大同市妇幼保健院
Datong Maternal and Child Health Hospital

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Datong Maternal and Child Health Hospital
大同市儿童医院
大同市妇产医院
大同市第一人民医院

RESEARCH PROTOCOL

研究方案

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Ethics Approval No.	KY2025-012	**Approval Date**	15 August 2025
Research Site	Datong Maternal and Child Health Hospital, China	**Document Type**	Concise protocol for clearance

1. Particulars of Researcher

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Research expertise	Clinical research; inpatient safety oversight; music intervention; Traditional Chinese Medicine; depressive disorders; psychophysiological indicators

2. List of Co-researchers

The following list should be confirmed against the final author list and institutional clearance requirements before submission.

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3. Research Proposal

Title of Research Proposal

Adjunctive Resonance-Based Chinese Five-Element Music Intervention for Depressive Disorders and Anxiety Symptoms in Male Inpatients: A Randomized Controlled Trial

Ethics-approved project title: The Novel Five-Element Resonance Music Intervention for Emotional Disorders in Chinese Men: A TCM-Inspired Randomized Controlled Trial.

Keywords

depressive disorders; anxiety symptoms; Five-Element music; resonance-based music intervention; Traditional Chinese Medicine; randomized controlled trial

Background / Justification

Depressive disorders are common clinical conditions and may be accompanied by anxiety symptoms, chronic stress, altered autonomic regulation, sleep disturbance, somatic discomfort, and impaired social functioning. Pharmacotherapy remains central to clinical care, but delayed onset, adverse effects, residual symptoms, and incomplete remission remain common concerns.

Music-based interventions are non-invasive, low-burden, and generally acceptable to many patients. Existing systematic reviews and clinical studies suggest that music therapy or music-based interventions may reduce depressive and anxiety symptoms, particularly when used as adjunctive interventions rather than replacements for standard psychiatric treatment.

Chinese Five-Element music is rooted in Traditional Chinese Medicine (TCM) theory and provides a culturally meaningful framework for selecting musical materials according to syndrome differentiation. Resonance-Based Chinese Five-Element Music Intervention (RFEMI) combines Five-Element tone selection with resonance-informed acoustic delivery, immersive sound exposure, and gentle tactile vibration. This study evaluates RFEMI as an adjunct to standard pharmacotherapy in male inpatients with depressive disorders and anxiety symptoms.

Objectives / Outcomes

Primary objective: To evaluate whether RFEMI plus pharmacotherapy is associated with greater reduction in Hamilton Depression Rating Scale (HAM-D) scores than pharmacotherapy alone or conventional music plus pharmacotherapy after four weeks.

Secondary objectives: To examine changes in anxiety symptoms, self-reported depressive and anxiety scales, TCM syndrome scores, clinical response and remission, serum biomarkers, cerebral oxygenation, and heart rate variability (HRV) indicators.

Expected outcomes: RFEMI is expected to be feasible and acceptable in an inpatient setting and may provide additional short-term benefit when used as an adjunct to pharmacotherapy. Physiological findings will be interpreted as exploratory correlates rather than as proof of a specific resonance mechanism.

Methodology

Study design

This is a single-center, randomized, assessor-blinded, parallel-group exploratory controlled trial. Three parallel groups will be compared: (1) pharmacotherapy only, (2) conventional music plus pharmacotherapy, and (3) RFEMI plus pharmacotherapy. The intervention period is four weeks. Outcome assessors and data analysts will be blinded to group allocation where feasible. Participants and intervention staff cannot be blinded because the intervention conditions are perceptibly different.

Study setting

The study will be conducted in the inpatient psychiatric clinical setting of Datong Maternal and Child Health Hospital, China. Interventions will be delivered in a quiet clinical room or designated treatment space suitable for music listening and RFEMI delivery.

Participants

Participants will be male inpatients aged 18-44 years who meet the International Classification of Diseases, 11th Revision (ICD-11) criteria for depressive episode or recurrent depressive disorder and the TCM diagnostic criteria for Yu disease. Anxiety symptoms will be assessed as a symptom dimension rather than as a primary anxiety-only diagnosis.

Randomization and blinding

Eligible participants will be randomized to one of the three study groups using a predetermined randomization procedure. Allocation information will be kept by designated study personnel and will not be disclosed to outcome assessors where feasible. Because participants can perceive whether they receive pharmacotherapy alone, conventional music listening, or RFEMI, participant blinding is not feasible.

Intervention Protocol

Group 1: Pharmacotherapy only. Participants will receive standard antidepressant pharmacotherapy once daily for four weeks. Medication plans will be prescribed and monitored by qualified psychiatrists according to clinical symptoms, treatment response, and side-effect profile. Medication plans should remain clinically stable during the intervention period where possible.

Group 2: Conventional music plus pharmacotherapy. Participants will receive standard pharmacotherapy plus receptive music listening. Sessions will be conducted in a quiet, softly lit room. The music will be comfortable, slow, and stable in rhythm, and will be selected as general relaxing music rather than Five-Element music. Each session will last approximately 30 minutes, five times per week, for four weeks.

Group 3: RFEMI plus pharmacotherapy. Participants will receive standard pharmacotherapy plus RFEMI. RFEMI will be delivered using the GuYuan rehabilitation music-therapy playback system, including a digital playback controller, multi-speaker immersive sound delivery, and a treatment bed providing gentle tactile vibration synchronized with the audio signal. Each session will last approximately 30 minutes, five times per week, for four weeks. Syndrome-matched RFEMI tracks will be selected according to TCM syndrome differentiation. Comfortable sound level, patient tolerance, interruptions, and adverse events will be monitored and recorded.

Inclusion Criteria

- Meeting both ICD-11 criteria for depressive episode or recurrent depressive disorder and TCM diagnostic criteria for Yu disease.
- Diagnosis confirmed by two senior clinical physicians.
- Planned inpatient stay longer than six weeks.
- No antidepressant medication in the previous six months and no music therapy in the previous year.
- Male sex, aged 18-44 years, junior secondary education or above, clear consciousness, and ability to communicate effectively.
- No other major physical disease or mental disorder that would interfere with participation.
- Voluntary written informed consent and complete clinical records.

Exclusion Criteria

- Depression due to organic mental disorder, psychoactive substance use, or non-addictive substance use.
- Serious organic disease or unstable vital signs.
- Suicidal or violent tendency, or refusal to cooperate with treatment.
- Hearing impairment that would prevent participation in music intervention.
- Inability to follow the intervention protocol.
- Incomplete scale data or clinical records.

Dropout, Removal, and Discontinuation Criteria

Participants may withdraw voluntarily at any time. Participants will be discontinued if they convert to bipolar disorder during treatment or if investigators judge that continued participation is unsafe. Participants may be removed from analysis if they do not

take medication as prescribed, have poor adherence that prevents accurate efficacy assessment, develop serious adverse events or complications, or have incomplete data affecting efficacy or safety evaluation.

Outcome Measures

Outcome domain	Measure	Timing / note
Primary outcome	Hamilton Depression Rating Scale (HAM-D)	Baseline and week 4; primary endpoint is change in score.
Anxiety symptoms	Hamilton Anxiety Rating Scale (HAM-A); Generalized Anxiety Disorder-7 (GAD-7)	Baseline and week 4.

Sample Size Calculation

The sample size was estimated a priori using G*Power 3.1. The calculation was based on an F test for one-way analysis of variance, with an assumed effect size of f = 0.35, a two-sided significance level of alpha = 0.05, statistical power of 0.80, and three groups. The required total sample size was approximately 82 participants. Considering an expected attrition rate of approximately 10%, the planned final sample size was 90 participants, with 30 participants allocated to each group.

Statistical Analysis

Data will be analyzed using SPSS 26.0 or equivalent statistical software. Normally distributed continuous variables will be expressed as mean ± standard deviation, and non-normally distributed variables will be summarized using median and interquartile range where appropriate. Categorical variables will be presented as frequency and percentage.

Baseline comparability among the three groups will be assessed using one-way analysis of variance or Kruskal-Wallis H tests for continuous variables and chi-square or Fisher exact tests for categorical variables. Within-group pre-post changes will be analyzed using paired-sample t tests or Wilcoxon signed-rank tests. Between-group post-treatment or change-score differences will be analyzed using ANOVA or non-parametric equivalents as appropriate. Repeated-measures analyses may be used for physiological indicators measured at multiple time points. A two-sided P value of <0.05 will be considered statistically significant. Secondary outcomes will be interpreted as exploratory and hypothesis-generating.

Safety Monitoring

Participants will be monitored before, during, and after intervention sessions for discomfort, dizziness, ear pain, unstable vital signs, emotional agitation, or other adverse events. Intervention sessions may be paused, adjusted, or discontinued if participants report discomfort or if clinical staff judge continued participation to be unsafe. Any adverse events will be recorded and managed promptly by the clinical team.

Research Data

Where will the data be kept? De-identified research data will be stored in password-protected electronic files and/or locked research folders at the clinical research site. Identifiable clinical records will remain under institutional medical-record management procedures.

Anonymity of data: Participants will be assigned study codes. Names and other direct identifiers will not be used in analysis files or shared research datasets.

Who will have access to the research data? Access will be limited to authorized members of the research team, the principal investigator, and designated institutional or ethics reviewers when required.

How long will the data be kept? Research data will be retained for seven years, or according to institutional and journal requirements, and then securely destroyed or archived according to institutional policy.

Ethical Considerations

This study was reviewed and approved by the Research Ethics Committee of Datong Maternal and Child Health Hospital, China (Approval No.: KY2025-012; approval date: 15 August 2025). The approved project title was “The Novel Five-Element Resonance Music Intervention for Emotional Disorders in Chinese Men: A TCM-Inspired Randomized Controlled Trial.” The study will be

conducted in accordance with the Declaration of Helsinki and relevant ethical guidelines for biomedical research involving human participants. Written informed consent will be obtained from all participants before enrolment. Participants will be informed that participation is voluntary and that they may withdraw at any time without affecting their clinical treatment.

Budget / Financial Support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. Existing clinical resources and study-site support will be used where appropriate.

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Potential Impact

This study may provide preliminary evidence supporting RFEMI as a culturally grounded, low-burden adjunctive intervention for depressive disorders and anxiety symptoms in inpatient psychiatric care. If feasible and clinically promising, the study may support larger sham-controlled trials, improved intervention reporting, and future development of protocol-based publications in music intervention, psychophysiology, and culturally informed mental health care.

Confidentiality Statement

This research protocol is prepared for institutional clearance, ethical documentation, and journal-submission support. It should be kept confidential and should not be shared outside the authorized research, ethics, or journal-clearance process without permission from the principal investigator or project leader.