Enhancement of one exposure session for social anxiety disorder with transcranial alternating current stimulation: a proof-of-concept study

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To investigate the effects of aPFC-SMC phase-coupled tACS on exposure for SAD.

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

Summary

ID

NL-OMON56518

Source
ToetsingOnline

Brief title
Exposure enhancement with tACS in SAD

Condition

- Anxiety disorders and symptoms

Synonym
performance anxiety, social anxiety disorder, social phobia, speech anxiety

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen
Source(s) of monetary or material Support: NWO

Intervention

Keyword: Enhancement, Exposure, Social Anxiety Disorder, tACS

Outcome measures

Primary outcome

The main outcome of the study is subjective anxiety during the speech delivery as assessed with subjective units of distress ratings.

Secondary outcome

Additional parameters are self-reported social anxiety symptoms (via the Social Phobia Scale questionnaire), in-session avoidance behaviour (body posture, speech prosody, eye gaze), magnetic resonance imaging scans, physiological measures (heart rate, skin conductance, salivary testosterone and cortisol), implicit measures of approach-avoidance biases to emotional faces (via the computerized Approach-Avoidance Task), and computational estimates of learning rate adaptation to volatility (via the computerized Reversal Learning Task).

Study description

Background summary

With a lifetime prevalence of 13.3%, social anxiety disorder (SAD) is the most common anxiety disorder and among the most common pyschiatric disorders (Kessler et al., 1994). If untreated, the disorder typically follows a chronic, unremitting course leading to substantial impairments in vocational and social functioning. Exposure therapy is a proven effective treatment for SAD, but remission rates tend to be low (Blanco et al., 2010; Davidson et al., 2004), underscoring the need for new treatment strategies that enhance remission rates. This can be done by pairing exposure therapy with an additional intervention that boosts its underlying mechanisms of fear reactivity. Avoidance is the main hampering factor in exposure therapy: as long as patients avoid, fear cannot be extinguished and patients cannot learn new behaviours (Beckers & Craske, 2017). Avoidance, for instance, can predict treatment

outcome, suggesting that improving in-session avoidance might augment the treatment effects. Using a proof-of-concept study (Hutschemaekers et al., 2021), we previously showed that improving control over in-session avoidance can indeed augment the efficacy of exposure therapy and improve in-session fear reactivity (i.e. higher peaks and steeper reductions in fear levels). However, those studies used an invasive method (pharmacological intervention). Recent developments in neuromodulation have shown that non-invasive methods can effectively improve control social avoidance in healthy and anxious participants (Bramson et al., 2020; Meijer et al., 2023).

Cortical oscillations play an important role in the control over automatic social emotional action tendencies. Specifically, social emotional action control has been shown to be supported by a mechanism where the phase of theta-band oscillations in the anterior prefrontal cortex (aPFC) is coupled to the amplitude of gamma-band rhythms in sensorimotor cortex (SMC). A transcranial alternating current stimulation (tACS) protocol has been developed that mimics this endogenous mechanism by stimulating the aPFC and the SMC with theta- and gamma-band rhythms respectively, and by coupling the phase of the theta stimulation to the amplitude of the gamma stimulation. It was shown that in-phase aPFC-SMC stimulation facilitates the selection of an appropriate emotional action alternative, improving social-emotional control in both healthy and socially-anxious individuals (Bramson et al., 2020; Meijer et al., 2023).

In this proof-of-concept study, we aim to investigate whether these effects of in-phase aPFC-SMC tACS can be used to non-invasively enhance an exposure session. We plan to conduct a double-blind intervention study comparing one session of exposure plus in-phase aPFC-SMC tACS against exposure plus an active sham tACS stimulation (anti-phase aPFC-SMC) as placebo. Standardized brief exposure will be delivered according to the protocol developed by Rodebaugh and colleagues (2013): in this clinical assay consisting of two exposure sessions one week apart, participants need to prepare and deliver a speech (6 - 8 minutes) in front of an audience and a video camera. The first exposure session is enhanced with tACS, and the second exposure session is not enhanced, allowing the detection of transfer effects. We expect to detect verum vs placebo effects on response to exposure in terms of improved fear reactivity during the first enhanced exposure session. Furthermore, we will investigate whether this effect is mediated by in-session changes in avoidance (as measured by body posture, speech prosody, and eye gaze during the speech delivery), and whether these effects transfer to a second exposure session without enhancement.

Study objective

To investigate the effects of aPFC-SMC phase-coupled tACS on exposure for SAD.

Study design

The planned study is a double-blind intervention study.

Intervention

Participants will receive brief standardized exposure consisting of two exposure sessions one week apart in which participants give a speech in front of an audience and a video camera. The first exposure is enhanced, and the second exposure is not. Participants will be randomly allocated to either in-phase aPFC-SMC tACS enhancement or active sham (anti-phase aPFC-SMC) tACS enhancement. tACS will be applied concurrently with the speech preparation and delivery (20 minutes).

Study burden and risks

We believe the burden and the risk to be limited. Participants will visit the site three times, but each visit is necessary: the baseline neuroimaging/behavioural/questionnaire data measured during the first visit are crucial to obtain predictors of the tACS effects, and the subsequent two exposure visits are required to investigate the effects of our intervention, i.e. both immediate as well as persistent effects of combined tACS-exposure. Moreover, tACS is considered to be safe (Antal et al., 2017), and our stimulation parameters have been tested before (Bramson et al., 2020; Meijer et al., 2023).

There are no direct benefits for the participants in the present study. Possibly, participants that receive in-phase tACS will have benefits compared to standard exposure, however this has yet to be determined. Participants will contribute to knowledge on a potential enhancer of exposure efficacy for SAD.

We require participants that meet the DSM-5 criteria for SAD so that our findings can be clinically-relevant and provide ground for future clinical trials.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

A. 18-45 years old
B. Meeting the DSM-5 criteria for SAD as assessed with the Mini International Neuropsychiatric Interview (MINI), with a predominant fear of public speaking
C. Self-reported SAD symptoms above clinical cut-off (score > 30 on the Liebowitz Social Anxiety Scale)
D. Magnetic resonance imaging (MRI) compatible
E. tACS compatible

Exclusion criteria

A. Prior non-response to exposure therapy (i.c. speech exposure) for SAD symptoms, as defined by the subject*s report of receiving specific and regular exposure assignments as part of previous therapy
B. Entry of subjects with other mood or anxiety disorders will be permitted in order to increase accrual of a clinically relevant sample; however, in cases where SAD is not judged to be the predominant disorder, participants will not be eligible
C. Psychosis or delusion disorders (current or in the past)
D. Subjects with significant suicide ideations or who have enacted suicidal behaviors within 6 months prior to intake will be excluded from participation and referred for appropriate clinical intervention
E. Intellectual disability

F. Substance or alcohol dependence
G. Somatic illness
H. Pregnancy or lactation
I. Antipsychotic medication
J. Participants that use antidepressants or benzodiazepines will not be excluded, but have to be on a stable dose for at least 6 weeks prior to enrollment
K. Insufficient ability to speak and write Dutch

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2023
Enrollment:	60
Type:	Anticipated

Ethics review

Approved WMO

Date:	12-02-2024
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL84921.091.23