Dysbiosis and the Gut-Brain Axis in ADHD: Mechanisms and Emerging Therapeutic Strategies

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Abstract

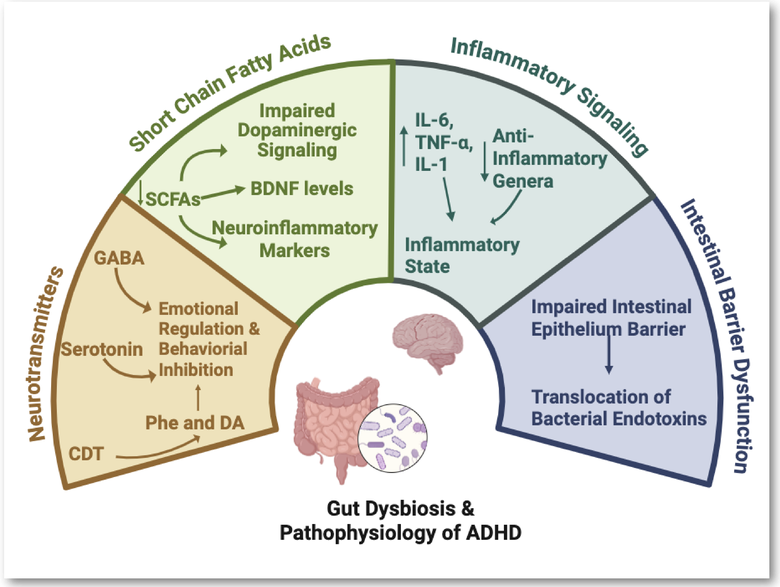
Dysbiosis, characterized by an imbalance in gut microbiota, significantly influences the pathogenesis of Attention-Deficit Hyperactivity Disorder (ADHD) by disrupting the gut-brain axis (GBA), a bidirectional network linking the gastrointestinal tract and central nervous system. Altered microbial diversity is consistently observed in ADHD patients. Evolving interventions, such as dietary modifications, probiotics, prebiotics, and fecal microbiota transplantation (FMT), show preliminary promise in restoring microbiota balance and mitigating ADHD symptoms. However, inter-individual variability in microbial responses highlights the need for personalized therapeutic approaches, while inconsistent study designs underscore the urgency for standardized research methodologies. By elucidating the mechanisms linking gut dysbiosis to ADHD, this review aims to guide targeted, GBA-focused interventions to improve clinical outcomes in ADHD management.

Introduction

- Attention-deficit/hyperactivity disorder (ADHD), a prevalent neurodevelopmental disorder characterized by inattention, impulsivity, and/or hyperactivity [1,2].
- The gut microbiome, a complex ecosystem of trillions of microorganisms including bacteria, fungi, and viruses, is essential for gastrointestinal, metabolic, and immune function [3].
- The gut-brain axis, a bidirectional communication network linking the gut and central nervous system (CNS), regulates key processes implicated in ADHD, such as dopamine synthesis and neuroinflammatory responses [4].
- Dysbiosis, an imbalance in microbial communities triggered by antibiotics, processed diets, or stress, can increase gut permeability, promote systemic inflammation, and exacerbate ADHD symptoms [5,6] particularly dopamine pathways critical to attention and impulse control.

Methods

- A search consisting of key terms “ADHD” AND “Dysbiosis”, “ADHD” AND “Osteopathic Manipulative Treatment”, and “dysbiosis” AND “neurological disorders” was conducted using PubMed and EMBASE.



Mechanistic Insights

Microbial Modulation of Neurotransmitters

- Gut microbiota impacts CNS function in ADHD by producing GABA for emotional regulation and regulates cyclohexadienyl dehydratase (CDT) activity in phenylalanine (Phe) metabolism and dopamine (DA) synthesis [7,8].

Short Chain Fatty Acids (SCFAs)

- Loss of Faecalibacterium reduces SCFAs, impairing intestinal barrier function, neuroimmune activity, brain-derived neurotrophic factor (BDNF) expression, and dopaminergic signaling, which worsens inattention and impulsivity [8,9].

Mechanistic Insights (continued)

Immune System and Inflammatory Signaling

- The inflammatory state is exacerbated by combination of innate and adaptive immune response specifically increased proinflammatory cytokines [10].

Intestinal Barrier Dysfunction

- The intestinal epithelial barrier is impaired by dysbiosis, leading to increased permeability and translocation of bacterial endotoxins like lipopolysaccharide [11].

Conclusion

- Mounting evidence supports the role of gut dysbiosis in the pathogenesis of ADHD through mechanisms involving neuroinflammation, altered neurotransmitter imbalance, and disruption of gut and blood-brain barrier integrity and the gut brain axis. Emerging microbiome-targeted therapies—including probiotics, prebiotics, omega-3 fatty acids, and dietary interventions—offer promising adjuncts to conventional treatment by addressing upstream biological processes but require more causal data and personalized approaches.

References