Clinical Trial Protocol
Iranian Registry of Clinical Trials

08 Nov 2026

Effectiveness of right unilateral and sequential bilateral repetitive transcranial magnetic stimulation (rTMS) on somatic-subjective anxiety in patients with comorbid anxiety and depression

Protocol summary

Study aim
Determining the effectiveness of Repetitive Transcranial Magnetic Stimulation on somatic-psychic anxiety in patients with anxiety-depression comorbidity

Design
A randomized, double-blind, sham controlled clinical trial with a parallel group design of 501 patients, enrolled between July 2026 and October 2026.

Settings and conduct
Study Location: This study will be conducted at the Department of Psychiatry, Farhikhtegan Hospital, Tehran, Iran. Study Population: The study population will consist of outpatients with a comorbid diagnosis of anxiety and depressive disorders. Blinding Type: Double-blind. Blinding Procedure: Both active and sham stimulation groups will be exposed to an identical apparatus, coil, auditory output, and stimulation positioning relative to the target site, with the sole exception that in the sham condition, no magnetic current is delivered to the brain. The clinician will receive and implement a uniform set of stimulation parameters (including duration, coil placement, and acoustic characteristics) from the principal investigator for all participants, while remaining blinded to both group allocation and the study hypotheses.

Participants/Inclusion and exclusion criteria
Inclusion criteria: Diagnosis of major depressive disorder and a anxiety disorder according to the DSM-5; a score of >17 on the HRSD-71 and >18 on thee HAMA; availability of documented pharmacological treatment history. Exclusion criteria: History of prior electromagnetictherapies; significant suicidal ideation; presence of ferromagnetic metallic implants; personal history of epilepsy.

Intervention groups
Intervention group 1: The right unilateral Repetitive Transcranial Magnetic Stimulation (rTMS); Intervention group 2: The Sequential bilateral Repetitive Transcranial Magnetic Stimulation (rTMS); Control group: The sham stimulation

Main outcome variables
Anxiety

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20180522039775N3**
Registration date: **2026-07-14, 1405/04/23**
Registration timing: **prospective**

Last update: **2026-07-14, 1405/04/23**
Update count: **0**

Registration date
2026-07-14, 1405/04/23

Registrant information

Name
Mehdi Rezaei

Name of organization / entity
Lorestan university

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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2026-07-31, 1405/05/09

Expected recruitment end date

2026-10-20, 1405/07/28

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Effectiveness of right unilateral and sequential bilateral repetitive transcranial magnetic stimulation (rTMS) on somatic-subjective anxiety in patients with comorbid anxiety and depression

Public title

Effectiveness of repetitive transcranial magnetic stimulation (rTMS) on patients with comorbid anxiety-depression

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Patients who meet the criteria for major depressive disorder and an anxiety disorder according to the DSM-5 The symptoms of depression and a baseline score greater than 17 on the HRSD-17 scale Symptoms of anxiety and a baseline score greater than 18 on the HAMA scale Having access to medication information is available

Exclusion criteria:

Under 18 years old History of receiving electromagnetic therapies (such as tDCS, rTMS, ECT) Having significant suicidal thoughts The presence of a pacemaker or metal implants Personal history of seizures or epilepsy History of head surgery or severe head trauma Diagnosing other psychiatric conditions, including substance use disorders, organic brain disorders, personality disorders, or bipolar disorder Pregnancy or breastfeeding High-dose benzodiazepine use (>2 mg of lorazepam equivalent per day)

Age

From **18 years** old

Gender

Both

Phase

N/A

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor

Sample size

Target sample size: **60**

Randomization (investigator's opinion)

Randomized

Randomization description

A computer-based randomization approach will be used (www.sealedenvelope.com). Sixty participants will be placed into ten equal-sized blocks of 6 to create a random allocation sequence. To conceal the randomization process, a unique code generated by the software will be provided to each participant. These codes will be randomly associated with cubes representing the intervention groups.

Blinding (investigator's opinion)

Double blinded

Blinding description

In this study, both the evaluator and the therapist will remain blinded to the administration of active versus sham interventions, as well as to the group allocation of participants. Furthermore, participants will be unaware of whether they receive active or sham intervention, and the researcher will be blinded to group assignments. The evaluator will administer and score identical questionnaires at three time points—pretest, posttest, and follow-up—without any knowledge of group allocation. The therapist will receive and implement a standardized stimulation protocol (including duration, coil positioning, and audible coil click) for all participants, as provided by the researcher, while remaining uninformed about group assignment and underlying hypotheses. Both groups (active and sham stimulation) will be exposed to identical equipment, coil, acoustic artifact, and stimulation positioning, with the sole distinction that in the sham condition, no magnetic current will be delivered to the brain.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Research Ethics Committee of University of Birjand

Street address

University of Birjand, Shahid Avini Boulevard

City

Birjand

Province

South Khorasan

Postal code

9717434765

Approval date

2026-05-11, 1405/02/21

Ethics committee reference number

IR.BIRJAND.REC.1405.020

Health conditions studied

1

Description of health condition studied

Mixed anxiety and depressive disorder

ICD-10 code

F41.2

ICD-10 code description

Mixed anxiety and depressive disorder

Primary outcomes

1

Description

Anxiety

Timepoint

Baseline, Final Treatment Session (Session 20), Three Months Post-Treatment (Follow-up)

Method of measurement

Hamilton Anxiety Rating Scale (HAM-A)

Secondary outcomes

1

Description

Depression

Timepoint

Baseline, Final Treatment Session (Session 20), Three Months Post-Treatment (Follow-up)

Method of measurement

Hamilton Depression Rating Scale (HAM-D)

Intervention groups

1

Description

Intervention group 1: In the bilateral stimulation protocol, the right dorsolateral prefrontal cortex (area F4) will be stimulated first at a frequency of 1 Hz. Each session will consist of 4 trains, each lasting 360 seconds, delivering a total of 1,440 pulses. Immediately thereafter, stimulation will be applied to the left dorsolateral prefrontal cortex (area F3) at a frequency of 10 Hz, such that each session comprises 75 trains of 5 seconds each, resulting in 3,750 pulses per session. The stimulation intensity for both hemispheres will be set at 120% of the resting motor threshold (rMT). All participants will receive repetitive transcranial magnetic stimulation (rTMS) sessions three times per week.

Category

Treatment - Devices

2

Description

Intervention group 2: In the right unilateral stimulation group, all stimulation parameters applied to the right dorsolateral prefrontal cortex (DLPFC) will be identical to those used in the bilateral protocol (targeting region F4), except that the number of stimulation trains per session will be increased to five, resulting in the delivery of 1,800 pulses per session. All participants will receive repetitive transcranial magnetic stimulation (rTMS) sessions three times per week.

Category

Treatment - Devices

3

Description

Control group: Sham repetitive transcranial magnetic stimulation (sham rTMS) will be administered to the same target regions (F3 and F4) using a placebo (sham) coil. This coil is fully matched to the active coil with respect to visual appearance, acoustic characteristics, and somatosensory perceptual features (e.g., a mild percussive sensation on the scalp). Critically, it lacks the capacity to generate focused magnetic field pulses and thus does not produce any neuromodulatory effect.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Farhikhtegan Hospital

Full name of responsible person

Mohamma-Mahdi Shariat-Bagheri

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Daneshgah Square, The terminus of the Shahid Sattari Expressway (northern segment)

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Sponsors / Funding sources

1

Sponsor

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Grant name

Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
University of Birjand
Proportion provided by this source
100
Public or private sector
Public
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Academic

Person responsible for general inquiries

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
No - There is not a plan to make this available
Justification/reason for indecision/not sharing IPD
he participant data file is confidential and only general information will be entered in the article.
Study Protocol
No - There is not a plan to make this available
Statistical Analysis Plan
No - There is not a plan to make this available
Informed Consent Form
No - There is not a plan to make this available
Clinical Study Report
No - There is not a plan to make this available
Analytic Code
No - There is not a plan to make this available
Data Dictionary
No - There is not a plan to make this available