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A study on the efficacy and multimodal brain mechanisms of acupuncture combined with probiotics in treating depression accompanied by mental fatigue in adolescents and college students

Submission date 26/11/2026	**Recruitment status** Not yet recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 26/11/2026	**Overall study status** Ongoing	
Last Edited 26/11/2026	**Condition category** Mental and Behavioural Disorders	

Plain English summary of protocol

Background and study aims

Depression is common among young people in China. A recent review estimated that almost four in ten Chinese university students have symptoms of depression. Many of them also have mental fatigue: a lasting feeling of mental tiredness, poor concentration and slow thinking that makes studying and everyday life difficult. Standard antidepressant medicines can cause side effects, and many young people do not want to take them for long periods.

Acupuncture is widely used in China for depression. The technique used in this study, called Shugan Tiaoshen, was developed by Professor Wenbin Fu. It uses fine needles at fixed points on the head, abdomen, hands, feet and ears. Probiotics, sometimes called good bacteria, may also affect mood and sleep through the link between the gut and the brain.

The study has three aims: first, to find out whether acupuncture combined with a probiotic reduces depression and mental fatigue more than acupuncture alone; second, to find out whether real acupuncture works better than a sham (pretend) acupuncture; third, to understand how the treatment might work, by studying brain waves, sleep recorded by a wrist-worn device, and blood and stool samples.

Who can participate?

The study will recruit 120 students aged 12 to 28 years who are either secondary school students in Bao'an District, Shenzhen, or full-time undergraduate students of Guangzhou University of Chinese Medicine doing their clinical training at the Seventh Clinical Medical College. Participants must have mild to moderate depression confirmed by a doctor, together with mental fatigue, and must be right-handed. Participants under 18 years of age will need written agreement from a parent or guardian, as well as their own agreement.

People cannot take part if they have chronic fatigue syndrome, epilepsy, a serious physical

illness, a history of severe mental illness, thoughts of harming themselves, a strong fear of needles, or if they are taking antidepressants or have taken antibiotics or probiotics in the past month.

What does the study involve?
Everyone who joins has a short screening visit and a waiting period of 3 to 7 days without sleep medicines. Before treatment starts, participants complete questionnaires, have a brain wave (EEG) recording of about 25 minutes, give a small blood sample (10 mL) and a stool sample, and wear a wrist device that records sleep for about one month.
Participants are then allocated by computer, by chance, to one of three groups of 40: acupuncture plus probiotic; acupuncture plus a placebo (inactive) probiotic; or sham acupuncture plus a placebo probiotic. Nobody can choose their group, and participants and the staff who assess them do not know which group they are in.
All groups have 12 acupuncture sessions over 4 weeks, three sessions a week, each lasting about 30 minutes, and take two sachets of powder every night before bed for 4 weeks. Questionnaires are repeated after 2 weeks and at the end of treatment, and there is a final check one month later. Taking part lasts about 8 weeks in total.

What are the possible benefits and risks of participating?
Participants may feel better in mood, mental energy and sleep, although this cannot be guaranteed. All treatment and tests are free of charge, and everyone receives regular acupuncture sessions and medical checks.
Acupuncture can cause brief discomfort, small bruises or minor bleeding where the needle goes in, and occasionally light-headedness or fainting, which the staff are trained to manage. The probiotic may cause mild bloating or loose stools. Blood sampling can cause brief pain or bruising, and the EEG gel is washed out afterwards. Stool samples are collected by participants at home using a provided kit. Personal information is kept confidential, and taking part is voluntary: participants can withdraw at any time without giving a reason and without affecting their studies or medical care.

Where is the study run from?
The study is run by the Department of Acupuncture and Moxibustion, Shenzhen Bao'an District Hospital of Traditional Chinese Medicine, Bao'an District, Shenzhen, Guangdong, China.

When is the study starting and how long is it expected to run for?
Recruitment is planned to start in December 2026 and to finish in December 2027. The whole study is expected to take about one year. Each participant takes part for about 8 weeks.

Who is funding the study?
The study is funded by the 2026 Special Project of the Joint Laboratory for Student Mental Health, Guangzhou University of Chinese Medicine.

Who is the main contact?
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Study information

Scientific Title
Acupuncture plus Lactiplantibacillus plantarum BGI-N6 probiotic versus acupuncture plus placebo and sham acupuncture plus placebo for mild-to-moderate depression with mental fatigue in adolescents and university students: a three-arm randomised controlled trial

Acronym
APDT

Study objectives
1. To characterise the baseline neurophysiological and sleep phenotype of adolescents and university students with mild-to-moderate depression and mental fatigue, by quantifying EEG markers (frontal-central theta and beta power during 10-minute resting state and 15-minute 2-back task; P300 amplitude) and habitual sleep parameters recorded continuously with a wearable device
2. To determine whether acupuncture combined with Lactiplantibacillus plantarum BGI-N6 probiotic, compared with acupuncture plus placebo probiotic, reduces depressive symptom severity (HAMD-17) and mental fatigue (MFI-20 mental fatigue subscale) after 4 weeks of treatment
3. To determine whether the combined intervention reverses EEG abnormalities (P300 amplitude attenuation, elevated theta and reduced beta power) and improves objective sleep architecture, and whether improvement in sleep parameters mediates the improvement in EEG markers
4. To explore the central–peripheral mechanisms of the intervention by integrating plasma proteomics, untargeted metabolomics, PBMC transcriptome and gut metagenomic data with EEG, sleep and clinical outcomes

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 24/11/2026, Medical Ethics Committee of Shenzhen Bao'an District Hospital of Traditional Chinese Medicine (No. 25, Yu'an 2nd Road, Bao'an District, Shenzhen, 518000, China; +86 755 23086529; weipenghuang@szbazyy.net), ref: KY-2026-054-02

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Placebo

Assignment
Parallel

Purpose
Treatment

Study type(s)

Health condition(s) or problem(s) studied
Depression (mild-to-moderate major depressive disorder, DSM-5) with comorbid mental fatigue

Interventions
This is a single-centre, three-arm, parallel-group, randomised, participant- and assessor-blinded, sham- and placebo-controlled trial. Eligible participants enter a 3- to 7-day washout period (3 days for those with no sleep-medication use and good sleep habits in the preceding month; 7 days for those who used hypnotics or reported poor sleep habits), then complete baseline assessment and are randomised 1:1:1 to one of three arms.

Arm 1 (acupuncture plus probiotic, n = 40): manual acupuncture at Baihui (GV20), Yintang, Touwei (ST8), Jiuwei (CV15), Zhongwan (CV12), Qihai (CV6), Taichong (LR3, bilateral), Hegu (LI4, bilateral) and Sanyinjiao (SP6, bilateral), with auricular acupoints (Heart, Liver, Kidney) applied to alternating ears; needles retained for 30 minutes after deqi, three sessions per week for 4 weeks (12 sessions). In addition, two sachets of Lactiplantibacillus plantarum BGI-N6 live-strain preparation are taken orally each night before sleep for 4 weeks.

Arm 2 (acupuncture plus placebo, n = 40): identical acupuncture protocol, plus two sachets nightly of maltodextrin placebo matched for appearance, taste, smell and packaging.

Arm 3 (sham acupuncture plus placebo, n = 40): non-penetrating Park sham needles at the same acupoints (needle tip touches but does not penetrate the skin; no deqi) and sham auricular pellets, three sessions per week for 4 weeks, plus two sachets nightly of maltodextrin placebo.

Randomisation is generated by a central randomisation system using block randomisation, with allocation concealment by sequentially numbered, opaque, sealed envelopes; allocation is requested only after eligibility confirmation and baseline assessment. Participants and outcome assessors are blinded to allocation; the acupuncturist is aware of allocation but takes no part in outcome assessment or data analysis. Total treatment duration is 4 weeks in all arms, followed by 1 month of follow-up (total study duration 8 weeks per participant). Assessments are performed at baseline, day 14, week 4 and 1 month after the end of treatment, and include clinical rating scales, EEG, sleep monitoring with a wearable device, stool sampling for metagenomic sequencing and fasting venous blood sampling for multi-omics analysis.

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. Depression severity measured using Hamilton Depression Rating Scale, 17-item version (HAMD-17): change in total score from baseline (score range 0–52, higher scores indicate greater severity), rated by a trained outcome assessor blinded to allocation at Baseline (day 0) and week 4 (day 28 ± 4 days)

2. Mental fatigue measured using Multidimensional Fatigue Inventory, 20-item version (MFI-20): change in the mental fatigue subscale score from baseline (subscale range 4–20, higher scores indicate greater fatigue), completed by the participant at Baseline (day 0) and week 4 (day 28 ± 4 days)

Key secondary outcome(s)
1. Depressive symptoms measured using the Patient Health Questionnaire-9 (PHQ-9) total score (range 0-27), assessed as change from baseline at baseline (day 0), week 2 (day 14 ± 2), week 4 (day 28 ± 4) and follow-up (week 8, 1 month ± 7 days after treatment)
2. Sleep quality measured using the Pittsburgh Sleep Quality Index (PSQI) global score (range 0-21), assessed as change from baseline at baseline (day 0), week 2, week 4 and follow-up (week 8)

3. Objective sleep parameters measured using a wrist-worn wearable device (Huawei Band 10) worn nightly to record sleep onset and offset time, total sleep time, sleep efficiency, number of awakenings, and duration of deep, light and REM sleep, assessed as change from baseline through continuous daily monitoring from 3 days before baseline (day -3) to the end of treatment (day 28), summarised for baseline, week 2 and week 4
4. Neurophysiological indices of cognitive resource allocation measured using electroencephalography (EEG) during a 10-minute resting state and 15-minute 2-back task to assess frontal-central theta (4-8 Hz) and beta (13-30 Hz) power, and P300 amplitude, assessed as change from baseline at baseline (day 0) and week 4 (day 28 ± 4)
5. Gut microbiome composition and function measured using shotgun metagenomic sequencing of faecal samples to assess alpha and beta diversity, taxonomic abundance and functional pathway profiles, assessed as change from baseline at baseline (day 0), week 2 (day 14) and week 4 (day 28)
6. Peripheral molecular profiles measured using plasma proteomics, untargeted metabolomics and peripheral blood mononuclear cell (PBMC) transcriptomics from fasting venous blood, assessed as change from baseline at baseline (day 0) and week 4 (day 28 ± 4)
7. Safety and tolerability measured using the incidence, severity and relatedness of adverse events (e.g. needle-site pain, bruising, needle syncope and gastrointestinal symptoms) recorded at each visit throughout the study from baseline to follow-up (week 8)

Completion date
31/12/2028

Eligibility

Key inclusion criteria
1. Adolescents and university students aged 12–28 years
2. Meet DSM-5 criteria for major depressive disorder (single episode or recurrent) and the traditional Chinese medicine pattern of liver-qi stagnation with spleen deficiency, according to the Criteria of Diagnosis and Therapeutic Effect of Diseases and Syndromes in Traditional Chinese Medicine (ZY/T001.1-94)
3. HAMD-17 total score of 8–23 (mild to moderate depression) and MFI-20 mental fatigue subscale score of ≥12
4. Right-handed
5. Signed written informed consent

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
12 Years

Upper age limit
28 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1.Diagnosis of chronic fatigue syndrome (CFS)
2.Severe organic disease, or history of epilepsy (an absolute contraindication to EEG recording)
3.Use of antidepressants or other psychoactive substances within the previous 4 weeks
4.Extreme fear of needling, or history of needle syncope
5.Suicidal ideation or suicidal behaviour at baseline, as screened with the Chinese version of the Columbia-Suicide Severity Rating Scale (C-SSRS)
6.Previous diagnosis of intellectual disability or other psychiatric disorder
7.Severe hepatic, renal, cardiovascular, endocrine, respiratory or haematological disease
8.Current participation in another clinical trial, or use of antibiotics or probiotics within the previous month that could affect study outcomes

Date of first enrolment
01/12/2026

Date of final enrolment
31/12/2027

Locations

Countries of recruitment
China

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Shenzhen Bao'an District Hospital of Traditional Chinese Medicine
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Sponsor information

Organisation
Guangzhou University of Traditional Chinese Medicine

Funder(s)

Funder type

Funder Name

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available