Efficacy and Mechanism of Abdominal Acupuncture as a Poststroke Intervention for Promoting Upper-limb Motor Recovery: A Study Protocol of A Randomized Controlled Trial

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Abstract

Background: How to promote true recovery from poststroke upper limb motor impairment has remained an urgent public health problem. Acupuncture has the potential to facilitate poststroke recovery. Abdominal acupuncture, based on the recently discovered acupoint system on the anterior abdominal wall, appears attractive because it induces less pain, and allows concurrent limb rehabilitative training during treatment. However, its clinical efficacy has not been systematically demonstrated, and its neurophysiological mechanism has remained obscure. **Methods:** First-onset stroke survivors (0.5-3 months post-stroke) will be randomly divided into 3 groups (N=22 in each), respectively receiving (1) abdominal acupuncture, (2) abdominal acupuncture with sham needles, and (3) no acupuncture. All subjects will concurrently receive basic treatment, including upper limb rehabilitative training and measures for secondary stroke prevention. Clinical scores reflective of motor functions and impairment (Wolf motor function test, Fugl-Meyer assessment, Brunnstrom staging), evaluation of daily life ability, surface electromyography, and motor-imagery functional magnetic resonance imaging will be collected as outcome measures before and after intervention. Upper-limb muscle synergies will be identified from the collected surface electromyography. **Discussion:** The study will use abdominal acupuncture to improve recovery from motor dysfunction of the upper limb after stroke, to observe the effects of abdominal acupuncture on post-stroke upper limb motor functions, and to analyze the relationship between changes in upper-limb functions and measurements from both multi-muscle surface electromyographic data and brain activations during motor imagery from functional magnetic resonance imaging, so as to explore possible mechanisms of neuroplasticity associated with abdominal acupuncture. **Trial registration:** This trial was registered with the ClinicalTrials.gov (ID: NCT03712085) on 7th July 2018, and last updated on 16th Oct 2018.

Background

Stroke is a severe disease that can endanger human life. With a high rate of morbidity, mortality, and recurrence, it is also the most common cause of adult disability worldwide [1, 2]. It was reported that 60-80% of stroke survivors have motor dysfunction, rendering them dependent on others in activities of daily living [3]. In particular, the incidence of upper limb dysfunction following stroke is extremely high [4]. Recovering upper-limb motor functions poses hard challenges to rehabilitation science. Even after high-intensity rehabilitation training, 15-30% of stroke survivors still have motor functional impairment in different degrees [5]. Since having high-functioning upper limbs – and especially hands – is a *sine qua non* for many daily motor tasks that demand accuracy and precision, upper limb dysfunction affects the quality of life of stroke survivors particularly seriously. In recent years, research on improving upper limb function after stroke has aroused great attention in medicine [6, 7].

Acupuncture, as a treatment modality of Traditional Chinese Medicine (TCM), has the potential to facilitate recovery of motor function, somatic sensation, speech, and self-help ability for stroke survivors [8]. According to TCM principles, Qi, Blood, Yin and Yang are the four basic elements that govern the operations of the human body through their mutual cooperative, and sometimes competitive,

interactions. Thus, for the body to remain in a healthy state, the activities of these four elements should be kept in balance. Acupuncture helps harmonize Yin and Yang, then clearing blocked channels of Qi and Blood in the body so as to restore the normal body state, thus reducing motor impairment. A number of previous clinical trials have demonstrated the efficacy of acupuncture as a post-stroke intervention [9-11].

Abdominal acupuncture is a new acupuncture method based on Dr. Zhi Yun Bo's discovery of a microsystemic meridian system whose surface acupoints are located on the anterior wall of the abdomen [12]. According to our previous research [13, 14], abdominal acupuncture is potentially an effective method for treating stroke. While the exact clinical efficacy and the repeatability of our previous observations remain to be established, we think abdominal acupuncture is a very promising and attractive intervention because it induces less pain to the patient than other conventional acupuncture methods. Also, at the center of the surface acupoints for abdominal acupuncture is the umbilicus, a landmark closely related to the circulation of Qi and Blood throughout the body. Thus, it should be easier for abdominal acupuncture to modulate and enhance the whole-body flow of Qi and Blood than traditional acupuncture. Besides, it only involves inserting needles into the abdomen, which means the patient can concurrently undergo additional upper- or lower-limb training during acupuncture [15]. Despite these advantages, the neurophysiological basis of why abdominal acupuncture works has remained obscure. Given the increasingly pressing need to rehabilitate a large number of stroke survivors and the growing popularity of acupuncture, it is ever more urgent to rigorously quantify the efficacies of different acupuncture types in different subject groups, and to elucidate its mechanisms of actions. This knowledge can then be the basis of an evidence-based decision on whether, and if so how, to incorporate acupuncture into the general guideline of treatment and rehabilitation for stroke [16].

The combination of acupuncture and early post-stroke rehabilitation may accelerate the establishment of collateral circulation that increases cerebral blood flow and promotes compensatory reorganization of the tissues and neurons surrounding the infarct, thus enhancing neuroplasticity [17, 18]. Neuroplasticity refers to the ability of the nervous system to modify itself to adapt to the changing internal and external environments. This modification involves functional reorganization of neuronal networks, underpinned by changes in neuronal physiology, biochemistry and morphology [19]. Much of true recovery from motor impairment after brain injury is the result of neuroplasticity [20].

Recent studies have suggested the application of surface electromyography (sEMG) for both quantitative and qualitative analyses of neuromuscular functions [21, 22]. However, in a clinical setting, the application of sEMG in neuromuscular assessments is still immature. There is a paucity of studies on the activation patterns of forearm and hand muscles and hand motor function in stroke survivors [23]. Similarly, there has been little research on the relationship between the extent and location of the stroke lesion and the post-stroke synergistic activation patterns of upper-limb muscle groups (known in the motor control literature as muscle synergies). Muscle synergies are hypothesized motor control modules, organized in the brain stem or spinal cord, usually derived from multi-muscle sEMG measurements, and functioning as elementary building blocks of movement generation [24]. Each motor behavior results from a specific combination of fixed synergies. The central nervous system (CNS) optimizes control

possibly by producing dynamic muscle activities through muscle synergy activations, thereby generates movement with a “simplified” strategy [25, 26]. It has been proposed that muscle synergy patterns can serve as neurologically based markers of the physiological status of stroke survivors [27]. Considering upper limb synergies, Cheung *et al.* observed how stroke influences the temporal activations of preserved muscle synergies using different movements and postures [24, 28]. However, to the best of our knowledge, how an acupuncture treatment may reduce motor impairment by altering the activations of muscle synergies post-stroke has never been studied. This knowledge would almost certainly shed light on the neurophysiological mechanisms behind the clinical efficacy of acupuncture.

Although sEMG, as an outcome measure, can indicate post-acupuncture changes in the muscle synergies of the hemiplegic limb, and thereby suggest changes in the motor-control strategy due to acupuncture, sEMG by itself cannot provide any information on how brain neuroplasticity facilitates recovery of motor functions. Fortunately, the application of functional Magnetic Resonance Imaging (fMRI) – a technology for exploring activities of cerebral neurons during the resting state, motor imagery, or other behavioral tasks – may solve this problem. The fMRI has been used in many prior studies that focus on revealing acupuncture mechanisms [29-31]. Motor imagery is an excellent strategy for characterizing brain activation patterns related to movement for stroke patients [32, 33], because the imagery tasks can involve movements identical to the ones used for eliciting sEMG, and that any overt, large-amplitude physical movement is not possible within the MRI scanner. But relevant neuroimaging research about motor imagery after stroke is still limited [34].

At present, there has not been any systematic research that strongly and adequately suggests any concrete, solid mechanism of post-stroke brain plasticity attributable to abdominal acupuncture treatment, and can account for any observed clinical efficacy of abdominal acupuncture. Moreover, in general there are very few studies that combine fMRI with sEMG for unveiling the mechanism of a post-stroke intervention by simultaneously characterizing brain neuroplasticity and changes in neuromuscular coordination. Since muscle coordination is ultimately accomplished by neuronal networks in the brain and spinal cord [24], collecting data from both the brain and muscle-activation levels can provide a more complete and integrated view of the neurophysiological underpinnings of the intervention. Given how little is known about abdominal acupuncture mechanisms, such a comprehensive approach of data collection seems even more reasonable and necessary for maximizing the chance of a breakthrough in our understanding.

In this clinical trial, we seek to use abdominal acupuncture to improve recovery from motor dysfunction of the upper limb after stroke, to observe the effects of abdominal acupuncture on post-stroke upper limb motor coordination through muscle synergy analysis on the sEMG, and to dissect the possible mechanism of cerebral plasticity after acupuncture treatment.

Methods/design

Our study is a prospective, assessor- and analyst-blinded randomized controlled trial. The Rehabilitation Department of the Guangdong Provincial Hospital of Chinese Medicine will be responsible for recruitment of subjects, providing acupuncture and basic treatments, performing assessments, analyzing part of the collected data. The Chinese University of Hong Kong will be responsible for analyzing another part of the collected data. Before commencement, each qualified subject will have to sign an informed consent form after being screened for eligibility. After that, they will receive baseline assessments before randomization. Eligible patients will be divided into 3 groups in a 1:1:1 ratio following a random number table. This study protocol is summarized in a flowchart (Fig.1).

Fig.1. A flowchart which summarizes the whole study protocol. All the recruited subjects will receive baseline assessment including the evaluation of qualification according to inclusion and exclusion criteria and signing the informed consent. 66 qualified patients will be randomly divided into three groups, receiving the same basic treatment throughout the study and different interventions for 4 weeks. Before the intervention (week 0), patients will receive the assessment of sEMG, fMRI, WMFT, FMA, Brunnstrom and MBI. During the intervention, the experimental group will receive abdominal acupuncture at the established abdominal acupoints. The sham experimental group will receive sham abdominal acupuncture at the same acupoints as the experimental group. There is no treatment of acupuncture in the control group. Besides, all the patients will receive the assessment of WMFT, FMA, Brunnstrom and MBI at the end of second week of intervention (week 2nd). After the intervention (week 4th), patients will receive the assessment of sEMG, fMRI, WMFT, FMA, Brunnstrom and MBI. Finally, all the collected data will be analyzed. SEMG, surface electromyographic; fMRI, functional magnetic resonance imaging; WMFT, Wolf motor function Test; FMA, Fugl-Meyer assessment(upper limbs); Brunnstrom, Brunnstrom staging of upper limb movement; MBI, modified barthel index.

Eligibility criteria

Inclusion criteria includes: (1)First-time stroke survivor with left hemiplegia, with diagnosis of lesions confirmed by brain CT or MRI; (2)Right-handed before stroke, aged between 35 and 75 years old; (3)Stroke survivor at 0.5 to 3 months post-stroke presented with stable vital signs; (4)No cognitive impairment, and can understand and execute commands with ≥ 7 points of mini-mental state examination (MMSE) scores; (5)Can control sitting balance without external support, with the Brunnstrom stage of hemiplegia (upper limb and hand) at IV or V, and a Fugl-Meyer Assessment score (upper limb; motor) between 20 and 50 points; (6)Agrees to sign the informed consent; (7)Presented with no unilateral neglect.

Exclusion criteria includes: (1)Any patient with recurrent stroke, subarachnoid hemorrhage, brain tumor; (2)Contraindication to undergo a 3T MR imaging; (3)Claustrophobia; (4)Have severe complications involving the heart or any hepatic or renal diseases; (5)Have a history of non-compliance to medical interventions; (6)Have participated in other clinical trials recently.

Intervention programme

Basic treatment

All the qualified subjects will be randomly divided into 3 groups and receive basic treatment. The basic treatment will include upper limb rehabilitative training and measures for secondary stroke prevention. According to the recommendations on upper limb movement in the guidelines for the rehabilitation of AHA-ASA-2016 [35], patients will receive rehabilitative training that focuses on correct limb placement, operation therapy, joint loosening, joint passive activity, neuromuscular function promotion training, and other active exercises. Patients will also receive treatments of secondary stroke prevention deemed necessary by the doctors, such as anti-platelet aggregation, plaque stabilization, anticoagulation, intracranial pressure reduction and other symptomatic treatments according to the Chinese Guidelines for the Prevention and Treatment of Cerebrovascular Diseases [36].

Treatment plan for Experimental Group

The experimental group will receive abdominal acupuncture and basic treatment. A pre-defined standardized acupuncture prescription will be employed [12]. The abdominal acupuncture points will be seen in Fig.2: Zhongwan (RN12), Xiawan (RN10), Qihai (RN6), Guanyuan (RN4), ipsilateral Shangqu (KI17), ipsilateral Huaroumen (ST24), ipsilateral Shangfengshidian (AB1), and ipsilateral Shangfengshiwaidian (AB2) [37]. Patients will lie in supine position, with Bo's abdominal needles inserted into the skin at the established abdominal acupoints listed above. Then Bo's abdominal needles (0.2 x 30 mm, produced by Changzhou Dayi Medical Device Co., Ltd, China) will be thrust into these abdominal acupoints straight after local disinfection. Operators can appropriately adjust the depths and angles of the needles according to the patient's condition with light manipulation. Treatment will last for 30 minutes per session, and be administered once a day, 5 days a week for a total of 4 weeks. The basic treatment prescribed for this group will be the same as that for the sham experimental group and the control group.

Fig.2. The figure shows the abdomen and the abdominal acupoints used in the experimental and the sham group, with umbilicus as center, pubic bone as bottom, and distance measured in cun. The eight white dots represent the abdominal acupoints used for treating patients with left hemiplegia, Zhongwan (RN12), Xiawan (RN10), Qihai (RN6), Guanyuan (RN4), left Shangqu (KI17), left Huaroumen (ST24), left Shangfengshidian (AB1), and left Shangfengshiwaidian (AB2).

Treatment plan for Sham Experimental Group

The sham experimental group will receive sham abdominal acupuncture and basic treatment. The acupuncture points will be the same as the ones listed for the experimental group (Fig.2). Patients will lie in a supine position with needles placed in the established abdominal acupoints. After disinfection,

locating the flat needles on the skin of the predefined abdominal acupoints (Fig.2). Disposable flat needles (0.3 x 30 mm; Huatuo Brand, produced by Changzhou Dayi Medical Device Co., Ltd, China) will be straightly thrust into the base of skin, but not into the dermis [38]. The manipulation and sessions of treatment are the same as those applied in the experimental group. The basic treatment prescribed for this group will be the same as that for the experimental group and the control group.

Treatment plan for control group

The control group will receive basic treatment only. The basic treatment prescribed for this group will be the same as that for the experimental group and the sham experimental group.

Outcome

Primary outcomes

The primary outcomes in this study include evaluations of sEMG and fMRI at baseline and 4 weeks into intervention, and evaluations of Wolf motor function Test (WMFT) and Fugl-Meyer assessment of upper limbs (FMA-U) scales 0 week, 2 weeks, and then 4 weeks into the intervention.

SEMG, a non-invasive examination method, can objectively, accurately and dynamically evaluate the functional state of neuromuscular control, and has been gradually introduced into the clinic for evaluation of stroke [21, 22]. Here, surface EMG activities will be collected from 16 muscles of each of the upper limbs. The muscles will include triceps brachii, lateral and medial heads; biceps brachii, short and long heads; deltoid, anterior, medial, and posterior parts; superior trapezius; rhomboid major; brachioradialis; supinator; brachialis; pronator teres; pectoralis major, clavicular head; infraspinatus; and teres major [28]. Electrodes for each muscle will be placed according to guidelines of the Surface Electromyography for the Non-Invasive Assessment of Muscles-European Community project (SENIAM) and Delagi et al [39]. To elicit EMG activities, all patients will be asked to perform 7 motor tasks, which will include simple upward reaching, shoulder abduction, forward reaching with elbow extension, hand pronation, shoulder circumduction, moving along a path together with hand pronation, and shoulder posterior extension. The tasks for both arms will be identical, except that their trajectories will be mirror images of each other. For every task, EMG signals of 5 to 6 trials will be collected.

Human neuroimaging methods have been widely used in acupuncture research [40]. In this study, we will perform 3 neuroimaging experiments, including resting-state fMRI, motor-imagery task-based fMRI, and DTI through the use of a 3T MRI scanner (standard orthogonal cranial coil; Toshiba Corporation, Japan). Resting-state fMRI and DTI will be performed with a predetermined programme. During motor imagery trials, participants will be instructed to imagine the following sequence of actions which are related to the sEMG motor tasks: ☐ When hearing "Sitting down", the participant will imagine himself or herself sitting

with hands on knees for 20 seconds. ☐ When hearing “Emptying”, the participant will imagine nothing for 20 seconds. ☐ When hearing "lifting hand", the participant will imagine sitting and lifting the stroke-affected hand to shoulder level for 20 seconds. ☐ When hearing “Emptying”, the participant will imagine nothing for 20 seconds. ☐ When hearing "abduction", the participant will imagine sitting and doing shoulder circumduction with a 360-degree turn repeatedly for 20 seconds. ☐ When hearing “Emptying”, the participant will again imagine nothing for 20 seconds. The above sequence will be repeated 4 times; across these replicates, the ordering of movement ☐, ☐ and ☐ will be randomized. The whole motor imagery sequence will last for 8 minutes. Before imaging, each participant will be asked to watch a video made by the researchers to learn the actions corresponding to the instructions, so that the participant may correctly imagine each movement associated with each instruction.

The WMFT Scale [41] is the acknowledged scale of choice for evaluating upper limb motor functional gain associated with compulsory exercise therapy [42]. The validity and reliability of WMFT have been repeatedly argued for and demonstrated [43, 44], and this clinical score has also been previously applied to assess upper limb functions of acute stroke survivors [45].

The FMA scale is widely used in clinical and scientific research because it reflects the level of motor impairment in stroke survivors [46]. For the upper limb portion of the FMA scale, the total maximum score is 66 points. This score assesses the quality of both common and specific movements, and can reflect subtle changes in impairment across time [47]. It is currently recognized as a motor function rating scale with good reliability and validity [48].

Secondary outcomes

The secondary outcome measures will include the Modified Barthel Index (MBI), and the Brunnstrom Staging of upper limb movement. They will be assessed at baseline, 2 weeks and then 4 weeks into the intervention.

The MBI is a quantitative evaluation of daily life ability. It consists of 10 areas of evaluation, ranging from personal hygiene, eating, taking care of bowel activities, to mobility ability [49]. The total score is 100 points; the higher the score, the better the self-care ability. Besides, it can also reflect the status of movement recovery.

Brunnstrom staging can indicate the overall neuromotor status of the stroke-affected limb [50] – for instance, whether the limb is affected by soft paralysis, spasm, or whether it is capable of common movement, separation movement, or coordinated movement *etc.* This staging can guide targeted rehabilitation training, but it cannot reflect any subtle changes of impairment level or motor function.

Adverse events

During the course of the study, any complaints and sudden illness, including local pain, subcutaneous bleeding, skin irritations, palpitations or dizziness, and any other unusual responses will be recorded throughout the whole study period. All of the serious adverse events will be reported to the ethics committee of the hospital in a timely manner.

A summary of our subject enrollment scheme, the treatment plan, and the outcome measures are presented in Fig.3.

Fig.3 A summary of the enrollment scheme, the intervention (the treatment plan), and the assessment (outcome measures) at different timepoints. The symbol × indicates the item is performed in a part of the trial at a time point.

Timeline of Intervention

In this trial, all acupuncture interventions will take approximately 30 minutes per session, administered once a day, 5 times a week, for 4 weeks in total. Subjects will undergo the first assessment of outcome measures on the day being enrolled, the second one at 2 weeks into the intervention, and the third one immediately after receiving all treatment sessions at the 4th week (Fig.3).

Sample size

The subject sample size determined for this study is based on results of previous reports [51]. We used the `sampsizepwr` function of the MATLAB software to calculate the sample size. Taking the FMA score as an outcome, and assuming that the FMA is 30 ± 10 before treatment and 37 after treatment, the effect size between groups is 0.7. For a statistical power of 0.8, a minimum of 19 cases per group is necessary. Taking into account some uncontrollable factors that may lead to a ~15% subject dropout rate, each group will need an additional 3 subjects. Thus, at least 66 subjects (22 per group) will need to be enrolled.

Recruitment

In order to achieve our targeted sample size (see above), we will post recruitment posters in both out-patient and in-patient departments in the Guangdong Provincial Hospital of Chinese Medicine. Inclusion criteria and contact information will be shown on the poster.

Randomization and allocation concealment

All eligible patients will be divided into 3 groups in a 1:1:1 ratio using a random number table. The matching between the subject's identity and the subject number will be revealed after subject recruitment, so that concealment of subject allocation can be ensured.

Blinding (masking)

In this study, the assessors and the analysts will be blinded to the grouping of subjects. Physicians from the Rehabilitation Department will be responsible for the assessment of the clinical scales and collecting sEMGs, and they will receive the same training before the trial begins. Physicians from the Imaging Department of the Guangdong Provincial Hospital of Chinese Medicine will be responsible for collecting fMRI data. The technical team of the hospital will be responsible for the randomized subject assignment and other statistical analyses. Thus, all assessors and analysts will not know to which group each subject will have been assigned, and what treatments each will have received.

Data management

We have set up standard operating procedures to standardize data collection, data entry, and data storage so as to promote data quality. Assessors are responsible for data collection following the basic principles of in-time, integrity, and accuracy. All data including clinical assessments and outcome measures, baseline, and other trial data will be recorded into Case Report Form (CRF). Collected data will be entered into computer in time to facilitate verification, identification, and correction of any potential errors and omissions. Research files will be stored according to standardized schemes to facilitate easy and correct data retrieval. Other measures for fireproofing, anti-thievery, anti-damage, and confidentiality will be employed to the extent possible to ensure file safety.

Statistical methods

All statistical analyses will be performed by a statistician. Statistical analysis will be performed using the software SPSS 20.0, and functions in the statistics toolbox of MATLAB. Two-sided significance will be determined with $\alpha = 0.05$.

An intention-to-treat approach will be adopted in our analysis of the available data. Any missing data will be handled with a multiple imputation approach. Results from quantitative data will be compared across groups with independent two-sample t-test; results from qualitative data will be compared across groups with Chi-square test. The Wilcoxon test or ANOVA will be used to compare the difference between groups according to the results of the Kolmogorov-Smirnov test.

Analysis of fMRI images will be implemented using the SPM8 software. Analysis of sEMG will be implemented using the DELSYS ANALYSIS P189 software and custom functions written in MATLAB. All sEMG and fMRI data will be analyzed offline.

Data monitoring and quality control

Data monitoring and quality control will be ensured and managed by the Methodology Team of the Guangdong Provincial Hospital of Chinese Medicine. This team conducts on-site supervision on research units regularly to ensure that all protocols in the research program are strictly observed, and the data collected are well managed.

Discussion

The most common dysfunction after stroke is upper limb hemiplegia. More than 80% of stroke survivors have acute upper limb hemiplegia [52]. Common manifestations of upper limb dysfunction include muscle weakness, abnormal muscle tone, and poor exercise control. Promoting recovery of the upper limb is a great challenge as well as a heavy burden for patients, their families, and the society in general [53].

Evidence suggests that brain plasticity involving reorganization of neuromotor circuitry is the basis for neurological recovery. However, the neurophysiological mechanisms underlying why and how rehabilitation facilitates recovery has remained unclear [24, 54].

Previous reviews and studies have shown that abdominal acupuncture have positive effect on upper limb motor function of stroke survivors by promoting brain plasticity [55, 56]. According to recent clinical observations, abdominal acupuncture is likely an effective method for treating stroke – in fact, one with potentially considerable clinical efficacy. Nevertheless, due to a lack of high-quality and well-designed studies that focus on evaluating this new type of acupuncture, its effectiveness is still inconclusive. We believe that in addition to assessing the effectiveness of abdominal acupuncture, it is also important to use modern medical technology to shed light on its mechanism of actions.

This study protocol is the first rigorously designed, evidence-based clinical trial that uses both objective neurophysiological measures (fMRI combined with sEMG) and commonly used, albeit less objective, clinical scores (WMFT, FMA-U and MBI scales) to evaluate the effects of abdominal acupuncture on brain plasticity in stroke survivors. Results of this study are expected to provide possible mechanism of improvement of limb function after acupuncture treatment – mechanisms that are based on structural changes in brain networks and alterations in the activation of muscle synergies. Such a unique and novel combination of outcome measures may eventually lead to a new evaluation system for post-stroke management in the future, and provide the much-needed scientific basis for the curative effect of acupuncture.

List Of Abbreviations

TCM, Traditional Chinese Medicine; sEMG, surface electromyography; CNS, central nervous system; fMRI, functional Magnetic Resonance Imaging; WMFT, Wolf motor function test; FMA, Fugl-Meyer assessment(upper limbs); FMA-U, Fugl-Meyer assessment of upper limbs; Brunnstrom, Brunnstrom staging of upper limb movement; MBI, modified barthel index; MMSE , mini-mental state examination;

SENIAM, Surface Electromyography for the Non-Invasive Assessment of Muscles-European Community project.

Declarations

Ethics approval and consent to participate

The study has been approved by the Ethics Committee of Guangdong Provincial Hospital of Chinese Medicine (NO. BF2018-164-01). All eligible patients are required to sign the informed consent before joining the research. Researchers are required to explain the background, objectives, procedures, possible benefits and risks of the study to all patients. Any public report about the results of this study will not reveal the personal identity of the subjects. All information related to patients is confidential.

Consent for publication

Not applicable.

Availability of data and material

All research data and material will be uploaded to [ClinicalTrials.gov](https://clinicaltrials.gov), and research results will be disseminated in the form of papers.

Competing interests

Not declared.

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Author's contributions

R.P. and S.L. designed the protocol and wrote the draft. J.X. and V.C.K.C revised the manuscript. Y.G. registered and submitted this trial to [ClinicalTrials.gov](https://clinicaltrials.gov). Y.Z. and Y.H. helped with operation training, including acupuncture and assessment tests involving sEMG and fMRI. J.Z. was responsible for statistical analyses. As co-senior contributors, H.C. and V.C.K.C conceived of this study. All authors have read this protocol and approved the final draft. The trial sponsor is responsible for selecting research unit, researchers and other resources. All costs for project implementation are supported by project funder.

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Trial status

This protocol is the 1.0 version, dated 1 January 2019. The recruitment of subject in this research has begun from 10 January 2019 and anticipated to end on 30 December 2020.

Confidentiality

Medical records (CRF, test sheets *etc.*) will be kept in a locked cabinet in the hospital, and the physicians will record the results of the examination on the patients' out-patient medical records. Researchers, the applicants' representatives, and the ethics committees will be allowed to access the medical records. Researchers will make every effort to protect the privacy of the personal medical data to the extent permitted by law.

Additional file

A checklist of defining standard protocol items for clinical trials (SPIRIT 2013 Checklist, DOC 119 kb) is attached in the additional file.

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Figures

Figure 1

A flowchart which summarizes the whole study protocol. All the recruited subjects will receive baseline assessment including the evaluation of qualification according to inclusion and exclusion criteria and signing the informed consent. 66 qualified patients will be randomly divided into three groups, receiving the same basic treatment throughout the study and different interventions for 4 weeks. Before the intervention (week 0), patients will receive the assessment of sEMG, fMRI, WMFT, FMA, Brunnstrom and

	Enrollment	Treatment period			
TIMEPOINT	-1 week	1 week	2 week	3 week	4 week
ENROLLMENT					
Inclusion criteria	×				
Exclusion criteria	×				
Informed consent	×				
Basic assessment and allocation	×				
INTERVENTION		×	×	×	×
Experiment group		×	×	×	×
Sham experiment group		×	×	×	×
Control group		×	×	×	×
ASSESSMENT					
Functional magnetic resonance	×				×
Surface electromyography	×				×
Wolf Motor Function Test	×		×		×
Brunnstrom Staging of upper-limb movement	×		×		×
Fugl-Meyer Motor Assessment of upper limbs	×		×		×
Modified Barthel Index	×		×		×
Adverse events	×		×		×

Figure 3

A summary of the enrollment scheme, the intervention (the treatment plan), and the assessment (outcome measures) at different timepoints. The symbol × indicates the item is performed in a part of the trial at a time point.

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