



## Review Article

## Gut microbiota and neurosurgery: understanding the gut-brain axis in postoperative recovery

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### Abstract

The gut-brain axis plays a pivotal role in postoperative recovery, particularly in the context of neurosurgery, where neuroinflammation and cognitive function are critical for patient outcomes. This complex bidirectional communication system between the gastrointestinal tract and the central nervous system is influenced by gut microbiota, which modulates neuroinflammation through short-chain fatty acids (SCFAs) and other metabolites. Dysbiosis, an imbalance in gut microbiota, can exacerbate neuroinflammatory responses and contribute to cognitive decline in surgical patients. Studies have demonstrated that maintaining gut health can enhance cognitive recovery and overall postoperative outcomes through the modulation of immune responses and neuroinflammatory pathways. Furthermore, nutritional interventions, including probiotics and prebiotics, have shown potential in optimizing microbiota composition to improve surgical recovery and cognitive function. This review article aims to elaborate on the intricate relationships among gut health, microbiota, and neurosurgical outcomes while exploring current scenarios, the role of nutritional supplements, and strategies to optimize postoperative recovery through gut microbiota modulation. Future directions in this field promise to unveil novel therapeutic approaches targeting the gut microbiome to improve neurosurgical outcomes and cognitive recovery.

**Keywords:** Gut microbiota, Gut-brain axis, Neuroinflammation, Neurosurgery, Postoperative recovery, Nutritional supplements

**Received:** 06-03-2025; **Accepted:** 09-04-2025; **Available Online:** 07-05-2025

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### 1. Introduction

The gut microbiome, a diverse community of microorganisms, is increasingly recognized for its significant role in both gastrointestinal and neurological health. The interaction between gut microbiota and the brain, known as the gut-brain axis, indicates that gut health can influence cognitive function and neuroinflammation, which are crucial factors in neurosurgical recovery.<sup>1</sup> Dysbiosis, characterized by an altered gut microbiota composition, has been associated with various neurological disorders, impairing postoperative recovery and increasing neuroinflammatory responses.<sup>2</sup> With the growing emphasis on personalized medicine, there is a need for a better understanding of how gut microbiota can be manipulated to enhance surgical outcomes.<sup>3</sup>

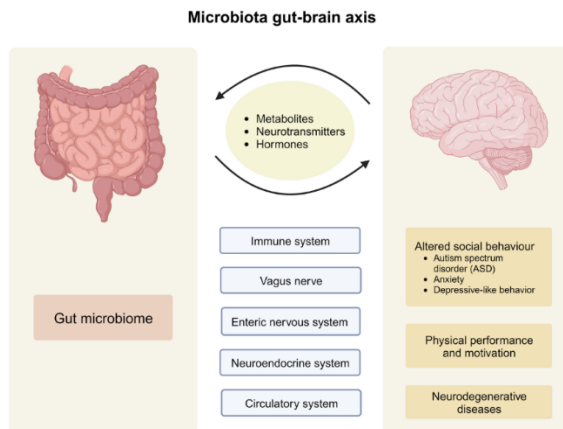
#### 1.1. Physiology of gut microbiota

The human gut microbiota encompasses trillions of microorganisms, predominantly bacteria that play indispensable roles in various physiological processes. These include metabolism, immune responses, and protection against pathogens.<sup>2,4</sup> Within this complex community, several microbial species have been identified as particularly significant for maintaining gut health and influencing the gut-brain axis, thereby affecting neurological functions.<sup>3</sup>

Notable bacterial genera within the gut microbiota include *Lactobacillus*, *Bifidobacterium*, and *Faecalibacterium*, which have been shown to contribute positively to gut health through various mechanisms.<sup>4,5</sup> For instance, *Lactobacillus* species are known for their role in fermenting lactose into lactic acid, which lowers gut pH and inhibits the growth of pathogenic bacteria. These beneficial

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bacteria also produce short-chain fatty acids like butyrate, which serve as energy sources for colonocytes and exhibit anti-inflammatory properties.<sup>5</sup> Similarly, *Bifidobacterium* species play a crucial role in modulating the immune system; they enhance intestinal barrier function and exert protective effects against gut inflammation.<sup>5,6</sup>



**Figure 1:** The Gut-brain axis: The immune system, vagus nerve, enteric nervous system, neuroendocrine system, and circulatory system facilitate bidirectional communication between the gut microbiome and the brain. Changes in gut microbiota have been associated with autism spectrum disorders, anxiety, depressive-like behaviour, reduced physical performance and motivation, as well as neurodegenerative diseases.<sup>7</sup>

Another key player, *Faecalibacterium prausnitzii*, is one of the most abundant and significant species in a healthy gut microbiota and is known for its beneficial effects on intestinal health and anti-inflammatory actions. Low levels of *Faecalibacterium prausnitzii* have been associated with various gastrointestinal diseases, underscoring its protective role.<sup>4</sup> Conversely, overgrowth of harmful bacteria, such as *Escherichia coli* or *Clostridium difficile*, can lead to dysbiosis, which is associated with heightened inflammation and a compromised gut barrier.<sup>5,6</sup>

Approximately 80% of the vagus nerve fibres are afferent, allowing it to convey gut signals to the brain, influencing cognitive recovery post-surgery. Activation of the vagus nerve by SCFAs has been shown to enhance anti-inflammatory responses in the brain.<sup>2,4</sup> The interaction of gut microbiota with the host is mediated through several pathways, including direct contact, microbial metabolites (like SCFAs), and signalling via the vagus nerve.<sup>2,7</sup> These interactions are critical for the maintenance of homeostasis and have far-reaching implications for both gastrointestinal and neurological health. For instance, the gut-brain axis facilitates communication between the gut microbiota and the brain, influencing not only cognitive function but also emotional regulation.<sup>6</sup> **Figure 1** shows the gut-brain axis.<sup>7,8</sup>

Research indicates that dysbiosis (the imbalance of gut microbiota) can alter the gut-brain axis and exacerbate

neuroinflammatory responses, which is particularly relevant in the context of neurosurgery.<sup>8</sup> This state is characterized by increased intestinal permeability, allowing microbial products and toxins to enter systemic circulation, potentially leading to neuroinflammation and cognitive impairments post-surgery and influencing postoperative recovery.<sup>6</sup> A comprehensive understanding of these interactions is crucial for developing targeted probiotic and prebiotic therapies to enhance surgical recovery and cognitive outcomes in neurosurgical patients.

Thus, the gut microbiota's composition, with specific emphasis on beneficial species such as *Lactobacillus*, *Bifidobacterium*, and *Faecalibacterium prausnitzii*, plays a pivotal role in maintaining gut health, influencing the gut-brain axis, and potentially impacting surgical outcomes in neurosurgery.<sup>9</sup> The disruption of this balance can lead to adverse health outcomes, elucidating the need for ongoing research and personalized medical approaches in managing gut health in neurosurgical practices.<sup>4</sup>

### 1.2. Effect of gut microbiota on neurosurgery and vice versa

Preoperative and postoperative gut health have profound implications for neurosurgical outcomes. Dysbiosis has been linked to increased neuroinflammation, which can hinder cognitive recovery post-surgery. Studies have revealed that certain gut microbiota can mitigate neuroinflammation via the production of SCFAs that exert anti-inflammatory properties.<sup>2</sup> Additionally, surgical stress can alter gut microbiota composition, leading to impaired gut permeability and subsequent neuroinflammatory responses.<sup>9,11</sup>

Conversely, postoperative recovery strategies can profoundly influence gut microbiota. Nutritional interventions aimed at restoring gut health, such as the use of probiotics, prebiotics, and synbiotics, have been associated with improved neurocognitive outcomes in neurosurgery patients.<sup>4</sup> These findings underscore the necessity to consider gut microbiota as a crucial component in the holistic management of neurosurgical patients.<sup>4</sup>

## 2. Current Scenarios

Recent research highlights an increasing recognition of the gut-brain axis in the context of neurosurgery. For instance, studies demonstrate that microbiota manipulation through dietary interventions can enhance cognitive function and reduce postoperative complications.<sup>2,5</sup> However, translating these findings into clinical practice remains challenging. Limitations include variability among individual microbiota profiles and the necessity for further research to establish standardized protocols for gut health optimization in surgical patients.<sup>3,5</sup>

### 2.1. Role of nutritional supplements and dietary additions in postoperative recovery and neuroinflammation

Nutritional support plays a vital role in the postoperative recovery of neurosurgery patients by influencing neuroinflammation and patient outcomes. Key components include:

**Probiotics:** These live microorganisms help restore gut microbiota balance and enhance immune responses. Clinical studies show that perioperative probiotic supplementation can significantly reduce postoperative complications by improving gut barrier function and modulating the immune system.<sup>2</sup>

**Prebiotics:** Non-digestible food ingredients that stimulate the growth of beneficial gut bacteria, prebiotics support overall gut health and enhance the production of short-chain fatty acids (SCFAs), which play a critical role in reducing inflammation and promoting cognitive recovery.<sup>9</sup>

**Omega-3 Fatty Acids:** Found in fish oil, omega-3 PUFAs, particularly DHA and EPA, have well-documented anti-inflammatory effects. Their supplementation can improve functional recovery and cognitive outcomes by promoting neuro protection and reducing neuroinflammation after surgical trauma.<sup>11</sup>

**Glutamine:** This amino acid supports immune function and intestinal health. Glutamine supplementation has been associated with improved postoperative recovery, highlighting its role in maintaining gut integrity and reducing complication rates.<sup>1</sup>

**High-protein diets:** Adequate protein intake is critical for wound healing and recovery. Increased protein consumption helps mitigate muscle loss and supports recovery, particularly in older patients following neurosurgery.<sup>1</sup>

**Timing of nutritional interventions:** The early introduction of nutritional support post-surgery is essential for further enhancing recovery and minimizing complications.<sup>1</sup> Timely interventions can significantly improve dietary intake and overall quality of recovery.<sup>3</sup>

Thus, targeted nutritional approaches, including probiotics, prebiotics, and omega-3 supplementation, along with dietary protein modifications, play a crucial role in improving postoperative outcomes and managing neuroinflammation in neurosurgical patients.<sup>1</sup>

## 3. Discussion

The relationship between gut microbiota and neurosurgery outcomes represents a burgeoning field of study that necessitates a nuanced understanding of the gut-brain axis and its implications for patient management strategies. Neurosurgical procedures, ranging from elective interventions such as tumour excision to emergency surgeries like traumatic brain injury repair, induce systemic stress

responses and can alter gut microbiota composition significantly. This phenomenon impacts both neuroinflammation and cognitive recovery post-surgery.

A considerable body of evidence indicates that dysbiosis—a state of microbial imbalance—can lead to increased intestinal permeability and systemic inflammation, both of which adversely affect neurological outcomes.<sup>1,2</sup> In neurosurgical patients, heightened neuroinflammation can exacerbate postoperative complications such as delirium, cognitive dysfunction, and prolonged ICU stays.<sup>3</sup> For example, increased levels of systemic pro-inflammatory cytokines have been correlated with poor cognitive outcomes in surgical patients, suggesting that the inflammatory state influenced by gut microbiota could extend to affect neural healing and recovery.<sup>4</sup>

Moreover, studies have shown that certain gut-derived metabolites, particularly SCFAs such as butyrate, exert neuroprotective effects that promote neuronal health and cognitive function.<sup>10</sup> SCFAs are produced by the fermentation of dietary fibres by beneficial gut microbiota and have been found to modulate the activity of microglia, the brain's resident immune cells, thereby influencing neuroinflammatory responses during postoperative recovery.<sup>11</sup>

The practical implications of these findings are profound for neurosurgeons. Strategies aimed at preserving or restoring gut microbiota during the perioperative period may mitigate the risk of neuroinflammation. For instance, the preoperative administration of probiotics and prebiotics to patients undergoing neurosurgery may enhance gut health, improve resilience against surgical stress, and promote faster cognitive recovery post-surgery.<sup>12</sup> There is emerging clinical evidence that supports this strategy: for example, in a pilot study, neurosurgical patients who received a specific probiotic formulation exhibited lower rates of postoperative delirium and improved cognitive scores compared to those who received a placebo.<sup>13</sup>

In parallel, perioperative nutritional strategies play a crucial role. Implementing a dietary regimen that emphasizes fibre-rich foods before surgery can help preserve a healthy gut microbiome by fostering the growth of beneficial bacteria, such as *Lactobacillus* and *Bifidobacterium*, which may, in turn, reduce inflammation and enhance cognitive outcomes post-surgery.<sup>14</sup> Furthermore, maintaining a well-balanced gut microbiota is critical for the regulation of the blood-brain barrier (BBB), which, when compromised, can lead to neuroinflammatory cascades that complicate postoperative recovery.<sup>15</sup> Therefore, strategies focusing on gut health can not only improve nutritional status but also serve as preventive measures against complications. Additionally, the timing of nutritional interventions is crucial. Preoperative optimization of the gut microbiota, combined with continued support through the early postoperative period, is essential for maximizing benefits and

minimizing the risk of complications. Given the critical nature of cognitive outcomes in neurosurgical patients—especially those undergoing major interventions or dealing with neurodegenerative conditions—tailoring such interventions becomes imperative.<sup>16</sup>

Neurosurgeons must also consider the individual patient's microbiome profile, which can be influenced by age, comorbidities, previous antibiotic therapy, and baseline dietary habits. Personalized approaches that consider these factors may enhance the effectiveness of therapies aimed at modulating gut microbiota.<sup>17</sup> Systematic screenings and the use of microbiome analysis could inform tailored strategies that align better with each patient's unique microbiota composition and metabolic requirements.<sup>18</sup> Moreover, further research is warranted to elucidate how specific surgical types and techniques might differentially affect gut microbiota and, by extension, cognitive outcomes. For instance, minimally invasive techniques might result in less surgical stress, potentially preserving gut integrity and microbiome function compared to traditional open surgery.<sup>12</sup>

Thus, the interplay between gut microbiota and neurosurgical outcomes is complex yet offers promising avenues for enhancing patient care. By integrating gut health strategies into the multidimensional management of neurosurgical patients, clinicians may improve not only postoperative recovery but also long-term cognitive outcomes. Future research is necessary to substantiate these links and to develop standardized protocols for the clinical management of gut health in the context of neurosurgery.<sup>19,20</sup>

#### 4. Future Prospects

As research into the gut-brain axis continues to advance, the potential for targeted microbiota manipulation as a therapeutic strategy in neurosurgery appears promising. A deeper understanding of the microbiome's role in neuroinflammatory processes and cognitive recovery could pave the way for innovative treatments aimed at improving surgical outcomes.<sup>2,21</sup> Additionally, emerging technologies in microbiome analysis may facilitate personalized treatments, ensuring that interventions are tailored to individual microbiota compositions and health needs.

#### 5. Conclusion

The intricate relationships between gut microbiota, neuroinflammation, and cognitive function underscore the importance of gut health in postoperative recovery following neurosurgery. Maintaining a balanced gut microbiome through nutritional interventions may enhance neurocognitive outcomes, highlighting a critical area for future research. As our understanding of the gut-brain axis deepens, the development of microbiota-centered strategies could transform the landscape of neurosurgical care, ultimately improving patient outcomes and quality of life.

#### 6. Source of Funding

None.

#### 7. Conflict of Interest

None.

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**Cite this article:** Patel V, Jain AP, Mehta V. Gut Microbiota and Neurosurgery: Understanding the Gut-Brain Axis in Postoperative Recovery. *IP J Nutr Metab Health Sci.* 2025;8(1):19–23