

Chapter 16

Pediatric and Adolescent Gut-Brain Axis - Developmental Perspectives

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Introduction

Childhood and adolescence are critical periods during which the gut microbiome-and subsequently the gut-brain axis-undergo significant maturation. Early microbial colonization interacts with immune ontogeny, synaptic refinement, metabolic programming, and HPA-axis calibration [1,2] Perturbations such as antibiotics, infections, and malnutrition can disrupt microbial diversity and influence long-term emotional regulation and cognitive development [3].

16.1 Early-Life Microbiome Development

Colonization Milestones:

The initial microbiome is shaped immediately at birth.

- **Mode of delivery:** Vaginal births promote *Lactobacillus*, *Bifidobacterium*, *Bacteroides* colonization, while cesarean births delay diversification and higher colonization by skin-associated bacteria, which may influence immune programming [4,5].
- **Feeding:** Breastfeeding supports *Bifidobacteria* through human milk oligosaccharides (HMOs), which promotes immune programming and mucosal barrier maturation. [6]. Formula feeding leads to faster diversification but may increase pathobionts.
- **Antibiotic exposure:** Maternal or neonatal antibiotics disrupt colonization patterns and may predispose to metabolic and immune dysregulation [7].

Immune System Training

- Early microbial signals regulate immune tolerance, T-cell differentiation, and gut-barrier stability [8].
- SCFAs-acetate, propionate, butyrate-play central roles in anti-inflammatory signaling and microglial maturation [9].
- Dysbiosis in infancy is linked to allergic disease, altered neuroinflammatory tone, and behavioral vulnerabilities [10].

16.2 Adolescence: A Second Window of Microbiome Plasticity

Adolescence introduces a second major shift driven by hormones, diet, and psychosocial stress.

Hormonal Transition

Sex steroids modulate gut permeability, immune function, and microbial composition, while microbes influence steroid metabolism and enterohepatic cycling [11]. These interactions contribute to emerging sex-specific patterns of stress reactivity and mood.

Dietary Shifts

Adolescent eating patterns like high sugar, processed foods, low fiber, reduce microbial diversity and SCFAs and increase inflammation, contributing to emotional instability and decreased attention [12].

Stress, Sleep, and Lifestyle

Academic load, screen exposure, and reduced physical activity alter circadian-microbial rhythms and elevate cortisol, disturbing microbial balance [13]. These factors collectively affect mood, cognition, and stress resilience.

16.3 Microbiome and Neurodevelopmental / Psychiatric Disorders

Autism Spectrum Disorder (ASD)

Children with ASD frequently show reduced *Bifidobacterium* and increased *Clostridium* [14]. Dysbiosis may contribute to SCFA imbalance, GI dysmotility, altered neuroinflammation and synaptic signaling [15]. Although causal pathways remain under investigation, gut alterations may exacerbate ASD-related sensory and behavioral symptoms.

Attention-Deficit/Hyperactivity Disorder (ADHD)

Altered microbiota may influence dopamine precursor metabolism and inflammatory signaling. Reduced alpha diversity in ADHD children suggests possible microbial contributions to attention regulation and impulse control [16].

Adolescent Mood Disorders

Adolescence is a high-risk period for anxiety and major depression. Dysbiosis is associated with reduced SCFA production and increased neuroinflammation [17], altered tryptophan-serotonin metabolism [18], increased intestinal permeability and cytokine activation. These pathways may influence emotional regulation and stress sensitivity.

16.4 Indian Context: Diet, Environment, and Developmental Microbiome Signatures

Microbiome development in Indian children and adolescents is uniquely shaped by nutritional deficits, recurrent infections, traditional dietary patterns, and high antibiotic exposure, creating trajectories distinct from Western populations.

1. Malnutrition and Microbial Immaturity

Childhood malnutrition in India is associated with reduced microbial diversity and an immature microbiome, marked by lower *Bifidobacterium* and *Lactobacillus* and higher enteropathogens [19]. This compromises immunity and neurodevelopment.

2. **Iron-Deficiency Anaemia:** Iron-deficiency anaemia alters SCFA profiles, promotes inflammation, and favours *Enterobacteriaceae* expansion, while reducing beneficial SCFA-producing taxa [20]. These disruptions can affect cognitive and stress pathways.

3. Recurrent Diarrheal Infections

Frequent diarrhoeal episodes cause microbiome instability, repeated loss of beneficial species, and delayed maturation, contributing to growth faltering and impaired gut-brain axis functioning [21].

4. Indian Dietary Patterns

Millet- and legume-rich diets, polyphenol-containing spices (e.g., turmeric, cumin), and fermented foods (curd, buttermilk, idli/dosa batter) increase *Lactobacillus*, *Bifidobacterium*, and SCFA-producing taxa [22]. These components support microbial richness during adolescence.

5. High Antibiotic Use

India's high antibiotic consumption leads to repeated microbial "resets", reduced diversity, and prolonged commensal recovery, elevating long-term risks of dysbiosis-related disorders [23].

16.5 Mechanistic Pathways

- Neurotransmitter Modulation

Gut microbes shape serotonin, dopamine, and GABA metabolism [24]. Microbial metabolites act via vagal, endocrine, and paracrine pathways, influencing emotional and cognitive outcomes.

- Immune-Neuroendocrine Crosstalk

Dysbiosis increases inflammatory cytokines (IL-6, TNF- α), modulating microglial activity and HPA-axis sensitivity [25]. These mechanisms affect fear, reward, and executive networks.

- Epigenetic Programming

SCFAs influence histone acetylation and DNA methylation, shaping neural plasticity during periods of high epigenetic responsiveness [26].

16.6 Interventions and Preventive Strategies

- Diet-Based Approaches

High-fiber foods, fruits, vegetables, legumes, and fermented foods such as yogurt, kefir, idli/dosa, and pickles support microbial resilience [27, 28]. Mediterranean-style patterns are associated with better mood and microbial diversity.

- Probiotics and Prebiotics

Select probiotic strains (*Lactobacillus rhamnosus*, *Bifidobacterium longum*) may improve emotional regulation and stress

recovery [29]. Prebiotics such as GOS and inulin reduce cortisol responses and modulate emotional processing [30].

- **Lifestyle Interventions**

Exercise increases microbial diversity and reduces inflammation [31]. Adequate sleep and stress management maintain circadian-microbial balance.

- **School-Based Strategies**

Nutrition education, healthier cafeteria policies, physical activity periods, and balanced hygiene practices can promote microbiome-friendly environments [32].

Conclusion

Childhood and adolescence are dynamic periods when the gut microbiome and developing brain influence each other through metabolic, immune, and neuroendocrine pathways. Early microbial disruptions can increase vulnerability to neurodevelopmental and psychiatric conditions, whereas diet, lifestyle, and supportive environments can enhance resilience and healthy development.

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