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The Sleep Microbiome: Insights into Probiotics and Sleep Health

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Abstract

Introduction

The World Health Organization (WHO) defines probiotics as "live microorganisms that, when administered in adequate amounts, confer health benefits to the host." A number of scientific reports show that their effects extend beyond the immune and gastrointestinal systems, and that poor sleep quality and insomnia are an increasingly important social problem. Studies indicate that 30-50% of adults experience sleep problems. Sleep deficiencies are associated with higher rates of obesity, hypertension, type 2 diabetes, cardiovascular diseases, mental health disorders and increased risk of death. One promising way to help treat sleep problems is through the use of probiotics. Interaction through the gut-brain axis suggests that altering the gut microbiota may become a useful tool for improving sleep quality.

Aim of the study

The purpose of this study was to investigate the potential effectiveness of probiotics in improving sleep quality and treating insomnia.

Materials and Methodology

PubMed and Google Scholar databases were analyzed. Articles were searched in English using the following keywords: probiotics; sleep quality.

Results

Probiotics resulted in a favorable cumulative effect on sleep quality as measured by the PSQI global questionnaire and a statistically significant positive effect on at least one of the components characterizing sleep quality (i.e., sleep latency, sleep length, sleep disturbance, daytime sleepiness). They allow to maintain a high percentage of slow-wave sleep, despite stressors, and indirectly affect sleep quality in athletes by reducing muscle soreness.

Conclusion

The results of studies to date indicate that probiotics are an effective, safe and clinically sound adjunctive method for improving sleep quality and treating insomnia. However, these studies are at an early stage and require further efforts using larger research groups.

Keywords: sleep quality; probiotics.

I. Introduction

Insomnia stands out as one of the most frequently reported subjective sleep issues among adults [1]. Sleep challenges impact 30% to 50% of the adult population, with diagnostic criteria for insomnia being met by 10% to 15% of individuals. Elevated frequencies are observed in women, those who are divorced or separated, individuals who have experienced the loss of a loved one, and older adults. [2]. The condition insomnia is defined by difficulties in initiating sleep, maintaining it, or experiencing diminished sleep quality [3]. Additionally, insomnia is marked by cognitive, mood or performance impairment during waking hours [4,5,6,7]. Chronic insomnia is the term for sleep difficulties that occur regularly for several days a week and persist for more than 3 months [8]. The origins of sleep disorders are diverse, arising from transient stressful life situations and underlying health conditions, both somatic and psychiatric. These disorders correlate with heightened risk of depression, psychosomatic ailments, increased rates of psychoactive substance use, and an elevated risk of suicide [9,10].

Sleep deficiency is also associated with a higher incidence of obesity, hypertension, cardiovascular diseases, type 2 diabetes, certain cancers, mental health disorders like depression, anxiety and dementia [11, 12, 13]. Research results indicate the important role of poor sleep in health, emphasizing the importance of treating sleep problems in primary health care [11]. According to the international classification of diseases, 10th edition (ICD-10), insomnia is a symptom of many somatic and mental disorders and should only be classified as a separate diagnosis when dominating the clinical picture [7]. Persistent sleep problems negatively impact social and family life, impede work performance, leading to reduced productivity, impaired judgment, and emotional reactions. Moreover, they incur substantial economic costs at both societal and individual levels, with some countries estimating the social cost of insomnia at 1.55% of the gross domestic product [10].

Primary insomnia treatment should involve behavioral modifications, encompassing practices like maintaining adequate sleep hygiene and engaging in cognitive-behavioral therapy tailored

to address insomnia. For individuals requiring pharmacotherapy, recommendations include nonbenzodiazepine sleep medications (commonly referred to as “Z drugs”) and antidepressants, tailored to the patient’s needs and specific comorbidities [4]. However, pharmacological approaches often lead to addiction and carry numerous side effects. Conversely, psychological/behavioral methods necessitate prolonged therapy sessions and can be time-consuming to yield satisfactory results. Hence, there exists a need for simpler methods to facilitate the maintenance of healthier sleep [14].

The role of the microbiome is increasingly emphasized, treating it as a separate organ of the body. Brain centers are linked to gut functions through the brain-gut axis, as evidenced by the association of gut microbiota imbalances with central nervous system and gastrointestinal disorders found in irritable bowel syndrome. It appears that the interaction between gut microflora and the brain is bidirectional, potentially allowing for the modulation of CNS function responses based on the composition of gut microflora. Probiotic administration could serve as a potential dietary signal influencing the diurnal rhythm through the gut microflora. A proposed mechanism of action of probiotics is also to reduce hypothalamic-pituitary-adrenal axis activity and lower cortisol levels due to their anti-inflammatory properties [15].

Ia. Subjective and objective methods of assessing sleep quality

The Pittsburgh Sleep Quality Index (PSQI) questionnaire is the most commonly used method for subjectively assessing sleep quality. Patient self-complete a 19-item questionnaire that evaluates individual components of sleep quality and generates a global score based on them. The 19 items result in seven "component" scores, covering subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction. The PSQI provides a subjective assessment of sleep quality and disturbances over a one-month interval. Higher global PSQI score indicating poorer sleep quality. A global PSQI score ≤ 5 indicates good sleep quality and > 5 indicates poor sleep quality [16,17].

Objective assessment of sleep quality involves measuring the continuity and depth of sleep through brain activity recordings using EEG electrodes. These electrodes capture the brain’s electrical activity, and the wave patterns are examined to classify sleep characteristics [15].

Ib. Probiotics, prebiotics, and symbiotics- worth to know

1. Probiotics:

The World Health Organization (WHO) defines probiotics as "live microorganisms that, when administered in adequate amounts, provide health benefits to the host." At first, these health benefits were considered only in the form of effects on the gastrointestinal tract (ensuring the balance of the intestinal microflora, lactose intolerance, diseases with diarrhea, peptic ulcers, providing immunity and even in colon cancer). The current state of knowledge suggests that they are finding use in the treatment or adjunctive treatment of a wider range of conditions, including potentially insomnia.

2. Prebiotics:

Are defined as "non-digestible food components that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon to improve host health," while the International Scientific Association for Probiotics and Prebiotics has expanded these definitions to include positive effects on other areas of health as well - not just action in the gastrointestinal tract [27].

3. Synbiotics:

In their composition, they contain both probiotics and prebiotics working together to improve the health of the host. They even work together, acting synergistically - probiotics use prebiotics as a source of growth for their bacteria [27].

II. Aim of the study

The purpose of this study was to investigate the potential effectiveness of probiotics in improving sleep quality and treating insomnia.

III. Materials and methodology

PubMed and Google Scholar databases were analyzed. Articles were searched in English using the following keywords: probiotics; sleep quality.

IV. Results

Probiotics play a crucial role in enhancing the internal homeostasis of the intestinal microflora to support the health of the gastrointestinal tract. Consequently, there is a reduction in the number of harmful bacteria incapable of surviving in an acidic environment. Simultaneously, beneficial bacteria thrive in this acidic environment, rebalancing the composition of the intestinal microbiota [18]. Ongoing research on probiotic bacteria extends beyond the gastrointestinal tract, exploring potential applications in areas such as mental health, including insomnia and sleep quality disorders.

IVa. *Lactobacillus gasseri* CP2305 and sleep quality

The microorganisms most commonly included in probiotics are Gram-positive bacteria, primarily derived from species of *Bifidobacterium* and *Lactobacillus*. Many *Lactobacillus* species have a well-established history of safe and effective use. It has been suggested that improving sleep quality can be achieved by modulating the composition of gut flora using probiotics containing *Lactobacillus gasseri* [15].

Correspondingly, Nishida et al. conducted three clinical studies in 2017 and 2019, each examining, among other factors, the impact of *Lactobacillus gasseri* on sleep quality in medical university students. The assessment utilized using the PSQI questionnaire or both the PSQI and EEG. All of these studies demonstrated a positive cumulative effect using the PSQI global score and a statistically significant improvement in sleep quality with *Lactobacillus gasseri*, as indicated by at least one of the PSQI components (such as sleep latency, sleep length, sleep disturbance, or daytime dysfunction due to sleepiness). EEG results provided objective data that corroborated the questionnaire findings [19,20,21].

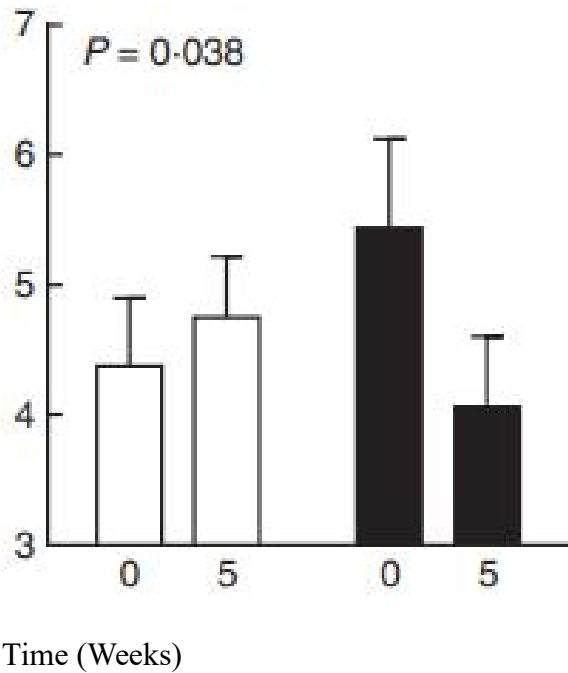


Figure 1. Changes in sleep quality as a result of the use of *Lactobacillus Gasseri* [19].

The column chart in Figure 1 shows time-dependent changes in global PSQI scores. White bars represent placebo treatment and black bars represent *Lactobacillus gasseri*. The left bar shows the mean score represented by mean SE before treatment, and the right bar shows after. The graph shows a significant improvement in sleep quality after 5 weeks of taking the probiotic, compared to placebo, assessed using the subjective PSQI scale (significance level $p=0.038$) [19].

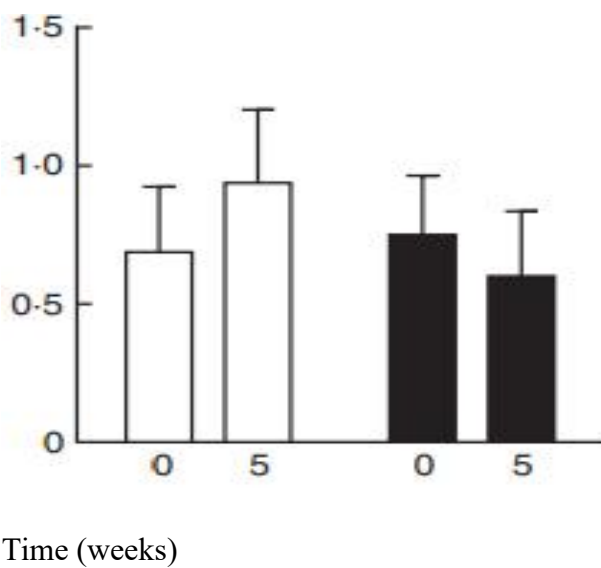


Figure 2. Changes in the PSQI sleep latency scores in both groups before and after 5 weeks [19].

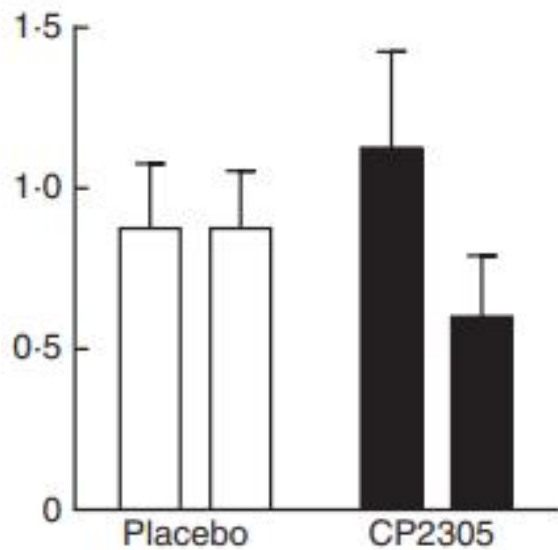


Figure 3. Presentation of the PSQI sleep duration scores in both groups [19].

Sawada et al., in 2017 and 2019 respectively, conducted two double-blind, randomized, placebo-controlled clinical trials to assess the potential health benefits of *Lactobacillus gasseri* use. In both studies, university students participated, and sleep quality was evaluated using the PSQI questionnaire. The 2017 study demonstrated a positive effect of the supplement on sleep quality, as indicated by a global PSQI score [22]. In contrast, another study found that *L. gasseri* CP2305 intervention increased the diversity of fecal microflora and prevented the proliferation of *Streptococcus* and *Enterobacteriaceae* species, suggesting potential effects on the gut-brain axis [23].

IVb. *Lactobacillus casei* and sleep quality

Takada's (2017) study aimed to investigate whether *Lactobacillus casei* could improve sleep quality in individuals experiencing stress. The research involved a cohort of medical students subjected to exam-related stress and was repeated over two consecutive years with different groups of students. The data from both were combined for analysis. The effects of *Lactobacillus casei* were assessed through participants' subjective anxiety levels, nocturnal EEG recordings, and a subjective sleep quality questionnaire. The study employed a double-blind, parallel-group, placebo-controlled trial.

According to the study results, the group receiving *Lactobacillus casei*, when compared to placebo group, did not exhibit a reduction in the percentage of N3 sleep, which represents slow-wave sleep often disrupted by stress factors. This suggests that individuals in the *Lactobacillus casei* group spent more time in deep sleep, contributing to subjectively better scores on sleep quality questionnaires [24].

IVc. Effect of probiotic supplementation on sleep in athletes

Harnett's 2020 study aimed to investigate the effects of a probiotic supplement on sleep quality and quantity among elite rugby athletes, recognizing sleep as an integral component of recovery crucial for sports performance. The double-blind, randomized, controlled study involved 19 athletes, divided into two groups. The first group received a daily probiotic supplement, Ultrabiotic 60™, containing 60 billion viable species of *Lactobacillus*, *Bifidobacterium* and *Streptococcus* species, and *Saccharomyces boulardii*. The second group received a placebo [25].

Participants assessed sleep amount and quality twice a week through a study-specific app, and saliva samples were collected at the same frequency for analysis of CRP and melatonin. The study revealed that a reduction in sleep quantity and quality led to increased perceived muscle soreness in the athletes. Comparing the placebo group and the probiotic group, the latter showed lower levels of muscle soreness and leg heaviness, correlating with improved sleep quality and quantity [25].

V. Summary

The findings from this review suggest that probiotic intake can lead to positive changes in an individual's perceived sleep health, as measured by the PSQI questionnaire [26]. Improvements in sleep quality may occur through various mechanisms, including reduced inflammation, secondary enhancements in sleep quality, impacts on immunity, or effects through the gut-brain axis. However, it is crucial to emphasize the necessity for long-term and rigorously controlled research on probiotics as a potential substitute for agents used in managing sleep disorders. The highly variable availability of preparations on the market, containing strains of different bacteria, further complicates development of specific indications with dosages for the treatment of sleep quality disorders. However, given the

percentage of the population that is affected by the problem of poor sleep quality, methods that do not require the use of addictive drugs to combat this condition should be one of the main goals of modern medical research.

DISCLOSURE

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