

Impact of 5-Hydroxytryptophan Supplementation on Gut Microbiota Composition of Older Adults With Different Sleep Status in Singapore: A Randomized Controlled Trial

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Objectives: The gut and brain communicate bidirectionally through the gut brain axis. Lower microbial diversity has been observed in populations with sleep disturbances. 5-Hydroxytryptophan (5-HTP) is known as a potential modulator of sleep quality, while its impact on the gut remains unclear. The aim of this study was to assess the impact of 5-HTP on gut microbiota in older Singaporeans with different sleep status.

Methods: This study is a single-blinded, 12-week parallel randomized controlled trial. Thirty older adults (66 ± 3 years, mean \pm SD) were randomly assigned to either consume or not consume 100 mg 5-HTP daily. Their baseline sleep status was evaluated using global sleep score (GSS): $GSS \leq 5$ (good sleepers, n:17); $GSS > 5$ (poor sleepers: n:13). Characterization of the bacterial population from the stool samples collected at week 0 and 12 was analyzed through 16S metagenomic

sequencing. Microbiota composition between $GSS \leq 5$ and $GSS > 5$ was compared via MetaStat analysis. The main effect and interaction of 5-HTP on gut microbiota composition was evaluated by mixed analysis of variance (ANOVA).

Results: At baseline, poor sleepers have a significantly lower relative abundance of *Firmicutes* than good sleepers ($GSS > 5$: $3.78 \times 10^{-1} \pm 5.43 \times 10^{-2}$; $GSS \leq 5$: $4.33 \times 10^{-1} \pm 9.32 \times 10^{-2}$; p-value: 0.048). After a 12-week consumption of 5-HTP, subjects with $GSS > 5$ showed an increase in α -diversity (Simpson_{5-HTP} vs. Simpson_{Control}: 0.037 ± 0.032 vs. -0.007 ± 0.022 ; $p_{\text{interaction}}$: 0.013). 5-HTP supplementation also showed interaction effects on the relative abundance of *Bacteroidota* (*Bacteroidota*_{5-HTP} vs. *Bacteroidota*_{Control}: $-1.03 \times 10^{-1} \pm 4.99 \times 10^{-2}$ vs. $-3.06 \times 10^{-2} \pm 4.39 \times 10^{-2}$; $p_{\text{interaction}}$: 0.019) and *Firmicutes* (*Firmicutes*_{5-HTP} vs. *Firmicutes*_{Control}: $1.10 \times 10^{-1} \pm 2.40 \times 10^{-2}$ vs. $2.02 \times 10^{-2} \pm 7.82 \times 10^{-2}$; $p_{\text{interaction}}$: 0.031). No significant changes were observed for $GSS \leq 5$ group.

Conclusions: In older adults, 5-HTP consumption modulated gut microbiota composition in poor sleepers ($GSS > 5$). However, no influence to the gut microbiota was observed in good sleepers ($GSS \leq 5$).

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