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Repetitive transcranial magnetic stimulation for the treatment of substance dependence

Submission date
26/09/2023

Recruitment status
No longer recruiting

Registration date
11/10/2023

Overall study status
Completed

Last Edited
18/04/2024

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Addiction is a growing problem worldwide, including in the United Arab Emirates (UAE). According to the National Rehabilitation Center in Abu Dhabi, drug addiction costs the UAE a total of Dh 5.5 billion every year. Therefore, it is paramount that substance use disorders (SUDs) are addressed vigorously.
As individuals with SUDs typically have other mental health problems such as depression, having a treatment that can potentially target both disorders simultaneously would be of high benefit and cost-effective.
Transcranial Magnetic Stimulation (TMS) is a non-invasive brain stimulation technique approved for the treatment of depression. Treatment with rTMS was also shown to reduce cravings in patients with SUDs.
This study aims to investigate the effectiveness of depression treatment using rTMS (as approved by the FDA) in reducing craving and consumption of illicit substances, and its effect on abstinence duration among patients with SUDs.

Who can participate?
Male patients aged 18-65 years meeting the criteria for psychoactive substance dependence, who are under the care of the Erada Center and who are admitted for detoxification and rehabilitation from November 2023 to November 2024.

What does the study involve?
Patients will receive rTMS treatment in two phases:
Phase 1: five times per week for 4 weeks (total 20 treatments)
Phase 2: two times as needed at 1 month, 3 months, and 6 months follow-up

What are the possible benefits and risks of participating?
Benefits include a decrease in cravings, maintenance of abstinence, and reduction in the severity of symptoms of depression, if present.
Risks are related to the side effects of rTMS (headache in 5-23% of cases and discomfort at the site of stimulation in 20-40% of cases).
The most serious side effect associated with rTMS is the accidental induction of a seizure. Although accidental seizures occur at a frequency of <0.1%, there are factors that may increase

the TMS risk of triggering a seizure such as family history of seizures, alcohol use, and previous neurological conditions. These are part of the exclusion criteria that will be used during the recruitment process. Furthermore, throughout the sessions, participants will be closely monitored by a team member for any side effects and managed accordingly.

Where is the study run from?
Erada Center for Treatment and Rehabilitation in Dubai (United Arab Emirates)

When is the study starting and how long is it expected to run for?
February 2021 to January 2026

Who is funding the study?
Erada Center for Treatment and Rehabilitation in Dubai (United Arab Emirates)

Who is the main contact?
Dr Samer El Hayek, s.elhayek@erada.ae

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Additional identifiers

Protocol serial number
DSREC-01/2021_12

Study information

Scientific Title
Repetitive transcranial magnetic stimulation effect on craving and period of abstinence in patients with substance use disorders

Acronym
rTMS-CASUD

Study objectives
This research aims, through a prospective longitudinal trial study, to investigate the effectiveness of depression treatment protocol of repetitive transcranial magnetic stimulation (rTMS) (as approved by the FDA) in reducing craving and consumption of illicit substances, and its effect on abstinence duration among patients with substance use disorders (SUDs).

Does treatment of individuals with SUDs with rTMS using FDA-approved depression protocol to the left dorsolateral prefrontal cortex (DLPFC):
1. Reduce consumption of, and craving for, substances of use?
2. Prolong the abstinence period?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/02/2021, Dubai Scientific Research Ethics Committee (Dubai Health Authority Headquarters - First Floor - Medical Education & Research Department - Medical Research Section; +971 (0)4 502 7518; DSREC@dha.gov.ae), ref: DSREC-01/2021_12

Primary study design
Interventional

Study design
Interventional double-blinded randomized controlled trial

Study type(s)
Treatment, Efficacy

Health condition(s) or problem(s) studied
Substance use disorders

Interventions
Participants will be randomized into one of two treatment groups: 1) active rTMS to the left dorsolateral prefrontal cortex and 2) sham rTMS to the left. Participants will be randomized by a third-party team member. The treating psychiatrist and the technician providing rTMS will be blinded to the randomization.

The study will be conducted in two phases:
During phase 1 (treatment initiation), participants will receive their assigned treatment five times weekly for 4 weeks (total of 20 treatments).
During phase 2 (follow-up), participants will receive two treatments as needed at 1 month, 3 months and 6 months follow-up points.

Intervention Type
Device

Phase
Phase III/IV

Drug/device/biological/vaccine name(s)
Repetitive transcranial magnetic stimulation (rTMS)

Primary outcome(s)
During phase 1 (treatment initiation), participants will receive their assigned treatment 5 times weekly for 4 weeks (total of 20 treatments). The outcomes will be:
1. Craving for the substances of use, measured using the Brief Substance Craving Scale (BSCS) total score at baseline and after every 5th session of TMS
2. Substance(s) of misuse consumption as evidenced by confirmed lab results of UDS at baseline, randomly twice per week during inpatient admission, and on every outpatient follow-up visit after discharge

During phase 2 (follow-up), participants will receive 2 treatments as needed at 1 month, 3 months and 6 months follow-up points. The outcomes will be:
1. Craving for the substances of use, measured using the Brief Substance Craving Scale (BSCS) total score at 1 month, 3 months and 6 months follow-up points
2. Substance(s) of misuse consumption as evidenced by confirmed lab results of UDS on every outpatient follow-up visit after discharge

Key secondary outcome(s)

During phase 1 (treatment initiation), participants will receive their assigned treatment 5 times weekly for 4 weeks (total of 20 treatments). The outcomes will be:
1. Time to relapse measured using the number of days with negative UDS, until positive UDS results
2. Anxiety and depression measured using the Hospital Anxiety and Depression Scale (HADS) at baseline and after every 10th session of TMS

During phase 2 (follow-up), participants will receive 2 treatments as needed at 1 month, 3 months and 6 months follow-up points. The outcomes will be:
2. Time to relapse measured using the number of days with negative UDS, until positive UDS results
2. Anxiety and depression measured using the Hospital Anxiety and Depression Scale (HADS) at 1 month, 3 months, and 6 months follow-up points

Completion date
01/01/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 18/04/2024:
1. Male patients aged 18-65 years
2. Meeting criteria for current SUD (moderate to severe) according to the International Classification of Diseases, Tenth Revision criteria (ICD-10)
3. Under the care of Erada Center and admitted for detoxification and rehabilitation and/or following at the outpatient clinic during the period of the trial
4. Abstinence from any substance of use for at least seven days as indicated by a negative urine drug screen (UDS) prior to initiation of sham or active rTMS

Previous inclusion criteria:
1. Male patients aged 18-65 years
2. Meeting criteria for psychoactive substance dependence according to the ICD-10 criteria
3. Under the care of Erada center and admitted for detoxification and rehabilitation from October 2023 to October 2024
4. Positive drug screen confirmed through urine analysis
5. HADS and BSCS will be routinely applied to all inpatients

As per the Neuromodulation Unit Criteria for rTMS treatment; patients need to meet the following criteria:
1. Current diagnosis of SUD (moderate to severe), based on the ICD-10 criteria
2. Abstinence from any substance of use for at least seven days as indicated by a negative urine drug screen

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Male

Key exclusion criteria
As per the Neuromodulation Unit existing criteria and as per the findings at the time of assessment for rTMS:
1. Current ICD-10 diagnoses of alcohol use disorder or any general mental health disorder (schizophrenia, major depressive disorder, bipolar disorder, anxiety disorder, obsessive-compulsive disorder, etc).
2. Use in the past 2 weeks of any medication with known pro-convulsant action; or current regular use of any of the following medications: benzodiazepines, antipsychotic medications and tricyclic antidepressants (in therapeutic doses), anti-epileptics, or mood stabilizers.
3. History of any clinically significant neurological disorder, including organic brain disease, epilepsy, stroke, brain lesions, multiple sclerosis, previous neurosurgery, or personal history of head trauma that resulted in loss of consciousness for >5 minutes and retrograde amnesia for >30 minutes.
4. Any personal or family history (1st-degree relatives) of seizures other than febrile childhood seizures.
5. Ferromagnetic object in the body rendering rTMS unsafe such as cardiac pacemaker or defibrillator, brain stimulator, shrapnel, surgical metal, clips in the brain or on blood vessels, or cochlear implants.
6. Patients started on, or imminently planned to start on Buprenorphine for Medication Assisted Treatment.

Date of first enrolment
15/01/2024

Date of final enrolment
01/06/2025

Locations

Countries of recruitment
United Arab Emirates

Study participating centre
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Sponsor information

Organisation
Dubai Health Authority

ROR
https://ror.org/01dcrt245

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Erada Center for Treatment and Rehabilitation

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Samer El Hayek (s.elhayek@erada.ae or samer.elhayek@gmail.com). The data will include the cleaned set of collected variables and scores on outcomes; it will be available up to 2 years from the publication of the study unless later on stated otherwise. Consent will be taken from all patients prior to enrolment and will include data sharing. All data will be anonymized.

IPD sharing plan summary
Available on request