












BMJ Open Tai Chi postural training for dyskinesia rehabilitation: a study protocol for a randomised controlled trial in convalescent ischaemic stroke patients

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ABSTRACT

Introduction Acute ischaemic stroke (AIS) is not only seriously damaging to the physical and mental health of patients, but also has become a major social public health problem. Effective dyskinesia rehabilitation treatment in convalescence is of great significance for AIS patients' prognosis and quality of life. Tai Chi (TC) shows great potential in improving motor function. This trial aims to evaluate the clinical efficacy of modified TC postural training (TPT), and to explore the related central-peripheral neurotransmitter mechanisms.

Methods/design The proposed study will be a multicentre randomised controlled trial. The trial will randomise 120 eligible AIS patients in a 1:1 ratio to receive TPT or Bobath rehabilitation training. Each training session will last 40 min and will be implemented once a day and five times per week (from Monday to Friday) in a duration of 4 weeks. After finishing the 4-week treatment, another 3-month follow-up period will be seen. Root mean square generated from the surface electromyogram (sEMG) will be the primary outcome. Other sEMG time-domain parameters and frequency-domain parameters and clinical scales assessment will be the secondary outcomes. Peripheral blood samples will be collected at baseline and at the end of 4-week treatment, which will be used to explore the related therapeutic mechanisms. Intention-to-treat analysis and per-protocol analysis will both be implemented in this trial.

Ethics and dissemination The study has been approved by Ethics Committee of Dongzhimen Hospital Affiliated to Beijing University of Chinese Medicine, being granted approval numbers DZMEC-KY-2020-22. The research results will be disseminated through (open access) peer-reviewed publications and presentations at conferences.
Trial registration number ChiCTR2000032999.

INTRODUCTION

Stroke is a type of cerebrovascular disease characterised by high morbidity, high disability rate and high mortality. An authoritative survey revealed that stroke had become the leading cause of disability and the second-leading cause of death around

Strengths and limitations of this study

- To the best of our knowledge, the study is the first randomised controlled trial evaluating the effect of modified Tai Chi postural training (TPT) for dyskinesia rehabilitation in convalescent ischaemic stroke patients by objective parameters (produced by surface electromyogram).
- Neurotransmitter detection will be helpful to explore the therapeutic mechanism of TPT for rehabilitation on dyskinesia.
- Due to the characters of the intervention, the trial could not be double blind. But the electronic data capture system will contribute to quality control of the trial.
- Changes in the patient's condition and a relatively long follow-up period may increase the patient's drop-out rate.

the world.¹ According to the epidemiological investigation, the incidence rate of stroke in China is as high as 116–219 per 100, 000 person-years, showing an increasing trend in the past years.² Previous studies showed that there were about 7 million stroke patients in China, among whom about 70% account as acute ischaemic stroke (AIS) patients.^{3,4} The mortality rate of hospitalised patients with AIS in China was 9%–9.6%. Meanwhile, the mortality/ disability rate was 34.5%–37.1% 3 months after onset. When the stroke onset is 1 year, the mortality rate was 14. 4%–15. 4% while the mortality/disability rate was 33.4%–33.8%.^{5,6} AIS has gradually become a major social public health problem because it not only seriously impairs motor function of AIS patients but also aggravates their mental anxiety.⁷ Since the motor function level of AIS patients is closely related to the prognosis and quality of life, it is particularly important to

carry out effective rehabilitation of dyskinesia especially in convalescence.

Currently, novel training methods based on virtual reality (VR) technology have been successively applied to the motor function rehabilitation of AIS patients. A number of small sample studies have shown that technology-assisted VR training can effectively improve stroke patients' motor function, active range of motion and dynamic and static balance.^{8 9} In terms of motor learning after stroke, some scholars have proposed that implicit motor learning may have additional benefits for stroke patients with cognitive impairment or deficits,¹⁰ since it relies less on working memory resources.¹¹ In addition, different frequency and intensity of training will also affect the final rehabilitation effect.¹² Although different types of novel technology-assisted rehabilitation training have shown good efficacy, their high cost of equipment, or strict and specific patient population selection make it difficult to popularise.⁹ In Chinese stroke rehabilitation practice, manual therapy based on neurodevelopment treatment is still the mainstream,¹³ among which Bobath therapy is the most representative one. The overall principle of Bobath is to give full play to the initiative of patients under the premise of controlling the abnormal movement mode of patients. Bobath rehabilitation also provides appropriate assistance to patients, completes joint and muscle group training, and maximises recovery of limbs motor function. Although Bobath Concept has been widely used in stroke rehabilitation,^{14 15} its clinical effect on AIS patients with severe dyskinesia still has limitations.^{16 17} In brief, the treatment needs to be conducted one-on-one under the guidance of a professional rehabilitation therapist and usually lasts for a period of months to years. This not only challenges the medical level in the region where the patients live, but also increases the economic burden of patients.¹ Therefore, a simpler and more effective therapy is urgently needed for improving the motor function and reducing disability. Tai Chi (TC), which can complement the deficiencies of modern medical treatment in AIS rehabilitation, shows great potential in improving motor function^{18 19} and has been expected to be a new option.

For more than half a century, the scholars have conducted a great number of researches on TC from the perspectives of medicine, nutrition, psychology and biomechanics.²⁰ Among them, the clinical application value of TC has been drawn attention to particularly.²¹⁻²³ Studies have shown that TC is effective in the treatment of fibromyalgia and Parkinson's disease^{24 25} and in reversing the risk factors for stroke in middle-aged and elderly adults.²⁶ In a study of TC with Berg Balance Scale and other clinical scales selected as outcome measures, the results revealed that the effect of TC training was significantly better than that of the conventional rehabilitation treatment.²⁷ However, the previous studies are mainly focused on the integral TC routine and there is still a lack of clinical efficacy study on single postures after decomposition. Furthermore, TC is still not widely applied to

the AIS patients with severe dyskinesia. At the same time, there are few studies on the efficacy mechanism of TC. In recent years, some scholars have completed exploratory studies on the biomechanical mechanism, but not many studies pay attention to the correlation between TC and neurotransmitters. The research on the central-peripheral neurotransmitter mechanism of TC promoting the recovery of motor function in AIS patients is still a blank. This study not only aims to evaluate the clinical efficacy and safety of TC postural training (TPT), but also to explore the association between neurotransmitters and TC for promoting the rehabilitation of motor function in AIS patients. The results are promising to establish a foundation for further development of a new, simple, safe and effective therapy applying in convalescence of AIS.

HYPOTHESES

We speculate that AIS patients may be more prone to exercise-induced central fatigue, thereby inhibiting the recovery of motor function. The special TPT improve this state and promote the rehabilitation of motor function by reducing central fatigue, which may show better results than traditional Bobath therapy.

OBJECTIVES

Primary objectives

The primary objectives of the study are:

1. Clinical efficacy of TPT is verified in promoting the rehabilitation of motor function in AIS patients through advanced objective outcome measures.
2. Advantages of curative effect of TPT is verified in convalescence of AIS by comparing the objective outcome measures.

Secondary objectives

The secondary objectives of the study are:

1. Finding the evidence of the improvement in exercise-induced central fatigue in ischaemic stroke patients applying TPT, and exploring the related central-peripheral mechanisms.
2. Analysing the therapeutic targets, and providing evidence-based medical evidences for the application of TPT in dyskinesia rehabilitation of ischaemic stroke patients.

METHODS AND ANALYSIS

Study design, recruitment and procedure

This multicentre randomised controlled trial will be conducted at three trial sites in Beijing in mainland China: (1) Dongcheng Campus of Dongzhimen Hospital Affiliated to Beijing University of Chinese Medicine, (2) Tongzhou Campus of Dongzhimen Hospital Affiliated to Beijing University of Chinese Medicine and (3) Pinggu Campus of Beijing Hospital of Traditional Chinese Medicine Affiliated to Capital Medical University. A total of 120 participants meeting the inclusion criteria will

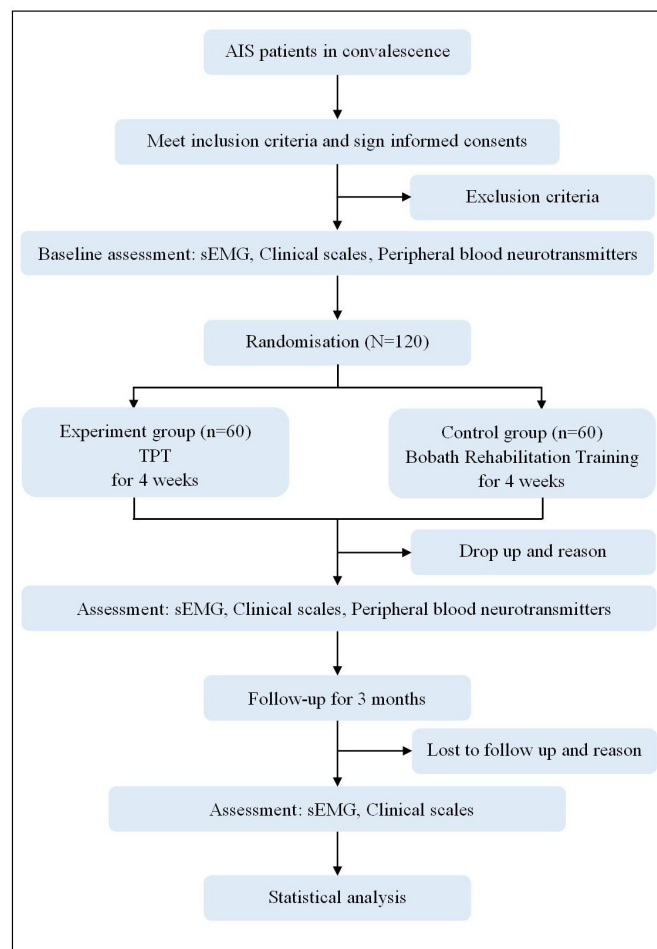


Figure 1 Flow chart of study procedure. AIS, acute ischaemic stroke; sEMG, surface electromyography; TPT, Tai Chi postural training.

be recruited from three trial sites. Patients can obtain specific public recruitment information through posters in the outpatient department or inpatient department. We will communicate with prospective participants about the study details. After the patient voluntarily signs the informed consent, he or she will be invited to participate in the trial. Recruitment will start from 1 June 2020, until when 120 participants are enrolled. The procedure of this trial is shown in [figure 1](#). The schedule of enrolment, intervention and assessments in this trial is shown in [table 1](#).

Eligibility criteria

Inclusion criteria

- ▶ In accordance with the diagnostic criteria of the ‘Chinese guidelines for diagnosis and treatment of AIS’ (2018 version),²⁸ and confirmed by CT or MRI examination.
- ▶ Aged 30–80 years old, male or female, right-handed habit.
- ▶ First episode of stroke or with a history of stroke but with no serious neurological dysfunction and modified Ranking Scale grade ≤ 2 .

- ▶ AIS patients who are in the subacute phase (from 2 weeks to less than 3 months after onset).
- ▶ With dyskinesia but muscle strength \geq III grade (including III grade).
- ▶ With symptom of lower limb hemiplegia but can walk more than six metres independently.
- ▶ Blood pressure is stable below 160/90 mm Hg.
- ▶ Enough cognition to follow commands and Mini-Mental State Examination score >24 .
- ▶ Never received standard Chinese or western medicine rehabilitation treatment before the study.
- ▶ No experience of TC exercise in the past.
- ▶ Patients or their legal guardians sign the informed consents.

Exclusion criteria

- ▶ Patients who meet the diagnostic criteria of AIS but are treated by thrombolysis or surgery.
- ▶ Younger than 30 years old or older than 80 years old; or aged 30–80 years old, but left-handed habit.
- ▶ The course of this disease is more than 3 months after onset.
- ▶ Although the onset of this disease resulted in dyskinesia, the muscle strength is less than III grade (excluding III grade).
- ▶ Patients with joint lesions that affect the motor function of the limbs.
- ▶ Patients with skin or muscle lesions of the extremities that affect surface electromyography (sEMG) examination.
- ▶ Patients with severe dysfunction of heart, lung, liver, kidney and other important organs and blood system.
- ▶ Patients with moderate and severe cognitive comprehension or visual impairment, unable to complete rehabilitation treatment and examination.
- ▶ Women during pregnancy or breast feeding.
- ▶ Patients who are participating in other clinical studies.

Participants withdrawal and dropout criteria

- ▶ Patients who require to quit initiatively.
- ▶ Patients with serious cardiovascular and cerebrovascular diseases and other systemic complications or serious adverse events, such as deterioration of the disease, requiring urgent measures.
- ▶ Patients who do not receive rehabilitation treatment as prescribed.
- ▶ Patients who do not complete the information recording as required and affect the outcome assessment.
- ▶ Patients who lost to follow-up.

Participants rejection criteria

- ▶ Patients who do not meet the inclusion criteria but is strayed.
- ▶ Patients who have been randomised but have not received rehabilitation treatment.

Table 1 Schedule of enrolment, intervention and assessments

Time point	Study period						Follow-up
	Enrolment	Baseline	Treatment				
	-1 week	0 week	1 week	2 weeks	3 weeks	4 weeks	
Enrolment							
Eligibility screen	X						
Informed consent	X						
Demographic information	X						
Descriptive information*		X					
Randomisation		X					
Allocation		X					
Intervention							
Tai Chi postural training			—————				
Bobath rehabilitation training			—————				
Assessments							
sEMG		X				X	X
NIHSS		X	X	X	X	X	X
BI		X	X	X	X	X	X
BBS		X	X	X	X	X	X
FMA							
5-HT		X				X	
DA		X				X	
Safety							
Adverse event	X	X	X	X	X	X	X
Physical examination	X	X	X	X	X	X	X
Neuroimaging examination		X				X	
Blood routine		X				X	
Urine routine		X				X	
Kidney and liver function		X				X	
Coagulation function		X				X	
Electrocardiograph		X				X	

*Descriptive information includes the personal general data, vital signs, clinical symptoms and signs, history of present illness, medical history, medication history and neurological examination.

BBS, Berg Balance Scale; BI, Barthel Index; DA, dopamine; FMA, Fugl-Meyer Assessment; 5-HT, 5-hydroxytryptamine; NIHSS, National Institutes of Health Stroke Scale; sEMG, surface electromyography.

Randomisation

A total of 120 eligible AIS patients will be randomly assigned into the experimental group or the control group (60 cases per group) in a 1:1 ratio with central randomisation method. The information of each selected participant will be uploaded to the electronic data capture (EDC) system of a third-party evaluation centre in real time. Then participants will be automatically randomised through the system network. The third-party evaluation centre is independent of the study and its EDC system passes the international certification. Four clinical research coordinators at three trial sites will be responsible for recruiting patients, using the EDC, and requesting randomisation.

Blinding

Due to the significant difference between the TPT and the Bobath rehabilitation training, masking the therapists is difficult. But patients, clinical research coordinators, outcome assessors and statisticians who conduct the final statistical analyses will be blinded to the group allocation. The bottom of the blind will not be revealed until the statistical analyses are completed. The EDC system and training of all researchers prior to the start of the trial will ensure the successful implementation of the blinding method.

Baseline assessment

Descriptive information will be collected at baseline. Descriptive information includes the patient's personal

general data, vital signs, clinical symptoms and signs, history of present illness, past medical history, medication history and neurological examination. At the same time, patients also need to receive head CT or MRI neuroimaging examination, blood routine, urine routine, liver and kidney function and other laboratory tests. The resulting data will be used to describe and compare the baseline characteristics of the two groups. In addition, the first sEMG data collection, the first clinical scales assessment and the first peripheral blood sample collection will be completed at baseline.

Intervention

All treatment will be implemented by the licensed rehabilitation therapists with at least 3 years of treatment experience. Each training session will last 40 min and will be implemented once a day and five times per week (from Monday to Friday) in a duration of 4 weeks. After each treatment, the corresponding therapist is required to sign for reference. Patients will be permitted to insist to the former treatment which benefit to their condition. Other treatment that may affect the patient's motor function will be banned, such as oral muscle relaxants, surgery and so forth.

The experience group

Patients in the control group received TPT. We selected six basic movements in the TC routine, namely, 'Starting Posture', 'Part the Wild Horse's Mane', 'Cloud Hands', 'Brush Knee and Twist Step', 'Forearm Rollings on Both Sides' and 'Closing Form', as the basic movements for patients to practice. The standard movements refer to the 24 simplified TC popularised by General Administration of Sport of China (<http://www.sport.gov.cn/>). In the actual training process, accuracy and coherence of postural routines will not be emphasised. Meanwhile, we will reduce the difficulty of reaching the standard of the postures appropriately according to the actual exercise ability of patients.

The upper limb training content required to complete by each basic movement is shown in [table 2](#). From easy to difficult, these six movements basically cover the trajectory of upper limb in daily life. Postural training also involves wrist and finger movement, which can achieve a more comprehensive upper limb rehabilitation training for patients. At the same time, the requirements of the six movements for the lower limbs include the single support movement moving forward, backward, left and right from the middle step, single limb weight training, hip, knee and ankle joint movement training, lumbar dorsal and lower limb muscle group control training, standing, and walking balance training and other rehabilitation training programmes. Depending on the patient's ability, the patient with poor muscle strength or high degree of spasm will be assisted by his or her therapist.

At the beginning of the training, the decomposition posture training of the limbs of the healthy and affected sides will be identical. With the improvement of the

Table 2 The upper limb training content of six basic movements

Name of the basic movement	The upper limb training content
Starting posture	1. Flex-stretch
Part the wild horse's mane	1. Stretch-adduction 2. Flex-adduction
Cloud hands	1. Flex-adduction-extorsion 2. Flex-stretch-abduction
Brush knee and twist step	1. Flex-abduction-extorsion-adduction 2. Flex-adduction-intorsion-stretch
Forearm rollings on both sides	1. Flex-abduction-extorsion-flex-adduction-intorsion 2. Flex-adduction-intorsion-flex-abduction-extorsion
Closing form	1. Stretch-flex

patients' active exercise ability, different posture training should be completed on the left and right sides at the same time. Each of the six basic movements requires a full postural interaction with a combination of the healthy and the affected side. The enrolled AIS patients do not need to practice all six basic movements, but repeated exercises selectively according to their respective dysfunction points, and gradually advanced exercises according to the difficulty of the movements.

To ensure the quality of the research, the therapists in the experimental group will receive instruction and training of TPT techniques. The content is divided into three parts, including the theoretical explanation of six basic movements, the demonstration of posture control techniques and the practice of actual operation. After the training, an assessment will be organised. Only the therapists who pass the examination can get the certificates. The intervention programme of the experimental group must be conducted by the certified rehabilitation therapists at all participating centres. Video recording is required during the treatment.

The control group

Patients in the control group will receive standard modern Bobath rehabilitation training. According to the 'Chinese Guidelines for Stroke Rehabilitation' (2011 version),¹³ the main contents of training include good limb position, muscle strength and joint activity training, knee-ankle joint control training, weight loss gait training and so on. The above rehabilitation training content can be selectively carried out to enhance training effect. All trainings focus on changing the patient's abnormal posture and abnormal movement patterns.

To ensure the quality of the research, the therapists in the control group will participate in the internationally certified Bobath technical training and obtain the certificates after the examination. The intervention programme

of the control group must be conducted by the certified rehabilitation therapists at all participating centres.

Follow-up

After the 4-week treatment, the participants will enter a 3-month follow-up period. During the follow-up period, all patients will be encouraged to continue community or family rehabilitation training. At the same time, patients in the experimental group will be encouraged to continue TPT. The training frequency is required to be more than three times per week. Patients in both groups will be given rehabilitation training diaries, and need to record the content and duration of rehabilitation training every day with the assistance of family members. Researchers will call the patients every 2 weeks to urge their rehabilitation training and keep a record of follow-up time. During the follow-up, the patients' combined medication status will be recorded in detail for further correlation analysis.

At the end of the 3-month follow-up period, all patients will be required to return to the hospital for sEMG examination and clinical scales assessment.

Outcome measures

In this study, the primary outcome and secondary outcomes will be measured at baseline, the end of the 4-week treatment and the end of the 3-month follow-up. Peripheral blood sample will be collected at baseline and the end of 4-week treatment. All outcome assessments will be independently performed by experienced and blinded assessors, who are also professional rehabilitation physicians.

Primary outcome

Root Mean Square

Since muscle strength is a major indicator of motor function, root mean square (RMS) generating from Flex-Comp sEMG system (Thought Technology, Canada) will be selected as the primary outcome. Such time-domain parameter reflects the effective value of the muscle discharge. Its peak value indicates the amplitude or contraction intensity, which mainly depends on the internal relationship between the muscle load factor and the physiological (also biochemical) processes of the muscle itself. RMS, an objective data indicator, is more sensitive and reliable in reflecting the changes of muscle strength than clinical muscle strength examination, which is only divided into 0–5 grades.

Electromyographic information will be collected from 11 muscles, including biceps brachii, triceps brachii, flexor carpi ulnaris, extensor digitorum, deltoid, quadriceps femoris, hamstring tendon, tibialis anterior, gastrocnemius, peroneus longus and erector spinae. Bilateral limb muscles collection will be conducted, a total of 22 muscles. Data from the healthy limbs will be used as a normal control.

The acquisition of single muscle EMG information will begin in the patient's resting state (Only if the heart rate ranging from 60 to 100 beats per minute will be

permitted). When connected to the sEMG system, the electrode plate will be pasted in the muscle abdomen according to the highest EMG signal point which will be automatically recognised by the sEMG system. When the EMG signal is stable, the assessors will ask the patient to exercise according to the time sequence of forced contraction and relaxation under the system prompt. After the collection of isometric movement, the data of muscle dynamic isotonic movement will be collected. The above tests will be performed again after an 1 min rest. With a total of three cycles, the average value of RMS will be taken.

Secondary outcomes

Integrated EMG

Integrated EMG (IEMG) is the total amount of electrical discharge of the motor units participating in muscle activities over a period of time, which is positively correlated with muscular tension. Under the premise of time invariable, IEMG can reflect the number of motor units and the discharge level of each motor unit. The value decreases linearly with the load duration. Considering the importance of muscular tension in the rehabilitation of motor function, IEMG will be selected to assess the state of muscular tension.

Average EMG

Similar to RMS, average EMG (AEMG) is also a characteristic indicator of signal amplitude variation, which is the average amplitude of instantaneous EMG over a period of time. AEMG can reflect the amount of motor unit activation, the type of motor unit participating in the activity, and the degree of synchronisation during muscle activity. Therefore, AEMG is also an important objective data indicator to express muscle strength level.

Mean Power Frequency and Median Frequency

Mean power frequency (MPF) and median frequency (MF) are both frequency-domain parameters that reflect the frequency characteristics of EMG signals. The former is related to the proportion of fast and slow muscle fibres in muscle tissue. The latter is related to the conduction velocity of action potential, the type of moving unit and the degree of synchronisation. These two parameters can be used to measure fatigue during muscle activity.

Clinical Scales Assessment

Fugl-Meyer Assessment (FMA), Berg Balance Scale (BBS), Barthel Index (BI) and National Institutes of Health Stroke Scale (NIHSS) will be selected to evaluate the rehabilitation effect of motor function in AIS patients. FMA will be used to assess reflexes, spasms, and motor coordination in patients. BBS will be used to assess balance ability of patients. BI will be used to assess the patients' daily living ability. NIHSS will be used to assess neurological function impairment in patients.

Safety outcomes

Routine blood and urine tests, coagulation function test, liver and kidney function tests and ECG test will be performed before and after the intervention. The test reports and the patient's vital signs will be used as the safety outcomes.

Collection, preservation and determination of peripheral blood sample

Peripheral blood samples will be collected at baseline and at the end of 4-week treatment. Patients will be required to refrain from eating and drinking after 12:00 pm the night before blood collection, followed by venous blood collection in the morning, with a single collection of 4mL. The collected blood samples will be preserved in the clinical biobank for classification and storage at low temperature, and will be detected within 1 week. Two monoamine neurotransmitters, 5-hydroxytryptamine (5-HT) and dopamine (DA) will be the main determination objects.

Data management and monitoring

Before the trial, an independent data safety and monitoring committee (DSMC) will be set up for the data management and monitoring. DSMC is composed of experts from third party evaluation centres and has no conflict of interest. Researchers who are responsible for data collection and entry will be trained by DSMC to ensure the accuracy, completeness and consistency of the data. During the trial, the inspectors from DSMC will regularly monitor the correct execution of the study protocol and the correct completion of the electronic case report form (eCRF).

The EDC system will be used in this study, and all participants' visit data will be directly input into the eCRF through the network user interface in all trial centres. The data of each eCRF will be logged twice by two independent operators. The inspectors from DSMC will regularly check and verify the consistency of the original data with the input data. The checked and qualified eCRF will be signed and then sent to the data management centre of EDC system in time. The third-party data manager will establish the corresponding database according to the contents of eCRF and the requirements of statistical analysis. After entry, verification and confirmation of all correct data, the chief researcher and statistical analysts will lock the database. The locked data file cannot be modified.

Quality control

A dedicated quality control group will be established for training four clinical research coordinators. The training includes patient recruitment, disease assessment and data collection, which will minimise selection bias. In the process of data collection, patients' combined medication and non-intervention treatment will be strictly noted. The influence of the above-mentioned interfering factors will be excluded in the statistical analysis.

The quality control group will also be answerable for the long-term communication and health education of patients. They will inform patients of the potential benefits and risks of participating in the research. If an adverse event occurs during the trial, the patient will receive consultation and free treatment from professional physicians, regardless of whether it is related to the research. The above measures will help to improve compliance of patients and reduce the lost rate of follow-up.

Statistical methods

Sample size

The sample size calculation was based on the parameters generated from the sEMG. According to a previous small simple size study,²⁹ 4 weeks after TC intervention, an increase in muscle strength of 12.86%±1.34% in patients treated with TC training vs 3.18%±23.45% in patients treated with routine rehabilitation therapy. We assume that the non-inferiority limit is 25%, with a type I error of 2.5% ($\alpha=0.025$) and 80% power ($\beta=0.20$), so the estimated required sample size is 50 participants per group based on the formula:

$$n = \frac{(Z_{1-\alpha} + Z_{1-\beta})^2 [p_1(1-p_1) + p_2(1-p_2)]}{(\varepsilon - \delta)^2}$$

Considering a 20% drop-out rate during the study, 60 patients will be enrolled in each group and the total sample size will be 120.

Data sets

In this study, three data sets will be established and analysed:

- ▶ Full analysis set (FAS): a collection of eligible and drop-out cases, but excluding rejection cases. The criteria are that the participants have been randomised and have had at least one treatment record. We will conduct intention-to-treat analysis through the FAS, which is mainly used for baseline comparability assessment and efficacy evaluation. Missing values will be filled in by the last observed carry-over.
- ▶ Per-protocol set (PPS): a collection of cases who met the inclusion criteria and completed all treatment measures. We will conduct PP analysis through the PPS, which is mainly used for efficacy evaluation.
- ▶ Safety Set (SS): a collection of cases who received at least one treatment and had a documented safety profile. Safety missing values cannot be carry-over. The SS will be used for safety analysis.

Statistical analysis

A statistician who is independent from the trial will be responsible for the statistical analysis. The SPSS V.25.0 (IBM) for Windows will be used. Statistical significance tests will be conducted on both sides, and $p < 0.05$ will be considered statistically significant. Descriptive statistical analysis of quantitative data will be conducted by means of mean, SD, number of cases, minimum, maximum, 95% CIs or median, upper quartile (Q1), lower quartile (Q3). Comparisons will

be made between and within groups as required. For intergroup comparison, if the data of the two groups conform to normal distribution and homogeneity of variance, independent sample t-test will be adopted; otherwise, Wilcoxon rank sum test will be adopted. For intra-group comparison, if the difference values conform to normal distribution, the paired sample t-test is adopted; otherwise, the sign rank sum test is adopted. The differences between the central effector and other confounding factors will be compared by using covariance analysis. Descriptive statistical analysis of qualitative data will be conducted by frequency and composition ratio. Comparisons will also be made between and within groups. X^2 or Fisher's exact test will be used for intergroup comparison, and Wilcoxon rank-sum test will be used for rank data. McNemar's test will be used for intra-group comparison. Cochran-Mantel-Haenszel test will be applied if the central effect is considered.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

ETHICS AND DISSEMINATION

Ethics

The study has been approved by Ethics Committee of Dongzhimen Hospital Affiliated to Beijing University of Chinese Medicine, being granted approval numbers DZMEC-KY-2020-22. We will follow the Declaration of Helsinki 2013 and will report the protocol according to the Standard Protocol Items: Recommendations for Interventional Trials 2013 Statement.

Safety

Any adverse events occurring during the trial will be recorded in detail regardless of whether they are related to the research. Once an adverse event occurs, the participant will be required to truthfully report changes in their condition before and after treatment. At the same time, the researchers will immediately take corresponding treatment measures until the participant's condition is stable. Within the next 24 hours, details of the adverse events will be reported to the hospital ethics committee, including the time of occurrence, clinical symptoms and signs, severity, duration, physical and chemical examination indexes, treatment methods and results, etc. The ethics committee will assess the correlation between the adverse events and the intervention, and will make a final decision on whether the participant will continue to participate in the trial. During the period of adverse events, the researchers will further record changes in the adverse events reported by the participant (such as whether the adverse event subsided or if it still exists, its severity and frequency), and

determine whether the adverse events occurred are related to the trial.

Dissemination

The research results will be disseminated through (open access) peer-reviewed publications and presentations at conferences.

DISCUSSION

Although preliminary progress has been made in the clinical practice of TC for dyskinesia rehabilitation, these researches are mainly based on integral TC routine. Meanwhile, as a complementary and alternative therapy, TC has its limitations and still hardly be applied for AIS patients with severe dyskinesia. In this trial, the standard practice postures of TC are simplified and decomposed according to the actual situation of the patients. 'Cloud Hands', for instance, can be simplified and decomposed into 'The unilateral upper limb movement of the Cloud Hands', 'The two-sided upper limb movement of the Cloud Hands', 'The unilateral upper limbs combined with trunk rotation movement of the Cloud Hands', 'The two-sided upper limbs combined with trunk rotation movement of the Cloud Hands', 'Standard Cloud Hands movement', 'Anti-resistance Cloud Hands movement'. Regardless of whether the patient is bedridden or able to stand or walk, the above training movements can meet the rehabilitation training requirements of different degrees of dyskinesia. The rehabilitation method performing from healthy side to the affected side is used in the specific training process, so that the affected side gradually adapt to the weight training. For the patients with weak balance and coordination function, the static training of fixed motion will be implemented. The dynamic postural training will be started based on strengthening static motion. Through simplifying and decomposing standard practice postures of TC, combined with the assistance of the therapist or moderate antiresistance postural training, TPT can be applied to convalescent ischaemic stroke patients in different Brunnstrom stages. In actual training, TPT will be selected according to the patients' changing characteristics of mechanics. The key point lies in improving muscle strength and inhibiting muscle spasm, which will further induce the corresponding cortical neural reflex development.

Studies on the application of TC for dyskinesia are short of unified standard for the efficacy evaluation, among which the subjective clinical scale assessment is the most widely used. sEMG, which reflects the state of neuromuscular activity by electromyographic signals during rest or movement, has been widely used in the field of rehabilitation medicine.³⁰ Based on the characteristic description of limb muscle strength, muscular tension and muscle group coordination, sEMG can provide more objective data supporting for the evaluation of limb motor function.³¹ In a previous study, researchers used sEMG to test healthy participants who are practicing TC. The results

indicated that the participants got significant improvement in muscle group stability, coordination and fatigue resistance.³² A recent study had also confirmed that sEMG can objectively evaluate the upper limb motor function and abnormal gait of AIS patients.³³ Therefore, sEMG will be introduced in this study to provide objective parameters for the efficacy evaluation of TPT.

In addition to verifying clinical efficacy, another important objective of this study is to explore the central-peripheral neurotransmitter mechanism of TPT. Changes of central excitatory or inhibitory functions have important effects on motor function, among which the regulation of monoamine neurotransmitters is the most critical.^{34–37} Several studies have shown that change of monoamine neurotransmitters level such as 5-HT and DA within the brain was closely related to central fatigue.^{38–41} One of the results showed that an increase in central ratio of 5-HT to DA was associated with feelings of tiredness and lethargy.³⁸ The interaction between 5-HT and DA was also reported to play a regulative role in the development of central fatigue,^{37,40} among which the 5-HT played the dominant role in the dynamic changes.^{36,41} A small sample trial about TC also showed significant differences in 5-HT and DA levels before and after the TC exercise, which suggested that the TC exercise was closely related to change of monoamine neurotransmitters level in the blood.⁴²

Some limitations are inevitable in this study. First, although the condition of AIS patients in convalescence is more stable than that in the acute phase, relapse or severe complications may lead to a high drop-out rate, which will affect the final statistical analysis. Second, because of the characters of the intervention, the therapists are not blind. Third, the limitation of sample size and region may affect the further popularisation of the research results. Despite facing above challenges, we will strive to standardise the steps in the trial. We hope that the results of this trial will provide more reliable evidence for the application of TPT in the convalescence of AIS, and attempt to elucidate the efficacy mechanisms.

Trial status

At the time of submission, the trial is currently in the recruitment phase. This trial started on 1 June 2020 and will end on 31 December 2022.

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