Delirium treatment with Transcranial Electrical Stimulation

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Deliria (incl confusion)
Study type	Interventional

Summary

ID

NL-OMON56548

Source
ToetsingOnline

Brief title
DELTES

Condition

- Deliria (incl confusion)

Synonym
acute encephalopathy, delirium

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMw funding met NWO voorwaarden

Intervention

Keyword: Delirium, Electroencephalogram, Non-invasive brain stimulation, Transcranial electrical stimulation

Outcome measures

Primary outcome

To study the effects of tACS treatment on delirium, our two primary objectives are as follows:

I. To investigate whether one session of standardized tACS reduces the relative delta power observed in delirium, measured using EEG.

II. To investigate whether one session of personalized tACS, based on a computational model and virtual trial using EEG as input, reduces the relative delta power in patients with delirium, measured using EEG.

The two main objectives of the study share the same outcome variable, namely relative delta power, measured immediately before and after the application of tACS or sham stimulation using a 64-channel EEG. Relative delta power has been chosen as the primary study parameter because delirium is consistently associated with increased delta EEG activity. As oscillatory synchronization can have cross-frequency effects, we hypothesize that tACS applied within the alpha frequency range improves functional connectivity, leading to reduced relative delta power.

Secondary outcome

The aim of the pilot study is to investigate whether the tACS treatment can be

safely applied to, and tolerated sufficiently by, patients with delirium.

Outcome measures include: the percentage of completed first stimulation sessions, increase in care needs within the first hour after tACS, and duration of delirium.

Secondary outcomes of the main study include: severity of delirium, duration of delirium, length of hospitalization, cognitive ability three months after tACS treatment, difference in effect between standardized and personalized tACS, changes in power and functional connectivity measured using EEG, subjective expectations and evaluations of tACS as a treatment for delirium and the effect of cumulative tACS sessions.

Study description

Background summary

Delirium, characterized by acute confusion and disturbances in cognition and perception, prolongs hospital stays, increases healthcare costs, and leads to long-term cognitive decline. Currently, there is no treatment that reduces the duration or severity of delirium. Delirium is characterized by a diffuse oscillating slowing of the electroencephalogram (EEG), including a pronounced loss of alpha activity and an increased relative delta power. Furthermore, functional connectivity between brain regions is reduced during delirium. Taking this into consideration, transcranial alternating current stimulation (tACS) is a potential treatment that directly addresses the brain dysfunction observed in delirium. Because tACS can improve multiple domains of cognition, including attention, it could be an effective treatment for delirium. In this study, we aim to investigate whether tACS results in normalization of the EEG in individuals with delirium. Additionally, we want to examine whether different approaches of tACS, standardized or personalized using EEG data as input, are effective compared to sham treatment.

Study objective

The aim of the study is to investigate whether standardized or personalized tACS induces EEG changes indicative of delirium reversal (primary outcome) or reduces the duration and/or severity of delirium (secondary outcome) compared to sham treatment. Additionally, we are interested in exploring the safety and tolerability of tACS as a treatment for delirium, which we are investigating through a pilot study as an integral component of the main study.

Study design

We will conduct a double-blind, randomized, sham-controlled, multicenter study to investigate the effectiveness of standardized and personalized tACS in patients with delirium. Participants will be randomized in two steps between standardized and personalized tACS, and then active or sham treatment. This randomization results in a 1:1:1 allocation between active standardized treatment, active personalized treatment, and sham treatment. During the initial months of study inclusion, personalized treatment will not be available, and randomization will occur between active standard treatment and sham treatment, with the first 30 patients being included as part of a pilot study to assess the tolerability of tACS in delirium. When the pilot study is completed and personalized treatment becomes available (expected in Q2-Q3 2024), randomization weights will be calculated to achieve a 1:1:1 allocation.

EEG measurements will be conducted immediately before and after the first stimulation session. Active tACS or sham treatment will be applied once daily for a maximum of 14 days, until delirium has resolved or until discharge from the hospital. During treatment, the presence and severity of delirium will be monitored daily. The treatment phase will conclude with a final visit, including a follow-up EEG. Three months after the study, cognitive status will be assessed using a validated telephone interview.

Intervention

Patients will receive tACS consisting of 2 mA (peak-to-peak) stimulation delivered for 30 minutes, using two 5x5 cm electrodes placed under a standard 64-channel EEG cap, for a maximum of 14 days. For the standardized tACS treatment, the frequency of tACS will be in the alpha range (10 Hz), and electrodes will be positioned over the frontal and occipito-parietal regions of the head. In contrast, the stimulation frequency and electrode placement in personalized tACS treatment will vary depending on the most optimal parameters determined by a computational model.

The sham treatment will consist of a 30-second ramp-up to 60 seconds of 10 Hz tACS, followed by a 30-second ramp-down, totaling 120 seconds of stimulation, for a maximum of 14 days.

Study burden and risks

All measurements in this study are non-invasive. Participants may temporarily experience mild tingling or itching under the electrodes during stimulation, or mild headache and fatigue shortly after stimulation. The proposed tACS protocol is considered safe according to the latest published international safety guidelines. All participants have been screened for their relevant medical history and contraindications for tACS. No serious or persistent side effects are expected during this study as a result of the tACS intervention, and therefore, the risks to the patients are considered low to very low. The visits require an additional time commitment for questionnaires, EEG data recording, and tACS stimulation. However, because these visits are conducted while the patient is hospitalized, the burden on the participants is considered low. Considering the negative effects of delirium on (long-term) functioning and the fact that there is currently no effective treatment available, the benefit of a potentially new treatment targeting the underlying brain dysfunction of delirium is considered high.

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 over 50 years.
Diagnosis of delirium
Richmond Agitation and Sedation Scale (RASS) score of -2 to +2.
Delirium duration of at least two days prior to study inclusion, based delirium assessments and/or descriptions in the medical and/or nursing files.
Known causes underlying delirium are being treated adequately, as assessed by the treating physician.

Exclusion criteria

Inability to conduct valid delirium screening assessment (e.g. coma, deaf, blind) or inability to speak the Dutch or English language.
Patients in a moribund state.
Alcohol/substance abuse withdrawal or stroke as precipitating factor for delirium.
Diagnosis of dementia, based on medical record review and/or a score of >=4.5 on the short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE).
Standard contra-indications for tACS (history of serious head trauma or brain surgery; large or ferromagnetic metal parts in the head (except for a dental wire);
implanted cardiac pacemaker or neurostimulator; skin diseases or inflammations; epilepsy)

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):	24-04-2024
Enrollment:	159
Type:	Actual

Medical products/devices used

Generic name:	Nurostym transcranial electrical stimulation
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	30-01-2024
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	26-06-2024
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	NL84043.041.23