Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Effects of Combined Exercise Training on Functional Brain Alterations During the Menopausal Transition: A Randomized Controlled Trial based on the Critical Window Hypothesis

Protocol summary

Study aim

To examine the effects of combined training on brain (fALFF, functional connectivity), cognitive (working memory, executive function, cognitive flexibility), vasomotor/quality-of-life, and functional indices in premenopausal and menopausal women, and to compare the two groups' responsiveness based on the critical window hypothesis.

Design

A randomized trial with 60 participants; blinding of participants and trainers is not possible, but outcome assessors and data analysts are blinded; 16-week combined training intervention; assessments at pre-test and post-test.

Settings and conduct

16 weeks of combined training (aerobic + resistance), 3 days per week, at Shahid Beheshti University gym; outcome assessors and data analysts are blind to the participants' group allocation.

Participants/Inclusion and exclusion criteria

Inclusion: Premenopausal or menopausal women with an intact uterus; PAR-Q+ clearance for physical activity; no severe chronic or neurological disease; no hormonal medication, specific supplements, or regular exercise in the past six months. Exclusion: Neurodegenerative disease; cognitive impairment; high cardiac risk during exercise; mobility-limiting disease; any hormone therapy; PCOS; chemotherapy; premature ovarian failure; claustrophobia; orthopedic devices or metal implants.

Intervention groups

Combined training group (16 weeks of aerobic + resistance training), control group (16 weeks of continuing usual lifestyle without physical activity)

Main outcome variables

Brain imaging indices (fractional amplitude of low-frequency fluctuations and functional connectivity), cognitive function (working memory, executive function, cognitive flexibility), vasomotor symptom interference with daily life and quality of life, and functional indices (maximal oxygen consumption, body composition, maximal voluntary contraction, rate of force development, fatigue index, grip strength).

General information

Reason for update

Acronym

women brain study

IRCT registration information

IRCT registration number: **IRCT20261010071367N1**
Registration date: **2026-11-02, 1405/08/11**
Registration timing: **registered_while_recruiting**

Last update: **2026-11-02, 1405/08/11**
Update count: **0**

Registration date

2026-11-02, 1405/08/11

Registrant information

Name

Elina Kiani Shahvandi

Name of organization / entity

Shahid Beheshti University

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Recruitment status

recruiting

Funding source

Expected recruitment start date

2026-10-23, 1405/08/01

Expected recruitment end date
2026-11-11, 1405/08/20
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Effects of Combined Exercise Training on Functional Brain Alterations During the Menopausal Transition: A Randomized Controlled Trial based on the Critical Window Hypothesis

Public title
Effect of Exercise Training on Brain Changes During the Menopausal Transition
Purpose
Health service research
Inclusion/Exclusion criteria
Inclusion criteria:
Women aged 45 to 55 years. Being in perimenopause or menopause according to the STRAW+10 system. Having an intact and healthy uterus. Being in good health for physical activity based on PAR-Q+. No severe chronic or neurological diseases. No use of hormonal medications or specific supplements in the last 6 months. No regular exercise training in the past 6 months. Written informed consent to participate in the study.
Exclusion criteria:
Diagnosis of neurodegenerative disease, cognitive impairment, or dementia. High risk of cardiac complications during exercise. Significant clinical neuropathy or severe musculoskeletal or joint disease that impairs mobility. Any hormone therapy (estrogen, androgen, or progesterone). Undergoing hysterectomy or endometrial ablation. Polycystic ovary syndrome (PCOS). Undergoing chemotherapy or having received chemotherapy in the past year. Premature ovarian failure. Absence from more than 15% of training sessions. Cardiac pacemaker, cardiac wires, or defibrillator. Presence of metal in the eye or orbital cavity. Steel clips for cerebral aneurysm. Intrauterine device made of stainless steel. Any surgery or tattooing (including cosmetic tattoos) within the past six weeks. History of radiotherapy or exposure to other high doses of radiation. Recurrent metastasis. Claustrophobia (fear of enclosed spaces). Artificial heart valve, ear implant. Implantable drug infusion pump. Nerve or bone electrical stimulator. Coil, catheter, or filter in any blood vessel. Orthopedic equipment (artificial joint, plate, screw, rod) or other metal parts in the body.
Age
From **45 years** old to **55 years** old
Gender
Female

Phase
N/A
Groups that have been masked
No information
Sample size
Target sample size: **60**
Randomization (investigator's opinion)
Randomized
Randomization description
After confirming the inclusion criteria and obtaining written informed consent, participants are stratified into two strata—perimenopause and menopause—based on the STRAW+10 system. Subsequently, within each stratum, random allocation to either the combined exercise training group or the control group is performed at a 1:1 ratio. The randomization sequence is generated using Random Allocation software (version 1.0) with a block randomization method employing variable block sizes (4 and 6). Block sizes are selected randomly and unpredictably to prevent selection bias. To ensure allocation concealment, the randomization sequence is placed in opaque, sealed, and sequentially numbered envelopes. These envelopes are prepared by an individual independent of the research (who has no role in the enrollment and assessment of participants) and are opened only after complete enrollment of the participant, verification of eligibility, and signing of the consent form. Consequently, the enroller remains unaware of the upcoming allocation, thereby eliminating the possibility of selection bias. The randomization sequence is generated by an independent researcher who has no role in the enrollment and assessment of participants, and is placed in the numbered envelopes. Enrollment of participants is conducted by another researcher who is unaware of the contents of the envelopes. Final allocation to the groups is performed by the same independent researcher by opening the corresponding envelope after complete enrollment.
Blinding (investigator's opinion)
Not blinded
Blinding description
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Biological Research Ethics Committee of Shahid Beheshti University
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Shahid Shahriari Square, Evin
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Approval date
2026-09-26, 1405/07/04
Ethics committee reference number
IR.SBU.REC.1405.179

Health conditions studied

1

Description of health condition studied
perimenopause: menopause
ICD-10 code
N95
ICD-10 code description
Menopausal and other perimenopausal disorders

Primary outcomes

1

Description
Functional brain changes measured by fALFF and FC indices.
Timepoint
Pre-test (pre-intervention) and post-test (at the end of week 16 after intervention start).
Method of measurement
Functional Magnetic Resonance Imaging

Secondary outcomes

1

Description
Cognitive performance (working memory, executive function, response inhibition, and processing speed)
Timepoint
Pre-test (before the start of the intervention) and post-test (at the end of the sixteenth week following the start of the intervention)
Method of measurement
Working memory: N-back test; executive function and response inhibition: Stroop test and processing speed; working memory: Digit Symbol subtest of the Wechsler Adult Intelligence Scale.

2

Description
Vasomotor Symptoms
Timepoint
Pre-test (before the start of the intervention) and post-test (at the end of the sixteenth week following the start of the intervention)
Method of measurement
Hot Flash-Related Daily Interference Scale and Menopause Rating Scale

3

Description
Physiological indicators (maximal oxygen consumption; body composition)
Timepoint
Pre-test (before the start of the intervention) and post-test (at the end of the sixteenth week following the start of the intervention)
Method of measurement
Maximal oxygen consumption will be measured using a maximal exercise test on a cycle ergometer via indirect spirometry; body composition will be assessed using an InBody body composition analyzer via the bioelectrical impedance analysis method.

4

Description
Force production-related indices (maximal voluntary contraction; rate of force development; fatigue index; grip strength)
Timepoint
Pre-test (before the start of the intervention) and post-test (at the end of the sixteenth week following the start of the intervention)
Method of measurement
Force-related parameters will be measured using a hand-grip dynamometer.

Intervention groups

1

Description
The intervention group participates in a 16-week combined exercise program, three sessions per week (48 sessions in total, with at least 48 hours between sessions). Each session lasts 80 to 90 minutes, including 10 to 15 minutes of warm-up, 60 to 70 minutes of main exercise, and 10 minutes of cool-down. High-intensity interval training is performed on a cycle ergometer, progressively consisting of 6 to 12 bouts of 30 to 75 seconds at high intensity interspersed with 30 to 60 seconds of active recovery. Resistance training is performed as full-body training using gym machines, free weights, and body weight, with three separate weekly session routines and progressive intensity (RPE 7 to 10). The first two weeks are dedicated to familiarization and low-intensity continuous exercise. All sessions are supervised by trainers with heart rate monitoring. Equipment includes a cycle ergometer, resistance machines, free weights.
Category
Lifestyle

2

Description
The control group receives no exercise intervention during the 16 weeks and is instructed to maintain usual lifestyle and avoid major changes in physical activity, diet, and supplement use. This group undergoes the same pre-test and post-test assessments as the training group.
Category

Lifestyle

Recruitment centers

1

Recruitment center

Name of recruitment center
Shahid Beheshti University

Full name of responsible person
Elina Kiani Shahvandi

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2

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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
Shahid Beheshti University

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
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Full name of responsible person
Elina Kiani Shahvandi

Position
PhD Candidate

Latest degree
Master

Other areas of specialty/work
Exercise Physiology

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Yes - There is a plan to make this 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

Yes - There is a plan to make this available

Data Dictionary

Yes - There is a plan to make this available

Title and more details about the data/document

De-identified individual participant data including all demographic, imaging, cognitive, functional, and questionnaire variables, along with the protocol and statistical analysis plan. Available from six months after publication of primary results for five years to qualified researchers.

When the data will become available and for how long

Access begins 6 months after publication of primary results and remains available for 5 years.

To whom data/document is available

Only researchers affiliated with accredited academic and scientific institutions, upon submission of a research proposal and signing a data sharing agreement; industry access is not permitted.

Under which criteria data/document could be used

For meta-analysis, reproduction of results, and secondary analyses related to midlife women's brain health; upon submission of a research proposal, signing a no-re-identification agreement, prohibition of commercial use, source citation, and ethics approval.

From where data/document is obtainable

To request data, applicants should contact the corresponding author, via email.

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

Applicant submits request to the corresponding author's email; after review by the research team and ethics committee approval, the agreement is signed and data are transferred within 2–4 weeks.

Comments