

Press Release

2022.2.22 | International Institute for Integrative Sleep Medicine (WPI-IIIS)

Sevoflurane Improves Sleep Alteration in Response to Inflammation

Researchers at the University of Tsukuba investigate the effect of the general anesthetic sevoflurane on sleep disturbance caused by systemic inflammation

Tsukuba, Japan – Getting a good night’s sleep can sometimes be a challenge, but inflammation may make it even more difficult. While the relationship between inflammation and sleep alteration has been previously shown, researchers in Japan have now identified a potential method to overcome sleep disturbance associated with systemic inflammation.

In a new study published in *Journal of sleep research*, researchers at the University of Tsukuba examined the effect of sevoflurane, an anesthetic agent used to maintain unconsciousness during surgery, on sleep recovery in a mouse model of systemic inflammation.

Systemic inflammation has been shown to affect sleep quality by reducing the amount of time spent in the rapid eye movement (REM) and waking states and increasing the amount of time spent in the non-REM state. Previous animal studies have illustrated the protective effects of sevoflurane on organs, including the brain, but the relationship between sevoflurane and sleep has not been explored under inflammatory conditions. Using a model in which mice are injected with the endotoxin lipopolysaccharide (LPS) to induce inflammation throughout the body, the research team evaluated the effects of sevoflurane on altered sleep patterns associated with systemic inflammation.

“We hypothesized that preconditioning with sevoflurane prior to inducing inflammation by LPS would promote sleep recovery,” says main

author Professor Takashi Kanbayashi.

The research team exposed mice to sevoflurane prior to LPS injection (“preconditioning”) and also examined the effects of sevoflurane exposure after LPS injection (“postconditioning”). Control mice without systemic inflammation were exposed to either sevoflurane or air and received either sterile saline or LPS injection. The researchers monitored the sleep patterns of the mice using electroencephalography and collected brain tissues for histological analysis.

“We found that mice that were preconditioned with sevoflurane showed a significant increase in REM sleep after LPS injection,” says Professor Kanbayashi. “This effect was not observed in mice that received postconditioning.”

Examination of brain tissues from mice treated with LPS alone revealed a reduction in neurons expressing the neuronal activation marker Fos in the pedunculo pontine tegmental nucleus and laterodorsal tegmental nucleus (PPTg/LDTg), which is an area of the brain involved in the regulation of REM sleep. However, the mice that received sevoflurane preconditioning before LPS treatment maintained similar levels of Fos-positive neurons as those observed in the control mice. These results demonstrate that maintained activation of neurons in the PPTg/LDTg region may represent a potential mechanism underlying the effect of sevoflurane on sleep reintegration under inflammatory conditions.

The findings of this study indicate a potential application for sevoflurane in the treatment of sleep disturbance associated with systemic inflammation.

The article, “Effect of sevoflurane preconditioning on sleep reintegration after alteration by lipopolysaccharide,” was published in *Journal of sleep research* at DOI: [10.1111/jsr.13556](https://doi.org/10.1111/jsr.13556).

This work was supported by a JSPS KAKENHI Grant-in-Aid (C) [grant numbers 19K07314 to YIT and 19 K08037 to TK]; The Japan Agency for Medical Research and Development [grant number JP20dm0107162] to TK; a Grant-in-Aid for Scientific Research on Innovative Areas, ‘Willdynamics’

[grant number 17H06049] to YIT; a grant from the World Premier International Research Centre Initiative (WPI), Japan, IIS; the Ministry of Education, Culture, Sports, Science and Technology World Premier Japan Society for the Promotion of Science KAKENHI [grant number 17H06095]; the International Research Centre Initiative, CREST [grant number A3A28043]; the Funding Program for World-Leading Innovative R&D on Science and Technology from JSPS; the Uehara Memorial Foundation research grant; and a Takeda Science Foundation research grant to MY. The study sponsors had no role in the study design, collection, analysis, or interpretation of data, writing the report, or the decision to submit the report for publication.

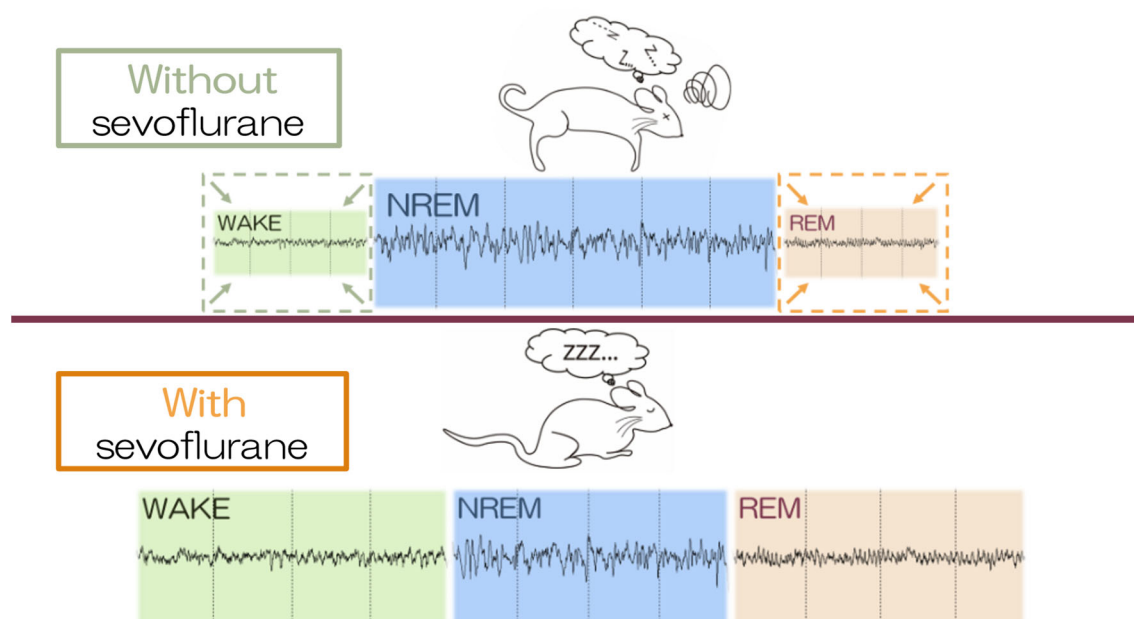


Fig1. Sevoflurane preconditioning promotes sleep recovery from lipopolysaccharide altered sleep

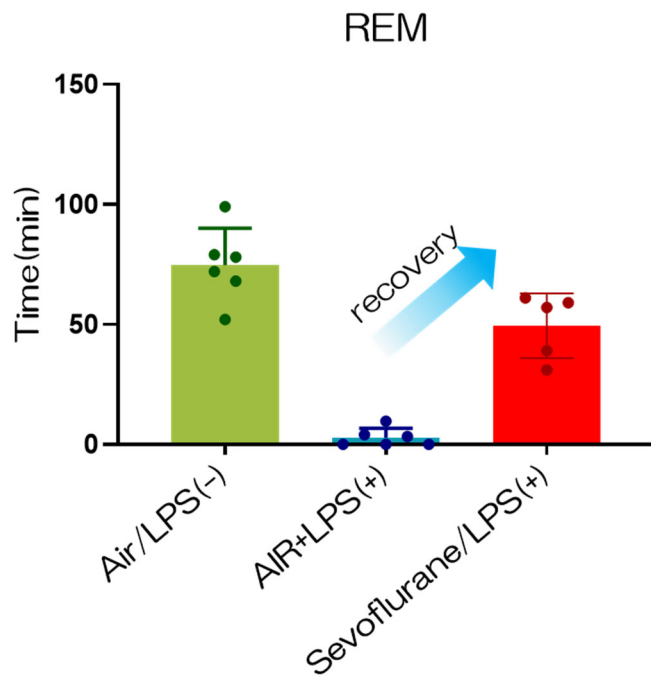


Fig2. The time spent in REM and waking states increases with sevoflurane preconditioning.

Bibliographic information

Nemoto T, Irukayama-Tomobe Y, Hirose Y, Tanaka H, Takahashi G, Takahashi S, Yanagisawa M, Kanbayashi T. (2022) Effect of sevoflurane preconditioning on sleep reintegration after alteration by lipopolysaccharide.

Journal of Sleep Research, e13556

doi: 10.1111/jsr.13556

Media Contact

Alliance and Communication Unit, International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba, Japan

E-mail: wpi-iiis-alliance@ml.cc.tsukuba.ac.jp