Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Nov 2026

The Effect of Trans-cranial Direct Current Stimulation and Cognitive Rehabilitation on Cognitive Functions and Neuronal plasticity in Patients with Multiple Sclerosis: A Randomized Controlled Trial

Protocol summary

Study aim

The aim is to evaluate the effect of transcranial direct current stimulation (tDCS) alone and combined with cognitive rehabilitation on attention, memory, and neuroplasticity markers including brain derived neurotrophic factor (BDNF) and diffusion tensor imaging (DTI) in multiple sclerosis patients.

Design

Interventional randomized controlled trial with block randomization, parallel design, double blind, sham controlled, phase not applicable, on 45 patients. Random sequence generated by statistical software and allocation concealment maintained using sealed opaque envelopes.

Settings and conduct

The study will be conducted at a multiple sclerosis center in tehran loghman hospital. After baseline assessment, patients will be randomly assigned to three groups. tDCS sessions will be delivered using preprogrammed devices. Patients, caregivers, and outcome assessors are blinded. Blood sampling for BDNF measurement and DTI imaging will be performed before and after the intervention.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Age 18 to 50 years, diagnosis of relapsing remitting multiple sclerosis, EDSS less than five, presence of cognitive impairment based on neuropsychological tests, willingness and informed consent. Exclusion criteria: History of seizure, psychiatric disorder requiring antipsychotics, pregnancy, left handedness, recent relapse requiring steroids, history of brain surgery or intracranial metallic clip, unwillingness or inability to complete sessions.

Intervention groups

Group 1: Transcranial direct current stimulation (tDCS). Group 2: Transcranial direct current stimulation combined with cognitive rehabilitation. Group 3: Sham stimulation (inactive stimulation without effective current).

Main outcome variables

Improvement of attention; improvement of verbal and spatial memory; improvement of inhibitory control; change in BDNF level; change in DTI indices.

General information

Reason for update

Acronym

MS-NEURO

IRCT registration information

IRCT registration number: **IRCT20220803055606N3**
Registration date: **2025-09-20, 1404/06/29**
Registration timing: **prospective**

Last update: **2025-09-20, 1404/06/29**
Update count: **0**

Registration date

2025-09-20, 1404/06/29

Registrant information

Name

alireza moradi

Name of organization / entity

Country

Iran (Islamic Republic of)

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Email address

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2025-09-23, 1404/07/01

Expected recruitment end date

2026-04-20, 1405/01/31

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

The Effect of Trans-cranial Direct Current Stimulation and Cognitive Rehabilitation on Cognitive Functions and Neuronal plasticity in Patients with Multiple Sclerosis: A Randomized Controlled Trial

Public title

Comparison of Transcranial Direct Current Stimulation (tDCS) Alone and Combined with Cognitive Rehabilitation on Improving Attention, Memory, and Inhibitory Control in Patients with Multiple Sclerosis

Purpose

Supportive

Inclusion/Exclusion criteria

Inclusion criteria:

Diagnosis of relapsing remitting multiple sclerosis (RRMS) by a neurologist Age between 18 and 50 years Mild disability with EDSS less than 5 Presence of cognitive impairment based on neurocognitive tests (more than 2 SD below the mean in attention or inhibitory control) Willingness and informed consent to participate in the study

Exclusion criteria:

Presence of psychiatric disorder requiring antipsychotic treatment History of seizure or epilepsy Left handed individuals Recent MS relapse in the past month requiring steroid therapy Pregnancy History of brain surgery or intracranial metallic clip Unwillingness or inability to complete intervention sessions

Age

From **18 years** old to **50 years** old

Gender

Both

Phase

N/A

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

Sample size

Target sample size: **45**

Randomization (investigator's opinion)

Randomized

Randomization description

Randomization will be performed using permuted block randomization. The unit of randomization is individual. Block sizes will be randomly varied and patients will be allocated to three groups (tDCS, tDCS+Rehacom, Sham). The random sequence will be generated using statistical software. Allocation concealment will be ensured using opaque sealed envelopes that are opened only at the time of patient enrollment. The referring neurologist, the patient, and the cognitive assessor will all be blinded to the group assignments.

Blinding (investigator's opinion)

Double blinded

Blinding description

In this study, patients are blinded to their allocation to the active or sham stimulation groups (participant blinding). The clinicians and staff responsible for administering tDCS sessions are blinded by using preprogrammed devices with random codes that conceal whether the stimulation is active or sham (care provider blinding). The principal investigator remains unaware of patient allocation throughout the data collection process due to the use of coded randomization and sealed opaque envelopes (investigator blinding). Outcome assessors who conduct neurocognitive tests and questionnaires are blinded to patient group assignment (outcome assessor blinding). Data analysts receive coded datasets and perform statistical analyses without knowledge of group allocation (data analyst blinding). No independent Data Safety and Monitoring Committee (DSMC) has been established for this study.

Placebo

Used

Assignment

Parallel

Other design features

This study is a randomized, double-blind, parallel-group clinical trial. Patients with multiple sclerosis will be randomly assigned to three groups (transcranial direct current stimulation, transcranial direct current stimulation combined with cognitive rehabilitation, and sham). The unique feature of this trial is the simultaneous use of a non-pharmacological intervention (tDCS) combined with cognitive rehabilitation, along with the assessment of neuroplasticity biomarkers (BDNF and DTI).

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics Committee of Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran

Street address

Next to Ayatollah Taleghani Hospital, Shahid Arabi St, Yemen St, Shahid Chamran Highway

City

Tehran

Province

Tehran

Postal code

1333635445

Approval date

2024-01-02, 1402/10/12

Ethics committee reference number
IR.SBMU.PHNS.REC.1402.121

Health conditions studied

1

Description of health condition studied
Multiple Sclerosis
ICD-10 code
G35
ICD-10 code description
Multiple sclerosis

Primary outcomes

1

Description
Change in attention score on the Integrated Visual and Auditory Continuous Performance Test in patients with multiple sclerosis
Timepoint
At baseline before starting the intervention; and immediately after completion of ten intervention sessions over two weeks
Method of measurement
Administration of the Integrated Visual and Auditory Continuous Performance Test using the standard computerized procedure, recording attention scores according to the official test manual

Secondary outcomes

1

Description
Change in serum level of brain derived neurotrophic factor in patients with multiple sclerosis
Timepoint
At baseline before starting the intervention; and immediately after completion of ten intervention sessions over two weeks
Method of measurement
Measurement of serum brain derived neurotrophic factor level using enzyme linked immunosorbent assay according to the manufacturer’s instructions

Intervention groups

1

Description
First intervention group: Patients will undergo ten sessions of transcranial direct current stimulation (tDCS). Each session lasts 30 minutes over two weeks (five sessions per week). The anodal electrode is placed over the left dorsolateral prefrontal cortex (F3 according to the 10-20 system) and the cathodal electrode over the right shoulder. Stimulation intensity is 2 mA.
Category
Treatment - Devices

2

Description
Second intervention group: Intervention group 2: Patients will receive ten sessions of transcranial direct current stimulation (tDCS) as in group 1, combined with cognitive rehabilitation using Rehacom software. Training modules focus on attention, memory, and inhibitory control during the same two-week period.
Category
Treatment - Devices

3

Description
Control group: Control group: Patients will undergo ten sessions of sham transcranial direct current stimulation. Electrodes are placed in the same positions as in the intervention groups, but the current is delivered only for the initial 30 seconds and then switched off, producing no physiological effect.
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Loghman Hakim Educational Hospital
Full name of responsible person
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https://lhmc.sbmu.ac.ir/index.jsp?pageid=18901&p=1

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Shahid Beheshti University of Medical Sciences
Full name of responsible person
Dr. Afshin Zarghi
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Next to Ayatollah Taleghani Hospital, Shahid Arabi St,

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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
Shahid Beheshti University of Medical Sciences
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

Contact
Name of organization / entity
Shahid Beheshti University of Medical Sciences
Full name of responsible person
Dr. Mehrdad Roozbeh
Position
physician
Latest degree
Specialist
Other areas of specialty/work
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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
Due to ethical considerations, patient confidentiality, and restrictions related to privacy protection, individual participant data will not be shared. No further information is available.
Study Protocol
Yes - There is a plan to make this available
Statistical Analysis Plan

Yes - There is a plan to make this available

Informed Consent Form

Yes - There is a plan to make this available

Clinical Study Report

Yes - There is 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

Title and more details about the data/document

The full study protocol, statistical analysis plan, informed consent form, and final clinical study report will be available.

When the data will become available and for how long

Access will start six months after publication of the main results and will remain available for at least five years.

To whom data/document is available

The documents will be available to academic researchers and recognized research institutions

Under which criteria data/document could be used

Use is permitted only for scientific and research purposes. Any commercial use or re-identification of patients is prohibited.

From where data/document is obtainable

Requests should be addressed to the principal investigator, Dr. Mehrdad Roozbeh, Shahid Beheshti University of Medical Sciences, Tehran. Email: mehrdadroozbeh@gmail.com

What processes are involved for a request to access data/document

Written requests will be reviewed, and upon approval by the research committee, the documents will be provided within two months.

Comments

No individual participant data will be shared.