Chapter 4
Microbiome and Brain–Gut Microbiota's Influence on Autism Pathogenesis

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ABSTRACT

Autism Spectrum Disorders (ASD) are neurodevelopmental conditions characterized by social communication challenges and repetitive behaviors. Emerging evidence suggests that gut microbiota, through the gut-brain axis, play a significant role in ASD pathogenesis. This complex communication network influences neurodevelopment by modulating immune responses, producing neuroactive metabolites, and maintaining gut barrier integrity. In individuals with ASD, specific microbial

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imbalances and reduced diversity are commonly observed, which are linked to these pathophysiological processes. Genetic predispositions and environmental factors, such as diet and antibiotic use, further affect gut microbiota composition, potentially exacerbating these imbalances. Therapeutic strategies targeting the gut microbiota, including probiotics, prebiotics, dietary modifications, and fecal microbiota transplantation, have shown potential in alleviating ASD symptoms. This chapter provides a comprehensive overview of the current understanding of the gut microbiota's role in ASD.

1. INTRODUCTION

Autism Spectrum Disorders (ASD) are a complex and diverse group of neurodevelopmental conditions, affecting approximately 1 in 54 children worldwide (Aymerich et al., 2024; Moschetti et al., 2024). Characterized by challenges in social communication, restricted interests, and repetitive behaviors, ASD encompasses a broad range of phenotypes and severities (Lai et al., 2014). The etiology of ASD is multifactorial, involving genetic, epigenetic, and environmental factors. Despite extensive research, the precise biological mechanisms underlying ASD remain elusive (Bölte et al., 2019; Yenkoyan et al., 2017). However, recent advances have highlighted the potential role of the gut-brain axis—a bidirectional communication network linking the gastrointestinal (GI) tract with the central nervous system (CNS)—in influencing neurodevelopment and contributing to the pathophysiology of ASD (Q. Li & Zhou, 2016; Saurman et al., 2020). The concept of a gut-brain connection is not new; historical medical traditions often emphasized the influence of the digestive system on mental health (Appleton, 2018; Berding et al., 2021). However, modern scientific exploration into the gut-brain axis has provided concrete evidence of its significance. This axis involves complex interactions mediated by neural pathways, such as the vagus nerve, hormonal signals, and immune responses (Makris et al., 2021). A key component of this system is the gut microbiota, a diverse community of microorganisms residing in the intestines. These microbes play a crucial role in numerous physiological processes, including digestion, metabolism, immune regulation, and the synthesis of neuroactive compounds. In the context of ASD, an increasing body of evidence suggests that alterations in the composition and function of the gut microbiota—termed dysbiosis—may have a profound impact on neurodevelopmental outcomes (Belizário & Faintuch, 2018; Laue et al., 2022; Warner, 2019). Children with ASD often exhibit GI symptoms, such as constipation, diarrhea, and abdominal pain, more frequently than their neurotypical peers (Chandler et al., 2013; V. Kang et al., 2014). These symptoms are not merely coincidental; they are believed to be linked to systemic physiological changes associated with