Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Nov 2026

Effects of Resistance, Aerobic, and Combination Training on serotonin and dopamine pathway and some Inflammatory Markers in Women with Multiple Sclerosis

Protocol summary

Study aim

Due to the limited number of studies on the effect of sports activity on the immune system of people with MS, our study is necessary to investigate the impact of aerobic, resistance, and combined exercises on the immune system of women with MS

Design

Patients enter the project randomly (Guilan MS Association) after having the criteria for entering the test and signing the consent form. The subjects will be divided into three groups: aerobic, resistance training, and a control group. A laboratory staff member will go to each person's house for fasting blood sampling.

Settings and conduct

The exercise sessions will be conducted at the patient's home, three days a week.

Participants/Inclusion and exclusion criteria

Entry requirements: Having Multiple Sclerosis 0-5/5 EDSS Age range 20 to 50 years Having Depressive Disorder 0-5/5 (DEPI) At least two months have passed since the last recurrence of the disease Exit conditions: Any heart-respiratory problem Persistent dizziness The unwillingness of the person to continue

Intervention groups

Intervention group: Intervention Groups: Aerobic Exercises Group: Participants in this group will perform aerobic exercises 2 to 3 days per week, starting with 2 days per week and gradually increasing to 3 days per week over time.Combined Exercises Group: This group will engage in aerobic and resistance exercises. The training conditions will be similar to those in the aerobic and resistance training groups. The exercises will alternate weekly between aerobic and combined routines. Aerobic exercises will be performed twice a week. Resistance Exercises Group: Participants will perform resistance exercises 3 days per week, with the intervention tailored to the individual's abilities.Control Group: This group will not receive any intervention.

Main outcome variables

serotonin, dopamine IL-17,IFN-γ,Foxp3 quality of life ,depression

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20220603055067N5**
Registration date: **2026-08-21, 1405/05/30**
Registration timing: **prospective**

Last update: **2026-08-21, 1405/05/30**
Update count: **0**

Registration date

2026-08-21, 1405/05/30

Registrant information

Name

Payam Saidie

Name of organization / entity

University of Guilan

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Iran (Islamic Republic of)

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Recruitment status

recruiting

Funding source

Expected recruitment start date

2026-08-29, 1405/06/07

Expected recruitment end date

2026-11-29, 1405/09/08

Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Effects of Resistance, Aerobic, and Combination Training on serotonin and dopamine pathway and some Inflammatory Markers in Women with Multiple Sclerosis

Public title
The Impact of Exercise on Multiple Sclerosis (MS)
Purpose
Supportive
Inclusion/Exclusion criteria
Inclusion criteria:
Having a depressive disorder Age range between 25 and 50 years having anxiety EDSS between 0.5 - 5.0 Absence of diseases such as: fatty liver, thyroid, kidney disease, cardiovascular disease Having at least 2 months gap from exercising No smoking No alcohol consumption Having a relapsing-remitting disease
Exclusion criteria:
Use of antidepressant, anti-anxiety, or other psychiatric medications Acute infection or use of anti-inflammatory / immunomodulatory drugs at study entry Musculoskeletal, orthopedic, or cardiopulmonary conditions preventing safe participation in the exercise program
Age
From **25 years** old to **50 years** old
Gender
Female

Phase
N/A
Groups that have been masked

- Outcome assessor
- Data analyser

Sample size
Target sample size: **52**
Randomization (investigator's opinion)
Randomized
Randomization description
In this study, we randomly allocated 40 women with relapsing-remitting MS to four groups (resistance, aerobic, combined exercise, and control) at the individual level, with 10 participants per group. We used simple randomization with no stratification. Each participant was assigned a number from 1 to 40; we drew the numbers by lottery and allocated them in sequence to the four groups until each group had 10 participants. Allocation concealment was ensured by having a person not involved in recruitment or outcome assessment perform the draw, and group assignments were kept concealed until after baseline measurements.
Blinding (investigator's opinion)
Double blinded
Blinding description
Because of the nature of the exercise intervention, participants and the trainers who delivered the sessions could not be blinded to group allocation; each participant necessarily knew which type of training (aerobic, resistance, combined, or control) she received. Blinding was therefore applied to outcome assessment and data analysis. Blood samples for biomarker measurement (serotonin, dopamine, IL-17, IFN-γ, FoxP3) were labeled with codes only, so the laboratory personnel measuring the outcomes were unaware of each participant's group. The statistician analyzed the data using coded group labels (A, B, C, D) and was unblinded only after the analysis was complete. On this basis the study is single-blind (outcome assessor– and analyst–blinded).
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Ethics Committee in Biomedical Research
Street address
5th Kilometer of Persian Gulf Highway
City
Rasht
Province
Guilan
Postal code
۴۱۹۹۶۱۳۷۷۶
Approval date
2023-12-27, 1402/10/06
Ethics committee reference number
IR.GUILAN.REC.1402.069

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
Serotonin, also known as 5-hydroxytryptamine (5-HT), is a neurotransmitter that plays a crucial role in regulating various physiological and psychological functions.

Timepoint

1 time before 8 weeks of training and 1 time after 8 weeks of training

Method of measurement

Serotonin/5-Hydroxytryptamine ELISA Kit

2

Description

Dopamine is a neurotransmitter and hormone that plays several critical roles in the brain and body. It belongs to the catecholamine and phenethylamine families and is a key chemical messenger involved in many important processes.

Timepoint

1 time before 8 weeks of training and 1 time after 8 weeks of training

Method of measurement

Dopamine ELISA Kit

3

Description

Interleukin-17 (IL-17) is a pro-inflammatory cytokine that plays a crucial role in the immune system, particularly in host defense and inflammatory responses. Here's a detailed overview of IL-17:Biological FunctionsImmune Response: IL-17 is primarily produced by a subset of T helper cells known as Th17 cells, but it can also be produced by other immune cells such as γδ T cells, natural killer (NK) cells, and innate lymphoid cells (ILCs). It is involved in the defense against bacterial and fungal infections by promoting the recruitment of neutrophils and macrophages to infection sites.Inflammation: IL-17 is a key mediator of inflammation. It stimulates the production of other pro-inflammatory cytokines, such as IL-6 and tumor necrosis factor-alpha (TNF-α), and promotes the release of chemokines that attract immune cells to sites of inflammation.Autoimmune Diseases: IL-17 plays a significant role in the pathogenesis of several autoimmune diseases, including psoriasis, rheumatoid arthritis, and multiple sclerosis. In these conditions, IL-17 contributes to chronic inflammation and tissue damage.

Timepoint

1 time before 8 weeks of training and 1 time after 8 weeks of training

Method of measurement

Human IL-17 Quantikine ELISA Kit (D1700)

4

Description

Interferon-gamma (IFN-γ) is a cytokine that plays a pivotal role in the immune system, particularly in the regulation of immune responses and inflammation. Here's a comprehensive overview of IFN-γ:Biological FunctionsImmune Activation: IFN-γ is a key activator of macrophages, enhancing their ability to phagocytose pathogens and present antigens. It also promotes the differentiation of T helper 1 (Th1) cells, which are essential for cell-mediated immunity.Antiviral and Antimicrobial Activity: IFN-γ has strong antiviral properties and is involved in the immune response against intracellular pathogens such as viruses, bacteria, and protozoa. It inhibits viral replication directly and activates immune cells to attack infected cells.Regulation of Adaptive Immunity: IFN-γ influences the adaptive immune response by promoting the differentiation of cytotoxic T cells (CD8+ T cells) and enhancing their ability to kill infected or cancerous cells. It also stimulates the production of antibodies by B cells.Inflammation and Autoimmunity: While IFN-γ is crucial for protective immunity, its dysregulation can contribute to chronic inflammation and autoimmune diseases. It is involved in the pathogenesis of conditions such as rheumatoid arthritis, multiple sclerosis, and inflammatory bowel disease.

Timepoint

1 time before 8 weeks of training and 1 time after 8 weeks of training

Method of measurement

Human IFN-gamma DuoSet ELISA DY285B-05

5

Description

FOXP3 (Forkhead Box P3) is a transcription factor that is critical for the development and function of regulatory T cells (Tregs), which are essential for maintaining immune tolerance and preventing autoimmune diseases. Here’s a detailed overview of FOXP3:Biological FunctionsRegulatory T Cells (Tregs): FOXP3 is a master regulator of Tregs, a subset of T cells that suppress immune responses to maintain homeostasis and prevent excessive inflammation. Tregs play a crucial role in:Immune Tolerance: Preventing autoimmunity by suppressing autoreactive T cells that could attack the body's own tissues.Immune Response Regulation: Controlling the intensity and duration of immune responses to prevent damage to the host from chronic inflammation or overactive immune responses.Gene Expression: FOXP3 controls the expression of various genes that are essential for Treg function. These include genes involved in Treg development, stability, and suppressive functions.Suppressive Mechanisms: FOXP3+ Tregs employ multiple mechanisms to suppress immune responses, including:Secretion of Anti-inflammatory Cytokines: Such as IL-10 and TGF-β.Cytolysis: Directly killing effector T cells.Metabolic Disruption: Modifying the local environment to inhibit effector T cell function.Inhibition of Dendritic Cells: Preventing the activation of other T cells by dendritic cells

Timepoint

1 time before 8 weeks of training and 1 time after 8 weeks of training

Method of measurement

Human Forkhead Box P3, FOXP3 ELISA Kit E0692Hu

6

Description

Depression is a prevalent and serious concern in individuals with multiple sclerosis (MS), affecting up to 50% of people with the condition at some point. This high prevalence highlights the need for careful monitoring

and management of depressive symptoms in MS patients

Timepoint

1 time before 8 weeks of training and 1 time after 8 weeks of training

Method of measurement

The Beck Depression Inventory is a 21-item

7

Description

Quality of life (QoL) in individuals with multiple sclerosis (MS) is influenced by a variety of factors, including physical, psychological, social, and environmental aspects. MS is a chronic and often disabling disease that can lead to significant impairments and challenges in daily life.

Timepoint

1 time before 8 weeks of training and 1 time after 8 weeks of training

Method of measurement

The multiple sclerosis impact scale (MSIS-29)

Secondary outcomes

empty

Intervention groups

1

Description

Intervention Group 1 (Aerobic Training):Participants in this group performed a supervised aerobic exercise program for 8 weeks, 2 to 3 sessions per week (starting at 2 sessions/week and gradually increasing to 3 sessions/week). Each session consisted of a 5-minute warm-up (light walking or cycling combined with dynamic stretching), 10 to 30 minutes of main aerobic exercise at 40–60% of peak heart rate, and a 5-minute cool-down (gradual reduction of activity intensity along with static stretching of the muscles used).

Category

Rehabilitation

2

Description

Intervention Group 2 (Resistance Training):Participants in this group performed a supervised resistance training program for 8 weeks, 3 sessions per week. Each session consisted of a 5-minute general warm-up (light aerobic activity combined with dynamic stretching to prepare the joints and muscles), 10 to 30 minutes of main resistance exercise (including weighted or resistance-based movements targeting major muscle groups), and a 5-minute cool-down (static stretching of the worked muscles).Intervention group:

Category

Rehabilitation

3

Description

Intervention Group 3 (Combined Training):Participants in this group performed a combination of aerobic and resistance exercises for 8 weeks, 2 to 3 sessions per week. The two types of training alternated on a weekly basis, and their intensity and volume were similar to those of the aerobic and resistance groups. Regardless of the type of training scheduled for that week, each session began with a 5-minute warm-up (light aerobic activity and dynamic stretching) and ended with a 5-minute cool-down (gradual reduction of intensity and static stretching).

Category

Rehabilitation

4

Description

Control group: Participants in this group did not receive any exercise intervention during the 8-week study period and continued their usual daily activities.

Category

N/A

Recruitment centers

1

Recruitment center

Name of recruitment center

Guilan Multiple Sclerosis Association

Full name of responsible person

Alia saberi

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

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Full name of responsible person

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Web page address
https://guilan.ac.ir/
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
No
Title of funding source
University of guilan
Proportion provided by this source
1
Public or private sector
Private
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Persons

Person responsible for general inquiries

Contact
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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
These data are confidential, and only researchers will have access to them
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