

BMJ Open 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 Wu ¹

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XW and QZ contributed equally. NC and XW contributed equally.

XW and QZ are joint first authors.

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For numbered affiliations see end of article.

Correspondence to
Professor Xie Wu;
wuxie_sus@163.com

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.

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.^{3,4} With the improved care in the hyperacute and acute periods of stroke, around 80% of stroke patients can survive from the initial injuries.⁵ However, stroke can usually lead to severe

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 convincingness 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.

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 poststroke 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,^{15–17} bilateral training,¹⁸ constraint-induced movement therapy (CIMT),¹⁹ robotic-assisted therapy,²⁰ mirror therapy²¹ and virtual reality.²² As the function recovery can last into the chronic phase of stroke,²³ 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.⁸ 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,^{19,24} so that treatment outcomes are compromised.^{25,26} 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^{27,28} and, thus, might not be widely accepted for long-term persistence. Therefore, economical and easy-to-adherence interventive 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.²⁹ Clinically, the CCH process has been suggested to facilitate people's psychosomatic and cognitive well-being³⁰ and to exert curative effects on autism, depression and posttraumatic stress disorder.²⁹ For example, it was reported that CCH could improve specific cognitive functions in patients with mild cognitive impairment.³¹ It was also suggested that CCH could stabilise physiological arousal parameters of cancer survivors, including slower heart rate, decreased blood pressure and decelerated respiration.³² 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.³³ 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.³⁴ 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 previsional 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.³⁴ 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 interventive 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).³⁵

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

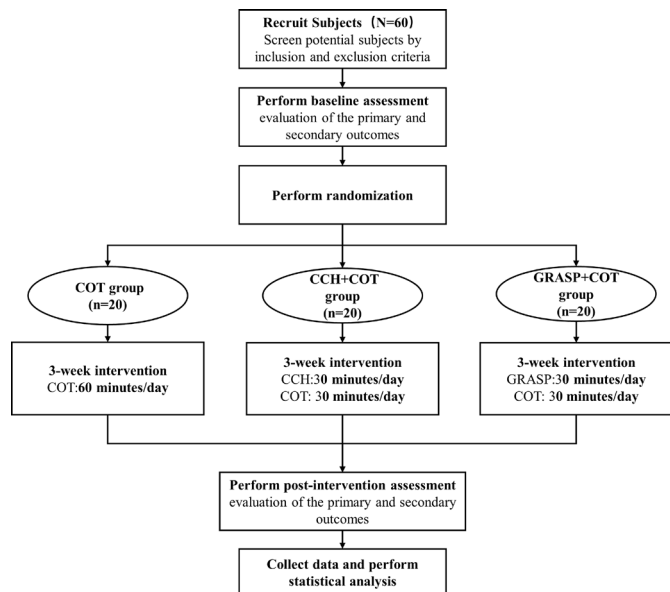


Figure 1 The study flowchart. CCH, Chinese calligraphy handwriting; COT, conventional occupational therapy; GRASP, Graded Repetitive Arm Supplementary Program.

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 pronation/supination, 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),³⁶ (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).³⁷

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).³⁸ 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,³⁹ 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 30.⁴⁰ 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% ($\alpha=0.05$), a minimum

	INTERVENTION PERIOD			
	Enrollment	Pre-allocation	Allocation	Post-allocation
TIMEPOINT	-T1	T0	0	T1
ENROLLEMENT				
Eligibility screens	×			
Informed consent	×			
Randomization	×			
Allocation	×			
INTERVENTIONS:				
COT			↔	
CCH+COT			↔	
GRASP+COT			↔	
ASSESSMENTS:				
Primary Outcome				
• Action research arm test		×		×
Secondary Outcome				
• Fugl-Meyer assessment-UE		×		×
• Gripping strength		×		×
• Purdue pegboard		×		×
• Disabilities of arm, shoulder, and hand		×		×
• Quality of life		×		×

Figure 2 The experiment schedule, including patient enrolment, intervention progresses and outcome assessments. The schedule was developed according to the standard protocol project statement for randomised trials. Time points: T1) before baseline screening; T0) baseline; T1) after intervention. CCH, Chinese calligraphy handwriting; COT, conventional occupational therapy; GRASP, Graded Repetitive Arm Supplementary Program.

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 60mins 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 30mins COT treatment and 30mins CCH training five times per week. The CCH training will be performed

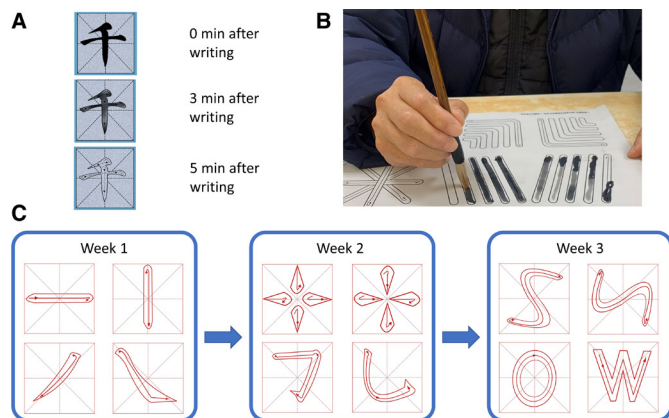


Figure 3 Calligraphy practising and copybook design. (A) Water drying out in 5 mins on the copybook. (B) A patient is practising the calligraphy handwriting. (C) The difficulty of calligraphy practising increases as the character frames become more complicated.

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

(ARAT)⁴⁵: the measure is a 19-items test divided into four subtests (grasp, grip, pinch and gross movement). For each item, the patient is asked to perform a simple task that involves a functional movement of the affected upper limb. The details of each scale are found in online supplemental material. In addition, on evaluating the score that patients can achieve, the overall time for patient to complete the ARAT will also be measured, in order to reduce the potential ceiling effect.⁴⁶

Secondary 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.
- ▶ Purdue pegboard (PPB)⁴⁸: the PPB is a reliable measure to assess the gross movement of the arm, hand and fingers as well as the fingertip dexterity. This measure requires patients to pick up pins one at a time and place them in a row of holes.
- ▶ Disabilities of arm, shoulder and hand⁴⁹: 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, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

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ORCID iD

Xie Wu <http://orcid.org/0000-0002-0459-7065>

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