Biasing decision flexibility with thalamic ultrasound stimulation

Published: 16-05-2024
Last updated: 18-01-2025

Our primary objective is to elucidate the neural and cognitive effects of short-term TUS to two thalamic subdivisions in humans. To this end, we target two thalamic subregions that are spatially adjacent yet feature divergent connectivity profiles...

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

Summary

ID

NL-OMON56757

Source
ToetsingOnline

Brief title
ThalStim

Condition

- Other condition

Synonym
normal brain function

Health condition

fundamental neuroscience in healthy adults

Research involving
Human

Sponsors and support

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

Intervention

Keyword: neuroimaging, perceptual decision-making, thalamus, transcranial ultrasonic stimulation

Outcome measures

Primary outcome

Intrinsic dynamics and task sensitivity of the cortical network partners of the stimulation targets (MD - prefrontal cortex, PUL - parietal cortex), estimated from electroencephalography (EEG) recordings, assess TUS effects. Changes in behavioural sensitivity to (1) perceptual and (2) task uncertainty manipulations following TUS application assess effects on decision computations. These are based on computational modelling of accuracy and response time measures.

Secondary outcome

We will explore TUS-related changes in physiological arousal based on measured of heart rate and pupil size. Anatomical MRI measurements will be acquired to perform personalized simulations of ultrasonic wave propagation; functional MR images will be used to test the dissociable involvement of the targeted thalamocortical networks in the decision task.

Study description

Background summary

The thalamus makes multifaceted contributions to neuro-cognitive function. By regulating cortical information processing, thalamocortical circuits define how external information guides behavior and critically support fundamental building blocks of cognition, including perception and executive function. However, the thalamus* deep location and differentiated composition challenges human research and limits causal interventions. The emerging technology of low-intensity Transcranial Ultrasonic Stimulation (TUS) promises to overcome such challenge. TUS enables reversible, non-invasive modulation of focal deep brain tissue, including the human thalamus with millimeter precision. However, no study to date has investigated the potential to interact with functionally heterogeneous subregions of the thalamus -a prerequisite for targeted engagement with this key structure. In this project, we aim to leverage TUS*s unprecedented precision to clarify the contribution of anatomically adjacent, yet distinctly projecting thalamic circuits to uncertainty resolution in human decision-making.

Study objective

Our primary objective is to elucidate the neural and cognitive effects of short-term TUS to two thalamic subdivisions in humans. To this end, we target two thalamic subregions that are spatially adjacent yet feature divergent connectivity profiles to distal cortical targets. We investigate the short-term effects of TUS to either the mediodorsal (MD) or pulvinar (PUL) thalamus while participants perform a perceptual decision-making task. Our primary outcomes are target-specific changes in (1) the engagement of cortical targets, and (2) decision computations relying on these circuits. As a secondary outcome, we probe TUS effects on physiological parameters.

Study design

Three-visit, single-blind, randomized, crossover trial. During the first session, structural and functional magnetic resonance imaging (MRI) scans will be obtained. The second and third sessions are ultrasonic intervention sessions. In these sessions, ultrasonic stimulation will be applied following and preceding acquisition of electroencephalography (EEG) during a perceptual decision-making task. We will use a factorial design with stimulation (MD-thalamus-TUS, PUL-thalamus-TUS) as a within-subject factor.

Intervention

Transcranial Ultrasonic Stimulation (TUS) aimed at bilateral mediodorsal thalamus, and bilateral pulvinar thalamus (in separate sessions). Experimental manipulations of (1) perceptual uncertainty and (2) task uncertainty serve to engage the two target networks.

Study burden and risks

Participants will receive no direct benefit from participating, though they often report enjoying their participation and the opportunity to experience MRI, EEG, and TUS. Participants will receive a standard financial compensation where applicable (¤15/hour; ¤120 in total for all three sessions). Before participation, all subjects will be screened for contraindications with respect to non-invasive brain stimulation and 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 may cause discomfort to some subjects. The EEG electrode application can cause a mild, transient skin irritation. Participants are informed about both possibilities in advance. TUS for human neuromodulation has never resulted in serious adverse events (Blackmore, Shrivastava, Sallet, Butler, & Cleveland, 2019; Pasquinelli, Hanson, Siebner, Lee, & Thielscher, 2019; Sarica et al., 2022). Like 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 U.S. Food and Drug Administration (2017)). In all cases we will adhere to the recommendations of the international expert group on Transcranial Ultrasonic Stimulation Safety and Standards (ITRUSST, https://itrusst.com). Minor side effects of participating in a TUS experiment 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

Public
Radboud Universiteit Nijmegen

Thomas van Aquinostraat 4
Nijmegen 6525
NL
Scientific
Radboud Universiteit Nijmegen

Thomas van Aquinostraat 4
Nijmegen 6525
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Between 18-40 years of age;
- The ability and agreement to provide informed consent in sound body and mind, and the ability to fulfil the study*s requirements.

Exclusion criteria

• Under 18 years of age;
• Current 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), orjewellery/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
• 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):	02-07-2024
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	16-05-2024
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	NL86115.091.24