BMC Complementary Medicine and Therapies

STUDY PROTOCOL

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Effects of the Qigong Tuina therapy on patients with Chronic fatigue syndrome: study protocol for a randomized controlled trial

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Abstract

Background Chronic fatigue syndrome (CFS) is a chronic disease characterized by fatigue, complex symptoms and long duration. It incurs significant economic costs every year. Qigong Tuina therapy (QTT), a traditional Chinese therapy, is skilled in the treatment of fatigue. The objective of this study is to observe the effectiveness of QTT in treating patients with CFS.

Methods A randomized controlled trial will recruit 128 patients with CFS. The patients will be allocated randomly in a 1:1 ratio to either the QTT group or the cognitive behavioral therapy (CBT) group. The interventions for both groups will be carried out once per week for 8 weeks. Then a 4 weeks follow-up will be conducted for all patients after the intervention. The primary outcome will be the changes in the Multidimensional Fatigue Inventory (MFI-20). Secondary outcomes will be measured by the 36-Item Short Form Health Survey (SF-36), Pittsburgh Sleep Quality Index (PSQI), Hospital Anxiety and Depression Scale (HADS), and functional magnetic resonance imaging (fMRI). The data will be analyzed at the baseline, 4 weeks into the intervention, at the end of the intervention, and 4 weeks after the intervention. The safety of interventions will be assessed after each treatment session.

Discussion The trial aims to establish whether QTT is not inferior to CBT for CFS patients. This study provides vital information for an alternative and complementary therapy aimed at patients afflicted with CFS.

Ethics and dissemination Ethical approval was granted by Ethics Committee of Shanghai Municipal Hospital of Traditional Chinese Medicine (2023SHL-KY-100–02). The findings will be disseminated through publications, conferences, and briefs to professional organizations.

Trial registration ChiCTR2400081828, Chinese Clinical Trial Registry. Registered on March 13, 2024.

Keywords Fatigue, Chronic fatigue syndrome, Cognitive behavioral therapy, Qigong Tuina therapy

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Introduction

CFS is a disease characterized by long-lasting profound disabling fatigue, post-exertional malaise, chronic pain, immune system disorder, poor memory, unrefreshing sleep, cognitive impairment and depression [1]. These symptoms could last more than 3 months which trouble patients a lot. It is approximately 836,000 to 2.5million individuals in the U.S. are affected by CFS [2].Moreover, following acute COVID-19, many patients continue to experience fatigue for many months, and a subset of these patients met the diagnostic criteria for CFS [3]. CFS also impairs occupational, educational, social, and personal activities, [4]which has become a severe problem with enormous effects on the public health [5].

However, the cause of CFS remains uncertain due to its intricate symptomatology, which affects various bodily systems. The symptoms of CFS are diverse and have interrelated effects. For instance, sleep disorders can exacerbate fatigue, resulting in reduced daytime productivity, memory loss, and cognitive impairment. Previous studies have found that CFS patients have abnormalities in the function of some brain regions [6]. CBT is a common intervention for CFS [7]. It can identify and adjust maladaptive behaviours and beliefs, leading to a decrease in symptom severity and improvement of functional capacity. However, involving professional counselors in the process proves to be challenging and expensive, making CBT a difficult approach to promote.

Tuina, a traditional Chinese massage therapy, is widely accepted by patients due to its safety and effectiveness [8, 9]. Previous studies show that Tuina relieves fatigue and improves daytime functioning in patients with CFS [10, 11]. Qigong is a traditional Chinese exercise method, which is characterized by slow and gentle movements and regulation of consciousness and breathing [12]. Study show that Qigong has the ability to enhance muscle strength and physical performance [13, 14], which are all vital factors for executing massage therapy effectively. Hence, it is advisable for Chinese Tuina practitioners to engage in Qigong exercises to enhance their clinical effectiveness. Previous research has also verified that Qigong can effectively enhance the quality of life and decrease pain in patients with CFS [15].

QTT is a kind of traditional Chinese therapy which combined Qigong and Tuina together. It had been named as Shanghai intangible cultural heritage [16]. Originating in northern China but later refined in Shanghai, this unique therapy has spread for over 100 years [17, 18]. In this therapy, both doctors and patients must engage in Qigong exercises, with doctors employing a unique massage manipulation procedure on their patients. Its main massage manipulation techniques is rubbing the trunk, making the heat generated by friction conduct to the deep tissue [19]. However, the effectiveness of this unique therapy still lacks clinical evidence, impeding extensive dissemination of this technique. Therefore, this clinical trial aims to find out the clinical effect of QTT thus explore a new effective therapy for CFS.

Methods

Design

The study is a single-center, randomized, assessor- and statistician-blinded, parallel-controlled trial. It will be conducted at the Shanghai municipal hospital of Traditional Chinese Medicine from March 2024 to December 2025. Participants will be allocated to the QTT group or the CBT group. The QTT group will use Qigong Tuina therapy, while the CBT group will use cognitive behavioral therapy. This protocol used the SPIRIT reporting guidelines [20].

Setting of the study

The 128 patients with CFS who are eligible for recruitment to this study will be randomized into the QTT and CBT groups with a sample size of 64 in each group. Participants in the QTT group will receive a 30 min Tuina treatment and 30 min of Qigong exercise per week. This will be for 8 consecutive weeks. On the other hand, participants in the CBT group receive a lecture for 1 h per week for 8 consecutive weeks. The outcome measures will be carried out after the end of intervention. The study design is illustrated in the flow chart in Fig. 1.

Randomization and allocation concealment

Eligible participants will be randomly assigned to the QTT group or the CBT group according to a rule of equal proportions, following a post-baseline assessment. The randomization list will be generated by a statistician using a computer program (Strategic Applications Software, version 9.1.3; SAS Institute Inc., Cary, NC, USA). The statistician, as the producer of the random sequence, numbers the random sequence one by one. The sequence is then placed in an opaque envelope by a designated project manager, who was not involved in the recruitment process, and finally handed over to a group of researchers. Before implementing random allocation, the team will record the details of each participant, including new ones (name, date of birth, participant and center code, date of enrolment) at the clinical center for use in reporting and in preparation for signing the informed consent. After assessing the participant's information to establish whether they meet the inclusion criteria, the research team will randomly choose a sequence from the envelopes, labeled with the patient's information, allocated to each group, and given to the participant.

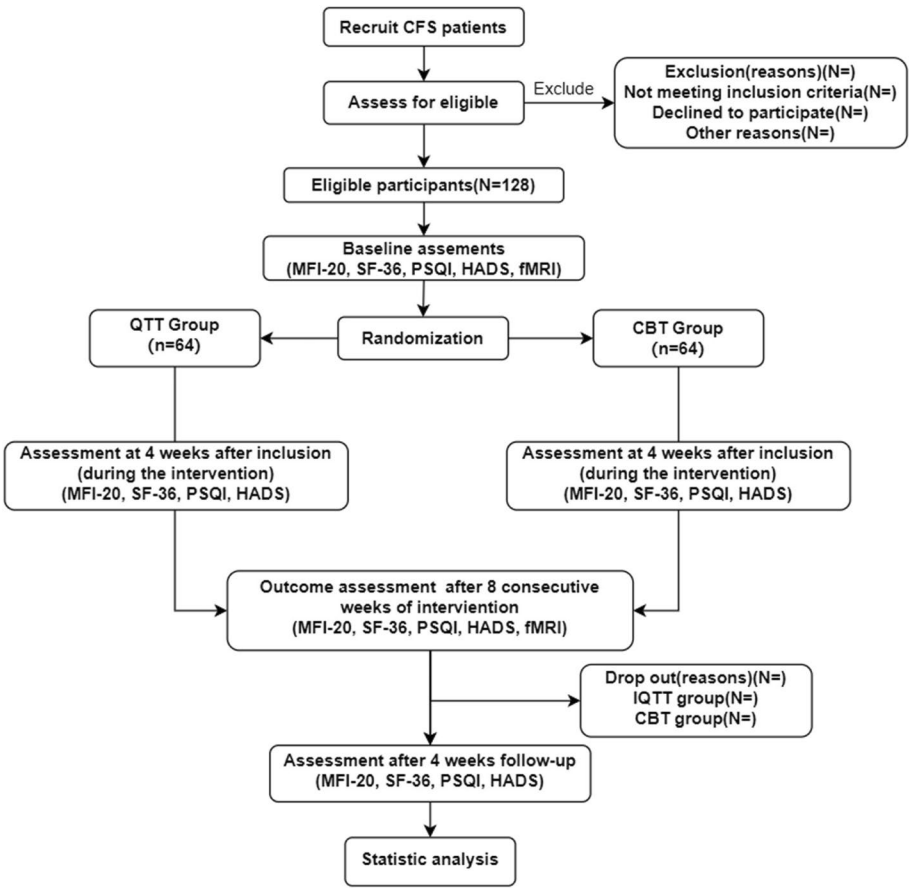

Fig. 1 Trial flow diagram. QTT: Qigong Tuina therapy. CBT: Cognitive behavioral therapy

Informed consent

Participants will be informed that the study collects data from patients with CFS. The data will be exclusively used by the group for the analysis of the experiment's findings. Moreover, the final results will be presented after omitting private information of the patients. Informed consent is a prerequisite for the intervention. Patients will be informed of the benefits that can be derived from the treatment as well as the risks that may be associated with it and they can terminate participation at any time. The study-related costs of all tests done during the research will be paid by the subject group. At the end of the clinical trial, patients will receive a refund for their participation and travel costs incurred. Informed consent was obtained from all subjects for publication of identifying information/images in an open access online publication.

Participants

Participants that meet the following criteria will be included.

I. According to the NICE guidelines for 2021 [1], all of the following 4 symptoms need to be present at the same time and last for at least 3 months:

   a) Debilitating fatigue worsened by activity.
   b) Post-exertional malaise.
   c) Cognitive difficulties.
   d) Unresolved fatigue on awakening from sleep.

II. Aged between 20 and 60 years old.
III. Rule out other potential medical causes which may lead to fatigue.
IV. Have not received any other treatment within 1 month.
V. Agree and sign informed consent.

Participants that meet any of the following criteria will be excluded.

I. Underlying diseases such as severe cardiovascular and cerebrovascular diseases, endocrine system

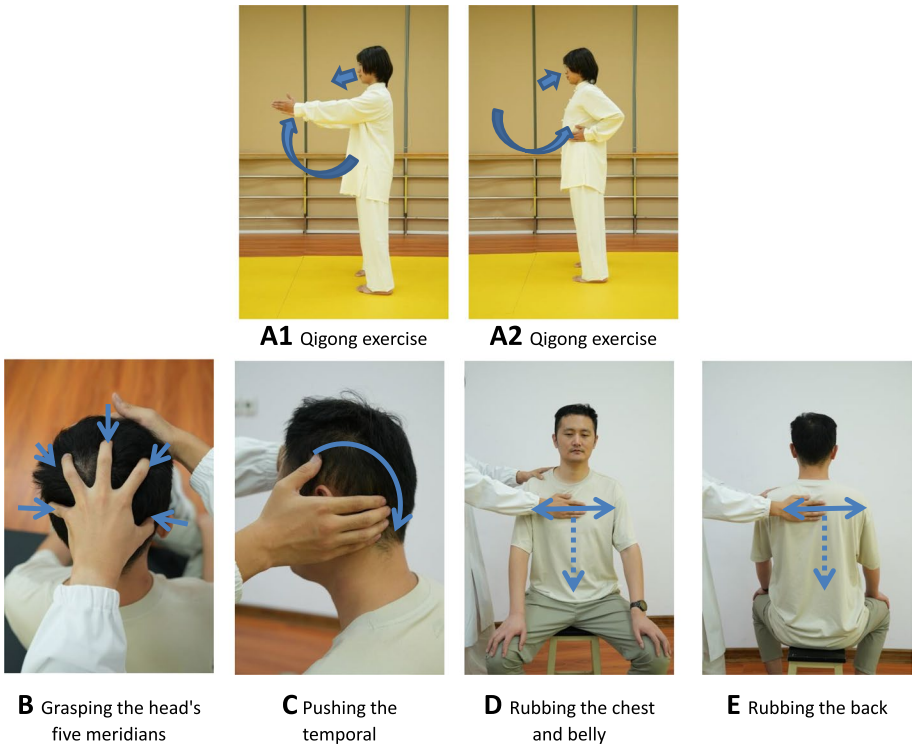

Fig. 2 The typical sequence of QTT. The operator in the picture is Haotian Han, a member of the research, while the other one is a participant. A1 and A2 are both Qigong exercises that involve elbow movements and controlled breathing

diseases, musculoskeletal diseases, autoimmune diseases, etc.

II. Taking medications that may affect the determination of results.
III. Have a definitive diagnosis of organic gastrointestinal pathology, abnormal liver or kidney function, tumor or other disease.

Participants who meet the following criteria will be excluded after the study has started.

I. Incorrect inclusion of experiments.
II. Poor subject compliance and fail to follow prescribed treatment.
III. Incomplete medical records, affecting the evaluation of efficacy.
IV. Self-withdrawal of subjects.
V. Adverse events or serious adverse events occurring during the course of the trial in which the subject is unfit to continue participation in the study.
VI. The subject has a serious deterioration of disease or certain comorbidities, complications and specific physiological changes that make him/her unsuitable for further participation in the study.
VII. Participants who are deemed ineligible by the researcher for further participation in the study.

Intervention

QTT group

The QTT intervention program and operating standards refer to the Chinese general higher TCM compiled college textbook of Internal Qigong Tuina [21]. Tuina therapy is performed once a week by a male certified therapist with TCM license and more than 5-years of clinical and Qigong exercise experience. He will receive training to provide patients with instruction on Qigong practice, as well as to administer Tuina. The treatment room will be regulated at 26–28 °C to ensure participant comfort. Each session will continue for 1 h. During Tuina, the participant shall be seated in an upright position. The typical sequence of QTT is as follows and Fig. 2.

A. *Qigong exercise:* The individual stands with their feet positioned apart at shoulder width, with toes turned inward at a 30-degree angle and gripping the floor, while maintaining tension in the leg muscles. Place the hands facing the torso, and rest them on each side of the chest. Extend the arms towards the front while keeping the muscles in the forearms tense, straighten the elbows, exhale and hold for ten seconds. (A1). Then slowly bend the elbows and bring the hands back to the chest, breathing in as he/she does so. (A2). Repeat the above exercise for 30 min.

B. *Grasping the head's five meridians:* The operator places one hand on the participant's forehead to stabilize it. Using the other hand, the operator flexes the interphalangeal joints and places the middle finger on the participant's governor vessel, the index and ring fingers on the bladder meridian and the thumb and little finger on the gallbladder meridian. Then, the operator performs grasping from front to back for 5 min.
C. *Pushing the temporal:* The operator stabilize the participant's head with one hand while the other hand's thumb placed at GB-8 and the remaining fingers placed at the back of the participant's head between GB-19 and GB-20(All the acupressure points are indicated by international standard serial numbers). Operator push with a single-directional straight-line from the front towards the back, downwards. Both sides of the head should be pushed for 5 min.(10 min in all)
D. *Rubbing the chest and belly:* The operator stabilizes the participant's shoulder with one hand and, using the palm of the other hand, rubs along the participant's lower edge of the clavicle in a right and left straight line, moving slowly from top towards the navel (avoiding the female participant's breasts). (7.5 min)
E. *Rubbing the back***:** The operator stabilizes the participant's shoulder with one hand and uses the other to apply left and right linear rubbing along the level of the seventh cervical spinous process. Then, the operator gradually moves their hand downwards to the level of the fourth lumbar vertebrae for rubbing manipulation. All the rubbing manipulations require the participant to feel a warm sensation in the friction area. (7.5 min)

CBT group

All cognitive behavioral therapies will be delivered with the aid of an experienced counselor and a research assistant. The treatment interviews will be recorded by the research assistant and submitted to the individual responsible for quality control. Participants will be requested to document daily exercise or study information pertaining to the therapy content. Counselor will be invited to the CBT group once a week for 1 h to give lectures or psychological counseling on CFS prevention and treatment. Cognitive behavioral therapy is collaborative, educational, consultative and emphasizes behavior. According to the previous study [22], weeks 1 to 2 were cognitive probes that involved engaging the patient in the treatment and providing details of the rationale for the treatment. Evaluate the questions asked and record details of the subject's activity, rest and fatigue on an hourly basis. Subjects were also encouraged to keep diaries (daily records of events, sensations, fatigue and muscle tension). Weeks 3 to 5 consisted of identifying core beliefs using techniques such as the three-column scale and the vertical arrow method. Throughout the process, the patient actively identifies their own adverse thought patterns and misconceptions, while the counselor carries out analysis, provides examples, engages in role-playing, and inspires without making moral judgments. Cognitive reconstruction was practiced between week 6 and week 8. The treatment involved progressive exposure therapy, graded activity programs, and addressed the severity and environmental specificity of cognitive fatigue, as well as its effects and outcomes. Other techniques used were cognitive rest, exercise to alleviate stress, and dietary adjustments to relieve fatigue.

fMRI examination procedure

fMRI data will be acquired from all the participants using a 3.0-T Trio Siemens System at the Shanghai Municipal Hospital of Traditional Chinese Medicine. All participants will be scanned: repetition time (TR) = 1,900 ms; effective echo times (TE) = 2.93 ms; sagittal slices = 188; thickness/skip = 1.2/0.6 mm; field of view (FOV) = 256 × 256 mm2; matrix = 240 × 256 mm2; Voxel size = 1.0 × 1.0 × 1.0, phase encoding direction = A > >P and flip angle (FA) = 90°. Participants will be instructed to rest with their eyes closed for 10 min prior to the scan, and requested not to think about anything during this time. Participants will be required to abstain from any head movement during data acquisition. We will acquire 242 three-dimensional image volumes, with the following parameters: TR = 2,000 ms; TE = 30 ms; section thickness = 1 mm; sagittal slices = 32; FOV = 256 × 256 mm2; matrix = 64 × 64 mm2; and FA = 90°. Both groups of participants will be examined before and after treatment.

fMRI data processing

Imaging data will be processed and analyzed using MATLAB 2015a (MathWorks, Natick, MA, USA), SPM12 (Wellcome Department of Cognitive Neurology, UK), VBM 8 (http://dbm.neuro.uni-jena.de/vbm8/), and CONN toolbox. MRICON will be used to convert the original scanned DICOM format to an NIFTI format [23]. The initial 10 time points and images will be independently eliminated and realigned for motion correction to prevent the identification of fake motion artifacts. The functional image will be coregistered with the T1 image, and the 10 mm full width half maximum (FWHM) kernel will used to smooth the space to reduce the noise of subsequent image subtraction [24]. The images will undergo detrending, and nuisance variables (including

the white matter signal and cerebral spinal fluid signal) will be regressed from the data. The amplitude of low-frequency fluctuations (ALFF) and fractional amplitude of low-frequency fluctuations (fALFF) indices will be computed for each participant. Functional connectivity (FC) analyses will be conducted using the CONN toolbox. Before conducting the correlation analysis, we will utilise the CompCor algorithm to execute a linear regression. This regression will eliminate the average signals of the white matter and ventricles from the data. This step decreases the spatial correlation induced by physiological noise. After preprocessing (i.e. motion correction, co-registration, subtracting, CBF estimation, smoothing, normalization, and masking), the data will be input into CONN. The seed-to-voxel FC analysis will be performed using a priori ROIs (i.e. superior frontal gyrus (SFG), anterior cingulate cortex (ACC), angular gyrus (AG), hippocampus, pallidum and postcentral gyrus (PCG)).Each voxel of the entire brain is functionally connected to the seed region, and each voxel will have a correlation value. The seed-to-voxel approach analysis produces a correlation graph of Fisher's r-z transformation for each participant and seeds, which are then subjected to independent T-tests.

Sample size calculation

The following two hypotheses are related to the differences between the two groups.

$$H0 : \mu 1 = \mu 2$$

$$H1 : \mu 1 \neq \mu 2$$

where μ1 represents the mean fatigue scale score following 8 weeks of treatment in the QTT group, and μ2 represents the mean fatigue scale score following 8 weeks of treatment in the CBT group. Referring to our previously published study [25] on the efficacy of CFS with respect to the MFI-20 scale, it was calculated that the final difference between the two groups in terms of MFI-20 average scores is 1.634 and the standard deviation is 3.238, $\alpha = 0.05$, $\beta = 0.2$, allowing for a dropout rate of 20 per cent, the sample size for each locus in each group would be 64. Therefore, a total of 128 subjects are required for this experiment. The following formula as used to calculate the sample size in this trial:

$$n = \frac{2(Z_{a/2} + Z_{\beta})^2 \times \sigma^2}{(\mu_2 - \mu_1)^2}$$

Outcome measurement

The assessment of the outcomes encompasses the following elements: changes in mental and physical fatigue, anxiety and depression, health status, sleep quality and functional connectivity between multiple brain areas. The relevant scale measurement such as the Multidimensional Fatigue Inventory-20 (MFI-20), 36-item Short Form Health Survey (SF-36), Pittsburgh Sleep Quality Index (PSQI) and Hospital Anxiety and Depression Scale (HADS) will be assessed at the baseline, 4 after inclusion (during the intervention), 8 weeks after inclusion (at the end of intervention) and 12 weeks after inclusion (at the end of follow-up). Professionals with expertise in the relevant departments but not involved in this particular trial at the Shanghai Municipal Hospital of Traditional Chinese Medicine will evaluate changes in functional connectivity between multiple brain areas and the characteristics of brain network activation at the baseline and the end of intervention(8 weeks). The detailed outcome assessment time points are provided in Table 1.

Primary outcome

MFI-20

Physical and Mental fatigue will be measured using the Multidimensional Fatigue Inventory (MFI-20), which is a questionnaire developed by Smets et al. (1995) with 5 dimensions: general fatigue, physical fatigue, mental fatigue, reduced motivation, and general activity [26]. The responses of each item are arranged in a Likert scale ranging from 1 (Yes, this is true) to 5 (No, this is not true) [27]. The scores of each dimension range from 4 to 20. Each of the dimensions contains 2 positively and 2 negatively orientated items. Higher scores indicate a higher degree of fatigue. The score of MFI-20 at 8 weeks after inclusion will be viewed as the primary outcome.

Secondary outcomes

SF-36

The health status will be assessed by the 36-item Short Form Health Survey (SF-36) [28], the assessment includes 9 dimensions with a total of 36 items. These dimensions are: physical functioning, body aches and pains, general health, vitality, social functioning, emotional functioning, mental health and health changes. Each of the 9 dimensions is assigned a code, which is then summed and expressed on a scale of 0–100. A higher score indicates a better health status.

PSQI

The Pittsburgh Sleep Quality Index (PSQI) was used to evaluate the sleep quality of the participants over the past month [29]. The PSQI comprises 19 self-assessment items and 5 other-assessment items. It is important to note that the 19th self-assessment item and 5 other-assessment items are not included in the scoring. Only the 18 self-assessment items that are involved in the

Table 1 Trail time points chart

Period	**Inclusion**	**Treatment**		**Follow-up**
Assessment	**Baseline**	**First**	**Second**	**Fourth**
Measure point(after inclusion)	**0 week**	**4 weeks**	**8 weeks**	**12 weeks**
Inclusion criteria	√			
Exclusion criteria	√			
Informed consent	√			
Randomization and allocation	√			
Intervention		1–8 week		
Multidimensional Fatigue Inventory (MFI-20)[a]	√	√	√	√
36-item Short Form Health Survey (SF-36)	√	√	√	√
Pittsburgh Sleep Quality Index (PSQI)	√	√	√	√
Hospital Anxiety and Depression Scale (HADS)	√	√	√	√
Amplitude of low-frequency fluctuations (ALFF)	√		√	
Fractional amplitude of low-frequency fluctuations (fALFF)	√		√	
Functional connectivity (FC)	√		√	
Adverse events	Any time during the intervention and follow-up			

[a] MFI-20 will be assessed at the baseline, 4, 8,12 weeks after inclusion, but only the score at 8 weeks will be viewed as the primary outcome

scoring are presented here (see the appended questionnaire for more information). The 18 items in the PSQI evaluate 7 different components of sleep quality. Each component is rated on a scale of 0–3 and the cumulative scores of each component are combined to produce the total score of the PSQI. The total score ranges from 0 to 21, where a higher score indicates poorer sleep quality.

HADS

Hospital Anxiety and Depression Scale (HADS) comprises several adjectives describing a person's feelings, irrespective of whether they are positive or negative [30]. Each adjective is rated from 0 to 4, indicating different levels of intensity (0 = no such feeling at all; 1 = a slight degree of such feeling; 2 = a moderate degree of such feeling; 3 = a considerable degree of such feeling; 4 = a fairly strong degree of such feeling). The scores that carry the highest impact on the mood factor of these feelings are totaled, with higher scores indicating a worse state of mind.

fMRI

This examination aims to find out the changes in functional connectivity between multiple brain areas and characteristics of brain network activation. The QTT and CBT groups were tested before and after the treatment for the structural and functional characteristics of brain regions such as the frontal lobe, temporal lobe, parietal lobe, occipital lobe, and hypothalamus [31]. The Matlab platform SPM software package was used to process the fMRI raw data in Dicom format. This was done to study the structural and functional features of several brain regions, including the occipital lobe and hypothalamus. Afterward, the statistical parametric mapping was created and the activation image was superimposed onto a standard brain to display the corresponding brain structure and the activation area's three-dimensional spatial location.

Safety evaluation and adverse events (AEs)

In this trial, any adverse reactions that occur during and after the intervention will be recorded on the case report form (CRF). QTT is an alternative therapy, so the passible risks include muscle pains after Qigong practice and minor skin injuries due to rubbing during Tuina. A patient experiencing an adverse reaction should seek necessary medical care without delay, and the reaction must be precisely documented on the CRF.

Date management

Raw data will be collected using paper case report forms (CRFs) at designated intervals. The completed CRFs will be received by two independent data managers who are not affiliated with the study team and are unaware of the subgroups. The raw data will then be entered into a Microsoft Excel database. These two administrators must be fully trained in data monitoring. At the end of the study period, all collected data will be locked and cannot be modified by the investigator. The CRFs will be securely stored for at least five years after the article's publication. Reviewers who have concerns about the validity or reliability of our trial may contact the corresponding author

for access to the raw data. To enhance the authenticity of the data, we have established an independent Data Safety Monitoring Board (DSMB) comprising of experts in Tuina, internal medicine and statistics. The DSMB ensures the overall quality and integrity of the information collected by performing spot checks on the raw data during meetings with the assessors to ensure compliance with the protocol guidelines. They have the authority to terminate the study early if necessary.

Statistical analysis

The Statistical Package for the Social Sciences (SPSSversion18.0, SPSS Inc., Chicago, IL, USA) will be used to statistically analyze the collected data. For normally distributed measures, we used the mean ± standard deviation, while for non-normally distributed measures; we used the median and interquartile range. For count data, we used frequency and percentage. The H test was used for the chi-square of the two groups before and after the intervention period to find out if the test of normal distribution and chi-square was satisfied. We set the significance level (α) at 0.05, and considered a difference statistically significant when the probability value (p-value) was less than 0.05.

Patient and public involvement

The design, conduct, reporting, and dissemination plans of this research were carried out without the involvement of any patients or members of the public.

Discussion

CFS patients are experiencing long-lasting profound fatigue and always accompanied affecting various bodily systems [32]. Although the symptoms are complex and varied, we can categorise them into two groups, somatic symptoms and mental symptoms. For example, fatigue, digestive disorder, and insomnia are somatic symptoms, while anxiety, depression, and even bad ideas in the mind are all mental symptoms. These two interact with each other. Evidence suggests that fatigue is closely linked to functional alterations within specific regions of the brain [33]. These changes affect the brain's ability to carry out cognitive and motor functions, finally lead to somatic symptoms. On the other hand, somatic symptoms such as fatigue and insomnia can in turn affect a person's mind, exacerbating anxiety and depression, for example. Therefore, adjusting the mind and body at the same time is the key to treating CFS.

Existing therapies mostly concentrate on one kind of symptom management, for example, CBT, which allows individuals to appreciate their condition, adjust their way of life and decrease their energy expenditure, consequently, reducing fatigue [34]. This therapy improves CFS by improving the patient's perspective, i.e. mental symptoms. However, in the QTT, either Qigong or Tuina can have a positive impact on both somatic symptoms and mental problems [35–37]. So QTT can treat CFS from two sides. Traditional Chinese medicine (TCM) suggests that fatigue arises from a lack of Qi and Yang energy in the body [38]. Both Qi and Yang energy can boost the body's metabolism, provides energy to carry out activities and raise spirits. QTT is a therapy that combines Qigong and Tuina. Tuina can generate heat, which corresponds to the concept of Yang energy in TCM. Similarly, Qigong can cultivate Qi within the body of practitioners, as its name suggests. Therefore, QTT can alleviate fatigue by supplying Qi and Yang energy to the body.

Fatigue is the primary symptom of CFS. Therefore, we employed the MFI-20 as the primary index of efficacy. CFS patients often suffer severely from fatigue and it greatly impacts their daily lives. Additionally, we used the SF-36 as a secondary efficacy index, to monitor whether the treatment enhanced the quality of life of the patients post-treatment. Insomnia is both a symptom of and a cause of CFS, and the two conditions interact with each other [39]. Therefore, improving sleep can lead to an improvement in CFS. Additionally, massage therapy has been shown to effectively improve sleep quality [40]. As a secondary outcome indicator, we employed the PSQI to assess the improvement of patients' sleep. Due to the long-term effects of fatigue and insomnia, patients may be susceptible to anxiety and depression [41]. Tuina, Qigong and CBT can all have a favorable impact on the psychosocial wellbeing of patients, improving their emotional and psychological state [36, 37, 42]. Therefore, we used the HADS to evaluate the psychological improvement of the patients in both groups.

In a prior study, it was discovered that functional magnetic resonance imaging (fMRI) of CFS patients displayed irregularities in the construction and connectivity of brain regions, especially in the right superior frontal gyrus (SFG), left median cingulate gyrus (DCG), left middle occipital gyrus (OG) and left middle temporal gyrus (MTG) [43]. Therefore, we utilised fMRI to observe alterations in the patient's brain region and analysed the mechanism of action of QTT.

However, this study still has limitations, such as its inability to implement a double-blind procedure (blinding both patients and operator) due to the nature of the intervention. And this is a single-centre experiment, the enrollment of patients has regional limitations..

In all, we carried out this experiment to present the efficacy of this therapy, elucidate its mechanism for treating CFS, explore a novel and effective method for treating CFS, and finally disseminate the therapy.

Trial status

At the time of submission, recruitment for the trial has been started. The first participant was included on 16 March 2024. The study is scheduled to end in December 2025.

Acknowledgements
The authors would like to would like to express their heartfelt gratitude to all trial participants, including study coordinators, participants, and their families, for their invaluable contributions and unwavering dedication to this trial.

Authors' contributions
HH and GA contributed to the concept and design of the study. FX and JC established the hypothesis and wrote the original proposal. HH, GA, JC, HY, FX, CX and JM contributed significantly in creating the manuscript. FY and GW performed critical revisions of the manuscript. HH drafted the manuscript and prepared figures and table. All authors read and revised the final version of the manuscript and will approve the final version.

Funding
This study has been partly funded by Future Plan for Traditional Chinese Medicine Inheritance and Development of Shanghai Municipal Hospital of Traditional Chinese Medicine (WLJH2021ZY-ZYY011). The sponsor, Shanghai Medical Innovation Development Foundation, is not involved in the trial's conduct, data collection, or statistical processing. The final trial results and publication of any reports are independent of the sponsor.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Competing interests
The authors declare no competing interests.

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Received: 1 April 2024 Accepted: 29 January 2025
Published online: 14 February 2025

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