior problems than normal children, and are a high-risk group for nutrient deficiency and nutritional diseases. The low fermentation diet of oligosaccharides, disaccharides, monosaccharides, and polyols (low FODMAP) not only improves constipation symptoms in children with ASD, but also has a positive impact on other gastrointestinal problems such as abdominal pain and bloating [22]. However, due to the widespread sensory sensitivity of pediatric patients, nursing staff need to collaborate with nutritionists to develop a progressive dietary intervention plan. Standardized

scales such as the Behavioral Pediatric Feeding Assessment Scale and the Simplified Sensory Scale can also be used to evaluate the dietary behavior and sensory characteristics of pediatric patients. Based on the evaluation results, specific interventions can be guided, such as changing the shape, appearance, frequency, and location of food, combined with behavioral reinforcement training to improve food acceptance and overcome taste sensitivity.

## **3. Construction of nursing practice framework based on MGB axis**

### **3.1 Primary prevention (perinatal intervention)**

The perinatal intervention based on MGB axis aims to reduce the risk of ASD by regulating the maternal and infant microbiomes. Research has shown that maternal gut microbiota imbalance during pregnancy is closely related to offspring neurodevelopmental disorders, immune abnormalities, and metabolic diseases [24]. In nursing practice, primary prevention can be achieved through the following measures: promoting probiotics/dietary fiber supplementation during pregnancy, optimizing the diversity of maternal gut microbiota, and inhibiting the proliferation of pathogenic bacteria; Advocate natural childbirth and breastfeeding, promote the colonization of a symbiotic microbiota dominated by bifidobacteria in the intestinal tract of newborns, and enhance intestinal barrier function; Carry out psychological health management during pregnancy, reduce maternal stress hormone levels (such as cortisol) through psychological intervention, and minimize their negative impact on fetal gut microbiota [25, 26].

### **3.2 Secondary Prevention (Early Identification)**

The core of secondary prevention lies in achieving early warning of ASD through dynamic monitoring of MGB axis related biomarkers. Dysbiosis of gut microbiota (such as abnormal ratio of Firmicutes/Bacteroidetes), decreased levels of short chain fatty acids (SCFAs), and elevated levels of serum inflammatory factors (IL-6, TNF -  $\alpha$ ) have been confirmed as early markers of MGB axis dysfunction [10, 11, 27]. In nursing practice, stratified screening can be carried out by combining multi omics techniques: fecal metagenomic sequencing can be performed on high-risk pregnant women (such as prenatal depression patients) to evaluate microbial functional modules (such as tryptophan metabolic pathways); Metabolomics analysis was performed on infants to analyze the levels of gamma aminobutyric acid in feces and predict neurodevelopmental risk [26, 28]. By developing the MGB axis risk assessment scale (covering environmental factors such as dietary patterns and antibiotic exposure history), nursing staff can accurately identify high-risk populations and gain a time window for subsequent interventions [29].

### **3.3 Third level intervention (personalized care)**

For ASD children with MGB axis dysfunction, a personalized intervention plan based on microbiome characteristics needs to be developed. By using 16S rRNA sequencing and metabolomics techniques, the characteristics of the gut microbiota in pediatric patients can be identified, and precise intervention strategies can be developed [30]. For example, adopting a low FODMAP diet or improving gut microbiota dysbiosis through methods such as FMT [11, 22]. In nursing practice, it is necessary to establish interdisciplinary teams (nutritionists, psychiatrists, and microbiome analysts) to dynamically monitor the alpha diversity index of fecal microbiota and plasma BDNF levels, and optimize intervention plans in real time [11].

When suspected ASD symptoms are detected in patients, self screening should be conducted first. After initial screening and re screening, if symptoms of ASD are found, it is necessary to go to the hospital for examination in a timely manner. At the same time, during the treatment process, not only should attention be paid to the daily performance and reactions of the child, but also to their diet, and a reasonable diet plan should be formulated to avoid the child's picky eating behavior affecting normal gastrointestinal reactions and worsening the condition.

## **4. Challenges and Prospects of Microbial Intervention in ASD Nursing**

### **4.1 Ethical Disputes and Safety Considerations**

There are significant ethical controversies and safety challenges regarding the application of microbial intervention in ASD nursing. At present, the privacy protection of donors in FMT is not yet standardized, which may lead to ethical disputes. It is recommended to establish an anonymous microbial community database and use multiple encryption technologies to store donor information [11]. In addition, ASD patients are mostly children whose physiological development is immature and their immune system is not sound. Microbial intervention may indirectly affect neural development by changing the gut microbiota, and its long-term safety is not fully understood. The heterogeneity of individual responses may also lead to different intervention outcomes. Therefore, a long-term follow-up plan needs to be developed to evaluate the long-term risks and benefits of intervention measures

### **4.2 Difficulties in Individualized Nursing**

The highly heterogeneous pattern of gut microbiota disruption in children with ASD poses multiple challenges for individualized design of microbial interventions [31]. In addition, ASD often coexists with comorbidities such as food allergies and gastrointestinal dysfunction, and the synergistic effect of dietary intervention and microbial therapy needs to be comprehensively considered, further increasing the complexity of individualized plans [4]. The current clinical practice lacks reliable biomarkers to guide treatment stratification, and dynamic monitoring technology is costly. In the future, it is necessary to combine multiple omics technologies to establish predictive models, and use artificial intelligence to integrate clinical phenotype and microbiome data to achieve precise intervention [32].

### **4.3 Technical bottlenecks**

The translational application of MGB axis theory in ASD nursing is limited by multiple technical bottlenecks. Firstly, existing research is mostly based on animal models, whose gut microbiota differs significantly from that of humans, and cannot fully simulate the social behavioral deficits of ASD, which limits the value of extrapolating experimental results to clinical practice. Secondly, the resolution and functional analysis capabilities of microbial detection technologies such as 16S rRNA sequencing and metagenomics are insufficient, making it difficult to reveal the causal relationship between specific strains and host immune and metabolic pathways. In addition, the delivery system of microbial intervention has limitations: oral probiotics are easily damaged by

gastric acid, while the standardized preparation of FMT is difficult, and there is a lack of specific microbial community formulas for ASD. Breaking through these bottlenecks requires the development of organoid co culture technology, the development of engineered bacterial strains to target metabolic pathways, and the use of bio optical imaging technology to achieve dynamic monitoring of microbial communities, thereby promoting the transformation of microbial intervention from empirical therapy to mechanism driven therapy [33, 34].

## 5. Summary

The MGB axis theory provides a new research direction and practical framework for the nursing of ASD. Children with ASD generally have dysbiosis of the gut microbiota.

Regulating the gut microbiota through probiotics, fecal microbiota transplantation, and dietary interventions can improve their gastrointestinal symptoms and behavioral problems. The construction of perinatal interventions, early biomarker monitoring, and personalized care plans further highlights the potential of MGB axis in the tertiary prevention of ASD. However, microbial intervention still faces challenges such as ethical controversies, individualized program design, and technical bottlenecks. In the future, it is necessary to combine multi omics technologies and interdisciplinary cooperation to promote the development of precision nursing and provide more effective health management strategies for children with ASD.

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