The Effects of Acupuncture on Cerebral Blood Flow in Post-Stroke Patients: A Randomized Controlled Trial

Motti Ratmansky, MD,^{1,2} Adi Levy, MD,^{2,3} Aviv Messinger, DipAC,⁴ Alla Birg, MD,¹
Lilach Front, MSc,¹ and Iuly Treger, MD, PhD^{1,2}

Abstract

Background/Objective: Stroke is a major cause of disability and death in the Western world. Studies have shown a direct relationship between specific mental and motor activity and changes in cerebral blood flow. Acupuncture is often used in post-stroke patients, but there is a lack of sham-controlled studies evaluating the effects of acupuncture on cerebral blood flow following a stroke. This pilot concept-assessment study sought to evaluate the effects of true acupuncture on cerebral blood flow velocity compared with sham acupuncture and lay a foundation for future work in this field.

Methods: Seventeen inpatients (age range, 44–79 years) 1–3 months post-stroke were allocated to acupuncture at true acupuncture (TA) points or at sham acupuncture (SA) points. The treatment was 20 minutes long. Transcranial Doppler ultrasonography was used to measure mean flow velocity (MFV) and peak flow velocity (PFV) at both healthy and damaged hemispheres before (T0), in the middle of (T15), and 5 minutes after (T25) treatment. Blood pressure was measured at T0 and T25.

Results: A statistically significant ($p < 0.04$) MFV increase in both hemispheres was found during and after TA; this increase was higher than that seen with SA ($p < 0.035$). Acupuncture had no significant effect on PFV. Systolic blood pressure significantly decreased after acupuncture ($p < 0.005$) in a similar manner for both TA and SA. National Institutes of Health Stroke Scale score was negatively correlated with MFV at T15 ($r = -0.825$; $p < 0.05$).

Conclusion: This pilot study showed a significant influence on cerebral blood flow velocity by TA. This study lays a foundation for larger-scale studies that may prove acupuncture to be a useful tool for cerebral blood flow enhancement during post-stroke rehabilitation.

Introduction

STROKE IS A MAJOR CAUSE of mortality and disability in the Western world. Post-stroke disability is a burden for patients and families.¹ Cerebral blood flow is normally correlated with cerebral glucose utilization rates and changes together with local glucose consumption in response to altered local functional activity.² Normal blood flow velocity in the damaged hemisphere after stroke is associated with better rehabilitation outcome.^{3,4}

In 1998, the National Institutes of Health published a consensus statement regarding the efficacy of acupuncture in adult stroke rehabilitation; it mentioned that acupuncture might be useful as an adjunct treatment or an acceptable alternative or be included in a comprehensive management program.⁵

Acupuncture is often used as an adjunct to standardized rehabilitation treatments after stroke, but its mode of action in the rehabilitation of these patients is yet to be discovered.^{6–9} Acupuncture influences cerebral blood flow in healthy persons^{10–12} and patients with stroke.^{13,14} However, few studies on cerebral blood flow in patients after stroke have used sham acupuncture.

The present study was designed as a pilot concept-assessment study to examine the influence of acupuncture on cerebral blood flow in post-stroke patients using transcranial Doppler imaging. The design was based on comparison of effects of true acupuncture (TA) to sham acupuncture (SA). The results suggest that TA has a significant influence on cerebral blood flow velocity and thus may be used for cerebral blood flow enhancement during post-stroke rehabilitation.

¹Pain Clinic, Loewenstein Rehabilitation Hospital, Raanana, Israel.

²Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.

³Sharett Institute of Oncology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.

⁴Complementary Medicine Services, Sheba Medical Center, Tel Hashomer, Israel.

FIG. 1. Study flow diagram. Twenty-one patients were randomly assigned in a blinded manner to receive a true acupuncture (TA)–sham acupuncture (SA) sequence (TA group) or an SA–TA sequence (SA group). Cerebral blood flow data collected during period 1 of the 2-period sequence were used for analysis.

Materials and Methods

Twenty-one inpatients from the neurological rehabilitation department at the Loewenstein Rehabilitation Hospital, Raanana, Israel, who had experienced an ischemic stroke and had been in the hospital for at least a month were enrolled in the study. To lower the risk of hemorrhagic transformation of the ischemic brain tissue, patients were not allowed in the study within less than 30 days after the stroke event. Other exclusion criteria were cardiac arrhythmias, needle phobia, and prior neurologic deficit not caused by the stroke.

The institutional review board approved the study. Informed consent was obtained before randomization and

treatment. Four patients whose informed consent forms were not properly signed were excluded from analysis (Fig. 1).

Twenty-one patients were randomly assigned in a blinded manner to receive a true acupuncture (TA)–sham acupuncture (SA) sequence (TA group) or an SA–TA sequence (SA group). The protocol included two 30-minute treatment periods (period 1 and period 2) separated by a 30-minute rest session. Each treatment period included 20 minutes of needle puncture (Fig. 2). With the crossover method, all patients received both treatments. The final numbers of patients in the TA and SA groups were 8 and 9, respectively (Fig. 1).

The treatment was performed by a medical doctor who is also a certified acupuncturist with 2 years' experience. Guidance was provided by a senior acupuncturist who had 12 years of practical experience in hospitals and other clinical settings following acupuncture studies in China as well as in Israel, with a certification in the Kiiko Matsumoto style of acupuncture.

The treatment was performed in a sitting position. The TA group received acupuncture in the LV-3, LV-4, SJ-5, and GB-34 points, which are fundamental points for regulation of blood flow according to Chinese medicine philosophy and are commonly used in acupuncture rehabilitation protocols. The points that were used in the SA group were in a nonspecific location, with no known acupuncture influence. These points were chosen to be as far as possible from known acupuncture points, not on any known meridian, and as far as possible from deep connective tissues¹⁵ as follows: (1) above the biceps muscle, (2) above the deltoid muscle, (3) above the gastrocnemius muscle (medial aspect), and (4) forearm (above the ulna). Acupuncture was performed in both groups under aseptic conditions using disposable acupuncture needles measuring 0.18 mm in diameter and 30 mm in length (DongBang Acupuncture, Inc., Chungnam, Korea). Needles were inserted to the subcutaneous layer with gentle stimulation (even technique). Twenty minutes after the insertion the needles were withdrawn.

Transcranial Doppler ultrasonography¹⁶ was used to record cerebral blood flow velocity. This is a portable, non-invasive, and inexpensive technique for measuring cerebral blood flow velocity through the skull. There is no need for

FIG. 2. Study protocol. The protocol included two 30-minute treatment periods (period 1 and period 2) separated by a 30-minute rest session. Each treatment period included 20 minutes of needle puncture. T₀, T₁₅, T₂₀, and T₂₅ refer to minutes after needle insertion.

patients' preparation, and it causes little discomfort. Transcranial Doppler ultrasonography is used to measure cerebral blood flow in post-stroke patients.^{3,4,14,17}

Cerebral blood flow velocity was measured by transcranial Doppler ultrasonography (Smart-Lite, Rimed Ltd., Raanana, Israel) at three time points: after 5 minutes of rest before needle insertion (T0, baseline), 15 minutes after needle insertion (T15), and 5 minutes after needle removal (T25). At T0 and T25, blood pressure was measured.

For each time point, mean flow velocity (MFV) and peak flow velocity (PFV) were recorded from both hemispheres. Results for the healthy and damaged hemispheres were analyzed separately. Analysis was performed only on data collected during period 1, with a comparison between the TA and SA groups. This was done because of the high readings at the beginning of period 2 for the TA group, showing that the lag time between the true and sham treatments should have been longer.

Acupuncture treatment and Doppler cerebral blood flow velocity recordings were performed in an unblinded manner.

Patients' demographic, clinical, and functional data were compared by *t* test for continuous variables or by Fisher exact test and chi-squared test for discrete variables. The *t* test was used to compare cerebral blood flow velocity at T0 between hemispheres and baseline cerebral blood flow and blood pressure between treatment groups. Repeated-measures analysis of variance (group $\times$ hemisphere $\times$ time) was used to identify a treatment and hemisphere effect on MFV and PFV at the middle of acupuncture session (T15) and 5 minutes after it ended (T25), as well as a treatment effect on blood pressure at T25.

MFV results for T15 and T25 were subtracted from those of T0, and the effect of demographic, clinical, and risk-related factors on differences was examined by using Pearson correlation for continuous variables and a *t* test for discrete variables (SPSS, Chicago, IL).

Results

Table 1 presents the characteristics of the 17 patients included in the analysis (12 men and 5 women). Patients'

TABLE 1. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF STUDY GROUPS

Characteristic	TA group (n=8)	SA group (n=9)	p-Value
Women/men (n/n)	2/6	3/6	NS
Age (y)	63.5 $\pm$ 11.9	60.2 $\pm$ 6.7	NS
Right/left hemispheric damage (n/n)	5/3	7/2	NS
Time after stroke at study recruitment (mo)	1.8 $\pm$ 0.6	1.5 $\pm$ 0.4	NS
NIHSS grade at admission	7.0 $\pm$ 3.5	7.0 $\pm$ 2.0	NS
FIM grade at admission	76.7 $\pm$ 15.4	66.9 $\pm$ 22.8	NS
Given tissue plasminogen activator (yes/no) (n/n)	2/6	1/7	NS
Receiving antiplatelet therapy (yes/no) (n/n)	7/1	5/4	NS

Values expressed with a plus/minus sign are the mean $\pm$ standard deviation.

TA, true acupuncture; SA, sham acupuncture; NS, not significant; NIHSS, National Institutes of Health Stroke Scale; FIM, Functional Independence Measure.

TABLE 2. GROUP RISK FACTORS

Characteristic	TA group (n=8)	SA group (n=9)	p-Value
Former stroke or cardiovascular illness (yes/no) (n/n)	1/7	6/3	<0.05
Stroke in family (yes/no) (n/n)	4/4	3/6	NS
Type 2 diabetes mellitus (yes/no) (n/n)	5/3	5/4	NS
Dyslipidemia (yes/no) (n/n)	5/3	7/2	NS
Hypertension (yes/no) (n/n)	6/2	7/2	NS
Smoking (yes/no) (n/n)	3/5	4/4	NS
Body-mass index (kg/m ²)	6.03 $\pm$ 8.9	1.03 $\pm$ 4.3	NS

Values expressed with a plus/minus sign are the mean $\pm$ standard deviation.

ages ranged between 44 and 79 years, time since stroke ranged between 32 and 90 days, and admission National Institutes of Health Stroke Scale (NIHSS) scores ranged from 4 to 13. Patients' characteristics did not significantly differ between the TA and SA groups (Table 1).

Stroke risk factors are described in Table 2. No significant differences were found between the groups other than prior stroke and cardiovascular condition, which were dominant in the SA group (Table 2).

For the entire patient population, at T0 (baseline) MFV and PFV were slightly higher for the healthy hemisphere than for the damaged hemisphere (mean MFV, 47.0 and 43.6 cm/s for healthy and damaged spheres, respectively; mean PFV, 73.2 and 69.2 cm/s). However, differences were not significant. Mean blood pressure and MFV at the damaged and healthy hemispheres at T0 (baseline) did not differ significantly between treatment groups. For TA group, the average blood pressure was 128.1/77.1 mmHg, average MFV in healthy hemisphere was 47.6 cm/s, and MFV for damaged hemisphere was 44.1 cm/s. The corresponding data for the SA group were 138.2/76.4 mmHg, 46.4 cm/s, and 43.1 cm/s.

TA increased MFV for the healthy and damaged hemispheres between baseline and T15 and between T15 and T25. SA showed no effect or only a short-term effect during the acupuncture session on the damaged hemisphere at T15 (Fig. 3). The repeated-measures analysis of variance indicates a significant time-point effect on MFV ($p=0.04$) and a significant time-point $\times$ group interaction ($p=0.035$). At the healthy hemisphere, TA increased PFV while SA decreased it. Damaged hemisphere PFV responded similarly to both TA and SA. For both hemispheres, time-point and treatment influence on PFV was nonsignificant (Fig. 4). Hemisphere factor (healthy or damaged) influence on MFV and PFV was not significant.

Between T0 and T25, blood pressure decreased from 128.1 $\pm$ 12.9/77.1 $\pm$ 15.3 mmHg to 122.0 $\pm$ 14.4/73.8 $\pm$ 13.9 mmHg in the TA group and from 138.2 $\pm$ 17.4/76.4 $\pm$ 11.3 mmHg to 125.9 $\pm$ 20.8/73.3 $\pm$ 13.0 mmHg in the SA group. The decrease in systolic blood pressure was significant ($p<0.005$) but was not affected by treatment. The decrease in diastolic blood pressure was not significant.

FIG. 3. Effects on mean flow velocity (MFV). In both hemispheres, TA led to an increase in MFV over time. In contrast, SA had no effect on MFV in the healthy hemisphere (**A**) and a transient elevation effect in the damaged hemisphere that was followed by a decrease (**B**).

Influence of clinical, demographic, and risk factors on cerebral blood flow was significantly evaluated only for the TA patients because SA had a minor influence on cerebral blood flow.

In the TA group, the NIHSS score at admission had a significant negative correlation with MFV for the healthy hemisphere at T15 ($r = -0.825$; $p < 0.05$). At T25, the effect of the Functional Independence Measure score at admission on the PFV in the damaged hemisphere for the TA group was nearly significant ($r = 0.745$; $p = 0.055$). Five of the eight patients from the TA group who had type 2 diabetes

mellitus showed a 11.2-cm/sec MFV increase at T15 for the damaged hemisphere, while the other three patients' MFV decreased by 6.8 cm/sec. The effect of type 2 diabetes mellitus was significant ($p < 0.05$). The effect of type 2 diabetes mellitus on the healthy hemisphere at T15 showed a similar trend but was not significant ($p = 0.066$); the influence of this disease on MFV at T25 was also not significant.

Age, sex, time from stroke, baseline blood pressure, smoking, body-mass index, or and Functional Impairment Measure score at admission had no significant influence on MFV results.

Discussion

In this pilot study, acupuncture at true acupoints significantly increased cerebral blood flow velocity in post-stroke patients undergoing rehabilitation. MFV increase after TA continued 5 minutes after needles were removed (T25; see Fig. 3). MFV was slightly increased after SA only during the session (T15) and for the damaged hemisphere alone. This effect diminished after needle removal (T25). SA had no effect on the healthy hemisphere (Fig. 3).

The insignificant influence of acupuncture on PFV may be explained by the sensitivity of PFV to extreme measurements, which increases variance and makes it more difficult to achieve statistical significance. The decrease in blood pressure during the acupuncture session (which may be attributed to relaxation during the treatment) indicates that cerebral blood flow increase was not mediated by an increase in systemic blood pressure.

Acupuncture affects cerebral blood flow in stroke patients.^{13,14} The current concept-assessment study shows that acupuncture at nonacupuncture points had a significantly smaller effect on MFV compared with true acupuncture, when patients were blinded to the treatment.

The elevation of MFV in both damaged and nondamaged hemispheres is in accordance with other studies that found acupuncture increases cerebral blood flow in healthy persons.¹⁰⁻¹³ Higher MFV in patients at admission to rehabilitation is associated with a better functional outcome and reduced impairment.^{3,4} The current study found sporadic and inconsistent evidence that patients with a smaller extent of neurologic deficit (lower NIHSS score) and better functional status (higher Functional Independence Measure score) responded better to acupuncture. The present results are in line with those of another study that found acupuncture more effective than SA in post-stroke patients with a relatively mild lesion, while both treatments were ineffective for patients with severe stroke.¹⁸ Nevertheless, other studies have suggested a better outcome in patients with a primary poorer neurologic status.¹⁹ This variance has yet to be studied in large-scale studies.

At baseline, patients' MFV did not significantly differ between the damaged and healthy hemispheres, possibly because of the time since the event; an earlier study found that patients may have increased cerebral blood flow velocity after stroke.¹⁷

Because the current patients had relatively normal initial cerebral blood flow and velocity values and nonsevere impairment, the clinical value of the cerebral blood flow velocity elevation is not clear. This finding suggests the need to further examine TA's influence on impairment and

FIG. 4. Effects on peak flow velocity (PFV). In the healthy hemisphere, TA increased PFV while SA decreased it (**A**). Damaged hemisphere PFV responded similarly to both TA and SA (**B**).

function in patients with minor to mild stroke and compare it with the effect of SA.

At present, there is no consensus regarding acupuncture influence on disability and function after stroke. Some systematic reviews and meta-analyses found acupuncture to be effective,^{7,9} while others did not.^{6,8}

It is hoped that this study will contribute to the favoring of acupuncture treatment in future meta-analyses for this population.

The main limitation of the present study is the small sample size. As mentioned earlier, this study was designed as a concept-assessment study and was meant to lay a foundation for future work in this field. A larger group could allow for more meaningful results and enable a better evaluation of the influence of different variables on outcomes. Another limitation is that acupuncture was applied only once, which is not typical in Chinese medicine. More treatments per patient are needed. Another disadvantage is the lack of assessor blinding. It would be desirable for the study to be conducted in a double-blind manner, in which both the assessors and patients are unaware of the treatment assignments. An important methodologic lesson gained from this study is that future studies should contain a longer washout period between true and sham acupuncture. In addition to short-term change in cerebral blood flow, there is a need to evaluate possible long-term effects of acupuncture on physical and functional outcomes; as mentioned earlier, such studies with sham control are relatively scarce.

In conclusion, the present pilot study demonstrated a significant increase in cerebral blood after acupuncture in stroke patients. Pending similar results in larger-scale studies, it suggests a possible future implementation of TA in stroke rehabilitation treatment.

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Author Disclosure Statement

No competing financial interests exist.

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Address correspondence to:
Motti Ratmansky, MD
Pain Clinic
Loewenstein Rehabilitation Hospital
278 Ahuza Street
43100 Raanana
Israel

E-mail: mottir@clalit.org.il