BRAIN STIMULATION AS NOVEL TREATMENT FOR INSOMNIA

A systematic review by L. B. Krone, K. D. Fehér, T. Rivero and X. Omlin. Published in Journal of Sleep Research (2023)



WHAT IS BRAIN STIMULATION?

Brain stimulation directly or indirectly modulates brain activity in targeted brain regions or cranial nerves using electric, magnetic, sound, ultrasound or thermal manipulations.



Insomnia is a sleep disorder defined by trouble falling asleep, staying asleep, or waking up too early. It impairs daytime functioning and may have long-term health consequences.



- 1. Adults with clinical insomnia
- 2. Brain stimulation as intervention, incl. control group
- 3. Used validated sleep outcomes

WHAT IS THE EVIDENCE FOR USING BRAIN STIMULATION IN **INSOMNIA TREATMENTS?**

TRANSCRANIAL MAGNETIC STIMULATION

9 studies

- Stimulation frequency: Low (1 Hz, inhibitory) or high (10 Hz, excitatory)
- Target region: Mostly left dorsolateral prefrontal cortex (dIPFC).
- Results: All report positive results or trends on insomnia symptoms. •
- To note: All studies raise concerns or have a high risk of bias.

TRANSCRANIAL ELECTRIC STIMULATION 5 studies

- **Stimulation type**: Transcranial direct or alternating current.
- Target region: Prefrontal and frontal cortical areas.
- **Results**: 4/5 report positive effects on insomnia symptoms.
- To note: All studies raise concerns or have a high risk of bias. One grossly exceeds recommended safety limits.

TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION

- 2 studies **Stimulation type**: Electrical stimulation at 20 Hz or 4 Hz.
 - **Target region**: Afferent auricular branch of the vagus nerve.
 - Results: Studies report no main effects on insomnia symptoms.
 - To note: One exploratory analysis suggests effects on sleep quality. One study raises concerns, one has low risk of bias.



FOREHEAD COOLING



- Stimulation condition: Fluid-filled bladder at 14-16°C. Target region: Forehead over the frontal cortex.
- **Results**: Study finds no effects on primary endpoints.
- **To note**: Exploratory analysis suggests faster sleep onset. Excellent study design with double-blinding and credible device control, low risk of bias.



WHAT ARE THE LIMITATIONS?

- >100 studies report positive effects of brain stimulation on insomnia symptoms.
- Only 17 studies meet inclusion criteria.
- 15/17 studies still raise concerns or have a high risk of bias.
- Evidence of strong pre-post effects with credible device control.



Sham brain stimulation elicits strong placebo effects

ARE THERE ALTERNATIVES?

Deep brain stimulation unsuitable due to invasiveness



Vestibular nerve stimulation suitability subject to further methodological development

Auditory stimulation - awaiting results; promising as it modulates sleep oscillations and functions Δ



WHAT IS THE TAKE-HOME MESSAGE?

To date, no brain-stimulation protocol can claim relevant therapeutic benefit for insomnia.



WHAT NEEDS TO BE DONE TO ADVANCE THE FIELD?

- Understand sleep-regulating brain circuitry to identify optimal stimulation targets.
- Use effective double-blinding and reliable sham conditions to prove superiority.
- Use predefined outcome measures, avoid overinterpretation of exploratory analyses.

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