Calligraphy-based rehabilitation exercise for improving the upper limb function of stroke patients: protocol for an evaluator-blinded randomised controlled trial

Xiaodi Wu,1 Qiang Zhang,2 Jun Qiao,3 Nan Chen,4,5 Xie Wu5

ABSTRACT

Introduction A common complication of stroke is upper limb dysfunction. Chinese calligraphy handwriting (CCH) is an aesthetical exercise developed from the traditional way of writing in China and holds potential to become a rehabilitation method to improve upper limb functions in patients with stroke. This study aims to design a randomised controlled trial to assess the effect of a customised CCH-based exercise for poststroke rehabilitation of upper limb dysfunction.

Methods and analysis A single-blinded randomised controlled trial will be conducted on 60 stroke patients. The patients will be randomly allocated into three groups: (1) conventional occupational therapy (COT) group, (2) COT+CCH group, (3) COT+Graded Repetitive Arm Supplementary Program (GRASP) group. For the COT group, patients will receive COT treatment of 1 hour/day. For the COT+CCH group, patients will receive 30 mins COT treatment and 30 mins CCH training. For the COT+GRASP group, patients will receive 30 mins COT treatment and 30 mins GRASP training. All the interventions will be performed 5 days per week for a total of 3 weeks. The upper limb functions will be assessed before and after the interventions using a series of rating scales.

Ethics and dissemination This study has been approved by the Research Ethics Committees of the Second Rehabilitation Hospital of Shanghai (study ID: 2020-32-01) and the Shanghai University of Sport (study ID: 102772021RT043). Results will be directly disseminated to the patients at the end of the study and to the public via publications in peer-reviewed journals and presentations in conferences.

Trial registration number ChiCTR 2100043036; Chinese Clinical Trials Registry.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ In this study, the efficacy of the proposed self-administrated Chinese calligraphy handwriting (CCH) exercise will be compared with that of the popular Graded Repetitive Arm Supplementary Program, which will strengthen the convinciness of the outcomes.

⇒ Outcome measures will include not only the performance of the affected arm in various activities but also the ability to use the affected arm for daily living will be evaluated using questionnaires.

⇒ The overall time to complete the action research arm test will be measured and analysed to reduce the ceiling effect.

⇒ This study is evaluator-blinded study, and, thus, patients and therapists will not be blinded to the intervention allocation.

⇒ This study has a short intervention period, and the long-term efficacy of CCH for improving poststroke upper limb functions will not be investigated.

INTRODUCTION

Recent epidemiological studies have revealed that each year nearly 17 million people suffer from stroke in the world,1–3 and in China alone over 2.5 million new stroke cases are diagnosed per year.4 With the improved care in the hyper-acute and acute periods of stroke, around 80% of stroke patients can survive from the initial injuries.5 However, stroke can usually lead to severe neuropsychiatric disorders in patients, such as motion capacities, sensory and cognitive impairments.6,7 As one of the most common complications, the motor impairment might affect the unilateral movement abilities of patients’ upper limbs.8,9 Patients with such upper limb dysfunctions would exhibit difficulties in contracting muscles as well as in the control and coordination of their arms, hands and fingers. The post-stroke upper limb dysfunctions can, thus, limit the patients in daily activities such as eating, dressing and washing,10-12 and can increase their dependences and affect the quality of life in a long time period.13 Therefore, poststroke rehabilitation of upper limb dysfunction is critical in restoring patients’ upper-limb functions and improving their quality of life.14 By leveraging different technologies, multiple poststroke rehabilitation therapies have been developed and used to restore...
upper limb functions, such as therapist-assisted practice, bilateral training, constraint-induced movement therapy (CIMT), robotic-assisted therapy, mirror therapy and virtual reality. As the function recovery can last into the chronic phase of stroke, there is an increasing interest in validating interventions that aim to enhance the physical and psychological well-being in both acute and chronic periods of poststroke rehabilitation. It is recognised that therapies involving high-intensity repetitive tasks, such as the CIMT, have the best effect on the recovery of upper limb functions. However, by limiting the contralateral arm, the CIMT forces the patient to use the impaired arm and, thus, challenges the patient’s compliance during therapy, so that treatment outcomes are compromised. Therefore, high-intensity repetitive therapies might not be optimal for long-term rehabilitation of poststroke upper limb dysfunctions as well as for the improvement of the psychological well-being of the patients. The therapies supervised by therapists or with sophisticated equipment can increase the financial pressure of the patients and, thus, might not be widely accepted for long-term persistence. Therefore, economical and easy-to-adherence interventional exercises should be developed and involved to current poststroke rehabilitation programmes to allow the patients to persist in the training to obtain ongoing benefits from the therapy.

Chinese calligraphy handwriting (CCH) is a culture-based exercise to express the aesthetics of Chinese characters and writers’ inner psyche. Clinically, the CCH process has been suggested to facilitate people’s psychosomatic and cognitive well-being and to exert curative effects on autism, depression and posttraumatic stress disorder. For example, it was reported that CCH could improve specific cognitive functions in patients with mild cognitive impairment. It was also suggested that CCH could stabilise physiological arousal parameters of cancer survivors, including slower heart rate, decreased blood pressure and decelerated respiration. Thus, the CCH might also be able to mitigate poststroke neuropsychiatric disorders.

The CCH may be a proper exercise to improve stroke patients’ upper limb functions because of its unique writing styles. First, long-term CCH training might facilitate the neuroplasticity in human brain. In this study, the cingulate gyrus area was found to be relatively small in people who had practiced calligraphy for over 5 years, which was possibly due to increased efficiency of cingulate gyrus neuron utilisation. The CCH involves dynamic feedforward and feedback between visuoperceptual, proprioception and upper limb motor system. Specifically, the writer first predicts and plans the size and positions of each character on the paper. During CCH, the writer needs to recall the planned configurations of the characters and compare them to the writings. Such visual feedback on the writings also forces the writer to adjust brush gripping, applied pressure and writing speed. As the main function of the cingulate neurons is the previsial stimulation and premotor planning, the CCH might stimulate the cingulate neurons in the brain. Therefore, the CCH may be able to improve the patient’s cognitive well-being, hand–eye coordination and real-time execution ability. Second, the writer needs to maintain the upper limb stability to smoothen the thickness of the character strokes during CCH, which may effectively stimulate muscle contractions in the upper limb. Third, the writer strives to control the writing speed and frequently alters the tilt angles during writing. Therefore, performing the CCH may be able to train coordinative movements and improve the flexibility of upper limb joints. As a consequence, the CCH holds great potential not only in facilitating the recovery of upper limb functions but also in improving the mental state of patients with stroke.

The cultural factors behind the CCH may make it more easily accepted by Chinese patients than many other exercises. Calligraphy copybook is prevalently used at the beginning of CCH self-practicing because the character frames in the copybook can regulate people’s writing styles without the need of instructors. Thus, the calligraphy copybook may be an excellent tool for patients with stroke to practice the CCH exercise at both hospital and home. In addition to Chinese characters, the copybook can also be designed by including characters of other languages to make it more suitable for patients with other cultural backgrounds. Therefore, the purpose of this study is to develop a CCH-based interventional exercise with a self-designed calligraphy copybook and validate its effect on the improvement of patients’ upper limb functions in the chronic period of stroke.

METHODS
Study design
This study will be a single-centre, three-arm, parallel group, assessor-blind randomised controlled trial. All the patients will be informed of the study content before the subject recruitment. The patients who meet the inclusion criteria and agree to participate in the study will sign the informed consent. As shown in the study flowchart (figure 1), the patients will be randomly allocated into three groups with equal sample size: (1) conventional occupational therapy (COT) group, (2) COT +CCH group, (3) COT +Graded Repetitive Arm Supplementary Program (GRASP) group. The rehabilitation interventions will last 3 weeks. Patients’ upper limb functions will be assessed using rating scales before and after the interventions. The study protocol is shown in figure 2 (recommended for interventional trials (Standard Protocol Items: Recommendations for Interventional Trials) 2013).

Subject recruitment and randomisation
From January 2021 to September 2021, patients will be screened and recruited in the Department of Neurological Rehabilitation in the Second Rehabilitation Hospital of Shanghai via reviewing their electronic medical records. This study will only recruit patients who meet the following criteria: (1) first-ever stroke through
neuroimaging assessment, (2) within the chronic phase of stroke, (3) able to sit without upper limb supporting, (4) sufficient active range of motion: 90° of shoulder flexion, 90° of elbow flexion, 30° of wrist flexion, (5) able to hold the calligraphy brush with the affected hand, (6) good cognitive ability (Mini-Mental State Exam scores >23), (7) no serious visual impairment or visual field defect, (8) 40–80 years old. The exclusion criteria of this study include: (1) other neurological diseases or upper limb surgical histories, (2) severe communication deficits, (3) obvious shoulder pain (pain rating at rest >5).

Subject randomisation will be performed by an external professional statistician. Number 1–60 will be randomly sequenced using the SPSS V.23.0. Of 60 envelopes will be prepared, each with an external series number corresponding to the random sequence generated and an internal group number: #1 (COT group), #2 (COT+CCH group), or #3 (COT+GRASP group). Once a patient is recruited, the authors will open an envelope sequentially and allocate the patient into a group according to the internal group number. The external series number on the envelope will also be used as the ID of each patient to track their information and data throughout the entire study, which makes the assessor blind to the group allocation.

Sample size
According to a previous study, the minimal clinical important difference for the Action Research Arm Test (ARAT) scale is 6 in patients with chronic stroke. The mean score that patients with chronic stroke can achieve was reported to be about 30. Thus, the effect size is estimated to be 0.2. The sample size was then calculated using this value in G*Power 3 (Erdfelder, Faul, & Buchner, 1996). To achieve a power of 80% (α=0.05), a minimum of 18 subjects is required for each group. Taking this rate into consideration, a total of 60 patients (20 per group) will be recruited in the study.

Interventions
All patients will receive rehabilitation interventions based on routine treatment and daily nursing in the hospital. The rehabilitation interventions will be carried out 5 days per week for a total of 3 weeks. In the COT group, the patients will receive 60 mins COT treatment five times per week. The treatment will be performed by a therapist, which comprises task-related practices for gross movements and dexterity, including different grips, selective finger movements, strength training, stretching and daily life activities.

In the COT+CCH group, the patients will receive 30 mins COT treatment and 30 mins CCH training five times per week. The CCH training will be performed...
on self-designed copybooks with hollowed-out character frames (figure 3A). The copybooks are reusable as the water dries out in 5 min. During writing, the patients will be required to sit in front of a desk. The patients hold a calligraphy brush using the thumb, index finger and middle finger of the affected hand, soak its head with water and then fill the character frames on the copybook (figure 3B). Three different copybooks with increasing difficulties are designed, and each will be used in the CCH training for 1 week (figure 3C). This design can enable the patients to imitate geometric shapes, beginning with straight lines, followed by more complicated circles and curves, which will comply with the skill relearning progression within the poststroke rehabilitation.41

In the COT+GRASP group, the patients will receive 30 mins COT treatment and 30 mins GRASP training everyday. The GRASP is a standardised poststroke upper limb rehabilitation programme42 and has been demonstrated to be effective in enhancing the motor function of the upper limb of chronic stroke patients.43 The patients will perform GRASP by referring to an exercise manual presenting the schematic diagrams of each exercise. During the GRASP training, the therapist will leverage simple tools (such as balls, cups, and towels) to guide the patients to practice the actions and skills involved in daily activities.44

### Outcome assessment

The effects of these interventions on patients’ upper limb functions and quality of life will be assessed using a couple of different rating scales by a senior physiotherapist with over 5 years of relevant experience. This physiotherapist will not be involved in the execution of the intervention and will remain blinded to the group of the patient during the entire trial. To ensure maximum blindness, the patients will also be requested not to discuss their intervention exercises with the physiotherapist during the assessment. The rating scales include:

#### Primary outcome measures

- Fugl-Meyer assessment-UE47: this measure is designed to assess motor function, sensation, balance, range of motion and joint pain.
- Gripping strength of the affected hand will be measured as the mean of three consecutive trials.
- Disabilities of arm, shoulder and hand:49 this measure is a 30-item self-report questionnaire, which is designed to assess individually rated upper limb impairments and impacts on activities for patients with musculoskeletal conditions in the upper limbs.
- Quality of life (short form 36):50 this measure is a generic self-report of health status for evaluating the quality of life that relates to physical and mental well-being.

#### Statistical method

Two-way analysis of variance will be applied to examine the interaction and the main effects of the intervention method and the assessment time. The effects of the intervention will be analysed by comparing the changes in the functionality of the affected upper extremity between groups using the analysis of covariance of change score, with the baseline as covariate and by adjusting for possible confounders. If significant interaction is found, Tukey post hoc tests will be performed. Demographic characteristics and other baseline values will be described using descriptive statistics for each group. Significant level for all tests will be set at p<0.05 for all statistical tests and corrected for multiple comparisons using the Bonferroni method. All statistical analyses will be performed using SPSS (V.13.0; SPSS, Chicago, Illinois).

#### Quality control and quality assurance

During patient recruitment, three senior neurologists will jointly evaluate each patient’s stroke status based on his medical record. The experimental data will be reviewed and verified by a senior researcher.

#### Management of adverse events

Possible adverse events include shoulder pain, hand soreness and numbness and muscle fatigue. The patients will be instructed to rate and report the severity of pain and...
fatigue from 0 (eg, no pain) to 10 (eg, unbearable pain) at the end of each treatment. The research team will record the adverse event, including duration, severity and position. If any patient reports severe adverse events that may affect the progressing of the intervention, the test will be paused, and relieving treatment will be provided. If the symptom cannot be relieved, the intervention will be terminated.

**Patient and public involvement**

The initial research idea was conceived by the authors and modified according to face-to-face interviews with patients with stroke and their guardians. Before the formal experiment, five stroke patients will be invited to practice the CCH and GRASP. The intervention protocols will be adjusted based on their feedback to ensure the safety and applicability of the intervention. The potential risks and benefits of the study will be fully explained to the patients and their guardians before signing the informed consent, and the study results will be released to them on request.

**Ethics and dissemination**

This study will be conducted in accordance with the principles of the Declaration of Helsinki. The ethics approvals have been obtained from the Research Ethics Committee of the Second Rehabilitation Hospital of Shanghai (study ID: 2020-32-01, approved date: 15 December 2020) and the Shanghai University of Sport (study ID: 102772021RT043, approved date: 19 January 2021). The authors will communicate the study information, including the study aims, the recruitment criteria, the study protocols, the potential risks and the expected outcomes to the recruited patients. The authors will provide direct consultation to all patients and their guardians to address any concerns they may encounter. The patients and their guardians will make the final decision to join or withdraw from the study. All the recruited patients will sign the informed consent before the study.

Patients’ identifiable information will be stored separately from their clinical information and research data by one of the authors who is in charge of the patient randomisation. In order to protect patients’ confidentiality, only the director of the study, this author and the ethics committee will have access to the patients’ personal information and medical records. At the end of the study, the data will be saved on a password-protected hard drive and will be discarded 3 years after the study.

The results of the study will be published in peer-reviewed scientific journals and presented at conferences and workshops within 12 months after study completion. According to the instructions of the International Committee of Medical Journal Editors, individuals who meet the criteria for authorship will be included as authors of the publications. The CCH exercise and the corresponding equipment (copybook, calligraphy brush, etc) will be optimised and promoted to the vast physiotherapists to enable the clinical transition.

**DISCUSSION**

The results of the study will demonstrate that CCH enhances the continuity of recovery with daily practicing. Many patients do not perform rehabilitation training at home after leaving the hospital due to financial burdens and, thus, fail to further recover their upper limb functions. The CCH is expected to become a home-based rehabilitation activity that can provide the patient with long-term benefits at low costs. Patients can independently execute the CCH exercise without the presence of a rehabilitation therapist and, therefore, are able to maximise time spent improving their upper limb function with a minimum financial expense. As a type of self-administered exercise, the CCH may not be suitable for patients in the early stages of stroke recovery, but more suitable for patients who have initially benefited from hospital-based treatments and expect to continue upper limb rehabilitations after leaving the hospital. On the completion of this study, future research should include the design of a special brush that will be much easier to be held by the patient with inferior hand functions, in order to allow more patients to practice CCH to get benefits at an earlier stage after stroke.

**Author affiliations**

1School of Kinesiology, Shanghai University of Sport, Shanghai, People’s Republic of China
2Institute for Biomechanics, ETH Zürich, Zurich, Switzerland
3Department of Treatment, The Second Rehabilitation Hospital of Shanghai, Shanghai, People’s Republic of China
4Department of Rehabilitation, Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, People’s Republic of China
5Department of Rehabilitation, Xinhua Hospital Chongming Branch, Shanghai, People’s Republic of China

**Contributors**

XW: perform the preliminary experiment; write the manuscript; QZ: design the experiment; write the manuscript (joined); edit the manuscript; JQ: perform the preliminary experiment; NC: supervise the experiment; XW: design the experiment, be the PI of the project.

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**Competing interests**

None declared.

**Patient and public involvement**

Patients and/or the public were involved in the design, conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

**Patient consent for publication**

Consent obtained directly from patient(s).

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**Supplemental material**

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ORCID ID
Xie Wu http://orcid.org/0000-0002-0459-7065

REFERENCES


Below describes the details of the rating scales that will be used in the experiment:

1) Primary outcome measures

- Action Research Arm Test (ARAT): The ARAT was developed by Lyle in 1981 to measure function of the arm and hand in a variety of tasks, with special focus on fine motor function of hands. all 19 items of the ARAT are scored on a 4-point scale (0-3). Scores are judged as follows. 0, the patient is unable to perform any part of the task; 1, the patient is able to completely lift the object from the flat platform; 2, the function is completely completed but is very clumsy or very difficult; and 3, the movement is completed normally. The scores for each item were calculated by summing the total score for each side, ranging from 0 to 57 [1]. In addition, the overall time for patient to complete the ARAT will be recorded. The ARAT has good predictive and concurrent validity [2].

2) Secondary outcome measures

- Fugl-Meyer assessment-UE (FMA-UE): The FMA was designed in 1975 as a global assessment index for quantitative assessment of recovery of post-stroke paraplegic limbs. It is a quantitative performance-based measure consisting of 33 items that measure motor function of the upper limb. Each item is scored on a 3-point scale (0=can't perform, 1=can partially perform, 2=can fully perform), and the maximum score is 66. The severe degree of paresis was distributed according to the FMA score as follows. ≤25 points: severe, 26 to 45 points: moderate, and 46 to 66 points: mild [3]. The FMA has a high inter-rater and test-reset reliability [4].

- Griping strength of the affected hand: The grip force of the affected hand was measured with a dynamometer (Xiangshan, EH-101). The patient insisted the griping at his/her best for three seconds, and then rested for 30 s. The test was performed three times, and the maximum value was recorded.

- Purdue pegboard (PPB): The PPB was developed by Tiffin in 1948 to measure gross motor skill in the use of the arm, hand, and fingers, as well as fingertip dexterity. It consists of five subtests: dominant hand (D), non-dominant hand (ND), both hands (B), dominant +non-dominant+ both hands (D+ND+B), and an assembly subtest. In the five subtests, very small pins, washers, and collars were manipulated with one and two hands, and participants were
asked to place as many pins as possible into the holes within 30 seconds. In subtests D, ND, and B, the number of pins placed within 30 s was recorded. scores for subtests D+ND+B could be calculated from the scores of the first three tests. The assembly subtest score is the total number of pins, washers, and collars placed in 60 s [5]. PPB has good predictive and concurrent validity [6].

- Disabilities of arm, shoulder, and hand (DASH) : DASH is a 30-item self-report questionnaire designed to assess individual ratings of upper limb impairment and effects on activity in patients with upper limb musculoskeletal disorders. The items ask about the level of difficulty in performing different physical activities due to upper limb problems (21 items), the severity of symptoms such as upper limb pain, weakness and stiffness (5 items), and the impact of the problem on social activity participation, etc. (4 items). Each item has five options for response, with scores ranging from 0 (no disability) to 100 (most severe disability), with higher scores indicating greater disability. DASH has good internal consistency and validity in adults following stroke [7].

- Quality of life (short form 36, SF-36) : SF-36 was normalized in 1990 as a self-report measure of functional health and well-being. The SF-36 consists of eight health scales. Physical Functioning (10 items), Role Limitation-Physical (4 items), Physical Pain (2 items), General Health (5 items), Vitality (4 items), Social Functioning (2 items), Role Limitation-Emotional (3 items), and Mental Health (5 items). A score from 0 (the worst health measure) to 100 (the best health measure) was calculated for each scale. SF-36 has good internal consistencies and group differences validity in stroke patients [8, 9].
Reference


