Proceedings of ICBioMed 2025 Symposium: Extended Reality (XR) Applications in Medical Imaging
DOI: 10.54254/2753-8818/2025.PJ25875

Relationship Between Gut Microorganisms and Sleep Quality in Animals

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Abstract: This paper investigated the relationship between gut microflora and sleep quality by reviewing a literature on changes in intestinal flora and animal metabolism. When the sleep state is intrinsically or externally disturbed, it can cause related disorders such as sleep deprivation, snoring, sleepwalking, leg twitching, and narcolepsy. The sleep process is a crucial period during which the body conducts metabolism. A decline in sleep quality will affect the normal operation of other organs. This paper focuses on the pathology associated with obstructive apnea-sleep in insomnia and its relationship with the intestinal flora. The intestinal flora contains about 1000 species of bacteria, such as specialized anaerobes of the genera Bacteroides, Eubacterium, Bifidobacterium, Ruminalococcus, and Clostridium. Their metabolic processes and products are involved in the production of hormones and neurotransmitters that regulate sleep. The results showed a decrease in the proportion of Bacteroidetes, as well as a reduction in certain bacteria with prebiotic potential. In contrast, there was an increase in the ratio of Proteobacteria and a decrease in the overall intestinal microflora among patients experiencing symptoms related to insomnia or those diagnosed with clinical insomnia.

Keywords: gut microflora, sleep, insomnia, obstructive respiratory sleep apnea, circadian rhythm

1. Introduction

The animal gut's digestive function is primarily carried out by complex microflora. Absorbed substances are transported through the bloodstream from gut cells to all parts of the body. The association of animal gut microbial communities with several indicators of animal sleep has been demonstrated in several studies, and there is also a link between sleep disorders and gut microbes, but the exact link is not clear [1]. It has been explained that microbes in the gut have evolved as symbionts in animals to manipulate host behavior for their benefit [2], in the course of evolution, thereby influencing and regulating the physiological state of the host. This paper explores the relationship between changes in gut microbial population ratios, species, and metabolic functions and the multiple, complex operations of the organism, including the influence on sleep quality and states. As well as animals influence basic gut functions through sleep, directly or indirectly influencing microflora changes in the gut, providing a microbial perspective on the regulation of

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sleep quality, integrating and linking multiple perspectives, and providing research perspectives to address insomnia and sleep-related disorders.

2. Common factors that trigger insomnia

Sleep-disorder-insomnia(Insomnia) can be categorized into various types according to clinical manifestations and etiology, which include insomnia, hypersomnia, and somnolence. Additionally, there are mixed types of sleep disorders, which are characterized by a combination of these symptoms. Insomnia can be divided into acute insomnia and chronic insomnia. Acute insomnia is typically triggered by sudden events and has a shorter duration and recovery period. Chronic insomnia is triggered by factors including, but not limited to, psychological factors, mechanical disturbances caused by changes in the body, neurotransmitter and hormonal imbalances, and family aggregation [3]. Current research suggests that changes in sleep status during the REM period of sleep stages are associated with insomnia [4]. The symptoms of insomnia usually last for a long time, and the long period of regulation, in addition to causing memory loss, daytime sleepiness, loss of appetite, and other symptoms, can also cause other diseases, such as high blood pressure, diabetes mellitus, depression, and so on [5].

3. Imbalanced gut flora can cause reactions in various parts of the body

3.1. Gut microbial enzymes are associated with neurotransmitter synthesis

Concentrations of neurotransmitters such as dopamine, serotonin, acetylcholine, glutamate, GABA, and norepinephrine are correlated with bacterial taxa such as Eubacterium funestus, Mycobacterium anthropophilum, Escherichia coli, and Bifidobacterium bifidum [6].

So me studies have shown that the mechanism of action between gut flora dysbiosis and anxiety can be obtained by comparing the mechanisms associated with gut flora balance and depression. The main cause of stress and anxiety symptoms is the activation of the hypothalamic-pituitary-adrenal axis through the activation and release of adrenocorticotropic hormone (ACTH), which stimulates the production of glucocorticoids (such as cortisol) in the blood [7]. Gut microbes influence neurogenesis, brain function, and sensitivity to stress. Imbalances in the gut microbiota can lead to the activation of the hypothalamic-pituitary-adrenal (HPA) axis. This activation can trigger altered mental status and mental disorders, such as anxiety [8].

A bilateral communication system that allows gut microbes to interact with the brain is comprised of the gut-brain-microbiota axis. Probiotics are live microorganisms that, when ingested in specific quantities, can interact with commensal gut bacteria (such as Lactobacillus and Bifidobacterium) and provide benefits to the host's mental health. These bacteria have been found to provide benefits primarily through the immune response, HPA axis, inflammation, neurohormone, and neurotransmitter production [9].

3.2. Gut microbes are associated with Obstructive Sleep Apnea (OSA)

Obstructive sleep apnea (OSA) is a prevalent sleep disorder that is manifested in adults who experience 30 or more episodes during a 7-hour sleep period each night. There are episodes of airflow cessation from the mouth and nose lasting 10 seconds or more, accompanied by snoring, night sweats, awakenings, and decreased oxygen saturation, characterized by repeated collapse of the upper airway during sleep [10]. These respiratory events lead to chronic intermittent hypoxemia and sleep fragmentation, and ultimately, OSA becomes a risk factor for cardiovascular, metabolic,

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and cognitive diseases [11]. Known causative factors include nasopharyngeal tumors, structural abnormalities of the airway, obesity, and endocrine abnormalities, which also increase the chances of OSA with increasing age.

It has been found that changes in the gut microflora are now one of the influencing factors. It has been demonstrated by experimental animal studies that alterations in the gut microbiome may be caused by both hypoxemia and sleep fragmentation [12]. Some experiments have shown, by designing controlled surveys with normal healthy peers, that OSA patients have a higher percentage of the Firmicutes/Bacteroides in the gut [13]. Experimenters without obstructive sleep apnea (OSA) but with snoring had lower proportions of Actinobacteria/Proteobacteria in their intestinal tracts, as well as lower diversity of microbiome and a higher Proteobacteria abundance. By analyzing fecal samples from patients and controls, it was shown that the genus level showed significant differences, which is the abundance of some short-chain fatty acid-producing (SCFA-producing) bacteria was reduced relative to. This may be the reason for the disruption of the epithelial barrier [14], chronic sleep fragmentation (CSF), and chronic intermittent hypoxia (CIH) have adverse effects on the host metabolism, composition, and function of the fecal microbiota [12]. The Gemmiger, Oscillibacter, Megamonas, and Dialister were all low in abundance, which was negatively correlated with the presence of hypertension [15]. Prevotella enterotypes were found to be significantly related to OSA [16].

Patients with OSA who have carotid atherosclerosis tend to have a lower abundance of Peptostreptococcaceae [17].

4. Factors leading to intestinal dysbiosis

4.1. Sleep deprivation, sleep fragmentation, circadian rhythms

By rearing Drosophila in Axenic and Gnotobiotic conditions [18]， observing and measuring their sleep cycles and behavioral changes, it was concluded that Drosophila axenica's circadian rhythms did not change significantly from those of normal Drosophila. Still, the total nighttime sleep lasted longer and showed a reduced sleep rebound after sleep deprivation [19]. Rapidly obtained data on relevant life indicators through multi-generation reproduction of Drosophila suggests that the reduction of microorganisms in the animal causes defects in sleep duration, reproduction, and memory, with little effect on circadian rhythms, thus providing different data and perspectives for the study of the interaction between animal sleep and its microorganisms in vivo.

Circadian rhythms affect gut bacterial populations, which fluctuate during the day [20].

4.2. Maternal influences on infant gut flora GM

In the early years of life, infants obtain their nutrition mainly from breast milk. One mechanism proposes that the nutrients in the breast milk they ingest influence long-term healthy development through the gut microbiome (GM). The gut microbiome of infants differs significantly from that of adults, with higher levels of Bifidobacteria and fewer Bacteroidetes, which matches their weaker digestive function. Studies have shown that total sleep time (TST), sleep efficiency, and sleep quality are positively correlated with adult GM diversity [21, 22].

Phylogenetic diversity is lower in young children with rapid weight gain from birth to 6 months, and early life nutrition, sleep patterns, and infancy growth rates may influence GM composition [23].

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The method of delivery can also have an impact on the infant's intestinal flora, e.g., planned births, high intake of unhealthy diets during pregnancy, smoking, alcohol abuse, and excessive intake of antibiotics can all have a negative impact.

5. Related and treatments

5.1. Dietary adjustments

The microflora of the gut is diverse, and there is a large number of undiscovered flora with the potential to regulate gut function. A healthy gut microbiota usually has the potential to synthesize more beneficial compounds than harmful compounds [24]. Therefore, a normal diet should include high-fiber foods, probiotic-rich fermented foods such as vegetables and fruits, and a reduced intake of foods high in fatty acids.

Psychobiotics can decrease levels of pro-inflammatory cytokines while downregulating the HPA axis, mitigating damage to the BBB. They also promote the secretion of neurotransmitters such as serotonin and GABA, and regulate neurotransmitter homeostasis. Another probiotics, which have similar mechanisms, may alleviate the symptoms of the disease in patients with sleep disorders [25].

5.2. Oral supplements for sleep disorders

Oral pyrroloquinoline quinone (PQQ) is a quinone that participates in microbial metabolism as a redox coenzyme. Some studies have shown that Oral Supplements can provide some relief for sleep disorders. Scores on the six indicators of vigor, fatigue, tension and anxiety, depression, anger and hostility, and confusion were significantly higher after using the PQQ compared to before using the PQQ. Indicators of pain, sleep, obsessive-compulsive disorder, appetite, and quality of life also improved significantly [26].

5.3. Transplantation of fecal microbiota

Fecal microbiota transplantation (FMT) is a flora transplantation technique that involves transplanting functional flora from the feces of healthy individuals into the gastrointestinal tract of relevant patients to treat gut-related disorders by re-establishing a new and healthy intestinal flora [27].

A similar technique was documented by Ge Hong in China during the Eastern Jin Dynasty in his book, "The Elbow After Preparing an Emergency Prescription", which demonstrated the efficacy of fecal medicines in clearing away heat, relieving pain, detoxifying toxins, and avoiding filth [28].

6. Conclusion

This paper investigates the relationship between sleep quality and gut microbiota, as well as the underlying bidirectional mechanisms. Gut microbiota metabolites regulate the synthesis of sleep-related hormones (e.g., melatonin, GABA, and serotonin) and affect brain function by regulating the "gut-brain axis." Research has revealed that patients with insomnia have been shown to have a lower abundance of beneficial bacteria (such as Bacteroides), and an increased proportion of Aspergillus spp. Additionally, their bacterial diversity has been found to be reduced. These findings suggest that dysbiosis may be related to sleep disorders.

Also, patients with obstructive sleep apnea (OSA) show abnormal gut flora, such as an elevated ratio of Phylum Firmicutes/anaplasmosis and a decrease in short-chain fatty acid (SCFA)-producing

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bacteria, which may be associated with chronic hypoxemia and sleep fragmentation. In addition, circadian rhythm disruption, sleep deprivation, or maternal factors (e.g., mode of delivery, breastfeeding) can indirectly affect sleep by altering the composition of the flora.

On the therapeutic side, modification of diet, use of psychotropic probiotics or supplements such as pyrroloquinoline quinone (PQQ) may regulate flora and improve sleep. Fecal microbiota transplantation (FMT), as an emerging therapy, shows potential application by reestablishing healthy flora.

In conclusion, there is a close association between sleep quality and gut microbiota. Future studies might offer novel strategies for sleep disorders by targeting and regulating the microbiota.

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