Effects of transcranial ultrasonic stimulation on eye movements

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

Summary

ID

NL-OMON53753

Source
ToetsingOnline

Brief title
Transcranial ultrasonic stimulation of the frontal eye fields

Condition

- Other condition

Synonym
brain

Health condition

Neuroscience research

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Eye-saccades, Frontal eye fields, Transcranial ultrasonic stimulation

Outcome measures

Primary outcome

Oculomotor behaviour (leftward/rightward saccades) in the saccade-task is used as the main outcome variable.

Secondary outcome

Secondary outcomes, such as saccade latency and duration will also be assessed to study how TUS of the FEFs affects saccade preparation and duration.
Additionally, GABA/glutamate levels in the stimulation sites (using MRS) and the intracranial stimulation intensity (calculated on each subjects structural MRI) will be examined per individual to explain any inter-individual differences in behavioural outcomes.
To assess individual location of the left/right FEF and the left/right M1, which we need for stimulation during intervention sessions, we perform a short functional MRI during the intake session.
Furthermore, as a quality control of this study, we have added the M1 as an active control site and we will perform a masking assessment at the end of the intervention sessions to guarantee the spatial specificity of TUS and the quality of our auditory mask, respectively. All of these measures will help ensure accuracy and precision of our findings

Study description

Background summary

Transcranial Ultrasonic Stimulation (TUS) is a non-invasive brain stimulation (NIBS) technique with unmatched spatial specificity and the ability to target nearly any brain region. To date, this technique is mostly studied in animal models, while its translation to human applications is still at an early phase. One of the current key aims is to develop TUS protocols to safely and effectively modulate behaviour in humans, and understand the neural basis of their effects. To achieve this critical translational goal, we leverage an experimental design from a non-human primate study (Kubanek et al., 2020) using TUS stimulation of the frontal eye field (FEF) to human participants. The FEF is involved in voluntary eye movements to the contralateral side. Exciting the FEF, therefore, drives eye saccades to the contralateral side, whereas inhibition of the FEF steers saccades to the ipsilateral direction. We measure the effect of FEF TUS stimulation on oculomotor behaviour to investigate the physiological and behavioural effects of TUS in humans. Based on the non-human primate findings reporting (Kubanek et al., 2020), we hypothesise that this online TUS protocol will bias eye saccades contralateral to the TUS stimulated FEF. This effort may indicate the potential of TUS in an online paradigm and will further serve to inform the experimental design of future studies.

Study objective

Our primary objective is to translate an in non-human primate established online TUS protocol to humans. To this end, we will investigate how this protocol influences choice behaviour in humans, by stimulating the left and right FEF in a saccade task.

Study design

The present study will be a single-blind, three-visit, randomised, sham- and active-controlled trial. In the first session, structural and functional MRI scans will be obtained, during which participants perform a FEF localiser task and a hand primary cortex (M1) localiser task. We will also obtain a MRS scan to assess the GABA/glutamate concentrations in the FEF and M1. The second and third session are the intervention sessions in which the left and right FEF, and left and right M1 will be stimulated (with sham) while the participants perform a saccade-task. The intervention sessions also include a final masking assessment, to ascertain that the participants were successfully blinded to the conditions.

Intervention

Participants will receive TUS at a standard sub-threshold intensity.

Study burden and risks

Participants, apart from the reimbursement they receive and the experience of participating in a brain stimulation study, have no further benefit from participating in this study. Participants will receive a standard financial compensation where applicable. Before participation, all subjects will be screened for contraindications with respect to TUS and magnetic resonance imaging (MRI). The estimated risk for participating in MRI measurements and TUS-based interventions is minimal. The noise and the relative confined space of the MRI scanner, and the requirement to remain seated during the TUS experiment, may cause discomfort to some subjects. TUS for human neuromodulation has never resulted in serious adverse events (Blackmore et al., 2019; Pasquinelli et al., 2019). Similar to applications of well-established biomedical ultrasound (Ter Haar, 2010), safety of study participants is ensured by adherence to internationally recognized practices and guidelines (e.g., from the Food and Drug Administration). Minor side effects of TUS may include light transient headache and fatigue (Legon et al., 2020). To conclude, the risk and burden associated with participation is considered minimal, and we do not expect any (serious) adverse events during the project.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Between 18-40 years of age
- Right handed
- The ability and agreement to provide informed consent, and the ability to fulfil the study's requirements

Exclusion criteria

• Under 18 years of age;
• Current or planned pregnancy;
• Claustrophobia;
• A history or brain surgery or serious head trauma;
• A history of or any close relatives (parents, siblings, children) with epilepsy, convulsion, or seizure;
• Predisposition for fainting spells (syncope);
• A cardiac pacemaker or intra-cardiac lines;
• An implanted neurostimulator;
• Implanted medication infusion device;
• Implanted metal devices or large ferromagnetic fragments in the head or upper body (excluding dental wire), or jewellery/piercing that cannot be removed;
• Use of a medical plaster that cannot or may not be taken off (e.g., nicotine plaster);
• Cochlear implants;
• Metal in the brain, skull, or elsewhere in your body (fragments, clips, etc.);
• Diagnosed neurological or psychiatric disorders;
• Use of psychoactive (prescription) medication (excluding anti-conception);
• Skin disease at intended stimulation sites;
• The consumption of more than four alcoholic units within 24 hours before participation or any alcoholic units within 6 hours before participation day;
• The consumption of recreational drugs within 48 hours before participation;
• Calcifications in the brain.
• All other criteria relevant to non-invasive brain stimulation as reported in the Donders Standard Operating Procedures for Non-Invasive Brain Stimulation.

Study design

Design

Study type: Interventional

Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	31-05-2023
Enrollment:	45
Type:	Actual

Medical products/devices used

Generic name:	NeuroFUS Pro - low intensity transcranial ultrasonic stimulation
Registration:	No

Ethics review

Approved WMO Date:	14-02-2023
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-06-2023
Application type:	Amendment
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	NL82309.091.22