Biasing approach/avoidance decisions using Transcranial Ultrasonic Stimulation of the Human Amygdala ventral Striatum

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The primary objective is to influence amygdala and ventral striatum neuronal activity, thereby changing their influence on consequent approach/avoidance decisions, as indicated with left or right button presses.

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

Summary

ID

NL-OMON51624

Source
ToetsingOnline

Brief title
Biasing approach avoidance behaviour using TUS

Condition

- Anxiety disorders and symptoms

Synonym
brain; anxiety

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen
Source(s) of monetary or material Support: Ministerie van OC&W,NWO crossover grant Innovative NeuroTEchNology for SociEty (INTENSE)

Intervention

Keyword: action selection, Amygdala, Approach/avoidance, Striatum, Transcranial Ultrasound Stimulation

Outcome measures

Primary outcome

Approach/avoidance choice behaviour as indicated by index-finger button-press

will be used to assess the neuromodulatory effects of TUS.

Secondary outcome

Pupil size; Heart rate.

These secondary study parameters fall under the blanket approval for standard

research (CMO2014/288, version 3; titled: *Imaging Human Cognition*).

Study description

Background summary

Avoidance behaviour is one of the key predictive factors in maintaining pervasive emotional disorders such as anxiety. Previous studies have shown that the Amygdalae are important regions involved in threat-assessment and consequent avoidance when people make approach or avoid decisions based on predicted reward or punishment. Disruption or ablation of the amygdala in animal models results in reduced avoidance and increased approach behaviour, allowing animals to gain rewards even in the presence of threat. Theoretically,being able to disrupt amygdala activity might provide a way to reduce avoidance biases in patients with anxiety-related disorders,allowing them to benefit from exposure treatment. Until recently, the only way to influence deep neural structures such as the amygdala was to open the skull and insert a deep-brain electrode. However, newly developed Transcranial focused Ultrasound Stimulation (TUS) can target and modulate neural activity in deep structures such as the amygdala non invasively, potentially providing a safe way to efficiently reduce threat avoidance. The current study is aimed at manipulating approach/avoidance behaviour through modulation of amygdala and ventral striatum, a neural region associated with reward processing, whilst participants make approach/avoid decisions based on threat (electrical shocks) and reward information (monetary bonusses).

Transcranial Ultrasonic Stimulation (TUS) is a non-invasive neuromodulation technique that can achieve focal modulation of deep brain structures such as the amygdala. Here, we will combine TUS with a well-validated decision making paradigm allowing us to test whether amygdala/striatal balance is causally related to approach/avoidance decision making. The outcomes of this study can provide a first stepping-stone for the development of TUS based interventions aimed at reducing anxiety disorders.

Study objective

The primary objective is to influence amygdala and ventral striatum neuronal activity, thereby changing their influence on consequent approach/avoidance decisions, as indicated with left or right button presses.

Study design

This study consists of three experimental sessions in a single-blind, randomized, sham-controlled trial. In the first session, a structural MRI scan will be obtained, followed by a behavioural approach/avoidance (AA) task. The second and third sessions are intervention sessions where TUS will be applied, aimed at bilateral ventral striatum or amygdalae in a counterbalanced fashion, whilst participants perform the same AA task.

Intervention

Transcranial Ultrasound Stimulation aimed at bilateral amygdalae and ventral striatum (in separate sessions).

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 and TUS. Participants will receive a standard financial compensation where applicable (¤10/hour). 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, 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.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Healthy participants between 18-40 years of age;
- 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 recreational drugs within 48 hours before participation

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2022
Enrollment:	85
Type:	Anticipated

Medical products/devices used

Generic name:	NeuroFUS Pro - low intensity transcranialultrasonic stimulation
Registration:	No

Ethics review

Approved WMO Date:	01-08-2022
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	NL81177.091.22