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ORIGINAL ARTICLE

Acupuncture of Motor-Implicated Acupoints on Subacute Stroke Patients: An fMRI Evaluation Study

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ABSTRACT

Background: Motor impairment is common after stroke. Along with classic integrated physical and occupational therapy, acupuncture is also suggested as an adjunctive therapy.
Objective: To evaluate the effectiveness of acupuncture on upper limb motor recovery of patients with subacute stroke.
Design, Setting, and Patients: Eighteen subacute stroke patients, transferred from a regional acute hospital to a convalescent hospital for rehabilitation in Hong Kong, from March 2005 to November 2007. Two clinical and behavioral evaluations for motor function were given to each participant along with 2 functional magnetic resonance imaging (fMRI) scans.
Intervention: Patients were treated with acupuncture 3 times a week over 8 weeks. The intervention set of 3 acupoints is known to influence the motor system, while a second control set does not. Physical and occupational therapy were also used as treatment (parallel to the interventions with acupuncture).
Main Outcome Measures: The primary outcome measure was fMRI, and the secondary measures were clinical and behavioral parameters, concentrating on motor function and disability using reliable and validated scales.
Results: Data on hand grip demonstrated reappearance of brain activations in the motor-related areas of the lesioned hemisphere in both groups after intervention. As with clinical and behavioral evaluations, the fMRI data on hand grip demonstrated no statistically significant differences between the groups.
Conclusions: These preliminary results suggest that acupuncture may be beneficial to motor recovery in subacute stroke patients. However, the application of control acupuncture points did not result in a different recovery. The supplemental effect of acupuncture to physical and occupational therapy needs to be explored in further studies.

Key Words: Acupuncture, Motor Recovery, Subacute Stroke, fMRI

INTRODUCTION

Acupuncture has been used in motor recovery after stroke in China and other parts of Asia for at least 2,000 years.[1–4] Acupuncture is recognized as an adjunct therapy in the West for stroke rehabilitation[4,5] but no evidence for its effectiveness is available based on randomized controlled clinical trials.

Four systematic reviews[2,6–8] were performed to assess the effectiveness of acupuncture in motor recovery after stroke.

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These reviews agreed that the effectiveness of acupuncture has not been proven in stroke rehabilitation. However, the authors did find a trend; although not statistically significant, patients using acupuncture as adjunct therapy after stroke did report some benefits. Nevertheless, it was agreed that well-designed randomized controlled clinical trials are lacking. It was suggested that studies should use both sham acupuncture and placebo control.[2,6,8] It is also clear that studies should be performed in a double-blinded manner.[2,6,8] In addition, the treatment schedule such as number of acupuncture sessions, acupoints used, and the duration of the whole treatment course should be standardized in all participants and administered by skilled practitioners.[2,8] Following therapy, internationally recognized outcome assessments should be used for quantification.[2,6–8]

Apart from assessing the effectiveness of acupuncture in motor recovery after stroke using functional outcome measures, neuroimaging (such as functional magnetic resonance imaging [fMRI]) may be used to assess the role of acupuncture in motor recovery. fMRI is able to show brain reorganization after stroke[9–12] using blood oxygen level–dependent (BOLD) signals.[13] In control participants under stimulation of motor-implicated acupoints, BOLD signals have also been detected in the sensorimotor area.[14,15] However, BOLD signals under stimulation of motor-implicated acupoints of stroke patients have not been studied in either cross-sectional or longitudinal studies.

Our objective was to investigate the effectiveness of acupuncture in motor recovery of stroke patients in the subacute stage by applying neuroimaging and functional outcome scales. The null hypothesis was that there would be no difference between motor-implicated acupoint stimulation and nonmotor-implicated acupuncture stimulation in supplementing routine physical and occupational therapy after stroke with respect to motor recovery.

METHODS

Recruited from March 2005 to November 2007 and admitted to a regional acute hospital were Chinese ischemic stroke patients (aged 18–80 years) experiencing a first stroke. Acute stroke was defined as stroke with onset of symptoms within 5 days from the date of admission.[16] All patients presented with significant hand weakness. Stroke severity at admission was measured using the National Institutes of Health Stroke Scale (NIHSS).[17] All patients gave written consent for their participation according to the Declaration of Helsinki[18] and they were free to withdraw from the study at any stage. Adverse effects and the number of deaths and recurrent strokes were recorded. The study was approved by the institutional review board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster.

Clinical and Behavioral Evaluations

Two clinical and behavioral evaluations for motor function were given to each participant. The first was performed within 1 week before initiation of the acupuncture intervention and repeated at the completion of the intervention. Each patient underwent neurological examinations using validated, internationally recognized neurological scales: the Barthel Index,[19] Motricity Index,[20] and Fugl-Meyer assessment.[21] For behavioral evaluation, patients were asked to execute grip strength with their paretic hand. Grip force[22] was measured in kilograms by a hand dynamometer. Evaluations were done by a registered physiotherapist on the affected hand only.

fMRI Scans

Two fMRI scans were administered to patients. The first one was performed within 1 week before the start of the acupuncture intervention and the second within 1 week after the completion of the acupuncture intervention. fMRI scans were administered using a 3T clinical MRI scanner (Magnetom Trio Tim syngo, Siemens Medical Solutions, Erlangen, Germany). Each patient underwent 2 structural MRI scans (T1- and T2-weighted) followed by 3 echo-planar imaging (EPI) T2*-weighted fMRI scan. Structural scans were used for the location of anatomy and pathology references.

For fMRI scans, BOLD images were performed using a T2*-weighted EPI sequence (TR [repetition time]/TE [echo time] = 3000/30 ms; flip angle = 90° field of view = 230 × 230 mm; matrix = 64 × 64; slice thickness = 3 mm contiguous; 44 slices; 60 time points for a total of 180 seconds). Image collection was preceded by 2 dummy scans. Each EPI sequence consisted of a boxcar paradigm composed of 4 alternating blocks with rest (R) and activation (A) (R-A-R-A). The duration of each block was 45 seconds. Three EPI sequences were acquired on each stroke patient: 1 for motor task performance, 1 for motor-implicated acupoint stimulation, and the other for nonmotor-implicated acupoint stimulation. The sequence of the 3 EPI scans administered was random.

Motor Task Performance

EPI scans of motor task performance were used to show brain reorganization before and after acupuncture interventions. Patients were instructed to squeeze a rubber ball with a force sufficient to cause indentation at their own constant pace[23] at A blocks of an EPI sequence. The cue to begin and to cease movements was indicated by tapping on the knee on the paretic side by an independent person who was present in the scan room with the patient. Mirror movement and involuntary movement were monitored as well.

Acupuncture Stimulation

EPI scans were used to show brain responses under acupoint stimulations and revealed differences between motor-implicated acupoint stimulation and nonmotor-implicated acupoint stimulation, if any. Patients were told that they would receive 2 sets of acupuncture stimulations on their paretic hand at 2 EPI sequences. Each set of stimulations involved 3 acupoints on the paretic forearm, and electric stimulation was provided on each acupoint. The intensity of electric stimulation was set depending on the presence of De Qi on the acupoints. De Qi was described as soreness, heaviness, and numbness.[14,24–26]

An electrode was stuck adjacent to each acupoint for electrical circulation. Needles were connected to the anode and electrodes were connected to the cathode by clips that were paired by a wire to an electronic acupunctoscope (Model WQ-6F, Donghua Electronic Instrument Factory, Beijing, China) that was located outside the scan room. Electric current was given at A blocks of EPI sequences. Frequency of stimulation was at 2 Hz.[14,27] Acupuncture was administered by a registered acupuncturist.

Randomization

This study adhered to checklists of Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA).[28] After the first clinical and behavioral evaluations and fMRI, patients were randomized using a computer program into a treatment and a control group, respectively. The treatment group received stimulation on 3 motor-implicated acupoints (LI 4 Hegu, PC 6 Neiguan, LI 11 Quchi), while the control group received stimulation on 3 nonmotor-implicated acupoints (TE 4 Yangchi, LU 6 Kongzui, LI 12 Zhouliao). The acupoints were the same as those used during fMRI EPI scan. Acupoints were stimulated unilaterally on the paretic hand of the patients while in a supine position. For patients who received acupuncture at LI 4, LI 12, and LU 6, needles were inserted at a depth of 0.5 to 1 inch. Puncture of acupoints LI 11, TE 4, and PC 6 was at a depth of 1 to 1.5 inches, 0.3 to 0.5 inches, and 0.5 to 0.8 inches, respectively. De Qi was provoked by manual stimulation at the beginning of the treatment. Needles were retained in place for 30 minutes and were stimulated by an electronic acupunctoscope. Current intensity was individualized to maintain De Qi. Single-use sterile acupuncture needles (0.25×40 mm and 0.25×25 mm) were used for intervention (Hwato, Suzhou Medical Appliance Factory, Suzhou, China). Each patient received 24 intervention sessions, 3 sessions a week.

Apart from acupuncture interventions, all patients were in the routine, in-patient stroke rehabilitation program at the convalescent hospital (3 times a week for 8 weeks). Reasons for termination of the treatment (if any) were recorded. A licensed acupuncturist with more than 20 years of experience and a postgraduate degree in acupuncture was responsible for acupuncture intervention with all patients throughout the study. The control intervention was a comparison between motor-implicated acupoints and nonmotor-implicated acupoints. Patients received a full explanation about the randomization of the study and they were free to choose whether or not to participate. Needling details of control interventions are previously described. Choices of nonmotor-implicated acupoints were recommended by the acupuncturist based on 3 intentions. First, the nonmotor-implicated acupoints were close in location to the motor-implicated acupoints, so they were effective in blinding the patients as to whether they were in the treatment or the control group. Second, the nonmotor-implicated acupoints were not recommended to be used for stroke treatment.[29,30] Third, the nonmotor-implicated acupoints were believed to have a localized effect only.[31,32]

Data Analysis

Clinical and behavioral evaluations and fMRI using BOLD images of motor performance, before and after acupuncture interventions, were compared in both the treatment and control groups.

Clinical and behavioral evaluation data analysis was processed using SPSS version 15.0 for Windows (SPSS Inc, Chicago, IL). Independent sample *t* test was used to compare the between-group changes in motor function scores. Differences in results in data, between before and after interventions within the group, were analyzed using paired *t* test. A P value $<.05$ was considered statistically significant.

fMRI images were analyzed using SPM2 (Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab 6.0 (Mathworks, Sherborn, MA) on a Windows XP platform. Realignment, coregisteration, and normalization of images were performed. Brain activations responsible for handgrip were found by a positive contrast setting in the general linear model of SPM2. The left hemisphere was assumed to be the lesioned hemisphere. Therefore, images from patients who had a right hemispheric infarct were flipped along the mid-sagittal plane.

Single subject contrasts were first created and then used for 1-sample *t* test to create group maps (corrected $P <.05$, extent threshold = 50 voxels), representing the 2 groups before and after the intervention. Paired sample *t* test was then used to analyze differences within treatment and control groups, whereas the 2-sample *t* test was used in testing for differences before and after acupuncture between groups.

EPI scans of motor-implicated acupoint stimulations and nonmotor-implicated acupoint stimulations of each participant were pooled to reveal brain responses. Using the same image analysis and general linear model statistics mentioned above, 2 group maps corresponding to brain activities under motor-implicated acupoint stimulation and nonmotor-implicated acupoint stimulation of stroke patients were found.

To show the role of acupuncture in stroke rehabilitation, conjunction analysis between motor task (after acupuncture only), and acupuncture EPI scans was performed.

RESULTS

Clinical Data

Twenty-six patients were initially recruited into the study, as shown in the flowchart of randomization (Figure 1). Eighteen patients were included in the final data analysis. Ten patients were in the treatment group and 8 in the control group. No recurrent stroke or death was recorded during the period of the study. Three patients did not receive intervention because they had hemorrhagic stroke. Three patients exited the study and did not finish the predetermined treatment and evaluation schedules.

Acupuncture intervention commenced at the subacute phase of stroke (mean [SD], 22 [6.1] days). Patient characteristics are listed in Table 1. The median NIHSS score was 5.5 (range, 0–15), indicating that most patients had moderate neurological deficits.[13] There were no statistically significant differences in the age, sex, NIHSS score, and paretic side between treatment and control groups. Six patients were paretic on the left side and their fMRI images were flipped along the midline for analysis. Therefore, the left hemisphere was the lesioned hemisphere for all patients in this study.

No adverse treatment response was reported during acupuncture intervention. Current intensity of treatment and control groups were a mean (SD) of 6.1 (2.63) and 7.4 (2.69), mA respectively. No significant differences in the current intensity used were found between the 2 groups.

Effectiveness of Acupuncture in Stroke Rehabilitation

Table 2 presents clinical and behavioral evaluations of the 18 patients assessed before and after acupuncture interventions. Figure 2 shows that both treatment and control groups demonstrated improvements in all 4 types of evaluations from baseline (*P* values <.05). However, no differences in these evaluations were found between the groups.

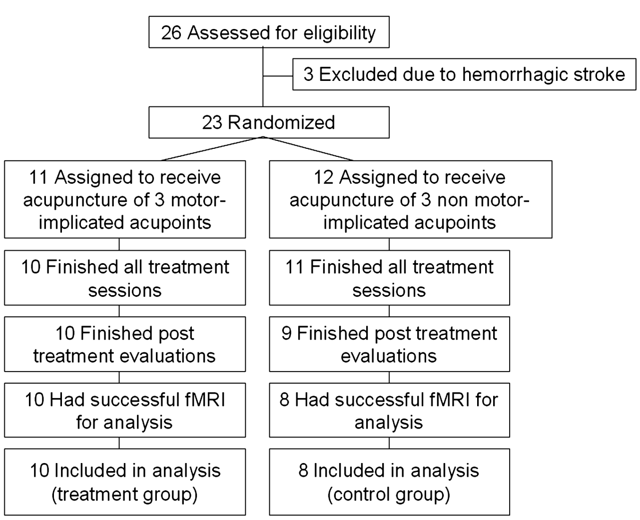

FIG. 1. Patient flow through the study.

Table 1. Demographic Details of Participants (N = 18)

No.	*Sex*	*Age, y*	*Paretic side*
1	F	69	L
2	M	72	R
3	M	73	R
4	M	75	R
5	M	74	L
6	F	71	L
7	M	69	R
8	F	71	R
9	M	55	R
10	F	62	R
11	F	75	L
12	M	55	R
13	M	70	R
14	M	73	R
15	M	75	L
16	F	63	R
17	F	48	R
18	M	71	L

fMRI data of hand grip demonstrated reappearance of brain activations in the motor-related areas of the lesioned hemisphere in both groups after acupuncture (Figures 3, 4). As with clinical and behavioral evaluations, the fMRI data of hand grip demonstrated no statistically significant differences between the 2 groups. However, paired *t* tests showed there was a significant difference in the postcentral gyrus in the lesioned hemisphere (BA 1 and BA 2, coordinates: 50, −32, 64) based on fMRI data of hand grip in the treatment group.

Brain Response to Acupuncture

Acupuncturing motor-implicated acupoints in the affected hands of stroke patients activated bilateral superior frontal gyri. No activation was found in the motor-related areas in the brain (Table 3).

Under acupuncture stimulation on nonmotor-implicated acupoints in the affected hand of stroke participants, the major activation was found in the nonlesioned temporal lobe (Table 4).

Conjunction analysis did not show any brain area that would be coactivated under motor task and acupuncture stimulation in the patients.

DISCUSSION

Preliminary data of subacute stroke patients in the present study showed significant improvements of motor function in the paretic hands after acupuncture intervention. However,

TABLE 2. CLINICAL AND BEHAVIORAL EVALUATION SCORES OF PARTICIPANTS (N = 18)

		Motricity Index [0–100 (normal)]		*Barthel Index [0–100 (normal)]*		*Fugl-Meyer Assessment [0–66 (normal)] Upper limb*		*Grip power, kg*	
No.	*Group*	*Before*	*After*	*Before*	*After*	*Before*	*After*	*Before*	*After*
1	Real	34	50	20	65	24	38	0	0
2	Real	10	35	5	40	6	9	0	0
3	Sham	56	85	85	100	35	57	0	11
4	Real	26	64	60	80	15	40	0	4
5	Real	34	67	10	55	12	53	0	4
6	Sham	53	92	20	95	27	66	0	9
7	Real	73	100	70	100	47	65	4	17
8	Real	43	58	35	55	12	32	0	2
9	Real	29	85	55	100	10	64	0	13
10	Sham	40	92	80	100	39	63	1	7
11	Sham	61	73	60	100	22	62	0	8
12	Real	0	10	30	80	5	6	0	0
13	Real	0	48	20	60	6	39	0	8
14	Real	67	100	40	100	48	65	6	28
15	Sham	0	10	10	40	5	10	0	2
16	Sham	0	64	35	40	6	23	0	2
17	Sham	76	76	85	100	41	52	5	8
18	Sham	0	39	70	90	6	19	0	0

there was no statistically significant difference of motor recovery between the motor-implicated acupoints plus conventional stroke rehabilitation group and the nonmotor-implicated acupoints plus conventional stroke rehabilitation group. Thus, the index of daily activity outcome (Barthel Index), neurological functional outcomes (Motricity Index, Fugl-Meyer Assessment), and behavioral outcome (grip power) did not reveal a more significant improvement in the treatment group than in the control group. Moreover, activations in motor-related brain regions of the treatment group were not larger than those of the control group.

Treatment acupuncture vs sham acupuncture, both with conventional stroke rehabilitation, was studied previously.[4,33,34] The results reported were in line with those of the present study. Treatment acupuncture patients in 1 study[33] did show at least a 10% increase in the Boston Motor Inventory score compared with the sham acupuncture patients, although after 20 treatment sessions over a period of 4 weeks, the differences between treatment and sham groups did not reach statistical significance. A randomized controlled trial[34] of acute stroke patients was unable to demonstrate any beneficial effects of deep acupuncture performed over 20 sessions in 10 weeks revealed by Barthel activities of daily living scores, neurological scores, use of health care and social services, and quality of life scales when comparing patients who had superficial acupuncture vs receiving no acupuncture at all. Another study on subacute phase stroke patients[4] compared a group of control patients who received subliminal electrostimulation on acupoints with another group of patients who were given treatment acupuncture at the same acupoints of those stimulated in the control group. Again, the acupuncture group showed no beneficial effects on functional outcomes or life satisfaction compared with the control group. From those results and on the basis of the present study, the effectiveness of treatment acupuncture in addition to conventional stroke rehabilitation must be questioned.

On a longitudinal basis, both test and control acupuncture resulted in improved outcomes of motor function after 8 weeks as documented by neuroimaging and functional outcome assessments. Whether acupuncture stimulation revealed any additional benefits to conventional stroke rehabilitation cannot be concluded from the present study. Contrary to the study performed by Gosman-Hedstrom et al,[34] in the present study, no patient group without treatment acupuncture was incorporated.

In the choice of sham acupuncture techniques, Naeser et al[33] inserted needles in nonexisting acupoints that were not connected to electricity. The control groups in the studies by Gosman-Hedstrom et al[34] and Johansson et al[4] used acupoints that were the same as those considered in the treatment group, but superficial acupuncture[34] (needle placed just under the skin) and transcutaneous electrical nerve stimulation[4] were applied to the control groups. In the present study, these sham acupuncture techniques were not adapted because the patient population in Hong Kong

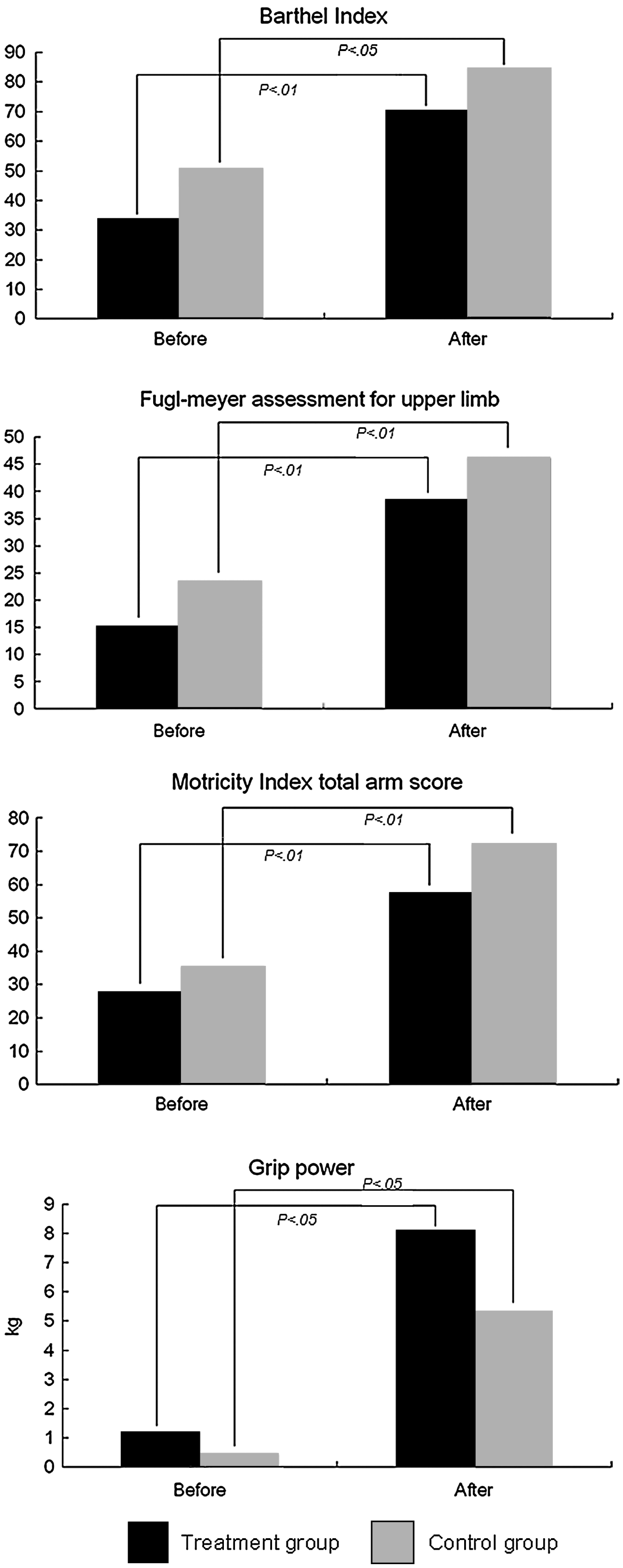

FIG. 2. Clinical and behavioral evaluations of treatment and control groups.

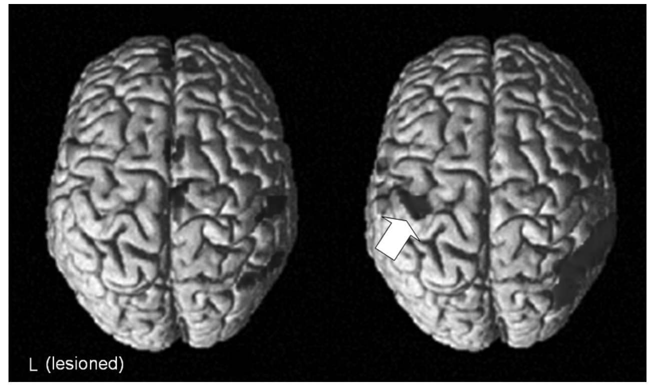

FIG. 3. Activation maps of fMRI data representing affected hand task of the treatment group before and after acupuncture intervention. White arrow indicates reappearance of brain activation in motor-related areas, consisting of the precentral and postcentral gyri (BA1, BA2, BA3, BA4, and BA6) in the lesioned hemisphere after acupuncture intervention.

includes mainly Chinese and Chinese patients, especially the elderly, are familiar with acupuncture. Application of superficial acupuncture, blunt-tipped needle on acupoints without skin penetration,[35] or nonexisting acupoints stimulation would have been insufficient to effectively blind the patients as to whether they were in the control or treatment groups.

The control acupuncture technique in the present study was the stimulation on nonmotor-implicated acupoints. These acupoints were chosen by an experienced acupuncturist. It was believed that stimulation of those acupoints would not induce a therapeutic effect in relation to upper limb recovery in stroke patients. Nonmotor-implicated acupoints located close to the motor-implicated acupoints were selected and electrical stimulation was applied until

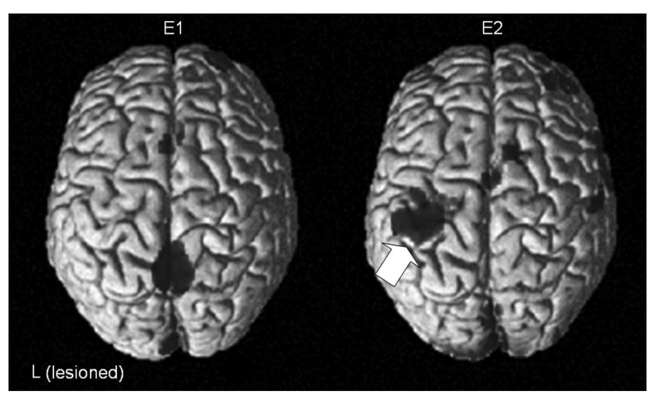

FIG. 4. Activation maps of fMRI data representing affected hand task of the control group before and after acupuncture intervention. White arrow indicates reappearance of brain activation in motor-related areas, consisting of the precentral and postcentral gyri (BA1, BA2, BA3, BA4, BA6, BA40) in the lesioned hemisphere after acupuncture intervention.

TABLE 3. REGIONS OF SIGNIFICANT ACTIVATION UNDER MOTOR-IMPLICATED ACUPOINT STIMULATIONS IN SUBACUTE STROKE PATIENTS

Clusters	$P_{corrected}$	Hemisphere	Coordinates of local maxima *x*	*y*	*z*	Regions in the cluster	No. of voxels
1	.02	Lesioned	4	4	74	Superior frontal gyrus	214
		Nonlesioned				Superior frontal gryus	353
2	.03	Nonlesioned	68	−40	20	Superior temporal gyrus	285
3	.03	Nonlesioned	42	30	44	Middle frontal gyrus	286
						Superior frontal gyrus	96

De Qi was achieved. Therefore, this control acupuncture technique was applied in the present study to provide satisfactory placebo and expectation effects.

Although nonmotor-implicated acupoints should not have therapeutic effectiveness on upper limb movement, they are nevertheless acupoints. Stimulation on an acupoint could elicit various physiological responses such as endogenous opioid release.[36] Needle insertions in nonmotor-implicated acupoints involving touching of the skin and stimulation of the nerves may produce therapeutic or clinically relevant effects.[37] In line with 2 other studies[38,39] that used nontherapeutic acupoints stimulation as the sham acupuncture technique, the indistinguishable effect between real and control acupuncture in this study could imply that any form of needle stimulation on the skin would produce similar results. Neither one had relevant therapeutic effects[40] because a De Qi effect was more important in improving motor function than the locations and choices of acupoints.

The selections of motor-implicated acupoints in this study (LI 4 Hegu, PC 6 Neiguan, and LI 11 Quchi) for the treatment group were based on 2 reasons. First, their effectiveness in upper limb motor recovery was relevant in stroke patients. Acupoints LI 4,[4,27,34,41–43] PC 6,[44] and LI 11[4,27,34,43] were chosen as the acupoints that facilitated motor recovery in many previous studies. Second, they were chosen because of the brain response to the stimulation of these acupoints. They have been designated as motor-implicated acupoints[14] because their stimulation induced activations in sensorimotor areas including the superior frontal gyrus, precentral gyrus, and postcentral gyrus (BA3, BA4, BA6, and BA7)[14] in fMRI images established in healthy participants.

From the fMRI data of the present study, acupuncture stimulations on motor-implicated acupoints did not activate motor-related areas in the brain. Acupoint specificity with brain responses, shown as an fMRI signal, is a point of controversy. Acupoint specificity appeared to be difficult to replicate.[45] As far as can be determined, acupuncture specificity in stroke patients has not been reported. fMRI data of stroke patients who were undergoing recovery showed a widespread activation when performing a predetermined test task. It was expected that acupuncture stimulation may produce a widespread activation in fMRI images.

In agreement with other studies,[4,34,46,47] this study provided acupuncture treatment to subacute ischemic stroke patients in addition to conventional inpatient physiotherapeutic and occupational therapies. Thus far, none of the studies mentioned were able to demonstrate any additional beneficial effects of acupuncture to conventional stroke rehabilitation.

CONCLUSIONS

This is the first study to apply fMRI images, together with functional outcome measures, to assess the effectiveness of acupuncture in motor recovery of patients with subacute stroke using a randomized controlled setting. From the preliminary data collected, there was no evidence that

TABLE 4. REGIONS OF SIGNIFICANT ACTIVATION UNDER NONMOTOR-IMPLICATED ACUPOINTS STIMULATIONS IN SUBACUTE STROKE PATIENTS

Clusters	$P_{corrected}$	Hemisphere	Coordinates of local maxima *x*	*y*	*z*	Regions in the cluster	No. of voxels
1	.16	Nonlesioned	48	20	−16	Superior temporal gyrus	327
						Inferior frontal gyrus	89
2	.17	Lesioned	−56	8	−4	Superior temporal gyrus	371
3	.18	Lesioned	−2	−58	70	Precuneus	21
		Nonlesioned				Precuneus	23

acupuncture on motor-implicated acupoints was superior to acupuncture on nonmotor-implicated acupoints in motor recovery of subacute stroke patients who received ongoing stroke rehabilitation. This raises a question on the choice of the control acupuncture technique that could be carried out on a Chinese population effectively, and without sensory or neurophysiological stimulations. Brain response under acupuncture stimulation in stroke patients was shown, but a larger study is needed to verify the findings. A pure control group, receiving stroke rehabilitation only in the absence of any form of acupuncture, is necessary to distinguish whether any motor recovery would benefit from additional acupuncture stimulation.

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DISCLOSURE STATEMENT

No competing financial interests exist.

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