ISSN 2345-1210 | Volume 10

Japanese Journal of Gastroenterology and Hepatology

Research Open Access

# Postbiotic's Role in the Gut-Brain Axis During Neonatal Age

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**Received:** 01 Apr 2025
**Accepted:** 12 Apr 2025
**Published:** 17 Apr 2025
**J Short Name:** JJGH



**Keywords:** Gut; Brain;Axis;Neonatal;Postbiotic

**Citation:** P Pavone. Postbiotic's Role in the Gut-Brain Axis During Neonatal Age. J Gastro Hepato. 2025; V10(14): 1-2

## 1. Abstract

### 1.1. Background

Postbiotics, biologically active compounds derived from probiotics, are increasingly recognized for their potential influence on the gut-brain axis (GBA), particularly during the neonatal period.

### 1.2. Methods

This narrative review explores the role of postbiotics in neonatal neurodevelopment, focusing on their mechanisms of action within the gut-brain communication network.

### 1.3. Results

By synthesizing findings from recent studies, we identify key pathways through which postbiotics exert their effects, including modulation of neuroinflammation, gut barrier integrity, neurotransmitter production, and epigenetic regulation.

### 1.4. Conclusions

Postbiotics represent a promising tool for early-life interventions aimed at optimizing neonatal neurodevelopment, meriting further investigation to translate these findings into clinical practice.

## 2. Introduction

The gut microbiome, comprising trillions of microorganisms, plays a pivotal role in the gut-brain axis (GBA), a complex communication network between the gut and the central nervous system (CNS). During the neonatal period, the establishment of gut microbiota and the development of the nervous system are tightly intertwined, influencing neurodevelopmental trajectories. Disruptions in this axis during early life can have long-term effects on cognition, behavior, and emotional regulation [1, 2].Gut microbial metabolites, including short-chain fatty acids (SCFAs) like butyrate, have been shown to enhance brain-derived neurotrophic factor (BDNF) expression, synaptic plasticity, andneurogenesis. Additionally, microbial products regulate the hypothalamic-pituitary-adrenal (HPA) axis, influencing stress responses and neuroendocrine functions [3, 4].This review aims to comprehensively examine the role of postbiotics in neonatal GBA modulation, highlighting their therapeutic applications and addressing existing challenges.

## 3. Materials and Methods

This narrative review synthesized data from peer-reviewed articles published in the last two decades, focusing on postbiotics' effects during the neonatal period. Keywords such as "postbiotics," "gut-brain axis," and "neonatal neurodevelopment" guided the literature search on PubMed and Scopus. Inclusion criteria encompassed studies examining postbiotics' impact on neurodevelopment, while exclusion criteria filtered out those focused solely on probiotics or unrelated to neonatal health. Emphasis was placed on mechanisms such as neuroinflammation, neurotransmitter synthesis, and gut barrier integrity.

## 4. Results

### 4.1. Neuroinflammation Modulation

Postbiotics, particularly SCFAs, reduce pro-inflammatory cytokines and promote anti-inflammatory responses. Studies have demonstrated increased regulatory T-cell activity, fostering immune tolerance and mitigating neuroinflammatory damage [5, 6].

### 4. 2.Gut Barrier Integrity

Postbiotics improve gut barrier function by strengthening tight junction proteins and enhancing mucus production. These effects mitigate the translocation of harmful substances, reducing systemic inflammation in neonatal mice models [7, 8].

### 4. 3.Neurotransmitter Production

Postbiotics stimulate enterochromaffin cells to produce serotonin and dopamine, essential for mood regulation and cognitive development. Enhanced microbial activity has been linked to improved neurotransmitter availability [5, 9].

**Table 1**: Summary Table of Evidence.

| Study | Postbiotic Component | Neonatal Outcome | Mechanism | Reference |
|---|---|---|---|---|
| Hsiao et al. (2013) | SCFAs (e.g., butyrate) | Enhanced neurodevelopment | Increased BDNF expression, synaptic plasticity | 5 |
| Sudo et al. (2004) | Microbial metabolites | Reduced stress response | Regulation of HPA axis and cortisol levels | 6 |
| Sharon et al. -2016 | Bacterial polysaccharides | Improved social behavior | Modulation of immune, neural pathways | 7 |
| Cerdo et al. (2023) | Lactobacillus- derived factors | Improved gut barrier | Strengthened tight junctions, reduced inflammation | 8 |

### 4. 4.Epigenetic Regulation

SCFAs act as histone deacetylase inhibitors, fostering a favorable transcriptional environment for neurotrophic factors like BDNF and resilience to stress. These epigenetic changes support long- term neurodevelopment [10].

## 5. Discussion

### 5.1. Neurodevelopmental Impact

Postbiotics enhance neurotrophic factors critical for neuronal growth and synaptic plasticity. This is particularly beneficial for preterm infants, who face elevated risks of neurodevelopmental delays. The non-invasive nature of postbiotic interventions makes them appealing for neonatal care [5, 7].

### 5.2. Stress Modulation

By regulating the HPA axis, postbiotics lower cortisol levels and improve stress resilience. These effects not only optimize immediate outcomes but also support long-term psychological health, particularly in neonates undergoing intensive care [6, 9,11].

### 5.3. Immune System Development

Postbiotics contribute to immune system maturation by modulating inflammatory pathways and promoting regulatory T-cell growth. This reduces the risk of chronic inflammatory conditions and infections, indirectly supporting neurodevelopment [8, 12].

### 5.4. Potential for Preventing Neurodevelopmental Disorders

Emerging data suggest that postbiotics may lower the risk of disorders such as autism spectrum disorder (ASD) and ADHD by mitigating neuroinflammation and promoting a balanced microbiota. These findings underline the importance of early-life interventions [7, 9].

### 5.5. Challenges and Future Directions

Standardizing postbiotic formulations remains a critical challenge. Large-scale randomized controlled trials are necessary to validate findings, optimize dosages, and establish delivery methods. Personalized approaches that consider microbiota profiles and genetic predispositions may enhance intervention efficacy. Additionally, longitudinal studies should assess the long-term effects of neonatal postbiotic supplementation on neurodevelopmental trajectories [10].

## 6. Conclusions

Postbiotics hold significant promise for neonatal health, particularly in enhancing neurodevelopment and supporting immune function through GBA modulation. While the current evidence is compelling, further research is essential to address existing challenges and facilitate the integration of postbiotics into routine neonatal care.

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