

Gut microbiome diversity associates with sleep quality in healthy adults



Poor sleep quality is a widespread problem and has been associated with several diseases in humans such as cardiovascular disease and cancer. Previous research has reported that the human gut microbiota may express endogenous circadian rhythms, together with findings showing alterations of the gut microbiota in response to sleep deprivation. On the other hand, the gut microbiota and its metabolites regulate the immune system including cytokine activity via bidirectional signaling of the brain-gut-microbiome axis, which may influence sleep and circadian rhythm.

Despite these findings, few studies have looked at the interaction between the gut microbiota composition and cytokine activity in the context of sleep. For example, interleukin 6 (IL-6) increases in times of stress and sleep loss, and the gut microbiota can induce IL-6 production, but this interaction is unknown in the context of sleep.

Therefore, Smith and colleagues from Nova Southeastern University in Fort Lauderdale, Florida, USA investigated the relationship between gut microbiome diversity, sleep, cognition, cortisol levels and the pro-inflammatory cytokines interleukin 6 (IL-6) and interleukin 1 beta (IL-1 β) in 26 healthy adult males.

Microbiome sequencing, actigraphy, cognitive and neurobehavioral testing and biochemical approaches were used. Actigraphy consisted of wearing an Actiwatch for 30 days that measured average bed time, average get up time, time in bed (hrs), total sleep time (hrs), onset latency (mins), sleep efficiency, wake after sleep onset (mins), and number of awakenings.

Overall, gut microbiome diversity positively correlated with sleep efficiency and total sleep time, and negatively correlated with wake after sleep onset, which suggests that gut microbiome could be involved in promoting better sleep. Additionally, increased microbiome diversity was also associated with cognitive flexibility and abstract thinking, which were assessed through cognition and emotion test battery.

Surprisingly, the authors found no significant association between the stress biomarker cortisol, sleep measures and gut microbiome diversity. On the other hand, they did discover that IL-6 levels positively correlated with time in bed (hrs) and total sleep time, microbial richness, as well as richness and diversity of the Bacteroidetes phyla and Firmicutes phyla richness. Therefore, the link between IL-6 and gut microbiome diversity is independent of stress despite the link between stress and IL-6.

At the phyla level, richness within Bacteroidetes and Firmicutes positively correlated with sleep efficiency, while only Bacteroidetes negatively correlated with sleep fragmentation. There is growing evidence that these two phyla may regulate sleep quality in humans. Increased richness within the Actinobacteria phyla was negatively associated with the number of sleep awakenings. Interestingly, Bacteroidetes, Actinobacteria and Firmicutes also produce γ -aminobutyric acid (GABA), which is an inhibitory neurotransmitter that promotes sleep activity in the brain.

Certain taxa whose metabolites signal via the gut-brain axis were also associated with sleep quality. For example, bacteria from the taxa *Corynebacterium*, which negatively correlated with the number of sleep awakenings, can synthesize the neurotransmitter serotonin that signals

through the gut-brain axis and can modulate sleep and may regulate melatonin production. Serotonin has also been found to increase IL-6 synthesis in some human cell types, and increased IL-6 production has been associated with poor emotional and cognitive performance.

On the other hand, SCFA producing taxa from the Lachnospiraceae family, including *Blautia*, *Coproccoccus* and *Oribacterium*, negatively correlated with healthy sleep. However, due to the inherently descriptive nature of the study it is unknown whether SCFA or other metabolites do indeed directly affect sleep quality in humans as further studies are needed.

Despite the study's limitations of analyzing a small sample group that consisted of only men, this novel study shows the connection between sleep quality and gut microbiome diversity in which IL-6 played an important role in the sleep-gut microbiome connection in humans. The authors also discovered several specific phyla and taxa that are related to sleep health which opens up the possibility to modulate the gut microbiota in order to improve sleep quality in the future.