Brainwave Entrainment and Stimulation

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To test whether tACS in a theta frequency enhances extinction of physiological stress responses to exposure to anxiety- or trauma-related stimuli or memories. Secondarily, to examine the influence of baseline neuroendocrinological response, baseline...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Anxiety disorders and symptoms
Study type	Interventional

Summary

ID

NL-OMON56492

Source
ToetsingOnline

Brief title
BEATS

Condition

- Anxiety disorders and symptoms

Synonym
trauma- and stressor-related disorder; anxiety disorder

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Nederlands Veteraneninstituut (NLVi) en het Ministerie van Defensie

Intervention

Keyword: anxiety, exposure therapy, posttraumatic stress disorder (PTSD), tACS

Outcome measures

Primary outcome

The primary study parameter is the stress response based on heart rate variability (HRV) and subjective units of distress (SUDs) during the exposure-based therapy sessions and subjective anxiety symptoms after the exposure-based therapy sessions.

Secondary outcome

Secondary study parameters are PTSD symptom severity and the influence of various baseline measures: resting-state heart rate variability, theta electroencephalography (EEG) activity, emotional working memory, stress hormone response, sleep quality and various mental health variables.

Study description

Background summary

The efficacy of treatments for trauma- and stressor-related disorders and anxiety disorders can potentially be improved in an innovative way. Evidence-based exposure therapies are aimed at extinguishing stress responses to anxiety- or trauma-related stimuli (fear extinction). The proposed mechanism behind this treatment is to weaken the fear memory and develop a safety memory, by formation of a so-called updated *stimulus-no trauma* association. The rationale behind this research proposal is that the administration of weak electric currents strengthens the consolidation of the safety memory by enhancing neural synchronization in the theta frequency (4-7 Hz), which plays an important role in learning and memory. We hypothesize that applying transcranial alternating current stimulation (tACS) in the theta frequency as add-on to exposure therapy will enhance the consolidation of the safety memory and ameliorates treatment outcome.

Study objective

To test whether tACS in a theta frequency enhances extinction of physiological

stress responses to exposure to anxiety- or trauma-related stimuli or memories. Secondarily, to examine the influence of baseline neuroendocrinological response, baseline resting state electroencephalogram (EEG) theta oscillations, sleep, age and use of medication on the effectiveness of tACS as add-on to treatment as usual (exposure therapy)

Study design

This is a double-blind placebo-controlled intervention study with an experimental group (active tACS) and a control group (sham tACS). Participants undergo a 6-session intervention with treatment as usual (exposure therapy for trauma- and stressor-related disorder or anxiety disorder) combined with tACS. Baseline, post-intervention assessments and follow-ups provide insight in effects over time on physiological stress responses during anxiety- or trauma-related stimulus exposure, PTSD and anxiety symptoms, electrophysiological brain activity (EEG), and emotional working memory performance.

Intervention

TACS is applied to the bilateral dorsolateral prefrontal cortex (DLPFC) at a frequency of 5 Hz with an intensity of 2 mA (peak-to-peak) in the active tACS group. In the control group (sham stimulation), the current is ramped up to 2 mA (30s) and immediately down (30s) again to 0 mA to mimic skin sensations without an active stimulation period. TACS is applied right after an exposure-based therapy session, for six consecutive exposure sessions in total.

Study burden and risks

The study involves a total of ten assessment time points for the participants, with six of them taking place in their own treatment facility (intervention sessions), two taking place in at the research center (baseline and post-intervention) and two taking place online only (follow-ups). Participants visit the research center for baseline and post-intervention assessments of PTSD or anxiety disorder symptoms (clinical interview), electroencephalogram (EEG) and working memory performance. Additionally, participants fill in online self-report symptom questionnaires. At baseline only, participants are asked to take saliva samples at home. Next, participants undergo the intervention (six tACS + exposure sessions). Finally, there are online naturalistic follow-ups, after the final tACS + exposure session that only includes the online questionnaires.
The application of tACS as in this study is considered safe and not associated with serious adverse events. Common adverse effects of tACS are minor (e.g., perceiving phosphenes, dizziness, headache, tingling, skin sensations)

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Age: 18 years or older
- People with uniformed professions or post-active military veterans
- Treatment with protocolized exposure-based therapy sessions for anxiety disorders or trauma- and stressor-related disorders (according to the Diagnostic and Statistical Manual of Mental Disorders, or DSM-5, criteria), e.g.
o Cognitive behavioural therapy with exposure, among which prolonged exposure (PE)
o Narrative exposure therapy (NET)
o Eye Movement Desensitization and Reprocessing (EMDR) therapy
- Willingness and ability to understand the nature and content of the study, to participate and to comply with the study requirements

- Willingness and ability to give written informed consent
- Provide written informed consent

Exclusion criteria

- Large metal or ferromagnetic objects in or around the head area, such as electronic hearing devices, cochlear implants, deep brain stimulators, or metal fragments near the skull (except for a dental wire).
- Opened skull or trepanation
- Pacemaker or neurostimulator
- Medication pump
- Epilepsy or family history of epilepsy
- Severe neurological condition or (a history of) brain damage
- Severe psychiatric condition comorbidity (e.g. schizophrenia, addiction)
- Skin damage or diseases around the intended tACS electrode sites (e.g. psoriasis, eczema)
- Concurrent or recent (within previous month) neuromodulation / neurostimulation (e.g., tDCS, TMS) treatment or study
- Pregnancy or possible pregnancy

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-06-2024
Enrollment:	56
Type:	Actual

Medical products/devices used

Generic name:	non-invasive brain stimulation: transcranial alternating current stimulation (tACS)
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	22-02-2024
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	03-04-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-06-2024
Application type:	Amendment
Review commission:	METC NedMec

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	NL84827.041.23