Peripheral Nerve Stimulation (PNS) to optimize military performance during and after sleep deprivation

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Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON53207

Source
ToetsingOnline

Brief title
Peripheral Nerve Stimulation and Sleep Deprivation

Condition

- Other condition

Synonym
Human performance, increasing alertness

Health condition

menselijk presteren

Research involving
Human

Sponsors and support

Primary sponsor: TNO
Source(s) of monetary or material Support: Defensie

Intervention

Keyword: Neurostimulation, PNS, Sleep deprivation, Vagus nerve

Outcome measures

Primary outcome

Cognitive performance on the cognitive task battery (e.g., reaction time, false alarms, lapses)

Secondary outcome

- VR test, including the percentage of decisions properly made as measured with a checklist for video-analysis. Quality of performance is also graded by instructors who are present during the VR test.

- Sleepiness levels after each cognitive performance test

- Mood ratings (pre- and post tests)

- Positive- and Negative affect ratings (pre- and post tests)

- Mental effort ratings after each cognitive performance test

- Symptoms of motion sickness after the VR test

Study description

Background summary

Sleep deprivation (SD) significantly impacts cognitive functioning and alertness, causing a decrease in performance. For military operators, (partial) SD is often unavoidable yet potentially endangers their performance such as maintaining alertness or making high impact decisions. A promising method to mitigate SD-induced cognitive performance impairment is transcutaneous

peripheral nerve stimulation (tPNS). This method involves applying a small electrical current non-invasively to the cervical branch of the vagus nerve (e.g., in the neck; ctVNS) with a medically approved device which is normally used for treatment of cluster headaches at home. Although studies on the effect of ctVNS on performance are scarce, initial results are very promising showing ctVNS increasing arousal, attention, and mood, but also counteracting feelings of fatigue. Here we propose to test whether ctVNS can (partially) restore cognitive performance under SD in lab settings as well as in the field.

Study objective

The main objective of the proposed study is to investigate the effect of ctVNS as a means to counteract the effects of SD on cognitive performance during and after SD. This will be tested using both well-controlled, established cognitive desktop tests, and a Virtual Reality (VR) scenario-based test which aims to more closely resemble the cognitive challenges encountered by dismounted soldiers in the field.

Study design

The study design will be a single-blind, sham-controlled, between-subjects intervention study with two groups of 20 participants. On the morning of day 1, both groups will perform a baseline test consisting of the desktop cognitive tests and the VR test. In the evening, the experimental group will receive ctVNS, whereas a control group will be treated with sham stimulation. Then, all participants will undergo one night of total SD. The desktop and VR tests are performed again on the morning of day 2 as a post-night test. To track effects of SD and ctVNS, the desktop tests are also performed every 3 hours during the night between day 1 and 2.

Intervention

Both groups will undergo one night of SD, with one group receiving ctVNS and the second group receiving sham stimulation. Electrical stimulation at 25 Hz is applied twice for 2 minutes in the neck using a handheld device (gammaCore® developed by electroCore®, FDA-approved and CE-marked to treat cluster headaches and treatment-resistant migraines at home), in the evening before SD occurs.

Study burden and risks

Participants will be invited for a single session of up to 36 hours, during which they are asked to participate in a number of activities. There are small burden and risks associated with participation, and there is no risk for any serious (adverse) event. The burden consists of the following activities:
- Sleep deprivation: Participants will be kept awake all night. After sleep

deprivation they will not be able to drive home safely, they will therefore be escorted home. Participants may experience increased fatigue the day after the experiment.
- Peripheral nerve stimulation: Stimulation will be done with a medically approved device (for at-home use) that applies a small current to the neck, targeting a branch of the vagus cranial nerve. Stimulation will be applied twice for 2 minutes, once on the left and once on the right side of the neck, with a 2 minute break in between. Some mild discomfort may occur locally, which stops when stimulation is stopped. Single session stimulation is associated with minimal side-effects, and use of the device is considered safe in healthy individuals.
- Behavioural testing: Throughout the session participants will be asked to participate in several cognitive tasks which are performed on a laptop. Each task takes 10-20 mins and tests different cognitive functions such as attention and memory.
- Virtual Reality test: After sleep deprivation participants will perform typical Special Operation Forces (SOF) tasks on foot in a VR environment. Virtual Reality can sometimes induce cyber-sickness, which is associated with feelings of dizziness, nausea, headache, and feeling warm. These symptoms start to improve as soon as the VR headset is taken off. To prevent cyber-sickness we will limit the amount of time in the VR and introduce breaks.

Benefits:
ctVNS is indicated in adults for the treatment of cluster headaches and migraines, with improvement of symptoms found after stimulation. ctVNS is a promising method for military applications, i.e. to counteract the decrease in cognitive performance in a military setting where maintaining wakefulness is necessary, and has the potential to support learning and memory, which may lead to improved performance in the field. On the day of stimulation participants may experience increased wakefulness and improved mood.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

1. The potential subject has given informed and written consent and is able to comply with all study assessments scheduled in the protocol.
2. All subjects need to be between 18 and 55 years of age.
3. All subjects have computer skills.
4. All subjects declare to be in good health, and declare not to have any chronic diseases.
5. Subjects must be able to communicate, participate, and comply with the requirements of the entire study.
6. One week prior to starting every trial day, all subjects need to be (and remain) in the same time zone as the CET time zone in which the research center lies. (GMT+1, daylight savings GMT+2). This to exclude jet lags which may confound the test results.
7. No signs of flue or viral infection in the last 5 days before the start.
8. Participant is active military personnel

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

1. Pregnancy
2. Atherosclerosis
3. Other cardiovascular health issues

4. Epilepsy and a history of psychiatric illness (including sleeping disorders).
5. Having an active implantable (metallic) device.
6. Using another device at the same time of testing or any portable electronic device (e.g., mobile phone).
7. Used alcohol the day before the start of a test day.
8. Used drugs in the last 3 months.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	02-10-2023
Enrollment:	40
Type:	Actual

Medical products/devices used

Generic name:	gammaCore
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO

Date:	28-08-2023
Application type:	First submission

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-02-2024
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL84403.028.23