Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

The effect of compassion-focused therapy on functional connectivity of brain networks and psychological symptoms in individuals with major depressive disorder

Protocol summary

Study aim
Effect of Compassion-Focused Therapy on Brain Connectivity and Psychological Symptoms in Major Depressive Disorder

Design
This study is a randomized controlled clinical trial conducted with 40 individuals diagnosed with major depressive disorder. After screening, participants are randomly assigned to two groups: experimental group (20 individuals) and control group (20 individuals

Settings and conduct
After obtaining the ethics code from the Ethics Committee of Shahid Beheshti University of Medical Sciences, 40 patients with major depressive disorder based on DSM-5-TR criteria will be referred by a collaborating psychiatrist. Then, initial assessments will be conducted by the researcher to check compliance with inclusion and exclusion criteria. Patients will then be randomly assigned to two groups: experimental and control.

Participants/Inclusion and exclusion criteria
Participants: 40 patients. Inclusion: Age 18-50 years, PHQ-9 score (10-27), informed consent, medication stability, no claustrophobia, no pregnancy or metal in body Exclusion: Absence from more than two sessions, withdrawal, or active suicidal ideation.

Intervention groups
The experimental group receives Compassion-Focused Therapy (CFT) based on Gilbert's standard protocol in 12 weekly 90-minute sessions. The control group receives pharmacotherapy during this period.

Main outcome variables
Change in functional connectivity of brain networks (DMN, SAN, CEN) measured by resting-state fMRI; Reduction in the severity of depressive symptoms based on the Patient Health Questionnaire-9 (PHQ-9) score; Reduction in depression severity based on the Hamilton Rating Scale for Depression score.

General information

Reason for update

Acronym
CFT

IRCT registration information
IRCT registration number: **IRCT20260607069694N1**
Registration date: **2026-07-02, 1405/04/11**
Registration timing: **prospective**

Last update: **2026-07-02, 1405/04/11**
Update count: **0**

Registration date
2026-07-02, 1405/04/11

Registrant information

Name
Ghazaleh آذر

Name of organization / entity

Country
Iran (Islamic Republic of)

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+98 21 2661 4755

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Recruitment status
recruiting

Funding source

Expected recruitment start date
2026-10-22, 1405/07/30

Expected recruitment end date
2027-03-21, 1406/01/01

Actual recruitment start date
empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

The effect of compassion-focused therapy on functional connectivity of brain networks and psychological symptoms in individuals with major depressive disorder

Public title

The effect of compassion-focused therapy on functional connectivity of brain networks and psychological symptoms in individuals with major depressive disorder

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Diagnosis of Major Depressive Disorder (MDD) based on a structured clinical interview conducted by a psychiatrist and a clinical psychologist Age between 18 and 50 years. A score between 10 and 27 on the Patient Health Questionnaire (PHQ-9) Ability to understand and complete the questionnaires (minimum educational level: middle school/junior high school) Provision of written informed consent for participation in the study and undergoing fMRI scanning Stable medication regimen during Compassion-Focused Therapy (CFT) No severe claustrophobia that would interfere with undergoing fMRI scanning Ability to remain motionless in the scanner for approximately 30 minutes No significant physical health problems or medical conditions, including pregnancy, that would contraindicate fMRI scanning. No diagnosis of bipolar disorder, psychotic disorders, or severe neurological disorders. No active use of illicit drugs or alcohol. No history of traumatic brain injury, epilepsy, or neurological diseases affecting brain function.

Exclusion criteria:

Active suicidal ideation with plan and intent. Inability to undergo fMRI scanning after the intervention due to any medical or technical reason. Voluntary withdrawal from the study.

Age

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

Gender

Both

Phase

N/A

Groups that have been masked

No information

Sample size

Target sample size: **40**

Randomization (investigator's opinion)

Randomized

Randomization description

After eligibility confirmation, the randomization sequence will be generated by an independent individual using random number generation software. The sequence will be placed in opaque, identical, numbered envelopes and kept inaccessible to the principal investigator until allocation. Following the completion of baseline assessments, the principal investigator will open each patient's envelope sequentially and assign them to experimental or control groups based on the number inside. The outcome assessor will be blinded to group allocation.

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

Ethics Committee of Shahid Beheshti University of Medical Sciences

Street address

Arabi Street , Daneshjo Boulevard, Velenjak, Tehran, Iran

City

Tehran

Province

Tehran

Postal code

4631- 19395.

Approval date

2026-06-07, 1405/03/17

Ethics committee reference number

IR.SBMU.MSP.REC.1405.161

Health conditions studied

1

Description of health condition studied

Major Depressive Disorder (MDD)

ICD-10 code

ICD-10 code description

2

Description of health condition studied

Major Depressive Disorder (MDD)

ICD-10 code

ICD-10 code description

Primary outcomes

1

Description

Change in functional connectivity of brain networks (DMN, SAN, CEN)

Timepoint
Before the start of the intervention and after the completion of the intervention
Method of measurement
fMRI

2

Description
Reduction in the severity of depressive symptoms
Timepoint
Before the start of the intervention and after the completion of the intervention
Method of measurement
Patient Health Questionnaire-9 (PHQ-9). Hamilton Rating Scale for Depression (HAM-D)

Secondary outcomes

1

Description
Increase in self-compassion score
Timepoint
Before the intervention and after the completion of the intervention
Method of measurement
Self-Compassion Scale (Short Form)

2

Description
Reduction in rumination score
Timepoint
Before the intervention and after the completion of the intervention
Method of measurement
Ruminative Response Scale

3

Description
Reduction in external shame score
Timepoint
Before the intervention and after the completion of the intervention
Method of measurement
External Shame Scale

4

Description
Increase in quality of life score
Timepoint
Before the intervention and after the completion of the intervention
Method of measurement
World Health Organization Quality of Life Questionnaire (Brief Version)

5

Description
Reduction in depression, anxiety, and stress scores
Timepoint
Before the intervention and after the completion of the intervention
Method of measurement
Depression, Anxiety, and Stress Scale

Intervention groups

1

Description
Participants in the experimental group receive Compassion-Focused Therapy (CFT) based on Gilbert's standard protocol (2009). The intervention consists of 12 weekly sessions, each lasting 90 minutes (total duration: approximately 3 months). Sessions are conducted individually by a PhD student in clinical psychology under the supervision of the supervisor at Taleghani Hospital Psychology Clinic, Tehran.Sessions 1-4: Psychoeducation (evolutionary model of depression, "tricky brain," three-system model: threat, drive, soothing), mindfulness, and rhythmic breathing exercises.Sessions 5-8: Defining compassion (kindness, common humanity, mindfulness), identifying the "inner critic," developing the "compassionate self" through imagery exercises (safe place, compassionate self, compassionate others), and cognitive restructuring with a supportive tone.Sessions 9-10: Identifying shame triggers and self-critical patterns, exploring developmental roots (childhood experiences), addressing fear of compassion, and reducing avoidance behaviors (e.g., perfectionism).Sessions 11-12: Writing a compassionate letter to oneself, reviewing all learned skills, and developing a relapse prevention plan.
Category
Treatment - Other

2

Description
Control group: Participants in the control group receive standard pharmacotherapy under the supervision of a collaborating psychiatrist for approximately 3 months. Based on standard guidelines for major depressive disorder treatment, first-line medications from the SSRI class (Selective Serotonin Reuptake Inhibitors) are prescribed. The type of medication, dosage, and treatment duration are determined by the treating psychiatrist based on clinical judgment and with the aim of achieving medication stability throughout the study period.Common medication options include Sertraline (starting dose: 50 mg/day, titrated up to 200 mg/day if needed) or Escitalopram (starting dose: 10 mg/day, titrated up to 20 mg/day). Prescriptions follow the latest clinical guidelines (e.g., American Psychiatric Association guidelines).Patients are monitored by the psychiatrist for side effects and treatment response throughout the study. The control group does not receive any additional psychological intervention (such as CFT or other psychotherapies) during the study period.
Category

Treatment - Other

Recruitment centers

1

Recruitment center

Name of recruitment center
Taleghani Hospital

Full name of responsible person
Dr. Hassan Khazraei

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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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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
50

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. Hassan Khazraei

Position
Assistant Professor

Latest degree
Ph.D.

Other areas of specialty/work
Psychology

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Person responsible for updating data

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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
The data from this study include fMRI brain images and sensitive clinical information from patients with major depressive disorder. Due to the potentially traceable nature of neuroimaging data (even after removal of identifiable features) and ethical commitments to participant confidentiality, sharing de-identified individual participant data is not possible. Furthermore, the original proposal did not include a plan for IPD sharing, and the informed consent form does not cover this option.
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
Undecided - It is not yet known if there will be a plan to make this available
Analytic Code
Undecided - It is not yet known if there will be a plan to make this available
Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available
Title and more details about the data/document
Title: Statistical Analysis Plan of the Randomized Clinical Trial of CFT in Major Depression Details: Includes methods for analyzing questionnaire data (SPSS, MANCOVA tests, repeated measures) and methods for preprocessing and analyzing fMRI data (SPM software, CONN toolbox, resting-state functional connectivity analysis).
When the data will become available and for how long
6 months after study completion and primary results publication (estimated late 2027)
To whom data/document is available
All researchers, professors, students, and specialists in clinical psychology, neuroscience, and psychiatry affiliated with accredited academic, research, or medical institutions.
Under which criteria data/document could be used
The study protocol is available for scientific study and citation only. Commercial use or reproduction without source attribution is not permitted. Any use must include full citation of the source (published article or IRCT-registered protocol).
From where data/document is obtainable
Primary contact: Principal investigator – Ms. Ghazaleh Azar Email: ghazalehazar.8540@sbmu.ac.ir Secondary contact: Supervisor – Dr. Hassan Khazraei Email: hassankhazaraee@sbmu.ac.ir Tertiary contact: Taleghani Hospital, Psychology Clinic – Address: Arabi Street, Daneshjo Blvd., Velenjak, Tehran, Iran
What processes are involved for a request to access data/document
Applicant submits a written request along with a letter of introduction from their academic institution to the principal investigator's email. The request will be reviewed within a maximum of 2 business weeks. If approved, the protocol file will be sent to the applicant via email.
Comments