

# Neurobiological Foundations of Autism Spectrum Disorder: Gut Microbiota, Epigenetic Modifications and Impaired Synaptic Plasticity

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Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition characterized by central nervous system dysfunction, arising from an intricate interplay of genetic, epigenetic, and environmental factors. Emerging evidence highlights the pivotal role of the Microbiota-Gut-Brain Axis in modulating ASD-related behavioral phenotypes and comorbid gastrointestinal symptoms. Bidirectional communication within this axis is mediated through neural, immune, and endocrine pathways, as well as microbial metabolites such as short-chain fatty acids (SCFAs) and the tryptophan-kynurenine pathway. Dysbiosis-induced intestinal inflammation and compromised blood-brain barrier integrity trigger systemic cytokine responses and glial hyperactivation, both of which are central to neuroinflammatory pathogenesis. A hallmark of ASD is epigenetic dysregulation—notably DNA methylation and histone deacetylation—which suppresses the transcription of genes vital for synaptic plasticity. These alterations impact key brain structures, including the cingulate gyrus, amygdala, striatum, and cerebellum. Within this genetic landscape, the ARID1B complex is of particular significance; its deficiency impairs dendritic development and disrupts excitatory synaptic signaling. Such morphological abnormalities in dendrites are considered primary drivers of impaired synaptic plasticity, fundamentally contributing to the pathogenesis of ASD.

This study examines the multifactorial neurobiological foundations of ASD, integrating gut microbiota dynamics, genetic mutations, and structural brain changes. While pharmacological and behavioral therapies remain the standard of care, future clinical priorities must focus on patient stratification based on biological phenotypes. The identification of specific biomarkers, such as fecal calprotectin and p-cresol, facilitates the development of personalized interventions—including probiotics and metabolic modulators—aimed at restoring the homeostatic function of the microbiota-gut-brain axis.