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The Role of Gut Microbiota on ADHD in Children: A Narrative Review

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Abstract

Background: Attention Deficit Hyperactivity Disorder (ADHD) is a prevalent neurodevelopmental disorder in children, impacting their cognitive, behavioral, and academic development. Recently, there has been increasing attention focused on the role of the gut microbiome in the pathogenesis of ADHD.

Methods: This narrative review synthesized data from recent studies evaluating the association between gut microbiota composition and ADHD in children. The literature was reviewed using databases including PubMed and Scopus up to early 2024.

Results: Findings suggest that children with ADHD often have altered gut microbiota compared to their healthy peers, potentially influencing the gut-brain axis and neurotransmitter activity. Interventions such as probiotics and dietary changes may support symptom management by modulating microbial diversity.

Conclusions: A growing body of evidence supports the role of gut microbiota in ADHD. While findings are promising, more robust, controlled clinical studies are needed to confirm causality and therapeutic applications.

Key Words: ADHD, Children, Gut microbiota, Neurodevelopment, Microbiome, Probiotics.

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1- INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common neurodevelopmental disorders affecting children globally. As of 2024, approximately 7.2% of children worldwide have been diagnosed with ADHD (1). This condition is characterized by persistent inattention, hyperactivity, and impulsivity that are inconsistent with a child's developmental stage, adversely affecting their cognitive, behavioral, and academic functioning (2). While genetic, environmental, and neurological factors contribute to ADHD, recent research has increasingly focused on the gut microbiota—the community of microorganisms residing in the gastrointestinal tract. This interest arises from evidence suggesting that the gut microbiota influences behavior and neurological function via the gut-brain axis (3).

The gut microbiota constitutes a complex ecosystem of diverse prokaryotes that maintain a symbiotic relationship with their host, playing a critical role in human health. Advances in sequencing and high-throughput technologies over recent decades have significantly enhanced our understanding of the gut microbiome's impact on health and disease. Given its high metabolic capacity, proximity to the intestinal mucosa, and interaction with the immune system, the gut microbiome's substantial contribution to human health is unsurprising. A growing number of conditions—including recurrent Clostridium difficile infections, inflammatory bowel disease, irritable bowel syndrome, colorectal cancer, allergies, neurological disorders, and metabolic diseases—are now linked to alterations in the resident gut microbiota (4). Research in this field continues to expand rapidly, with the gut microbiome increasingly recognized as our "second genome." Targeting the gut microbiome to restore or modulate its composition, through antibiotics, probiotics, prebiotics, or fecal microbiota transplantation (FMT), is considered a promising strategy for developing novel treatments for diseases associated with microbial imbalances (4).
Recently, the gut microbiome's role in mental health and neurological function has garnered heightened attention. The gut-brain axis, which facilitates bidirectional communication between the gastrointestinal and central nervous systems, has emerged as a critical pathway in this context (3). Preliminary evidence suggests that alterations in gut microbiome composition may be associated with neurodevelopmental disorders, including ADHD (5). However, existing studies are heterogeneous and require systematic synthesis.

This article begins by outlining the gut-brain axis and its relevance to neurodevelopmental disorders. It then examines specific gut microbiota changes in children with ADHD, explores potential mechanisms linking these changes to ADHD symptoms, and concludes by discussing microbiome-based interventions and future research directions to provide a comprehensive overview of this emerging field.

Research suggests that children with ADHD often exhibit distinct gut microbial compositions, which may correlate with symptom severity. The significance of this topic is multifaceted. First, elucidating the gut microbiota-ADHD relationship could uncover novel biological mechanisms, paving the way for innovative treatments such as probiotics or dietary modifications (6). Second, given the limitations and side effects of conventional pharmacological treatments (e.g., stimulants), identifying complementary approaches rooted in gut health is highly valuable (4).

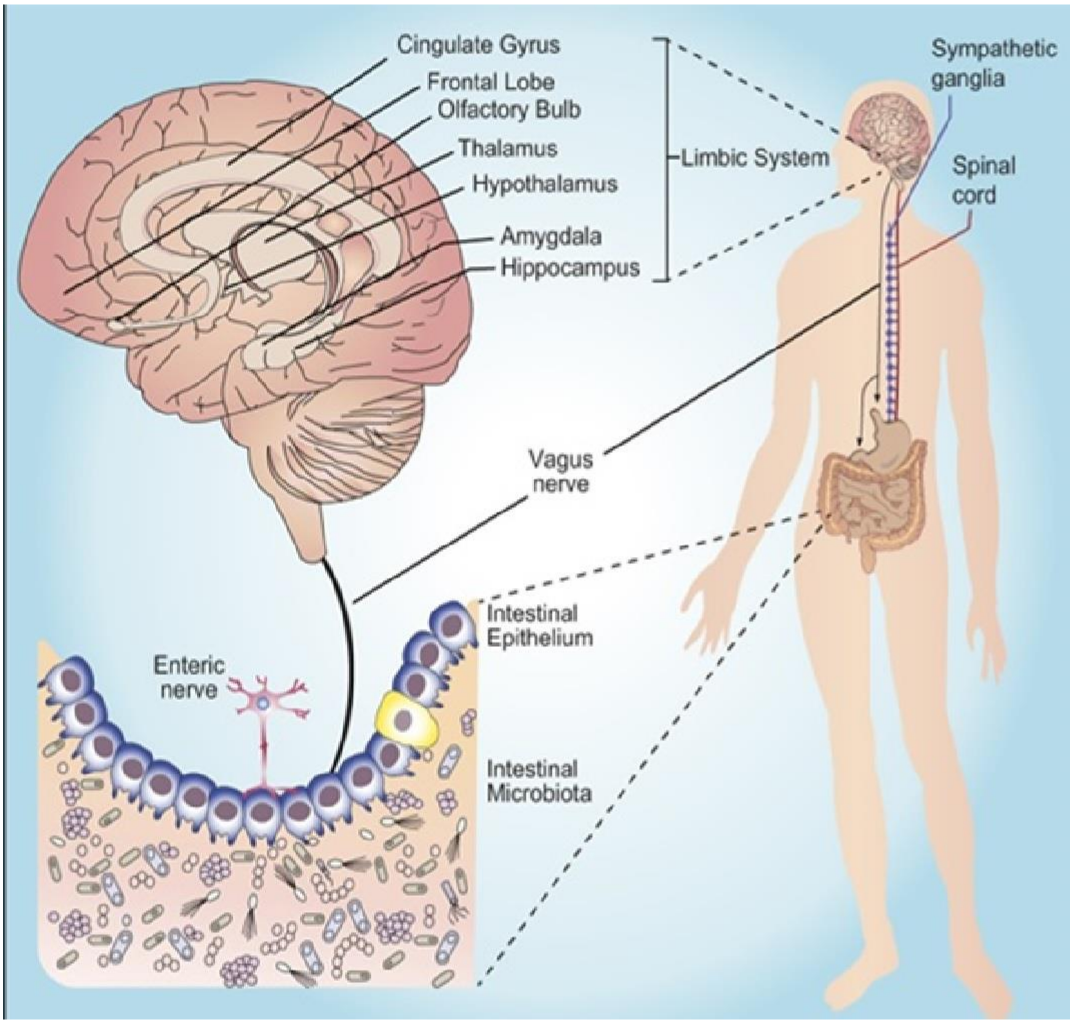

Figure-1: Gut-brain axis (8).

Third, as childhood is a critical period for neurodevelopment, early microbiome-targeted interventions may mitigate ADHD symptom severity or prevent progression (7).

Nonetheless, current studies vary in methodology and sample size. Many rely on cross-sectional data, with only a few exploring probiotic interventions. Inconsistencies in findings, such as the role of specific bacterial species, further underscore the need for a systematic review and meta-analysis to offer a more cohesive understanding of this relationship.

2- METHODS

This study is a narrative review that aims to explore the connection between the gut microbiota and ADHD in children by analyzing prior research. Relevant studies published in recent years were reviewed and synthesized.

2-1. Sources and Search Process

Databases: Scientific articles were retrieved from reputable sources, including PubMed, Scopus, Web of Science, and Google Scholar.

Keywords: Combinations of terms such as "gut microbiota and ADHD," "microbiome and attention-deficit hyperactivity disorder," "gut-brain axis in ADHD," and "childhood ADHD and gut bacteria" were used to identify relevant sources.

2-1-1. Inclusion Criteria

- Articles published between 2013 and 2024.

- Studies investigating the gut microbiome's role in ADHD in children.

- Review articles, clinical studies, and human laboratory research.

2-1-2. Exclusion Criteria

- Animal studies lacking human-relevant data.

- Theoretical articles without experimental or clinical evidence.

- Articles published in non-reputable or non-peer-reviewed journals.

2-2. Framework for Analysis and Interpretation

Selected articles were categorized based on study design, population, microbiota assessment methods, and reported outcomes. This study seeks to provide a comprehensive perspective on the gut microbiome's role in ADHD in children through comparative interpretation of diverse research findings.

2-3. Considerations and Limitations

As a narrative review, this study does not employ rigorous analytical methods such as meta-analysis or systematic review. It focuses on qualitative data interpretation and synthesis of various research perspectives to lay the groundwork for future investigations.

3- RESULT

3-1. Impact of Diet on ADHD

One study found that diets high in refined sugar and saturated fats increase the risk of ADHD, while diets rich in fruits and vegetables offer protective effects (8). Additional research indicates that fiber-rich, omega-3-supplemented, and probiotic-enhanced diets, such as the Mediterranean diet, enhance microbial diversity and reduce ADHD behavioral symptoms (8).

Diets dominated by processed foods correlate with higher abundances of harmful bacteria (e.g., Enterobacter and Escherichia coli) and lower levels of beneficial bacteria (e.g., Bifidobacterium), potentially exacerbating ADHD symptoms. Conversely, healthier dietary patterns are associated with a more balanced gut microbiota (9). Another study reported that kefir, a fermented dairy product, improved ADHD symptoms in children, likely due to alterations in gut microbial flora (10). Additionally, a low-lectin diet implemented alongside traditional ADHD treatments improved symptoms and gut microbiota composition, suggesting its potential as an adjunctive therapy (11).

3-2. Impact of Gut Microbiome on ADHD

Previous studies demonstrate that children with ADHD exhibit reduced gut microbial diversity compared to healthy peers, with an elevated Firmicutes to Bacteroidetes ratio (5). A decrease in beneficial species (e.g., Faecalibacterium) and an increase in pro-inflammatory bacteria (e.g., Clostridium) have also been observed, potentially intensifying systemic inflammation and disrupting neurotransmitter regulation (e.g., dopamine and serotonin) (12). Reduced Faecalibacterium levels lead to lower butyrate production—a potent anti-inflammatory compound—contributing to heightened systemic inflammation (10, 13). Some studies report positive effects of microbiome-based interventions, such as probiotic supplementation and diets rich in fiber and omega-3, on reducing ADHD symptoms (14, 15).

This research aims to provide a narrative review of existing literature on the gut microbiota's role in ADHD in children, synthesizing evidence on microbial dysbiosis, associated mechanisms, and intervention potential, while proposing directions for future research. The central question is: How does the gut microbiota influence ADHD in children, and what implications does this knowledge hold for improving management strategies for this disorder?

4- DISCUSSIONS

The findings of this narrative review reinforce the gut microbiota's role as a potential factor in ADHD pathophysiology in children. Aggregated evidence highlights distinct microbial patterns in ADHD-affected children, including reduced alpha diversity (5), an increased Firmicutes to Bacteroidetes ratio (12), and diminished abundance of anti-inflammatory genera like Faecalibacterium, known for producing butyrate, a short-chain fatty acid (SCFA) that modulates neuroinflammation (16). These microbial variations may affect the gut-brain axis through multiple mechanisms: first, disruptions in microbial metabolite production (e.g., SCFAs) could compromise blood-brain barrier integrity, increasing permeability to pro-inflammatory molecules (17); alterations in microbial neurotransmitter secretion (e.g., gamma-aminobutyric acid and serotonin) may disrupt dopaminergic balance in the prefrontal cortex, a key region for attention and impulse control (17,18).

These findings align with recent research on neurodevelopmental disorders (e.g., autism), confirming links between gut dysbiosis and behavioral abnormalities (7). However, this review's novelty lies in its specific focus on ADHD and its stratified analysis of bacterial species tied to symptom severity. For instance, reduced Bifidobacteria, involved in tryptophan metabolism (a serotonin precursor), may relate to mood disturbances common in ADHD (14). Similarly, elevated Proteobacteria (e.g., Escherichia/Shigella), which produce lipopolysaccharide (LPS) to drive systemic inflammation, may impair hippocampal neurogenesis (15).

4-1. Clinical Implications and Therapeutic Interventions

While precise causal mechanisms remain unclear, these findings suggest microbiome-targeted interventions as a potential ADHD management strategy. Preliminary evidence from randomized controlled trials (RCTs) indicates that probiotics containing Lactobacillus rhamnosus GG and Bifidobacterium lactis yield statistically significant improvements in Conners' scale scores, particularly for inattention (6). Likewise, polyphenol-rich diets (e.g., Mediterranean diet) correlate with increased Roseburia and Akkermansia genera linked to propionate production, potentially influencing behavior by suppressing inflammatory microglial activity (4).

4-2. Limitations and Future Directions

Despite recent progress, methodological limitations persist. Most studies adopt cross-sectional designs, limiting causal inference. Variability in sampling (e.g., stool vs. intestinal biopsies) and sequencing techniques (16S rRNA vs. metagenomics) hinders cross-study comparisons (19). Additionally, confounding factors—such as antibiotic use, diet, and ADHD subtype—are rarely controlled.

To address these gaps, four research frameworks are proposed:

1. *Prospective Longitudinal Studies:*

   Monitoring children from infancy to ADHD onset to identify predictive microbial markers.

2. *Multi-Omics Approaches:*

   Integrating metagenomics, metabolomics, and epigenetics for comprehensive gut-brain pathway mapping.

3. *Humanized Animal Models:*

   Using ADHD genetic mouse models (e.g., SHR) with human microbiota transplants to explore causality.

4. *Refined Trials:*

   Conducting phase II/III RCTs with standardized protocols for probiotics/prebiotics and monitoring inflammatory/neural markers.

5- CONCLUSTION

This review positions the gut microbiota as a "potential modifier" in ADHD pathophysiology, meriting deeper investigation into its functional and clinical implications. Integrating microbiome insights into current ADHD diagnostic and therapeutic frameworks could advance personalized medicine, leveraging microbial profiles in treatment decisions. Achieving this vision requires interdisciplinary collaboration across neurology, microbiology, and nutritional epidemiology to translate laboratory findings into safe, effective interventions.

6- DECLARATION

Not applicable.

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