

## Correlation between acupuncture and left-handed patients after stroke

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Optimal rehabilitation treatment of stroke often requires more than one therapeutic approach.<sup>1</sup> Often, one or more standard treatment modalities may be used in order to provide the most complete treatment for the patient. Increasingly, it is common to use several treatment modalities concurrently or in sequence, with the goal of improving the outcome of stroke rehabilitation. These modalities are occupational therapy (OT), speech therapy and physiotherapy (PT), combined with skilled medical and nursing care. In spite of intensive rehabilitation with these modalities, 36% of acute stroke patients stay moderately to severely disable at discharge.<sup>1</sup> Acupuncture as adjuvant modalities of treatment is widely practiced in China, and it can be traced back for at least 2000 years. It has become a subject of major interest, and one of the most popular practiced therapies in the West in recent years.

There have been many studies in the Chinese literature on the effectiveness of acupuncture in stroke rehabilitation, and its possible usefulness as shown in our previous study.<sup>2</sup> However with a few exceptions,<sup>2,3</sup> many of these studies have not been randomized and properly controlled. The trials in China support the effectiveness of acupuncture, but the quality of trials make the results less convincing. Trials published in the English literature propose that acupuncture may, or may not be effective for functional recovery<sup>4</sup> with the exception of trial by Abuhamed et al.<sup>2</sup> All other trials have not defined handedness and side of stroke as a differentiating variable, so they could not answer this question. Motor function of the limbs is predominantly depicted in the contralateral primary motor cortex in right-handed healthy subjects. Therefore, injury to primary motor cortex and other motor pathway components (such as, premotor cortex, supplementary motor areas, parietal cortex, and subcortical or brain stem) is able to cause contralateral hemiparesis or hemiplegia, a common neurological ailment in stroke. Although functional recovery after stroke is the rule more than the exception, mechanisms and determinants of this recovery are poorly comprehended. The goal of this study was to compare the effects of acupuncture, and no acupuncture in the acute stroke with respect to the ability in the activities of daily living (ADL) in

left-handed patients suffering from right hemiplegia (LHRH), or left hemiplegia (LHLH).

This study was approved by the Human Research Ethics Committee of Xiangya Hospital, Central South University. This study included 40 consecutive patient's suffering from acute cerebral infarction from Xiangya Hospital in Xiangya Medical College of Central South University, Changsha city, Hunan province, People's Republic of China after obtaining their informed consent. The study was conducted from September 2005 to March 2008. All patients were left-handed according to the Edinburgh Handedness Inventory. Inclusion criteria included: 1. left-handed patients with ischemic stroke (either computed tomography [CT] scan confirmed or CT scan normal, but clinically consistent with the World Health Organization's definition of stroke) 2. age >45 years 3. admission within 7 days post-ischemic stroke 4. no prior stroke with sensorimotor deficits 5. Glasgow coma scale of 15 6. ability to follow simple commands 7. the patient could not walk without support, and/or could not eat, and/or dress without assistance, and 8. the patient had to be able to cooperate mentally and be willing to participate in the study. Exclusion criteria included: 1. admission Barthel index (BI) <3 or >15, 2. no motor deficit 3. hemodynamic instability 4. history of dementia 5. inability to give agreement because of impaired cognition or receptive aphasia 6. deafness and/or blindness, and 7. right-handed patients. After inclusion, patients were stratified into LHRH (n=21), and LHLH (n=19). Patients in LHRH and LHLH were then separately randomized to the acupuncture group (LHRH [n=11] and LHLH [n=9]), and the control group (LHRH [n=10] and LHLH [n=9]). Randomization was sequential, and it occurred after the therapist's evaluation (concealed allocation). All patients received 4 weeks ( $\pm$ one week) of intervention in the neurological department. In both groups, treatment was started 7 days after a stroke onset. The total treatment duration was 4 weeks. The dropout cases were documented with causes, and analysis was based on intention to treat.

Intervention for the control groups' inpatients standard treatment included: PT (4 sessions per week and 45 minutes per session), OT (4 sessions per week and 30 minutes per session), speech therapy, and psychological counseling as indicated, and skilled nursing care, and a daily medical round. Drug therapy was not prespecified. Acupuncture group patients received the same treatment as described for the control group, with the addition of the acupuncture sessions of a total of 5 sessions per week, throughout the duration of 4 weeks of trial. Each acupuncture session lasted for 25 minutes.

Acupuncture was carried out by means of standard stainless-steel needles (0.30 mm diameter, 40 mm length), and performed by a well-trained acupuncturist. The acupuncture (body acupuncture) method used in this research is as follows: the acupuncture points selected for the upper limb were jian yu (large intestine meridian [LI] 15), zhi gou (sanjiao [sj] 6), qu chi (LI 11), wai guan (stomach meridian [S] 5), he gu (LI 4), and/or supplementary points as bi nao (LI 14), shou san li (LI 10).<sup>2</sup> The points selected for the lower limb were: fengchi (gall bladder [GB] 31), xue hai (spleen meridian [SP] 10), zu san li (S 36), san yin jiao (SP 6), tai chong (liver meridian 3), and/or supplementary points as tai xi (kidney meridian 3), san yin jiao (SP 6). Needling was carried out on the paretic side, following the traditional Chinese medicine principle of “neither augmentation nor depletion (of essence).” The special needle sensation (called *teh-chi*, meaning obtained essence) was evoked at every point. Once the needle was put *in situ*, low-frequency electrostimulation was applied (at LI 11 and LI 4 in the upper limb, and ST 36 and GB 31 in the lower limb). Frequency was preset to 2 Hertz with the amplitude regulated to be strong enough to elicit obvious muscle contractions. The non-electrostimulated needles were manipulated, and needle sensation was evoked every 10 minutes for 25 minutes. Defaulters (dropped out) were considered if they missed 4 concurrent sessions of acupuncture.

Supplementary points were used for all patients in the acupuncture groups. Traditional method of acupuncture was followed, so the acupuncturist was allowed to add, or omit a certain number of acupoints from a set of agreed-upon classical acupoints. To compare expectations of the patients in the acupuncture and control groups, we designed an expectancy scale based on questionnaires used to assess patients' expectation of effectiveness in a study on acupuncture in stroke rehabilitation.<sup>4</sup> After the first and the fifth treatment sessions, the expectation effect was tested by asking all patients the following question: “Do you think that this treatment will help you?” and “Would you recommend this treatment to others with the same problem as you have?” For each question, patients were asked to choose one of 5 alternatives: yes, probably, I have no opinion, probably not, or no.

Outcome measures was based on the neurological score in accordance with the Scandinavian Stroke Study group, comprising motor function of the arm, hand, and leg, orientation, ambulation, and speech. The highest score is 48 points. The ADL outcome was appraised with the Barthel index. The Barthel index is a tool with a highest of 100 points that includes 10 personal activities: feeding, personal hygiene, dressing, bathing

self, toilet, bowel control, bladder control, chair/bed transfer, ambulation/wheelchair, and stair/climbing. The Sunnaas index is an instrument for measuring ADL function, persona as well, and instrumental, it comprises 12 ADL, comprising eating, continence, indoor mobility, toilet management, and dressing and undressing, transfer hygiene, bath/shower, housework, cooking, outdoor mobility, and communication. The highest score is 36 points. Level of independence for each activity of daily living is scored from 0-3, with 0 as the lowest possible score, and 3 as the highest. A higher score shows fewer problems in both of these ADL indexes. The comparisons for outcome measures were planned to be carried out in 4 steps. In the first step, the LHRH and the LHLH control groups were compared. In the second step, the LHRH and the LHLH acupuncture groups were compared. In the next step, comparisons were made between the LHRH acupuncture group and the LHRH or LHLH control group. In the fourth step, the LHLH acupuncture group and the LHRH or LHLH control group. Comparisons were then carried out for entry characteristics.

Statistical methods utilized for the analysis of data are  $\chi^2$  test, Kruskal-Wallis test for the entry characteristics, and t test for the comparison between groups. Analyses were carried out using SPSS for Windows statistical software version 13.0. A  $p < 0.05$  was regarded as statistically significant.

**Table 1** - Entry characteristics of patients.

Characteristics	Acupuncture groups		Control groups	
	LHRH (n=11)	LHLH (n=10)	LHRH (n=10)	LHLH (n=9)
<i>Age, years</i>				
Male	75	77	74	76
Female	72	73	74	73
<i>Gender, n (%)</i>				
Male	7 (63.6)	6 (60.0)	5 (50.0)	5 (55.6)
Female	4 (36.3)	4 (40.0)	5 (50.5)	4 (44.4)
<i>Lesion site, n (%)</i>				
Normal	0	0	0	0
Cortical	2 (18.2)	1 (10.0)	1 (10)	1 (11.11)
Basal ganglion	5 (45.5)	4 (40.0)	4 (40)	4 (44.4)
Cerebellar	1 (9.1)	1 (10.0)	1 (10)	1 (11.1)
Brain stem	1 (9.1)	1 (10.0)	1 (10)	1 (11.1)
Multiple	2 (18.2)	2 (20.0)	2 (20)	2 (22.2)
<i>Other findings, n (%)</i>				
Previous stroke	3 (27.3)	3 (30.0)	3 (30.0)	3 (33.3)
Hypertension	8 (72.7)	7 (70.0)	7 (70.0)	6 (66.7)
Hypercholesterolemia	5 (45.5)	4 (40.0)	4 (40.0)	4 (44.4)
Atrial fibrillation	1 (9.1)	1 (10.0)	1 (10.0)	1 (11.1)
Smoking	5 (45.5)	4 (40.0)	4 (40.0)	4 (44.4)
Diabetes mellitus	2 (18.2)	2 (20)	2 (20)	2 (22.2)

Values are mean, LHRH - left-handed right hemiplegia, LHLH - left-handed left hemiplegia

A total of 40 left-handed patients were included at days 3-7 after acute ischemic stroke, and 21 patients each were randomized to LHRH and LHLH acupuncture group, and 19 patients each were randomized to LHRH and LHLH control group. Patient characteristics shown in Table 1 were comparable between the acupuncture groups and the control groups. Three patients had dropped out during the trial. There were no deaths or protocol offenders during the trial. Among the 3 dropouts, 1 patient had recurrent stroke, 1 defaulted on treatments, and 1 withdrew as a result of congestive heart failure. There were no statistical differences in dropouts between the groups.

At the first session of treatment, patients were asked on expectations of treatment. The proportion of patients with positive response (probably, or yes) to the question "Do you think that this treatment will help you?" was high in the acupuncture (85.7%) and control (84.2%) groups. When the question was repeated at the fifth treatment session, the proportion of patients with positive expectations remained high in the control (84.2%), and decreased somewhat in the acupuncture (81%) group, and the differences between the 2 groups at session 5 were not statistically significant. Responses to the question "Would you recommend this treatment for others with the same problem as you have?" showed a similar pattern (data not presented).<sup>4</sup> All patients receiving acupuncture tolerated it well without side effects. The total number of acupuncture sessions ranged from 16-20 for the acupuncture group. Nine (LHRH [n=5], LHLH [n=4]) patients received acupuncture at one additional acupoint in addition to the 10 main acupoints, 8 patients (LHRH [n=4], LHLH [n=4]) at 2 additional acupoints, and 4 patients (LHRH [n=2], LHLH [n=2]) at 3 additional acupoints. These acupoints were added according to the traditional Chinese medicine theory. Out of 21 patients receiving acupuncture, 19 were reported to have *teh-chi* ("obtained essence").

There were no statistically significant differences in the entry characteristics between the groups (Table 1). In both the acupuncture and control groups, all outcome measures showed that most of the improvement occurred at 2 weeks. After that time, the improvement continued. No differences were seen between the LHRH and the LHLH control groups when comparing the changes in the neurological score and the Barthel and Sunnaas index scores. For the ADL index scores after 2 and 4 weeks, also no differences were seen between the LHLH acupuncture groups and the LHRH or LHLH control groups making the same comparisons. Also, no differences were seen between the LHRH acupuncture groups and the LHRH or LHLH control groups ( $p>0.05$ ).

This randomized study in patients with acute ischemic stroke showed that acupuncture, given 5 times weekly for 4 weeks was associated with no beneficial effect in LHRH patients, as measured in different dimensions. For the design of the study, we chose a randomized parallel group study with 4 groups. The reasoning for having both a LHRH and a LHLH control groups was to explain whether the no acupuncture treatment situation was associated with any effect. As no such effect was discovered ( $p>0.05$ ), these 2 groups were utilized as a control groups in the following comparisons with the acupuncture groups.

Here, we will discuss whether any factors might have confounded the study. First, as we used the traditional method of acupuncture, in which the acupuncturist was allowed to supplement a certain number of acupoints, so we could not utilize sham acupuncture in the control group. Supplement acupoints were used for all patients. Thus, this could not cause bias. A number of previous randomized control trial of sham acupuncture treatments have been used as placebo controls, but sham acupuncture cannot exactly simulate true acupuncture.<sup>3</sup> We chose 10 main acupoints by referring to the books of acupuncture treatment in China. Our acupuncture sessions and its frequency was comparable with those from earlier studies. This study had greater sessions than others. Eighty percent of patient had *teh-chi*, and this is reasonable to be as important as the sites of acupuncture utilized in traditional Chinese medicine. Therefore, the positive result could not be confounded by these factors. In term of choosing instruments for evaluation, improvements in neurological impairment and ADL over 4 weeks were well discovered by neurological score, and Barthel and Sunnaas index in all groups, which propose that these outcome measures were properly chosen. These instruments have been widely used in other stroke studies, we think therefore, a clinically significant difference between the groups was improbably to have been missed. Furthermore, sum scores were used. Using a sum score has its limitations, but gives the reader the opportunity to compare the result with those in previous studies.<sup>2,3</sup>

Second, entry characteristics, which could affect the outcomes over time was taken into consideration in statistical analysis. Therefore, the results could not have been confounded by these characteristics. Third, the patient's expectancy of the efficacy of treatment may affect the result. The use of a credibility scale is one way of ascertaining the strength of the patient's expectations of improvement. Such a scale was used in this study. Fourth, this study used continuous electrical stimulation when the needle was put *in situ* hence, giving the evidence of the present strengthening stimulation

during the session could have produced a positive result. Previous randomized studies of acupuncture after stroke has reported positive results in  $\geq$ one outcome measure. The acupuncture procedure usually has been alike to the present one, with a combination of manual acupuncture and electroacupuncture. Fifth, the mean age of our study patients was high (74 years), as it was in the other positive study.<sup>4</sup> The patient age does not seem to be the only factor that distinguishes studies with positive versus negative result. Timing of the intervention may also be of significance. In this study and in other studies reporting negative or positive results, acupuncture treatment was started in the acute or sub-acute phase (first few weeks). Thus, the studies reported so far provide clear pattern as to the timing of treatment versus result.

Various types of sensory stimulation can affect rehabilitation. A number of studies have shown that acupuncture has circulatory and biochemical influence on the release of transmitters and peptides in the brain and spinal cord. Acupuncture has physiological effects that could affect brain plasticity and thus, the rehabilitation process. In the term of the side lesion, the side of brain lesion affects motor and function recovery post-stroke onset. Histological data point out that there is a greater proportion of neuropil volume in the left hemisphere of the primary cortex hand representation area, proposing the presence of more interconnectivity among neurons. Transcranial magnetic stimulation was used to demonstrate alters in motor cortex excitability with acupuncture. Right cortex transcranial magnetic stimulation showed decreased cortical excitability, and an inclination to an increase in cortical excitability was remarked with left cortex transcranial magnetic stimulation.<sup>5</sup> A study<sup>5</sup> does confirm the findings in previous studies with positive and negative outcomes, which have indicated that acupuncture treatment may have an additional effect on acute stroke patients as shown in RHRH acupuncture group, and may have no additional effect on LH acupuncture group in terms of functional ability.

The patients' number, short period of the study (4 weeks), and the use of a sum score seem to be the only limitation in our study. The sum scores do not show in which activities the problems occur.

In conclusion, acupuncture treatment may have no effect on stroke left-handed patients' in terms of daily life activities. Some activities are more necessary for independence than others. Therefore, in designing future trials of acupuncture after stroke, paying attention to the above mentioned limitations could provide supplementary information.

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