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BRIEF REPORT

An fMRI Study Showing the Effect of Acupuncture in Chronic Stage Stroke Patients With Aphasia

Anson C.M. Chau[1], Raymond Tak Fai Cheung[2]*, Xianyong Jiang[3], Paul K.M. Au-Yeung[4], Leonard S.W. Li[5]

[1]*Department of Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong*
[2]*Department of Medicine, Research Centre of Heart, Brain, Hormone and Healthy Aging, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong*
[3]*Clinical Centre for Teaching and Research in Chinese Medicine, Tung Wah Hospital, Hong Kong*
[4]*Department of Diagnostic and Interventional Radiology, Hong Kong Sanatorium and Hospital, Hong Kong*
[5]*Department of Medicine, Tung Wah Hospital, Hong Kong*

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Abstract
Acupuncture is used as a treatment in stroke patients with aphasia, yet the underlying neural mechanisms are unknown. This study aims to examine the relationship between changes in language function and brain activation using functional magnetic resonance imaging in chronic stroke patients with aphasia who underwent an 8-week acupuncture protocol. Seven chronic stroke patients were identified from a stroke database of a regional acute hospital in Hong Kong between January and July 2007. Patients were treated three times a week over a period of 8 weeks. Four acupoints were stimulated on the weak side of the patient's body. No other rehabilitation was given during the study period. Changes in language function were measured by aphasia quotient (AQ) of Cantonese Aphasia Battery (CAB). Functional magnetic resonance imaging blood oxygen level dependent signals were used to demonstrate the correlation between changes in AQ and brain activation after treatment. The patients were divided into well-recovered and poorly-recovered groups based on their CAB scores at entry. The well-recovered group showed significant improvement in CAB scores after receiving acupuncture treatment. A significant correlation between changes in AQ and blood oxygen level dependent activation in the lesioned Wernicke's speech area was found. These preliminary results suggest that acupuncture may be beneficial to language recovery in chronic stroke patients.

1. Introduction

Aphasia is a complication of stroke. Studies from different populations have revealed an incidence rate of aphasia ranging from 15% on the 10th day to 34% at 1 year following stroke [1]. In Western medicine, speech and language therapy is used to treat aphasia. However, this mode of therapy needs to be intensively administered for a prolonged period in order to achieve improvement of language deficits [2]. Aphasia has a negative impact on the patient's well-being, independence and financial situation.

*Corresponding author. Department of Medicine, 4/F Professional Block, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong.
E-mail: rtcheung@hku.hk

Chronic stroke patients with aphasia search for complementary and alternative medicine as long term treatment at a lower cost. Acupuncture is one of their choices. Acupuncture has been used in stroke rehabilitation in Asia for over 2000 years [3]. Studies have shown a positive therapeutic effect of acupuncture on aphasia in acute stage stroke patients [4]. Furthermore, acupuncture stimulation of certain acupoints has been shown, using functional magnetic resonance imaging (fMRI), to modulate the language network in the healthy brain [5].

Hence, this study aimed to investigate the therapeutic effect of acupuncture on language function in stroke patients with aphasia at the chronic stage. An internationally recognized quantitative linguistic functional scale for outcome evaluations and fMRI were used.

2. Materials and Methods

2.1. Subjects

Seven Chinese out-patients experiencing one ischemic stroke (2 females; mean age 63±10 years) were recruited. Their strokes occurred 17±8 months earlier. The patients were aphasic when they were discharged from the convalescent hospital. The infarct site was in the left hemisphere of these right-handed patients. The patient's characteristics are listed in Table 1. This study adhered to checklists of Standards for Reporting Interventions in Controlled Trials of Acupuncture [6]. Patients received stimulation on four acupoints (LI4-Hegu, PC6-Neiguan, LR3-Taichong and ST36-Zusanli). Acupoints were stimulated unilaterally on the weak side of the body, i.e., the right side, with the patient in a supine position. For patients who received acupuncture at LI4 and ST36, the needle was inserted at a depth of 1.3 cm to 2.5 cm and 1.3 cm to 3.0 cm, respectively. Needling over acupoints PC6 and LR3 was at a depth of 0.8 cm to 1.3 cm. De qi sensation was provoked by manual stimulation at the beginning of the treatment. The needles were retained in place for 30 minutes, and the acupoints were continuously stimulated by an electronic acupunctoscope (Model WQ-6F; Donghua Electronic Instrument Factory, Beijing, China). Current intensity was individualized to maintain de qi sensation. Sterile acupuncture needles (sizes: 0.25×40 mm and 0.25×25 mm) made for single use were used for this study (Hwato, Suzhou Medical Appliance Factory, Suzhou, China). One licensed acupuncturist with over 20 years experience and a postgraduate degree in acupuncture was responsible for selection of these acupoints and delivery of acupuncture therapy to all patients throughout the study. Each patient received 24 intervention sessions, with three sessions a week. All patients gave written consent for their participation according to the Declaration of Helsinki [7]. They were free to withdraw from the study at any stage. The study was approved by the institutional review board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster.

2.2. fMRI scans

Two fMRI scans were performed on patients. The first one was performed within one week before the start of the acupuncture therapy and the second was performed within one week after the completion of the therapy. At each fMRI visit, a patient underwent two structural MRI scans (T1- and T2-weighted) followed by a fMRI scan. Structural scans were used for anatomical localization and reference to the pathology.

For functional scans, the blood oxygen level dependent (BOLD) signals were collected using a T2*-weighted echo planar imaging (EPI) sequence (TR/TE=3000/30 ms; flip angle=90°; FOV=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 two dummy scans. Each EPI sequence consisted of a box-car paradigm composing of six alternating blocks with rest

Table 1 Demographic characteristics of patients

Subject	Sex	Age (yr)	Stroke chronicity (mo)	Infract sites
1	M	56	15	L lentiform nucleus
2	M	56	9	L basal ganglion
3	M	79	28	L frontal lobe
4	F	75	24	L middle cerebral artery territory
5	F	59	8	L middle cerebral artery territory
6	M	59	12	L middle cerebral artery territory, brainstem
7	M	59	26	L frontal lobe

M=male; F=female; L=left.

(R) and activation (A), i.e., RARARA. The duration of each block was 45 seconds.

EPI scan showing BOLD signal activation under linguistic task lasted for 4.5 minutes. The patient was in a supine position, wearing headphones with their hands resting on their abdomen. The patient was instructed to look at a reflective image of a screen through a mirror attached onto the receiving head coil which was connected to the MRI scanner. The scan started with the R block. In the R block, a crosshair was projected onto the screen at three positions: center, left and right. The projection was controlled by software installed in a laptop that was connected to the projector. The patient was then instructed to look at the crosshair when it was in the centre of the screen. When the crosshair was at a left or right position on the screen, the patient was instructed to indicate its position by raising the left or right index finger accordingly. Nine modified questions from Cantonese Aphasia Battery (CAB) were presented in each A block. Questions included sentence completion, sentence comprehension and auditory word recognition. The patient heard the questions through the headphones. Two answers for each question were then projected on the left and right side of the screen. The patient was then required to use their left and right index fingers to indicate the correct answer.

2.3. Linguistic function evaluation

Changes in linguistic function were measured using CAB [8]. CAB is modified from the Western Aphasia Battery (WAB) [9] and used for assessing aphasia in a native Cantonese speakers. Two CAB evaluations were given to each subject. The first was performed within 1 week before initiation of acupuncture therapy and the second at the completion of therapy. CAB contains the same assessing components as WAB, and includes spontaneous speech, comprehension, repetition and naming. The total score is expressed as an aphasia quotient (AQ) with the maximum AQ being 100, indicating no linguistic impairment. CAB evaluations were performed by a licensed speech therapist throughout the study.

2.4. Data analysis

Two AQ from each patient were compared using pair sample *t* test to reveal differences in language function before and after acupuncture treatment. Change in AQ of each patient was used in correlation analysis. fMRI images were analyzed using SPM2 (Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab 6.0 (Mathworks, Sherborn, MA, USA) on a Windows XP platform. Realignment, coregistration and normalization of images were performed. BOLD signal activations responsible for linguistic function were found by positive contrast setting in the general linear model of SPM2. Single subject contrasts were first created and then used for one-sample *t* test to create group maps (corrected $p<0.05$, extent threshold=50 voxels). To reveal any correlation between changes in linguistic function and language-related areas activation, we used a general linear test to detect the difference in the fMRI signal between the pre- and post-acupuncture scans. Regression analysis was then used to estimate the correlation between change in AQ and brain activation. Regression maps were evaluated at a corrected significance level of $p<0.05$.

3. Results

The AQ scores among our patients were uneven. AQ scores upon entry into the study were above 75% in five out of seven patients but below 25% in the remaining two patients. Thus, data were analyzed in two groups. Patients with AQ scores above 75% were assigned to the well-recovered group. Those with AQ scores below 30% were placed into the poorly-recovered group. Stroke occurred 21 ± 7.1 months earlier in the well-recovered group ($n=5$) and 9 ± 0.5 months earlier in the poorly-recovered group ($n=2$).

The seven patients showed a range of change in language function, based on AQ, after acupuncture treatment relative to baseline (−15% to 12%). A positive change in AQ in patients from the well-recovered group was observed after treatment ($7.7\%\pm4.10$). By contrast, a negative change was observed in the poorly-recovered group (−1.1% and −15.4%). Patients in the well-recovered group showed significant improvement of AQ after receiving 8 weeks of acupuncture therapy (pair sample *t* test, $p<0.05$; Figure 1).

Results of a simple regression analysis showed statistically significant correlation ($p<0.05$) between change in AQ scores and BOLD signal activations in the left middle and superior temporal gyri (Figures 2A and 2B). The findings suggested that a greater improvement in language function was associated with a larger activation in these areas. Details of activations are listed in Table 2.

4. Discussion

The main finding of this fMRI study was a significant correlation between positive changes in AQ and BOLD signal activation of the Wernicke's speech areas (BA22) in the lesioned hemisphere after an acupuncture treatment in chronic stroke patients with

aphasia. A previous fMRI study has shown dynamic patterns reflecting different stages of recovery after stroke [10]. The left temporofrontal region is responsible for linguistic function in normal subjects.

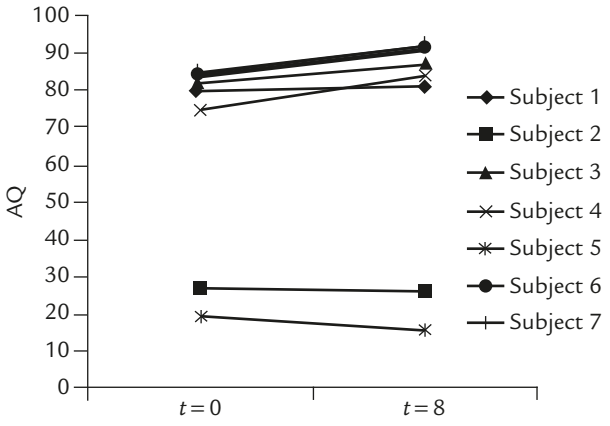

Figure 1 Changes in aphasia quotient (AQ) of Cantonese Aphasia Battery (CAB) of patients before ($t=0$) and after 8 weeks ($t=8$) of acupuncture therapy.

It has been suggested that perilesional regions or the contralesional hemisphere (right frontal lobe) are recruited for linguistic functional recovery after stroke, and that the degree of right-hemispheric participation may be a function of lesion size and aphasia severity [11]. Therefore, right-hemispheric recruitment would be greater with a large lesion in severely aphasic patients. Longitudinal studies have revealed a shift from the right hemisphere in the initial stages of recovery to the left hemisphere at a later stage of recovery [11]. The present study also found fMRI activation in the left middle and superior temporal gyri. A larger increase in AQ score is associated with a greater activation in the lesioned (left) language areas. Group analysis did not show significant activations during language task in either well-recovered patients or poorly-recovered patients. This may be due to weak signals generated by our small sample size which could not pass the statistical threshold. Apart from increasing the sample size, a homogeneous patient pool is essential to demonstrate activation in a lesioned brain. Variations in size, shape and location of infarct did not

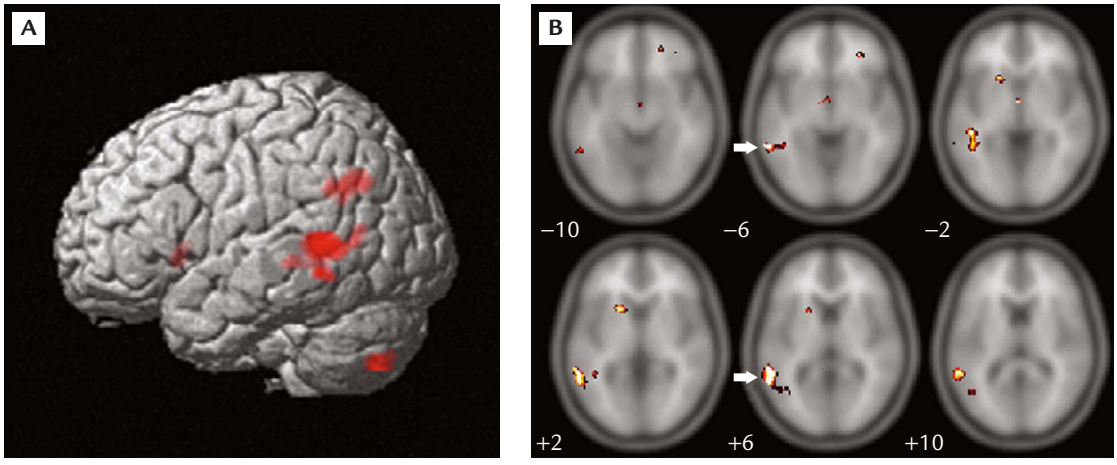

Figure 2 Correlation maps show change in aphasia quotient (AQ) and blood oxygen level dependent (BOLD) signal activations after an acupuncture treatment ($p<0.05$). (A) Results are surface-rendered onto a canonical brain viewing from the left side. (B) Results are displayed on normalized axial T1-images. The numbers below each image refer to z-plane coordinates in Table 2. Each image is 4 mm apart from each other. The left hemisphere of the brain is on the left side of the image. Arrows indicate clusters listed in Table 2.

Table 2 Brain activations on functional magnetic resonance imaging during the language task

Clusters	Hemispheres	Coordinates of local maxima			Anatomical location	BA	No. of voxels
		x	y	z			
1	Lesioned	−56	−44	6	Middle Temporal Gyrus	22, 21	260
					Superior Temporal Gyrus	–	–
2	Lesioned	−60	−46	−6	Middle Temporal Gyrus	21	149
					Superior Temporal Gyrus	–	–

BA = Brodmann's area.

allow detection of perilesional activity in aphasic patients under group analyses using fMRI [11,12].

To the best of our knowledge, acupuncture treatment for aphasia has not been evaluated in stroke patients in the Western literature. In China, a randomized controlled clinical trial [4] reported a statistically significant difference in WAB between the treatment group and control group of patients in the acute stage of stroke. The treatment group received acupuncture treatment plus standard medication and speech therapy whilst the control group received standard medication and speech therapy only. Acupuncture treatment was administered daily and lasted for 30 days. In common with the present study, acupoints LI4 and LR3 were chosen. Patients recruited in this study did not receive any other form of rehabilitation during the study period, and so their improvement in language function was related to the acupuncture treatment. It is unclear why poorly-recovered patients experienced a decrease in language function after acupuncture treatment. Therefore, future studies of acupuncture effectiveness on aphasia should recruit patients with some residual language function of similar severity.

Among the acupoints used in this study, brain activation during LI4 and LR3 stimulation have been reported in healthy subjects [13]. Apart from LI4 and LR3, acupoints GV20, GV26, CV23, GB20, and HT5 have been selected for treating aphasia [4]. These acupoints are mainly located in the head and neck region. As part of a sham-controlled, randomized clinical trial, we also aimed to find activation during acupuncture stimulation for aphasia. Therefore, acupoints in the head and neck region were not compatible with our experimental design. The precise mechanism underlying this effect of acupuncture is unknown. However, it is possible that by increasing language-related activity in the lesioned hemisphere, acupuncture should increase blood flow and blood volume to the frontal and temporal lobes and to modulate language areas damaged by stroke. Although active brain reorganization is not expected in chronic stroke patients, a sham group with superficial needle insertion at non-acupoints without needle stimulation is helpful in illustrating the specificity of acupuncture, which is different from the physiological response of needling anywhere. The results of this preliminary fMRI study suggest that acupuncture in chronic stroke patients with well-recovered aphasia (AQ scored higher than 75) may modestly improve their linguistic function by increasing brain activity in the lesioned language areas. Further studies with a large sample size and a sham group are needed to determine whether acupoint specificity has a unique effect on brain activity as compared with the physiological response to needling.

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