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Using sound to improve sleep quality in people with insomnia: a pilot study

Submission date
24/02/2025

Recruitment status
No longer recruiting

Registration date
04/03/2025

Overall study status
Completed

Last Edited
03/03/2025

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Consistent difficulties falling asleep and/or staying asleep can lead to a diagnosis of insomnia, a common sleep disorder that impacts daytime functioning and quality of life. Neural oscillations that occur during sleep such as sleep spindles are considered individual biomarkers of sleep quality, due to a major functional role in gating of external stimuli during sleep to preserve sleep stability. Individuals suffering from chronic insomnia may benefit from alternative treatments, such as enhancing spindle activity, which has the potential to ameliorate the detrimental effects of sleep loss in patients with insomnia. In young healthy adults, auditory tones phase-locked to the brain's endogenous oscillations have been shown to increase the amplitude of slow oscillations and in turn, boost the occurrence of sleep spindles. This pilot study thus aims to (1) test the effectiveness of increasing sleep spindle activity in adults with insomnia using a paradigm of slow oscillation enhancement through auditory tones (called closed-loop auditory stimulation; CLAS); and, (2) investigate if these changes contribute to an increase in both objective and subjective sleep quality, in addition to changes in neurocognitive performance.

Who can participate?
Patients above 21 years old meeting DSM-V diagnostic criteria for chronic insomnia

What does the study involve?
Subjects will be evaluated across three conditions, each separated by a week. These are:
(1) Adaptation night to screen for sleep disorders, record sleep EEG characteristics and acclimatization to a new sleeping environment;
(2) Stimulation night during which CLAS will be played during sleep, and;
(3) Sham night, during which no tones are played.
Questionnaires and cognitive tasks will be administered before and after sleep in (2) and (3) to assess the efficacy of stimulation on sleep quality and cognition. The order of sessions 2 and 3 will be counterbalanced.

What are the possible benefits and risks of participating?
There is no direct benefit from this study. However, their voluntary participation will contribute to the better understanding of human brain function towards sleep quality and memory consolidation during sleep.

Possible risks may concern the EEG component: adhesive tape/paste are used to attach electrodes. In rare cases, this could cause some minor skin irritation or acne. Such discomfort is monitored and may be removed if necessary.

Where is the study run from?
Duke-NUS Medical School, Singapore

When is the study starting and how long is it expected to run for?
January 2018 to August 2019

Who is funding the study?
1. National Medical Research Council (NMRC) Singapore
2. Canadian Institutes of Health Research

Who is the main contact?
Prof Thien Thanh Dang Vu, tt.dangvu@concordia.ca

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Canadian Institutes of Health Research Project Grant PJT 153115

Study information

Scientific Title
Auditory entrainment of sleep spindles and the impact on sleep quality in insomniacs: a pilot study

Study objectives
Auditory closed-loop stimulation (CLAS) will increase spindle activity compared to SHAM night. The increase in spindle density will be correlated with increased sleep efficiency, subjective sleep quality and better overnight memory performance.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 23/01/2018, National University of Singapore Institutional Review Board (10 Medical Drive, Singapore, 117597, Singapore; 65-6516 4311; irb@nus.edu.sg), ref: H-18-004

Study design
Randomized crossover sham-controlled study

Primary study design
Interventional

Study type(s)
Treatment, Efficacy

Health condition(s) or problem(s) studied
Insomnia disorder

Interventions
Auditory closed-loop stimulation (CLAS).

The study uses a randomized crossover sham-controlled study so all participants undergo a habituation night followed by two experimental nights with polysomnographic (PSG) recording in a counterbalanced order: one with closed-loop auditory stimulation (CLAS) stimulation and one without stimulation (SHAM). There are 7 days between each night.
All nights took place in the laboratory

CLAS: Real-time automated sleep stage detection and up-state targeting of slow oscillations (SOs) is used during N2 and N3 on electrode F3:A2. Auditory tones (50ms bursts of pink noise) locked to SO upstates are played in 2-ON-OFF blocks. Tone presentation is halted if an arousal occurs or if voltage thresholds (40uV) are not met. This intervention has been used previously by the host team (Singapore) (see Ong et al., Sleep Medicine 2016; Ong et al., SLEEP, 2018)

SHAM: Real-time automated sleep stage detection and up-state targeting of slow oscillations (SOs) is used during N2 and N3 on electrode F3:A2. The SO up-state locations are detected but no tones is played.

Intervention Type
Device

Phase

Not Applicable

Drug/device/biological/vaccine name(s)
Auditory closed-loop stimulation (CLAS)

Primary outcome(s)
Spindle activity (including spindle density, amplitude, duration, and peak frequency) is measured using automatic spindle detection during SHAM and STIM nights

Key secondary outcome(s))
1. Sleep macro-architecture (total sleep time (min), time in bed (min), wake after sleep onset (min), sleep onset latency (min), sleep efficiency (%; total sleep time/time in bed*100), time spent in each stage (%total sleep period), sleep fragmentation index (n/h)) measured using data extracted from sleep scoring during SHAM and STIM nights
2. Arousal index (n/h) measured using data extracted from manual detection of arousal during SHAM and STIMS
3. Slow oscillatory activity (<1.25Hz; including density, amplitude, and peak frequency) is measured using automatic SO detection during SHAM and STIM nights
4. Delta power (0.25-4Hz) is measured using Fast Fourier Transformation on frontal derivations during SHAM and STIM nights
5. Self-reported sleep assessment (including sleep quality rating, sleep duration, and number of awakenings) measured using data extracted from the questionnaire in the morning after STIM and SHAM nights
6. Declarative memory accuracy (correct minus wrong) measured using data extracted from the performance at the word paired-associate learning task performed before and after sleep during SHAM and STIM nights

Completion date
05/08/2019

Eligibility

Key inclusion criteria
1. Above 21 years
2. Meeting DSM-V diagnostic criteria for chronic insomnia
3. English as a first language
4. Have a minimum of 12 years of formal education
5. Have consistent sleeping habits at least 7 days prior to the study
6. Not be on any long-term medications affecting sleep
7. No other known medical conditions than insomnia that could affect sleep
8. Consume less than 2 units (200mg) of caffeine a day
9. Consume less than 21 units of alcohol per week
10. Score at the mini-mental state examination should be ≥ 26 if ≥ 55 years old

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Mixed

Lower age limit
21 years

Upper age limit
80 years

Sex
All

Total final enrolment
27

Key exclusion criteria
1. History of any psychiatric or neurological disorders
2. History of severe medical illnesses
3. Shift workers
4. Save travelled across more than 1 time zone one month prior to the study
5. Not taking any psychoactive medication 1 week prior to or during the study

Date of first enrolment
13/02/2018

Date of final enrolment
05/08/2019

Locations

Countries of recruitment
Singapore

Study participating centre
Duke-NUS Medical School
8 College Rd
Singapore
Singapore
169857

Sponsor information

Organisation
Duke-NUS Medical School

ROR

https://ror.org/02j1m6098

Funder(s)

Funder type
Government

Funder Name
Canadian Institutes of Health Research

Alternative Name(s)
Instituts de Recherche en Santé du Canada, Canadian Institutes of Health Research (CIHR), CIHR_IRSC, Canadian Institutes of Health Research | Ottawa ON, CIHR - Welcome to the Canadian Institutes of Health Research, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Funder Name
National Medical Research Council

Alternative Name(s)
The National Medical Research Council, National Medical Research Council (NMRC) Singapore, NMRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Singapore

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request from Prof Thien Thanh Dang Vu (tt.dangvu@concordia.ca)

• The type of data that will be shared : coded EEG raw dataset and memory performances
• Timing for availability: once manuscript in published (expected end of 2025)
• Whether consent from participants was required and obtained : yes
• Comments on data anonymization: coded - no identifiable information (i.e., name, email address and contact number) can be shared
• Any ethical or legal restrictions: no identifiable information can be shared

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.2	15/01/2018	03/03/2025	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes