Official Title: A Multimodal MRI-Based Study on the Rapid Antidepressant Mechanisms of Acupuncture and Individualized Treatment Response Prediction in Depression

NCT Number： Not yet assigned

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Research Plan

1. Research Design

1.1 Study Type

A randomized, blinded, sham-acupuncture controlled clinical trial.

1.2 Randomization and Blinding

Randomization: A block randomization method will be used. A computer-generated random sequence will allocate eligible depressed subjects in a 1:1 ratio to either the "Acupuncture Group" or the "Sham Acupuncture Group". The random sequence will be generated and sealed by an independent statistician not involved in recruitment, intervention, or outcome assessment. Random numbers will be kept in opaque, sealed envelopes, which will be opened by the acupuncturist after the subject completes the baseline assessment.

Blinding Implementation: Subjects, outcome assessors, and data statisticians will be blinded to the group assignment throughout the study. The acupuncture treatment will be administered by a fixed acupuncturist who cannot be blinded; this individual will not participate in subsequent outcome assessments or data analysis.

1.3 Acupuncture Intervention Protocol

① Acupuncture Group: Acupoints including Baihui (GV20), Sishencong (EX-HN1), Shenting (GV24), Touwei (ST8), Fengchi (GB20), Anmian (EX), Neiguan (PC6), Shenmen (HT7), and Sanyinjiao (SP6) will be selected according to the Chinese National Standard "Nomenclature and Location of Acupuncture Points" (GB/T 12346-2006). Electrical stimulation will be applied using dense-sparse waves.

② Sham Acupuncture Group: The treatment received by subjects in this group will show no obvious external difference from the acupuncture group. Sham acupuncture will use non-meridian, non-acupoint points, and the electroacupuncture device will not output an electrical current.

③ Electroacupuncture Parameters: Dense-sparse wave, frequency 2Hz/100Hz, current intensity adjustable between 0.1-1mA, adjusted to the subject's tolerance (Huatuo Brand SDZ-II Electronic Acupuncture Treatment Device, Production License No.: Su Shi Yao Jian Xie Qi Sheng Chan Xu 20010020), with a fixed duration of 30 minutes.

2. Study Subjects (Including Inclusion and Exclusion Criteria)

Study subjects will be recruited from patients attending Yuquan Hospital of Tsinghua University

and Tsinghua University Hospital. Healthy subjects will be recruited from the Physical Examination Center of Yuquan Hospital of Tsinghua University and from Tsinghua University students.

2.1 Diagnostic Criteria for Depression

Subjects must meet the diagnostic criteria for depression as defined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) published by the American Psychiatric Association.

2.2 Inclusion Criteria

(1) Age 18–59 years, right-handed;

(2) No prior systematic antidepressant treatment (including antidepressant medication, sedative-hypnotic drugs, electroconvulsive therapy, transcranial magnetic stimulation); or have not received any antidepressant treatment for at least 4 weeks prior to enrollment;

(3) $7 <$ Hamilton Depression Rating Scale (HAMD-17) total score ≤ 24;

(4) Voluntary participation in this study with signed informed consent from the subject or their legal guardian.

2.3 Exclusion Criteria

(1) Presence of other major mental disorders or psychotic symptoms;

(2) Presence of other serious physical illnesses, such as cardiovascular or cerebrovascular diseases and autoimmune diseases, or current or past neurological disorders or organic brain diseases;

(3) Current or past history of alcohol dependence or other psychoactive substance abuse;

(4) Women who are lactating, pregnant, or menstruating;

(5) Participation in other clinical drug trials within the past 3 months.

2.4 Criteria for Discontinuation/Elimination

(1) Withdrawal from the study by the subject;

(2) Occurrence of adverse reactions during treatment that make continued treatment unsuitable;

(3) Non-compliance with the study protocol (e.g., inability to attend treatment and assessment sessions on time).

2.5 Inclusion, Exclusion, and Discontinuation Criteria for Multimodal MRI Healthy Subjects

(1) Inclusion Criteria:

a. Age 18–59 years, right-handed;

b. No physical abnormalities at enrollment and not taking stimulant medications;

c. Voluntary participation with signed informed consent.

(2) Exclusion Criteria:

a. Personal or family history of psychiatric disorders;

b. History of neurological disorders;

c. Current or past history of alcohol dependence or other substance abuse;

d. Women who are lactating, pregnant, or menstruating;

e. Presence of contraindications for MRI examination.

(3) Discontinuation Criteria:

a. MRI detection reveals intracranial structural asymmetry, vascular malformation, or definite pathological lesions;

b. Trial discontinuation due to adverse reactions or inability to complete MRI scanning.

3. Outcome Measures and Follow-up Plan

3.1 Primary Outcome Measure

Montgomery-Åsberg Depression Rating Scale (MADRS) score measured before acupuncture, and at 1 hour, 24 hours, 3 days, and 7 days post-acupuncture.

3.2 Secondary Outcome Measures

Hamilton Depression Rating Scale (HAMD-17), Maudsley Three-Dimensional Visual Analogue Scale (M3VAS), and Positive and Negative Affect Schedule (PANAS) scores measured before acupuncture, and at 1 hour, 24 hours, 3 days, and 7 days post-acupuncture.

3.3 Multimodal MRI Measures

Observe changes in multimodal MRI (MRS, p-CASL, rs-fMRI) before and after the intervention. Healthy subjects will undergo a single multimodal MRI scan at enrollment.

3.4 Safety Measures

Vital signs including blood pressure, respiratory rate, body temperature, and heart rate will be measured before and after treatment. All adverse events will be recorded in detail on case report forms for effective monitoring and evaluation.

3.5 Follow-up Plan

This study primarily observes the rapid effect of a single intervention; the follow-up period is 7 days.

4. Study Objectives

4.1 To verify the rapid amelioration effect and mechanism of a single acupuncture intervention on depressive symptoms in patients with depression.

4.2 To establish an individualized subtype identification model and construct a personalized model for predicting acupuncture efficacy.

5. Statistical Analysis Methods

Statistical analysis will be performed using SPSS 24.0 statistical software (IBM, Armonk, NY). Normally distributed continuous data will be presented as mean ± standard deviation (mean ± SD), with intergroup comparisons using t-tests. Non-normally distributed continuous data will be presented as median (interquartile range), with intergroup comparisons using the Mann-Whitney test. Count data will be presented as n (%), with intergroup comparisons using the chi-square test or Fisher's exact test. A significance level of $P < 0.05$ will be used.