The effect of the Prolong Life With Nine Turn Method (Yan nian jiu zhuan) Qigong on patients with chronic fatigue syndrome: Study protocol for a randomized controlled trial

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Study protocol

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Abstract

Background Chronic fatigue syndrome (CFS) is characterized by persistent fatigue, which often leads to physical and psychological damage. However, there is currently no clear explanation for this syndrome. Most treatments are based on symptoms, and cognitive behavioral therapy (CBT) is considered to be one of the most effective treatments. Little is known about the Prolong Life With Nine Turn Method (PLWNT) Qigong, a combination of complex two-way traffic path connecting the cognitive center and the enteric nerves. In this study protocol, we explored the effectiveness of PLWNT on gastrointestinal function, physical and mental fatigue, and sleep quality in patients with CFS. Methods/design A randomized controlled trial consisting of 90 patients will be divided into treatment A and B groups. The treatment group will be treated with either CBT or PLWNT. Both treatment groups will include a supervised intervention at the Shanghai University of Traditional Chinese Medicine once a week, and the remaining six days will be completed at home over 12 consecutive weeks. Both treatments will take three months. Qualified participants in accordance with the inclusion criteria and signed informed consent will be recruited. The primary outcome variable is to explore the regulation mechanism of the brain-gut axis in patients with chronic fatigue and the Multidimensional Fatigue Inventory (MFI-20). Secondary outcomes are the Short Form 36-item Health Survey (SF-36), Pittsburgh Sleep Quality Index (PSQI), and Hospital Anxiety and Depression Scale (HADS), which will be completed before and after the intervention. Discussion This will be the first randomized controlled clinical trial to introduce the PLWNT method for the treatment of CFS. If our results demonstrate that CBT or PLWNT nterventions are more effective, this will provide a quality treatment for patients with chronic fatigue and optimize their guidance.

Background

Chronic fatigue syndrome (CFS) is a complex chronic medical condition characterized by symptom clusters, including pathological fatigue and malaise, that get worse after exertion, cognitive dysfunction, immune dysfunction, unrefreshing sleep, pain, autonomic dysfunction, and neuroendocrine and immune symptoms.[1] Most research on CFS has been conducted using a broad definition of CFS. The International Chronic Fatigue Syndrome Study Group criteria for the illness, often termed the Fukuda criteria, require at least six months of unexplained fatigue, together with the concurrent presence (for at least six months) of at least four of eight symptom criteria (unrefreshing sleep, self-reported impairment in short-term memory or concentration, sore throat, tender cervical or axillary lymph glands, muscle pain, multi-joint pain without joint swelling or redness, headaches of a new type, pattern, or severity, and post-exertional malaise lasting more than 24 h). [2] Depending on the criteria of definition used, CFS affects between 0.006% and 3% of the population.[3] There has been a high occurrence of fatigue, sleep disturbance, psychiatric comorbidity, and cognitive symptoms [4–7]. The functional impact of CFS was classified as mild for 20%, moderate for 66%, and severe for 14% of patients.[8]

CFS is diagnosed very rarely, which may be associated with the fact that the etiology of the disease is still poorly known, with diagnostic problems resulting from a lack of detailed and uniform guidelines allowing

an unambiguous diagnosis.[9] There is no pharmacological cure for the illness. Various drugs such as NSAIDs, antidepressants, and COX-2 inhibitors are only used in order to help relieve and manage the symptoms, especially in cases in which there is a specific medical intervention using highly individualized treatments. [10]Additionally, the use of antidepressants is controversial and has significant side effects.[11, 12] Several reviews have concluded that cognitive behavior therapy (CBT) seems to be a promising treatment for CFS.[13, 14] However, few people show persistent or sustained significant outcomes in this patient population.[15] Various non-pharmacological treatments have been explored in recent years, and complementary and alternative medicine (CAM), which is widely perceived to be “natural”, is one of the most promising treatments for CFS[16 17]. Many CAM modalities, such as traditional Japanese herbal medicine (Kampo)[18], acupuncture[19], and Qigong[20], have demonstrated to be an effective treatment and prevention method in relieving fatigue, depression, and insomnia. Qigong (pronounced “chee gung”) is a branch of Traditional Chinese Medicine (TCM) that includes two theories: “qi,” the vital energy of the body, and “gong,” the training or cultivation of qi[21]. The practice of Qigong combines breathing, movement, and meditation, and therefore it is often classified by Western providers under the category of “mind-body medicine”[22].

Evidence to date supports Qigong’s potential benefits of improving depression, quality of life, and motor function in patients with CFS, such as Tai Chi,[23] Baduanjin (also called Eight-Section Brocades,□□□)[24] and Liuzijue[25]. More importantly, Qigong can promote beneficial changes in the central nervous system (CNS), including favorable changes in the dopaminergic and other neurochemical systems, and depression, anxiety in the sympathetic nervous system (SNS) and/or hypothalamic-pituitary-adrenal axis (HPAA), perceived stress levels, fibromyalgia, pain, and hormonal changes [26, 27]. The PLWNT method is a kind of Chinese Qigong, including eight kinds of massage manipulations on the abdomen and a kind of upper body shaking, which can strengthen the connection between the brain and the intestine through the Brain-Gut Axis, and connect the cognitive and emotional centers with the neuroendocrine and intestinal system immunity. PLWNT, with its nine techniques, is easy to master and has low requirements for the body and cognition of the practitioner. It will be popular as a safe Qigong exercise that prolongs life, cures health, relieves fatigue, and regulates pain, sleep, mood, and gastrointestinal discomfort.

However, no one has studied the regulation of CFS by PLWNT in spite of its long history. In this study protocol, we will design an RCT to study a PLWNT intervention on CFS based on the brain-intestinal axis regulation theory to observe the patients’ fatigue symptoms, gastrointestinal function, sleep quality, anxiety, and depression.

Methods/design

Design

The study was designed as a randomized, evaluators and statisticians blinded, parallel-controlled trial. It will be conducted at the Shanghai University of Traditional Chinese Medicine and the Yueyang Hospital

of Integrated Traditional Chinese and Western Medicine. Participants

will be allocated to the PLWNT group and CBT group. The PLWNT group will be treated with Qigong and the CBT group will be treated with cognitive behavior therapy.

Setting of the study

Ninety CFS patients fulfilling the conditions for recruitment of this study will be randomly divided into the PLWNT group and CBT group, distributed according to a 1:1 allocation ratio for a sample size of 45 in each group. However, taking into account the shedding of clinical cases, we estimated that this study would require a sample size of 60 in each group, allowing a 25% dropout. The participants in the PLWNT group and CBT group will receive a 12 consecutive weeks' treatment and conduct a weekly supervised exercise at the Shanghai University of Traditional Chinese Medicine, taught by a dedicated senior faculty teacher. The number of exercises at home is not less than six times per week. The total study time will take 21 weeks: a screening period of 1 week, a treatment period of 12 weeks, and a follow-up period of 8 weeks. The study flow is depicted in Figure 1.

Randomization and allocation concealment

The eligible participants will be randomly allocated into the PLWNT and CBT groups according to a 1:1 equal proportion rule after the post-baseline assess. 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 sequences in order. The sequence is then placed in a non-transparent envelope by a specified project manager who is not involved in the recruitment, and it is ultimately handed over to the group of researchers. Prior to the implementation of the random assignment, the group of researchers will record details of each participant in the clinical center including new participants (name, date of birth, and participant and center code, including date) in case of reporting and preparation of a signed informed consent. Additionally, after a revision of the participant's information by the group of researchers to determine if the participant meets the inclusion criteria, a sequence will be randomly selected from the envelope to be labeled on the patient's data, assigned to each group and informed to the participant.

Informed consent

Prior to the start of the trial, the participants will be briefed on the course of the study and informed about their responsibilities. They will be informed of the physical examinations and precautions. Most importantly, they will be informed that their participation is entirely voluntary, and they can refuse or withdraw at any time, which will not affect their medical or other benefits. Once the participant withdraws, the collected data will not be deleted and will be used for the final analysis. A written informed consent of

each participant should be obtained prior to the initiation of any study-related treatment. A research assistant will be responsible for obtaining informed consent from all participants.

Participants

Participants meeting the following criteria will be included.

(1) Age between 2060 years; no gender requirement;

(2) Severe chronic fatigue that is unexplained after clinical evaluation and has a history of no less than six months. Fatigue is not caused by the work performed in the trail, and cannot be alleviated after rest;

(3) At least four from the following eight items: (a) Memory or attention drops. Its severity has led to a substantial decline in work capacity, ability to receive education, and ability to engage in social activities and personal life. (b) Sore throat; (c) Tender neck or axillary lymph nodes; (d) Muscle pain; (e) Migratory polyarticular pain without redness and swelling; (f) The type of attack, and type and severity of headaches different from before; (g) Cannot be alleviated after rest; and (h) More than 24 ho of muscle pain after exertion;

(4) Blood, urine routine tests, and liver and kidney functions are normal;

(5) Has not received any other treatment plan within one month;

(6) Agreed and signed the informed consent.

Participants meeting any of the following criteria will be excluded.

(1) No fatigue complaints, or less than four symptoms;

(2) Severe cardiovascular and/or cerebrovascular diseases, endocrine system diseases, sports system diseases, autoimmune diseases, infectious diseases, diabetes, or other mental diseases;

(3) Taking drugs that may affect the outcome judgment;

(4) Fatigue symptoms can be alleviated after rest;

(5) Fatigue symptoms do not cause a substantial decline in work ability, educational ability, social activities, recreational activities, and personal life skills;

(6) A definitive diagnosis of gastrointestinal organic disease, liver and kidney dysfunction, tumor, or other diseases;

(7) Pregnant or lactating women, drug addiction, heavy metal poisoning, etc.

Participants meeting the following criteria will be excluded after the trial starts.

(1) The patient has severe physical discomfort or adverse reactions;

(2) Subject requested withdrawal of informed consent;

(3) The investigator considers it necessary for the subject to discontinue the study from a medical perspective.

Intervention

PLWNT group

PLWNT includes eight kinds of massage manipulations on the abdomen and an upper body shake, which integrate the technique of abdominal massage and Qigong guiding. The exercise promotes gastrointestinal motility and secretion and promotes the intestinal nerve chain connection with the advanced nerve center, so as to achieve a state in which the body, mind, and spirit are relaxed and harmonious (Figure 2). A Qigong teacher of Shanghai University of Traditional Chinese Medicine who has been engaged in Qigong education for at least five years will lead a concentrated supervision exercise and correct the exercise posture during the whole intervention period for one hour once a week. The teacher will first lead a five-minute stretching and relaxation exercise that will be performed before the Qigong exercise, and then the teacher will introduce and demonstrate each movement, explain the precautions, and answer questions from participants for five minutes. Subsequently, the teacher will give individual guidance to 15 participants by correcting their movements for 30 minutes. Finally, all the participants will practice Qigong together for 20 minutes. Participants in the intervention group will be advised to practice Qigong for at least 30 minutes every day, and a “Working Practice Record” will be handed out and the subjects, who will be required to fill it after each exercise. The entire treatment process will last for 12 weeks.

CBT group

The experts in relevant fields will be invited for the CBT group to make lectures or psychological counseling on CFS prevention and treatment once a week for two hours. The remaining six days of self-psychological counseling at home are to ensure that the interventions are similar to those of the Qigong group. Treatment will last for 12 weeks. CBT is a psychotherapeutic approach in which elements of behavioral therapy and cognitive therapy approaches are incorporated. In CBT, links are made between the person’s feelings and the patterns of thinking that underpin his or her distress. We will invite qualified CBT therapists possessing appropriate professional qualifications for the provision of CBT (e.g., diploma in CBT, or other professionally accredited qualifications involving CBT as a major part of training [e.g., a clinical or counseling psychologist degree]).

Screening Measures and Demographics

This study will collect the online screening questionnaire, which includes (1) the CDC diagnostic checklist for CFS[28]; (2) a list of medical illnesses based on the CDC exclusion criteria for CFS; (3) socio-demographic data, including age, gender, employment status, educational level, marital status, and nationality; (4) lifestyle variables, including smoking, alcohol consumption, and physical activity or exercise habits; and (5) anthropometric variables, including weight, height, and blood pressure, also measured at baseline.

Outcome measures

The outcome assessment includes the following items: changes in functional connectivity between multiple brain areas, mental and physical fatigue, anxiety and depression, health status, and sleep quality. The relevant primary outcomes, secondary outcomes, and related self-assessment scale measurement such as Multidimensional Fatigue Inventory–20 (MFI–20), Short Form 36-item Health Survey (SF–36), Pittsburgh Sleep Quality Index (PSQI), and Hospital Anxiety and Depression Scale (HADS) will be assessed at the baseline and at 13 weeks (at the end of intervention). Changes in functional connectivity between multiple brain areas, characteristics of brain network activation, and the gastrointestinal microbiome will be tested by the doctors who are experienced in the corresponding departments but not involved in this trail at the Shanghai Yueyang Hospital of Integrated Traditional Chinese and Western Medicine. The detailed outcome assessment time points are provided in Table 1.

Primary outcomes

Multidimensional Fatigue Inventory–20 (MFI–20)

Mental and physical fatigue will be measured by the Multidimensional Fatigue Inventory–20 MFI–20, which is a 20-item self-report instrument designed to measure fatigue. It covers the following dimensions: General Fatigue, Physical Fatigue, Mental Fatigue, Reduced Motivation, and Reduced Activity. MFI–20 consists of 24 statements for which the person has to indicate on a 7-point scale to what extent the particular statement applies to him or her. The statements refer to aspects of fatigue experienced during the previous days. Higher scores indicate a higher degree of fatigue.[29]

Secondary outcomes

1. Changes in functional connectivity between multiple brain areas and characteristics of brain network activation

Changes in functional connectivity between multiple brain areas including the relationship between the insula, precuneus, thalamus/striatum, cerebellum, occipital and temporal structures, hippocampus, parietal lobule,, and characteristics of brain network activation will be explained by temporal changes in functional connectivity between multiple brain areas. These changes and characteristics will be assessed by using Siemens 3.0-T MR scanner with a 32-channel head coil.

2. Short Form 36-item Health Survey (SF–36)

Health status will be assessed using the Short Form 36-item Health Survey (SF–36), which includes 36 questions related to an individual's QOL that is summarized in two component summary scores: the Physical Component Summary (PCS) and the Mental Component Summary (MCS) scores.[30] The SF–36 evaluates the following eight physical and mental health areas: physical functioning (PF), physical role functioning (RP), bodily pain (BP), general health (GH), vitality (VT), social role functioning (SF), emotional role functioning (RE), and mental health (MH) (7). Each of the eight areas is scored on a scale of 0–100, where a higher score indicates better health subjectively. These scores are calculated from the questionnaires as described previously.[31]

3. Pittsburgh Sleep Quality Index (PSQI)

Sleep quality will be measured by the Pittsburgh Sleep Quality Index (PSQI), which is a self-rated questionnaire that assesses sleep quality and disturbances over a one-month time interval. Nineteen individual items generate seven "component" scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The sum of the scores for these seven components yields one global score.[32] The total score ranges from 0 to 21, and the higher the score, the poorer the sleep quality.[33]

4. Hospital Anxiety and Depression Scale (HADS)

Anxiety and depression will be assessed using the Hospital Anxiety and Depression Scale (HADS). The questionnaire comprises seven questions for anxiety and seven questions for depression and takes 2–5 min to complete. Although the anxiety and depression questions are interspersed within the questionnaire, it is vital that these are scored separately.[34] In most studies, an optimal balance between sensitivity and specificity is achieved when caseness is defined by a score of eight or above on both HADS-A and HADS-D. A sensitivity and specificity for both HADS-A and HADS-D of approximately 0.80 are very similar to the sensitivity and specificity achieved by the General Health Questionnaire (GHQ). Correlations between HADS and other commonly used questionnaires are typically in the range of 4983[35].

Adverse events and safety measurements

Adverse events (AEs) can be any adverse and non-significant signs (including abnormal experimental findings), symptoms, and diseases associated with the study in time, regardless of drug-related causes.[36] Most authors declared that Qigong is a relatively safe approach for various conditions, including hypertension. No severe AEs have been reported. If unexpected AEs occur, defined as any functional lesion caused by the intervention, such as headache, dizziness or vertigo, distension of head, tinnitus, stuffiness in the chest and worsening shortness of breath, heart-pounding or palpitations, muscular soreness or pain, profuse cold perspiration, irritability, neurasthenia, hallucination and paranoia, and psychological stress, regardless of whether it is related to treatment, the nearest affiliated Shuguang Hospital doctor will be notified in time, and he/she will make judgments and start medical treatment.

If serious AEs occur, the investigator will report to the primary investigator and ethics committee to determine whether the participant needs to withdraw from the study and treatment. The investigator will do the utmost to prevent and treat the damage that may result from this study. If, according to the experts' committee, the adverse event is related to the treatment of the Qigong, the research team will provide the cost of treatment and the corresponding financial compensation for the damage related to the trial.

Statistical analysis

Collected information will be entered into Excel, and the Statistical Package for the Social Sciences (SPSSversion18.0, SPSS Inc., Chicago, IL, USA) will be used to statistically analyze the data. Continuous variables will be summarized by the mean and standard deviation (SD), and median (IQR) interquartile range will be used for non-normal distribution. Categorical variables will be presented by frequency or percentages. The chi-square test will be used to measure the comparability between-group differences for counting data. Analysis of variance will be applied to measurement data such as age and the fatigue scale. For normal distributions of measurement data, independent t tests will be used to compare the differences between groups. Normality will be tested using the Kolmogorov Smirnov test. Two-sample independent sample t tests will be used for the between-group differences, and the effect size will be calculated by Cohen's d statistics. For within-group comparisons, we will use the paired t test. Additionally, demographic characteristics between the two groups, baseline measurements, and changes in measurements from baseline to completion of the study will be analyzed using two-sample independent t tests. If the baseline measurements are different, we will use covariance analysis (ANCOVA) to control the baseline when comparing the two groups. The clinical overall efficacy evaluation will be performed using a nonparametric test of two independent samples. If the number of volunteers on the subject is too short or there is some missing data, the Mann–Whitney U-test will be used to evaluate the difference between the groups. A P-value less than 0.05 indicates that the difference is statistically significant.

Ethics issue

The study protocol is carried out in accordance with the Declaration of Helsinki and the International ethical guidelines for biomedical research involving human subjects.[37, 38] This study protocol and consent forms were approved by the Ethics Committee of the Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai Affiliated Hospital of Shanghai University of Traditional Chinese Medicine (approval number: 81774443) and both were registered in the Clinical Trial Registry (WHO ICTRP member). The registration number is NCT03496961.

All participants will be fully informed about the inclusion and exclusion criteria for this study prior to the start of the trial, sign the informed consent form prior to the trial, and be informed of the right to withdraw from the trial at any time. Both recruitment and randomization will be open. If our research protocol changes, we must submit a written application to the Research Ethics Committee. Committee members will decide if it is necessary to change the protocol plan. Upon completion of the clinical study, we will submit a study completion report.

Discussion

The impact of chronic fatigue on individuals and society is great, affecting not only the physical and mental health of individuals but also the social development and the economy. [1, 39] However, CFS, although highly debilitating, has so far lacked an effective treatment. What is more regrettable is the limited use of evidence-based interventions designed to control symptoms and improve the patient's functions. Qigong therapy, one of the traditional Chinese wellness practices, is a gentle low-impact mind-body aerobic exercise that mainly emphasizes the combination of the "three regulations": body focus (posture and movement), breath focus, and mental focus (meditative components).[40] It is simply referred to as optimizing and restoring the body, mind, and spirit[41]. Qigong is a relatively safer and more effective treatment for treating CFS compared with other therapy methods.[42] It does not require sports space or sports equipment. In recent years, more and more studies have confirmed that Qigong can help to reduce anxiety, improve sleep, and has beneficial effects on the digestive and endocrine systems, both of which contribute to physical and mental health.[43–46]

PLWNT is one of the traditional exercises. It was written by a hundred-year-old man named Kai Fang in the Qing Dynasty, and it has a long history. However, no one has ever studied the influence of PLWNT on CFS. According to the self-massage exercise rule, the phrase emphasizing that "Insufficient supplementation, shed excess" is of great significance. Other phrases such as "Why borrow medicine to burn Dan, if oneself has the ability to remove disease and prolong life-span?" are found in Yi Shen Ji. PLWNT is composed of eight kinds of massage manipulations on the abdomen and a kind of upper body shaking. It is characterized by static work as an aid, focusing on the manipulation of the abdomen in terms of breathing and thinking regulation, the main use of normal abdominal breathing, gradually increasing the concentration of thinking in the lower Dantian.[26] More importantly, during a session, the participants can practice while lying down or sitting, completely free from time and space constraints.

The effect of PLWNT is mainly to strengthen the connection between the brain and the intestine through the Brain-Gut Axis (BGA), which affects the digestive and nervous systems. The connection between the two systems is strengthened primarily through the BGA, which is a complex two-way communication pathway that links the neuroendocrine, intestinal, and immune systems. Abdominal manipulation can stimulate the abdominal and intestinal smooth muscles, enhance gastrointestinal motility, regulate abdominal blood flow and lymphatic system function, and improve the peristaltic function of large and small intestines, effectively preventing digestive diseases. At the same time, the pain, emotion, and behavior of the nerve chain linked to the central nervous system and the high-grade nerve center strengthen the connection between the brain nerve and the gastrointestinal digestive system to regulate fatigue, sleep, and mood. In addition, abdominal manipulation can affect the fat in the abdomen, which can help to prevent diseases such as obesity. In previous studies, Qigong improved fatigue, depression, and sleep in patients with CFS.[46, 47] However, so far, no studies have been conducted to introduce PLWNT Qigong to regulate fatigue, depression, and sleep. Although in recent years the PLWNT has become an area of interest for both researchers and clinicians, few related interventions have been proposed or tested. This study will use some advanced instruments including a Siemens 3.0-T MR scanner with a 32-channel head coil and self-evaluation scales to test how PLWNT improves the fatigue, depression, and sleep symptoms of CFS patients through the BGA.

Although the findings of our study are promising, there are several notable limitations. First, the screening of the participants into the inclusion criteria is based solely on the self-evaluation scale with no specialized mental and psychological testing equipment, which leads to the inclusion of CFS patients is not strict. However, the probability of chronic fatigue caused by medical and mental illness is reduced by questionnaires that limit the age of participants who are recruited between the ages of 20 and 60. Second, there may be some potential limitations to the protocol. Ideally, each participant should be blind to the procedure, but this is difficult to achieve in non-pharmaceutical trials, so performance bias may be unavoidable. However, we will make an effort to ensure that laboratory technicians, data managers, and statisticians are not involved in both the recruitment and processing of the subject's data. Finally, the results of the study are limited to ≤60-year-old participants, so the results cannot be extended to the elderly.

Despite the above limitations of the study, there are still many advantages. Compared with other treatments, such as medication and psychological counseling, Qigong has distinct advantages for CFS patients, as it is easy to learn, it is self-administered, and it is not limited by time and space. In addition, this is the first Qigong study conducted to achieve therapeutic effects by connecting the intestines and brain. More importantly, no one has ever studied PLWNT Qigong so far. Finally, we use posters and social platforms to recruit individuals at various social levels, which may increase the sample representativeness.

In short, this is a strict, complete, randomization, and adequate concealment RCT study. There has been no published report about the effect of the PLWNT Qigong exercise. If this study demonstrates a

significant intervention effect of PLWNT, it will validate a higher quality treatment for patients with chronic fatigue compared to the current treatment options, and it will optimize their guidance.

Trial status

The clinical registration of this trial was completed on April 12, 2018. The current version of the protocol that has been approved by the Yueyang Hospital of Integrated Traditional Chinese and Western Medicine human research ethics committees is 5.0 (June 5, 2018). The first patient was recruited on December 1, 2018. It is expected that the recruitment (N = 135) will be completed by June 2021.

Abbreviations

PLWNT: Prolong Life With Nine Turn Method; CBT: Cognitive Behavioral Therapy; CFS: Chronic Fatigue Syndrome; MFI–20: Multidimensional Fatigue Inventory; SF–36: Short Form 36-item Health Survey; PSQI: Pittsburgh Sleep Quality Index; HADS: Hospital Anxiety and Depression Scale.

Declarations

Acknowledgments

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Authors’ contributions

The study was conceived and designed by FFX; FY, JCT, GC, YLY, and WJY were responsible for planning the draft. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

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Availability of data and materials

This trial is ongoing and the data will be shared through scientific articles.

Ethics approval and consent to participate

The study protocol is carried out in accordance with the Declaration of Helsinki and International ethical guidelines for biomedical research involving human subjects. This study protocol and consent forms were approved by the Ethics Committee of Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai Affiliated Hospital of Shanghai University of Traditional Chinese Medicine (approval number: 81774443) and registered in Clinical Trial Registry (WHO ICTRP member). The registration number is NCT03496961. All participants provide informed consent prior to participation.

Consent for publication

The images in Figure 2 is called Chong Guan and is one of the authors of this article. He agrees to use this images and the images will be freely available on the internet and may be seen by the general public. He is agree to made available to the Editor if requested, and will be treated confidentially.

Competing interests

The authors declare no competing interests

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Table 1

Due to technical limitations, Table 1 is only available as a download in the supplemental files section.

Figures

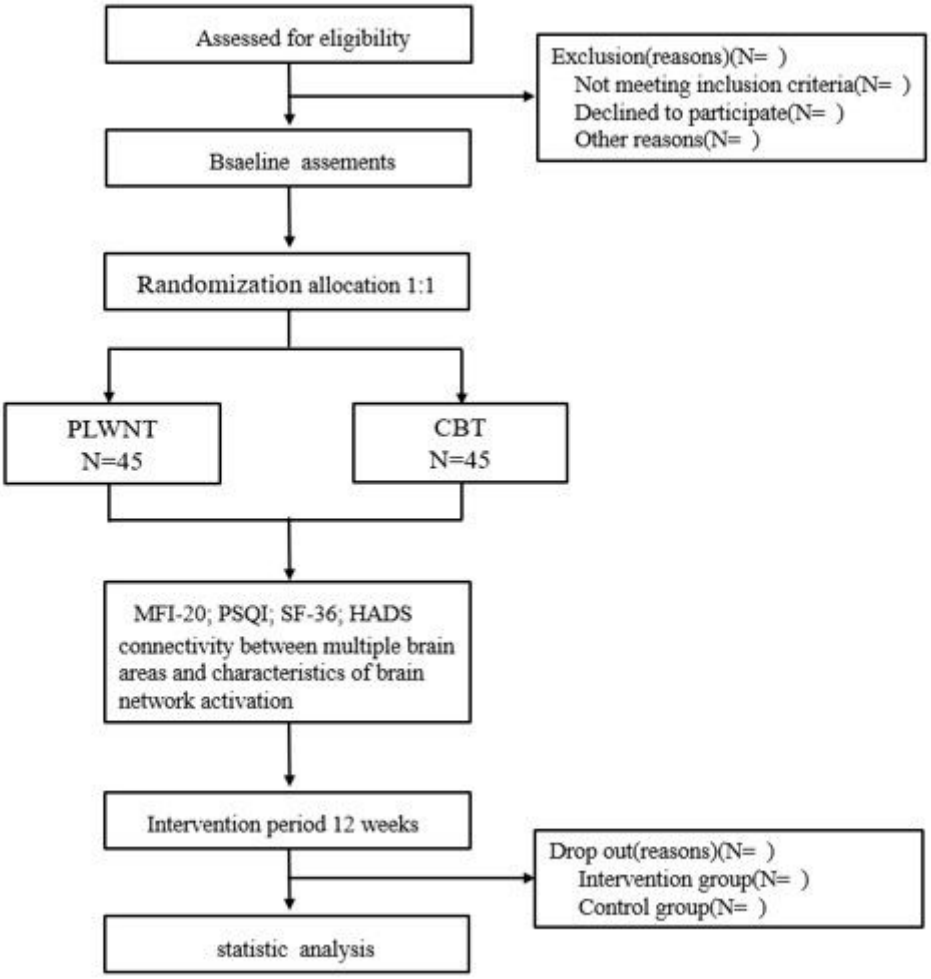

Figure 1

Flow diagram of study design.

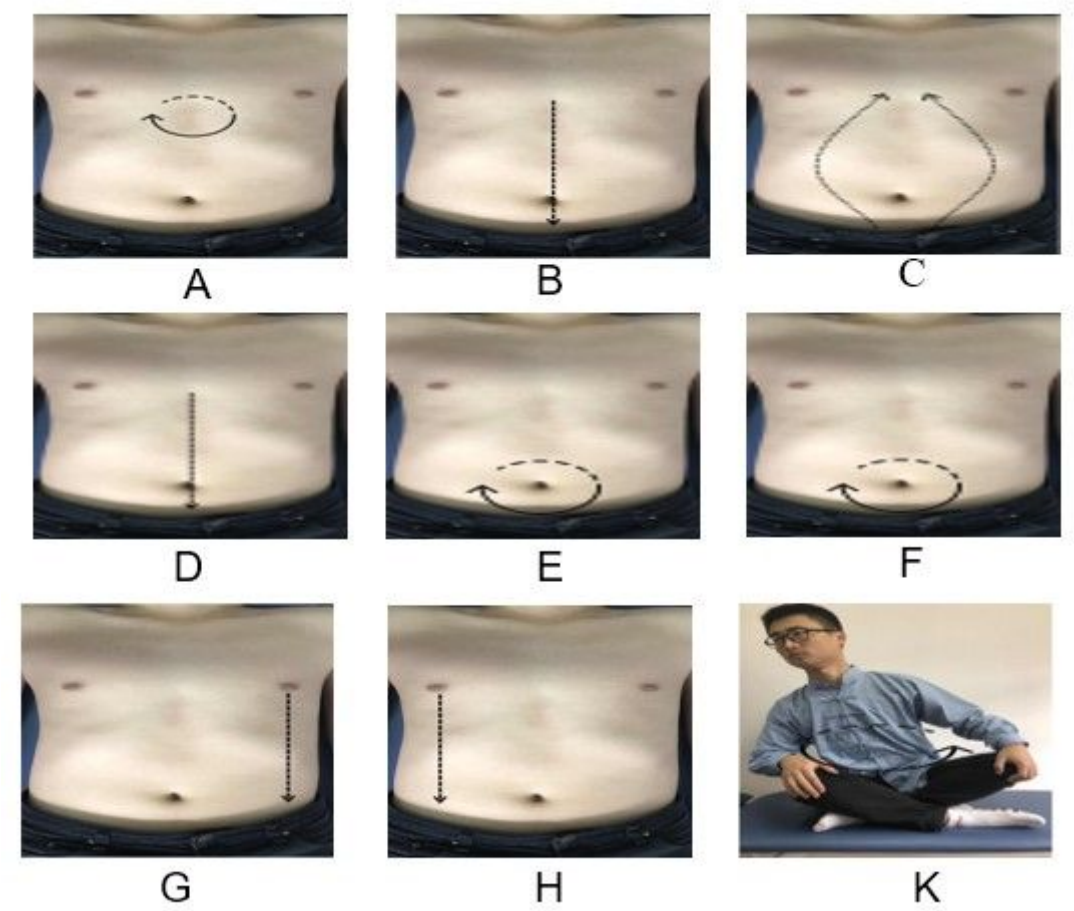

Figure 2

The postures of PLWNT. (A)Press and knead acupoint in Shanzhong.(B) Rubbing from Shanzhong Acupoint to Pubic Symphysis. (C) Rubbing from Pubic Symphysis to Shanzhong Acupoint. (D) Pushing from Shanzhong Acupoint to Pubic Symphysis. (E) Rubing with the right hand from the left. (F) Rubing with the left hand from the right. (G) Pushing with the right hand from the left breast to the groin. (H) Pushing with the left hand from the right breast to the groin. (K) Turn left and right. Every movements will be carried out 21 times.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.xlsx
- SPIRITChecklistforTRLSD18003431.doc