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Review Article

The Gut–Brain Axis in Sleep Deprivation: Mechanisms, Dysbiosis, and Potential Therapeutic Avenues

Esmail Karami[1], PhD; Mohammad Taghi Mohammadi[2], PhD; Hossein Shirvani[1], PhD; Behzad Bazgir[1], PhD

[1]Exercise Physiology Research Center, Life Style Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran;
[2]Department of Physiology and Medical Physics, Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran

Correspondence:
Behzad Bazgir, PhD;
Baqiyatullah University of Medical Sciences, Vanak Sq., Mulla Sadra St., Sheikh Bahai St., Postal code: 14155-64371, Tehran, Iran
Tel: +98 21 88754475
Email: bazgirbehzad@yahoo.com
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Abstract

Sleep is fundamental to metabolic regulation, cardiovascular health, immune balance, and cognitive performance. Emerging evidence indicates that sleep deprivation alters gut microbial communities and immune signaling, thereby influencing the gut-brain axis. This narrative review synthesized current findings on how sleep loss engages gut–brain pathways and evaluated therapeutic avenues linked to specific mechanisms, drawing on peer-reviewed human and animal studies and prioritizing sleep- and brain-relevant outcomes. Evidence converged on three mechanistic pillars: (1) circadian and microbial misalignment, which disrupts diurnal microbiome dynamics; (2) inflammatory and barrier dysfunction loops that increase permeability and immune activation; and (3) altered neurotransmitter and metabolite signaling, including shifts in tryptophan pathways and reduced short-chain fatty acid production, with downstream effects on neuroinflammation and plasticity. Human data supported associations between sleep loss, poor sleep quality, and impaired cognition. However, causal inference was limited by small sample sizes, study heterogeneity, and mixed endpoints. Interventions such as probiotics, prebiotics, postbiotics, synbiotics, diet-based short-chain fatty acid strategies, and chronobiotics are biologically plausible, yet they are supported mainly by small trials or preclinical models. Fecal microbiota transplantation shows exploratory, yet faces significant safety, standardization, and regulatory challenges. Collectively, the evidence indicated that sleep deprivation disrupts gut microbiota composition and gut-brain signaling, with consequences for neuroinflammation, neurotransmitter balance, and cognition. This review highlighted the consequent need for standardized endpoints, strain-resolved microbiome analyses, and well-powered randomized controlled trials.

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Keywords ● Sleep deprivation ● Gut–brain axis (GBA) ● Microbiota ● Neuroinflammation ● Probiotics

What's Known

- Insufficient sleep is associated with metabolic, cardiovascular, and mental health risks.
- Sleep loss perturbs gut microbial communities and immune signaling, which can influence brain function.

What's New

- We propose a tiered model illustrating how sleep loss disrupts the gut–brain axis through (i) circadian and microbial misalignment, (ii) inflammatory and barrier dysfunction loops, and (iii) altered neurotransmitter and metabolite signaling.
- We mapped interventions to these specific mechanisms, including nutritional strategies targeting short-chain fatty acids, postbiotics, microbiota-informed chronobiotics, probiotics, and fecal microbiota transplantation.

Introduction

Sleep deprivation has become a widespread problem in contemporary life, exerting a substantial negative influence on productivity and general well-being across diverse populations.[1] Chronic sleep deprivation is linked to several major health issues, such as metabolic disorders, cardiovascular diseases, and mental health impairments, in addition to the obvious ones, such as impaired cognitive performance and excessive daytime sleepiness.[2] The established connection between sleep deprivation and brain or mental health issues underscores the urgency of addressing this public health challenge.[3]

According to recent research, sleep deprivation has a significant impact on the gut microbiota, which is the intricate ecosystem of microorganisms residing in the gastrointestinal tract.[4] Sleep disturbances can cause dysbiosis, characterized by an imbalance between beneficial and harmful bacteria and a reduction in microbial diversity.[5] Numerous factors, such as changes in circadian rhythms, dietary practices, and stress hormone levels, are thought to be responsible for these changes in the composition of the gut microbiota. Since many physiological processes depend on the gut microbiota, its disruption can have cascading effects on overall health.[6-8]

Notably, the gut–brain axis (GBA) serves as the bidirectional communication network linking the gut and the brain, influencing emotion, cognition, and behavior.[9] Dysbiosis induced by sleep deprivation may disrupt GBA signaling, potentially exacerbating neurological dysfunction.[10] This complex relationship emphasizes the critical need to understand the specific mechanisms by which sleep deprivation impairs gut–brain communication.[11]

This narrative review aimed to investigate the effects of sleep deprivation on gut–brain crosstalk and to evaluate the potential of emerging interventions designed to mitigate these detrimental effects. By synthesizing the current literature, this review aimed to provide a mechanistic foundation for future research and therapeutic strategies aimed at preserving gut and brain health in the context of sleep loss.

Literature Selection

This narrative review integrated multidisciplinary evidence on how sleep deprivation alters the gut–brain axis, prioritizing mechanistic and translational synthesis over quantitative meta-analysis. A structured search of MEDLINE (via PubMed) and Scopus was conducted for literature published up to June 2025. The search strategy was designed to identify studies on sleep loss, microbiome dynamics, inflammation, neurotransmitters, short-chain fatty acids (SCFAs), and fecal microbiota transplantation (FMT). Relevant studies were also identified through hand-searching of reference lists.

Eligible studies included peer-reviewed, English-language reports of human, animal, and *in vitro* studies that specifically addressed microbiota composition, microbial metabolites, intestinal barrier and immune integrity, neurological outcomes, or microbiota-directed interventions. Non-English reports, conference abstracts, and opinion pieces were excluded. Data pertaining to study design, populations, outcomes, and mechanisms were extracted and narratively synthesized. The synthesis was organized around three focal domains: (i) circadian microbial misalignment, (ii) inflammatory and barrier dysfunction, and (iii) neurotransmitter and metabolite signaling. This structure provided an integrative framework for linking sleep deprivation-induced dysbiosis to neuroinflammation and cognitive impairment.

Effects of Sleep Deprivation on the Gut Microbiota

As discussed, sleep deprivation significantly disrupts the balance of the gut microbiota, leading to substantial alterations in its diversity and composition. It is associated not only with a general decline in microbial richness but also with specific changes in the relative abundance of specific bacterial species.[12, 13]

A primary cause of this disruption is the disturbance of circadian rhythms, which are crucial for regulating the diurnal oscillations of gut bacteria.[14] Circadian rhythms coordinate the timing of microbial growth and activity, which is why beneficial microorganisms thrive during wakefulness and digestion periods.[15] This timing is disrupted when sleep is interrupted, which can result in changes in intestinal motility and nutrient absorption, thereby creating an environment conducive to dysbiosis.[16, 17]

Furthermore, sleep deprivation activates the hypothalamic-pituitary-adrenal axis, elevating levels of stress hormones such as cortisol.[18] These hormones directly impact the gut environment, promoting the proliferation of stress- resistant species while suppressing beneficial ones. This modification establishes a deleterious feedback loop: the altered microbiome exacerbates local inflammation, which in turn further compromises gut barrier integrity.[6, 19, 20]

Compounding the issue, sleep deprivation induces dysregulation of the immune system, impairing gut mucosal immunity. In addition to exacerbating dysbiosis, the subsequent immune dysfunction feeds systemic inflammation, which can subsequently affect the central nervous system (CNS) and other organ systems.[21]

Dietary patterns are also altered by inadequate sleep, frequently resulting in increased consumption of high-fat and high-calorie foods.[22, 23] These dietary modifications further influence the composition and metabolic activity of the gut microbiota by providing substrates that promote the growth of specific microbial populations. For example, a diet high in processed foods can favor the proliferation of bacteria that thrive on simple sugars and fats, while depleting beneficial microbes dependent on dietary fiber. This imbalance can contribute to metabolic disorders such as insulin resistance and obesity, which promote inflammation detrimental to gastrointestinal health.[24]

Additionally, inadequate sleep can induce epigenetic modifications in both the gut microbiota and host cells. These alterations in gene expression can influence microbial metabolic activity and the overall gut ecosystem. Such epigenetic modifications have the potential to further complicate the relationship between sleep, diet, and gut health by modulating how gut bacteria interact with the host and metabolize nutrients.[25, 26]

Of note, the systemic effects of sleep deprivation extend beyond the intestine, substantially impacting the production of gut microbial metabolites, particularly SCFAs.[27] SCFAs, including butyrate, acetate, and propionate, are primarily produced through the bacterial fermentation of indigestible dietary fiber.[28] These metabolites are essential for maintaining gastrointestinal health and influence diverse physiological processes, including brain function.[29]

A critical role of SCFAs is to regulate the gut barrier integrity. They serve as a primary energy source for colonocytes and enhance the expression of tight junction proteins. However, sleep deprivation disrupts SCFA synthesis, leading to a decrease in the concentration of these beneficial metabolites.[30-32] This reduction can compromise intestinal barrier integrity and impair immunological responses.[33, 34]

As SCFAs can cross the blood-brain barrier (BBB), their altered production has significant implications for brain health. Reduced levels of butyrate, for instance, may exacerbate neuroinflammation by failing to inhibit the production of pro-inflammatory cytokines, thereby increasing susceptibility to cognitive impairment, mood disorders, and neurodegenerative diseases.[35, 36] Additionally, SCFAs influence the expression of brain-derived neurotrophic factor (BDNF), a key regulator of synaptic plasticity and neurogenesis, directly linking gut metabolic output to brain function and resilience.[37]

Therapeutic Implications and Research Priorities

This narrative review provided an integrative synthesis of the current evidence linking sleep deprivation to GBA dysfunction. It emphasized the mechanistic interplay between circadian misalignment, microbial dysbiosis, immune–barrier disruption, and altered neurochemical signaling. Rather than performing a quantitative meta-analysis, this review critically consolidated mechanistic insights from human and animal studies to delineate how chronic sleep loss could reprogram gut microbiota composition, disrupt metabolite and neurotransmitter pathways, and ultimately impair cognitive and emotional regulation.[38-44]

The analysis identified three interconnected mechanistic domains through which sleep deprivation exerts its deleterious effects: (i) the disruption of circadian–microbial synchronization, (ii) the induction of inflammatory and epithelial barrier dysfunction loops, and (iii) the alteration of neurotransmitter and metabolite signaling, particularly involving tryptophan derivatives and SCFAs.[27, 28, 32, 35-37] Collectively, these findings suggest that gut microbial imbalance serves as both a mediator and amplifier of sleep-related neurophysiological disturbances.[21, 39, 40, 43, 44]

By integrating these mechanisms, the review advanced a conceptual understanding of gut–brain cross-talk in sleep biology and highlighted several biologically plausible therapeutic strategies, such as probiotics, prebiotics, and FMT, that may restore microbial homeostasis and mitigate neuroinflammatory consequences of sleep deprivation.[45-50]

The Promising Role of Newly Emerged Interventions

Building on these mechanistic insights, recent studies have explored potential interventions targeting the gut–brain axis to mitigate the effects of sleep deprivation. Clinical and preclinical data suggest that modulating the gut microbiota can have beneficial effects on mood, cognition, and sleep regulation.[51-53] Probiotics and prebiotics have demonstrated potential in restoring microbial balance and enhancing the production of beneficial metabolites, such as SCFAs, which are known to strengthen intestinal barrier integrity and reduce systemic inflammation.[46, 48]

The FMT has emerged as a particularly promising, though still experimental, intervention. Studies indicated that FMT can improve sleep quality and neurocognitive outcomes by correcting dysbiosis and enhancing microbial diversity.[45, 50] In patients with chronic fatigue or sleep-related cognitive impairment, FMT interventions was shown to partially restore a healthy microbial composition and alleviate neuroinflammatory symptoms.[47, 49]

Despite its promise, FMT faces significant safety, standardization, and regulatory challenges that currently limit its broad clinical application.[49] Collectively, this converging evidence underscores the translational potential of microbiota-targeted therapies for addressing sleep deprivation–related dysfunctions.[45-53]

These findings collectively underscored the complex interplay between sleep deprivation, the gut microbiota, and neurological outcomes, and pointed to probiotics, prebiotics, and other microbiota-focused strategies as promising therapeutic avenues. A summary of the main findings is presented in table 1.

Integrative Conceptual Framework: Linking Gut Dysbiosis to Neuroinflammation and Cognitive Impairment

To move beyond descriptive reporting, this current synthesis proposes an integrative conceptual framework that illustrates how sleep deprivation may causally perturb gut–brain communication. Chronic sleep loss disrupts the circadian regulation of gut microbial oscillations, leading to dysbiosis characterized by a loss of beneficial taxa (e.g., *Lactobacillus, Bifidobacterium*) and reduced microbial diversity.[12, 13, 16] This imbalance increases intestinal permeability ("leaky gut"), allowing translocation of bacterial components such as lipopolysaccharides (LPS) into systemic circulation.[43, 44]

The resulting systemic and neuroinflammation activates immune–neuroendocrine cascades, particularly via the HPA axis, elevating levels of cortisol and pro-inflammatory cytokines (e.g., IL-6, TNF-α).[39, 40, 42] Concurrently, dysbiosis alters the metabolism of tryptophan and SCFAs, reducing the production of serotonin and butyrate—metabolites that are crucial for neuronal plasticity and mood regulation.[27, 28, 30, 32, 37, 54, 55]

Several studies demonstrated that this disruption extends to neurotransmitter synthesis and signaling, particularly serotonin, dopamine, and γ-aminobutyric acid (GABA) pathways. Sleep deprivation impairs tryptophan metabolism, reducing serotonin synthesis in both gut and brain, which contributes to mood instability and anxiety.[54-58] Dopaminergic signaling is also affected; gut-derived dopamine precursors are reduced during dysbiosis, thereby altering reward and cognitive processing circuits.[59-64] Similarly, populations of GABA-producing microbes, such as *Lactobacillus* and *Bifidobacterium,* are diminished by sleep deprivation, which impairs inhibitory neurotransmission and sleep quality.[65-69]

Collectively, these multi-level alterations; circadian dysregulation, barrier breakdown, immune activation, and neurochemical

Table 1: Summary of main findings

Main context	Main findings	References
Disruption of gut microbiota by sleep deprivation	Sleep deprivation leads to reduced diversity and altered bacteria; circadian rhythms are crucial for gut health.	12-14
Impact on gut health and dysbiosis	Disrupted sleep negatively affects intestinal motility and nutrient absorption, promoting dysbiosis and harming beneficial bacteria.	16-18
Dietary changes due to sleep deprivation	Sleep loss alters dietary habits, increasing the consumption of high-fat and calorie-dense foods, which fosters harmful gut microbes and metabolic disorders.	22-24
Epigenetic changes in gut microbiota	Sleep deprivation causes epigenetic modifications that impact microbial gene expression, complicating the interplay between sleep, diet, and gut health.	25, 26
Effects of gut microbial metabolites	Reduced production of SCFAs leads to neuroinflammation and cognitive decline.	28
Neurotransmitter production and sleep	Disruption affects tryptophan metabolism and neurotransmitters (serotonin, GABA), contributing to mood disorders.	54, 55
Inflammation and gut-brain crosstalk	Inflammatory molecules from gut bacteria contribute to systemic inflammation, increasing risks for neurological conditions such as Alzheimer's and depression.	39, 40, 43, 44
Experimental evidence of gut microbial changes	Animal studies show increased Firmicutes and decreased Bacteroidetes linked to colonic inflammation and cognitive impairments.	38, 42, 43
Clinical evidence on sleep deprivation and neurological outcomes	Sleep deprivation is linked to cognitive decline and mood disorders; specific microbiota are associated with cognition.	51-53
Gut microbiota and mental health	Insomnia, lower diversity, and mood disorder links; FMT improves sleep quality and mood.	45, 50
Interventional studies linking sleep and gut health	FMT may mitigate sleep deprivation effects, potential for chronic fatigue syndrome treatment.	47, 49
Probiotics and cognitive decline in older adults	Poor sleep quality in older adults is linked to cognitive decline; probiotics are a potential intervention.	46, 48

SCFAs: Short-chain fatty acids; GABA: γ-Aminobutyric acid; FMT: Fecal microbiota transplant imbalance; disrupt the balance between excitatory and inhibitory neurotransmission, sustain a state of neuroinflammation, and ultimately exacerbate cognitive and emotional deficits.[38, 41, 70, 71]

Therapeutic Implications

The proposed framework underscores a bidirectional, self-perpetuating cycle: sleep deprivation induces dysbiosis and systemic inflammation, which in turn worsen sleep architecture and cognitive function.[39, 40, 43, 44] Breaking this cycle through microbiota-targeted interventions, such as probiotics, prebiotics, SCFA-enhancing diets, and FMT, offers a promising mechanistic strategy.[45-50]

Future research should prioritize longitudinal, mechanism-anchored randomized controlled trials (RCTs) that integrate multi-omic profiling (e.g., metagenomics, metabolomics) with neuroimaging to validate these proposed causal pathways and intervention efficacy.[47, 49, 52]

Policy Implications and Future Directions

The findings of this review underscore the urgent need for public health policies that prioritize sleep health as a critical determinant of physical and mental well-being. Public awareness programs should highlight the established links between chronic sleep deprivation, gut dysbiosis, and cognitive or emotional disorders.[21, 41] Preventive health strategies that incorporate sleep hygiene education, dietary regulation, and microbiota-supportive nutrition could play a pivotal role in reducing the societal burden of sleep-related illnesses.[7, 24, 27]

Future research must prioritize longitudinal and multi-omics clinical trials to evaluate how targeted microbiome interventions, such as specific probiotic strains, prebiotic formulations, or FMT, can effectively restore gut–brain homeostasis.[47, 49, 50, 52] Collaborative efforts between clinicians, neuroscientists, and microbiome researchers are essential to translate these mechanistic findings into actionable therapeutic guidelines and informed public health frameworks.[46, 48]

Such integrative, translational approaches will not only deepen our understanding of the gut–brain–sleep triad but also guide the development of evidence-based strategies to improve sleep and neurological health at a population level.

Conclusion

In conclusion, this narrative review synthesized evidence establishing that sleep deprivation induces gut dysbiosis, which subsequently disrupts the gut-brain axis, primarily through increased systemic inflammation and the dysregulation of key neurotransmitters. This mechanism ultimately contributes to cognitive deficits and mood disorders. The collective findings underscored the critical public health importance of addressing sleep deprivation. Furthermore, they indicated that microbiota-targeted interventions, such as specific probiotic formulations and FMT, represent a promising therapeutic avenue for restoring gut–brain homeostasis and improving neurological outcomes in affected individuals.

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Authors' Contribution

E.K and B.B were involved in all stages of the review, including conceptualization, literature search, analysis, and manuscript drafting. H.S and M.T.M contributed to the literature review, manuscript drafting, and critical revision. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of AI

During the preparation of this manuscript, PaperGuide AI (web-based platform) was used to assist with literature searches, identification of relevant references, and organization of the bibliography. ChatGPT (OpenAI; GPT-4o) was used to improve the language, grammar, clarity, and overall academic writing style of the manuscript. AI tools were used solely to support these tasks and were not involved in generating scientific data, analyzing results, interpreting findings, or drawing the study's conclusions. All AI-assisted content was carefully reviewed, verified, and edited by the authors, who accept full responsibility for the accuracy, integrity, and final content of the manuscript.

Conflict of Interest: None declared.

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