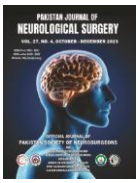

PAKISTAN JOURNAL OF NEUROLOGICAL SURGERY (QUARTERLY) – OFFICIAL JOURNAL OF PAKISTAN SOCIETY OF NEUROSURGEONS

DOI: 10.36552/pjns.v29i4.1096

EDITORIAL

Gut–Brain Axis (GBA) and Neurosurgical Practice:
Treatment Implications of Gut Microbiota Modulation

Prof. Dr. Saman Shahid (Head EH-DS Lab, National University of Computer & Emerging Sciences -NUCES, FAST Lahore)
Prof. Dr. Muhammad Anwar Chaudary. Chief Editor, Ex-Head of Department Neurosurgery Unit II, (PINS), Department of Neurosurgery, Farooq Hospital, Lahore, Pakistan

Introduction:
The gut–brain axis (GBA) is emerging as a clinically relevant dimension of neurosurgical care. Numerous studies have demonstrated the presence of a group of pathways known as the GBA that connect the gut microbiota to the central nervous system (CNS). The bacterial diversity of the gut microbiome appears to vary with age, exposure to antibiotics, and a variety of internal and environmental variables, which complicates this link. The gut–brain axis (GBA) is a bidirectional network linking gut microbiota, the enteric nervous system, immune and endocrine pathways, with central nervous system (CNS) function. Disturbance of this axis is increasingly relevant to neurosurgical decision-making and perioperative care [1-2] . The focus should be on how major surgeries like bariatric surgery or neurosurgery alter the GBA, and how to use that understanding to improve outcomes, often through interventions that modulate the gut microbiome. We can use probiotics/prebiotics to support gut health during neurosurgery recovery or understand how bariatric surgery changes gut hormones and metabolites, which can affect mental health. Surgeries can cause neuroinflammation, and perioperative neurocognitive disorders are being reported; therefore, current researchers are targeting the GBA that may help. There is a recommendation to use the Microbiome Modulation, in which probiotics or prebiotics are administered before or after surgery may help improve cognitive function by balancing the gut microbiome and reducing inflammation. Neurosurgeons also need to prevent surgical brain injury (SBI) by a novel strategy of correcting gut dysbiosis to enhance fine recovery. Further, Neuromodulation can be employed for GBA disturbances, such as functional digestive disorders. There is an option of Vagus Nerve Stimulation (VNS) as well, because this nerve is a key conduit for gut-brain communication. VNS has shown promise in treating conditions like depression and epilepsy [1-10].

Mechanisms of the Microbiota–Gut–Brain Axis Relevant to Neurosurgery: Gut microbes communicate with the brain via vagal and spinal autonomic nerves, immune signaling, and microbial metabolites (short-chain fatty acids, tryptophan metabolites, bile acids, neurotransmitters) [1-3]. These signals influence microglia, astrocytes, and blood–brain barrier (BBB) integrity, thereby modulating neuroinflammation, neurogenesis, and synaptic plasticity [2, 4]. Dysbiosis (disrupted microbial communities) can increase gut permeability and peripheral inflammation, which in turn promotes neuroinflammation and neuronal injury [3-5]. Surgery, anesthesia, opioids, antibiotics, and perioperative stress all perturb microbiota composition, especially in older or frail patients [6-8]. Experimental and clinical data suggest that these disturbances contribute to perioperative neurocognitive disorders (PND), including delirium and postoperative cognitive dysfunction, by triggering neuroinflammatory cascades via the microbiota–gut–brain axis [6-9].

Acute CNS Injury, Spine/Brain Surgery and the Gut: Neurosurgical conditions such as traumatic brain injury (TBI), spinal cord injury (SCI), and stroke induce profound, bidirectional disruption of the gut–brain axis. CNS injury alters autonomic outflow, gut motility, and mucosal immunity, rapidly driving dysbiosis. In turn, dysbiotic microbiota promote secondary brain injury through systemic inflammation, translocation of microbial products, and microglial activation, worsening cognition and functional outcome [10-13]. A similar two-way interaction appears after brain and spinal neurosurgery: CNS injury and perioperative factors disrupt gastrointestinal function via the hypothalamic–pituitary–adrenal axis and vagus nerve, while resultant dysbiosis and intestinal inflammation can exacerbate cerebral damage [12-14].

Perioperative Neurocognitive Disorders and Surgical Choices: Multiple reviews now link microbiota–gut–brain signaling to PND (Paroxysmal Nocturnal Dyspnea) pathogenesis. Elderly and high-risk patients show anesthesia- and surgery-induced loss of beneficial taxa (e.g., lactobacilli, bifidobacteria) with expansion of pro-inflammatory species, correlating with cognitive decline [6-9]. These findings raise several neurosurgical implications:

- **Risk stratification:** Pre-existing dysbiosis (age, obesity, chronic antibiotics) may identify patients at higher risk of delirium or delayed recovery [7-8].
- **Choice and timing of antibiotics and opioids:** Broad-spectrum regimens and prolonged opioid use are major microbiota disruptors; judicious use may reduce PND risk [14].
- **Anesthetic and analgesic strategies:** Minimizing systemic inflammation and stress may help preserve gut barrier and microbial homeostasis, though direct comparative trials in neurosurgery are limited [9].
- **Enhanced recovery protocols:** Early enteral nutrition and mobilization support microbiota stability and might lower infectious and cognitive complications after neurosurgical procedures [14].

Microbiota-Targeted Therapies in Neurosurgical Contexts

1. **Probiotics and Synbiotics (functional foods /supplements containing probiotics)**
    - Clinical studies in neuro-trauma and spine surgery suggest probiotic supplementation can improve gastrointestinal motility, reduce infection rates, modulate inflammatory cytokines, and may support cognitive recovery after TBI or spinal procedures [14-15].
    - Probiotic strains (e.g., Lactobacillus, Bifidobacterium) can enhance SCFA (short-chain fatty acid) production, upregulate neurotrophic factors (e.g., BDNF- Brain-Derived Neurotrophic Factor), strengthen BBB integrity, and dampen neuroinflammation [15].
    - However, strain-specific effects, heterogeneous trial designs, and small sample sizes mean evidence is promising but not definitive; better-designed RCTs are needed before routine neurosurgical use [14].
2. **Fecal Microbiota Transplantation (FMT)**
    - FMT has shown capacity to restore microbial diversity, reduce neuroinflammation, and improve cognitive or motor deficits in preclinical models and early clinical work in Parkinson's and Alzheimer's disease [16].
    - Conceptually, FMT or rationally designed microbial consortia could be used to break the toxic gut–CNS feedback loop after stroke, TBI, or PND, but safety, donor selection, and standardization remain major barriers, and neurosurgical-specific trials are lacking [16].
3. **Dietary Interventions and Prebiotics**
    - Diets that promote SCFA-producing commensals and reduce systemic inflammation may support microglial homeostasis and limit secondary injury after stroke or TBI [3-4].
    - Prebiotics (non-digestible fibers) and synbiotics can selectively encourage beneficial taxa, but controlled neurosurgical trials are still sparse [3].
4. **Neuromodulation of the GBA**
    - VNS, already used in epilepsy and depression, also modulates gut motility and immune tone. Experimental data suggest it can influence microbiota composition and attenuate neuroinflammation, positioning it as a potential tool to reshape the GBA in select neurosurgical patients [10].

Table: Key gut–brain axis (GBA) mechanisms shaping neurosurgical management

Clinical context / neurosurgical issue	GBA / microbiota involvement	Potential therapeutic implications
Perioperative neurocognitive disorders	Anesthesia/surgery-induced dysbiosis, neuroinflammation via MGB axis	Optimize antibiotics/opioids; test perioperative probiotics/FMT[6-9]
TBI, SCI, acute stroke	CNS injury → dysbiosis → secondary injury	Microbiota modulation to limit neuroinflammation, improve outcomes[10-13]
Brain/spine tumor treatment	Microbiota affect treatment response, immunity	Use microbiome-supportive diets/probiotics alongside oncologic care[10, 16]
Neurodegenerative disorders in neurosurgical patients	Chronic dysbiosis, GBA dysfunction	Adjunct probiotics, prebiotics, and FMT under trial conditions[2-4]

References

1. Cryan JF, O'Riordan KJ, Cowan CS, Sandhu KV, Bastiaanssen TF, Boehme M, Codagnone MG, Cussotto S, Fulling C, Golubeva AV, Guzzetta KE. The microbiota-gut-brain axis. Physiological reviews. 2019; 99 4. https://doi.org/10.1152/physrev.00018.2018
2. Zheng Y, Bonfili L, Wei T, Eleuteri AM. Understanding the gut–brain axis and its therapeutic implications for neurodegenerative disorders. Nutrients. 2023;15(21):4631.https://doi.org/10.3390/nu15214631
3. Suganya K, Koo BS. Gut–brain axis: role of gut microbiota on neurological disorders and how probiotics/prebiotics beneficially modulate microbial and immune pathways to improve brain functions. International journal of molecular sciences. 2020;21(20):7551. https://doi.org/10.3390/ijms21207551
4. Loh JS, Mak WQ, Tan LK, Ng CX, Chan HH, Yeow SH, Foo JB, Ong YS, How CW, Khaw KY. Microbiota–gut–brain axis and its therapeutic applications in neurodegenerative diseases. Signal transduction and targeted therapy. 2024;9(1):37. https://doi.org/10.1038/s41392-024-01743-1
5. Almheiri RT, Hajjar B, Alkhaaldi SM, Rabeh N, Aljoudi S, Abd-Elrahman KS, Hamdan H. Beyond weight loss: exploring the neurological ramifications of altered gut microbiota post-bariatric surgery. Journal of Translational Medicine. 2025;23(1):223.. https://doi.org/10.1186/s12967-025-06201-2
6. Lu J, Hou W, Gao S, Zhang Y, Zong Y. The Role of Gut Microbiota—Gut—Brain Axis in Perioperative Neurocognitive Dysfunction. Frontiers in Pharmacology. 2022;13:879745. https://doi.org/10.3389/fphar.2022.879745
7. Que M, Li S, Xia Q, Li X, Luo X, Zhan G, Luo A. Microbiota-gut-brain axis in perioperative neurocognitive and depressive disorders: Pathogenesis to treatment. Neurobiology of Disease. 2024;200:106627.https://doi.org/10.1016/j.nbd.2024.106627
8. Sun Y, Wang K, Zhao W. Gut microbiota in perioperative neurocognitive disorders: current evidence and future directions. Frontiers in Immunology. 2023;14:1178691.https://doi.org/10.3389/fimmu.2023.1178691
9. Zhou Q, Chen T, Wang X, Xu Z, Song Y, Liu S, Ge Y, Gao J. Role of gut microbiota in neuroinflammation: a focus on perioperative neurocognitive disorders. Frontiers in Cellular and Infection Microbiology. 2025;15:1582909. https://doi.org/10.3389/fcimb.2025.1582909
10. Willman J, Willman M, Reddy R, Fusco A, Sriram S, Mehkri Y, Charles J, Goeckeritz J, Lucke-Wold B. Gut microbiome and neurosurgery: Implications for treatment. Clinical and translational discovery. 2022;2(4):e139.https://doi.org/10.1002/ctd2.139
11. Ashique S, Mohanto S, Ahmed MG, Mishra N, Garg A, Chellappan DK, Omara T, Iqbal S, Kahwa I. Gut-brain axis: A cutting-edge approach to target neurological disorders and potential synbiotic application. Heliyon. 2024;10(13).https://doi.org/10.1016/j.heliyon.2024.e34092
12. Yuan B, Lu XJ, Wu Q. Gut microbiota and acute central nervous system injury: a new target for therapeutic intervention. Frontiers in immunology. 2021;12:800796. https://doi.org/10.3389/fimmu.2021.800796
13. Oyovwi MO, Udi OA. The gut-brain axis and neuroinflammation in traumatic brain injury. Molecular neurobiology. 2025;62(4):4576-90.https://doi.org/10.1007/s12035-024-04585-8
14. Fijan S, Šmigoc T. Overview of the efficacy of using probiotics for neurosurgical and potential neurosurgical patients. Microorganisms. 2024;12(7):1361.https://doi.org/10.3390/microorganisms12071361
15. Nandal K, Rathee J, Nandal R, Dahiya P, Kaur M. Probiotics in Neurosurgery and Neurodegenerative Diseases: Harnessing the Gut-brain Axis for Recovery. Journal of Biology and Nature. 2025;17(2):22-34.https://doi.org/10.56557/joban/2025/v17i29413
16. Liu L, Huh JR, Shah K. Microbiota and the gut-brain-axis: Implications for new therapeutic design in the CNS. EBioMedicine. 2022;77.https://doi.org/10.1016/j.ebiom.2022.103908