

Acupuncture and Transcutaneous Nerve Stimulation in Stroke Rehabilitation

A Randomized, Controlled Trial

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Background and Purpose—In small trials with control groups that receive no intervention, acupuncture has been reported to improve functional outcome after stroke. We studied effects of acupuncture and transcutaneous electrical nerve stimulation on functional outcome and quality of life after stroke versus a control group that received subliminal electrostimulation.

Methods—In a multicenter randomized controlled trial involving 7 university and district hospitals in Sweden, 150 patients with moderate or severe functional impairment were included. At days 5 to 10 after acute stroke, patients were randomized to 1 of 3 intervention groups: (a) acupuncture, including electroacupuncture; (b) sensory stimulation with high-intensity, low-frequency transcutaneous electrical nerve stimulation that induces muscle contractions; and (c) low-intensity (subliminal) high-frequency electrostimulation (control group). A total of 20 treatment sessions were performed over a 10-week period. Outcome variables included motor function, activities of daily living function, walking ability, social activities, and life satisfaction at 3-month and 1-year follow-up.

Results—At baseline, patients in each group were closely similar in all important prognostic variables. At 3-month and 1-year follow-ups, no clinically important or statistically significant differences were observed between groups for any of the outcome variables. The 3 treatment modalities were all conducted without major adverse effects.

Conclusions—When compared with a control group that received subliminal electrostimulation, treatment during the subacute phase of stroke with acupuncture or transcutaneous electrical nerve stimulation with muscle contractions had no beneficial effects on functional outcome or life satisfaction. (*Stroke*. 2001;32:707-713.)

Key Words acupuncture ■ transcutaneous electric nerve stimulation ■ activities of daily living
■ quality of life ■ outcome

Acupuncture has been used for the treatment of stroke patients in China from ancient times.¹ Although not generally accepted in the absence of convincing evidence of efficacy, acupuncture is increasingly applied in stroke patients in western countries.^{2,3} Beneficial results have been reported in studies with different designs and treatments from 24 hours to 8 years after stroke onset.⁴⁻¹¹ Few studies have been randomized, and the use of control or sham groups has varied. In its Conclusions and Recommendations section, the panel of the NIH Consensus Development Conference on Acupuncture recently stated that “[t]here are other situations such as...stroke rehabilitation...where acupuncture may be

useful as an adjunct treatment or an acceptable alternative or be included in a comprehensive management program.”¹²

Experimental studies have demonstrated that acupuncture and electroacupuncture have circulatory and biochemical effects in common with physical exercise on the release of transmitters and peptides in brain and spinal cord.¹³⁻¹⁸ Electrophysiologically, both acupuncture and electroacupuncture stimulate skin and muscle afferents. Intracellular recordings of cortical neurons in primates as well as neuroimaging and neurophysiological studies in humans have demonstrated that cortical sensorimotor representation areas (“cortical maps”) can be modified by sensory stimulation.¹⁹ Representation

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*See Appendix for list of participants.

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areas may also be modified by loss of sensory input, such as peripheral nerve blockade and amputation, and in response to focal brain lesions, including stroke.¹⁹ These areas may be modified by training and experience. Reorganization occurs not only in cortical areas but also in subcortical regions and the spinal cord.

In a previous study performed at a participating center in the present trial, 78 patients were randomized to treatment with acupuncture and electroacupuncture versus no specific sensory stimulation.⁵ Significant improvements in activities of daily living, quality of life, and motor function were observed in the treated patients, a difference that remained at 1- and 2.8-year follow-ups.⁸ Stimulation of muscle afferents by acupuncture was proposed as a method to increase poststroke plasticity processes in the brain. However, control patients did not receive sham or alternative treatment, and the possibility of an expectation effect, positive in patients treated with acupuncture or negative in control patients, could not be excluded. In addition, other types of deep-muscle stimulation (for instance, high-intensity, low-frequency transcutaneous electrical nerve stimulation [TENS]) that induces muscle contraction could have the same effect as electroacupuncture with needles.

The present study was designed to test 2 main hypotheses (with and without adjustment for comorbidity and other prognostic variables):

1. Sensory stimulation by acupuncture (including electroacupuncture) improves motor function and/or activities of daily living (ADL) after stroke.
2. Sensory stimulation by high-intensity low-frequency TENS, that induces muscle contractions comparable to those induced by electroacupuncture, improves motor function and/or ADL after stroke.

A secondary hypothesis was that sensory stimulation with acupuncture or high-intensity, low-frequency TENS improves quality of life after stroke.

Subjects and Methods

Study Design and Patients

After informed consent was obtained, 150 patients with acute stroke from 7 medical and neurological centers in Sweden were included in the study, from November 1994 to May 1997 (see Appendix 1). Patients of all ages and both sexes were eligible if they had had an acute stroke between 5 and 10 days before randomization. Criteria for the qualifying event were according to World Health Organization criteria for acute cerebrovascular disease.²⁰ If the stroke was a recurrent one, the patient could not have been functionally impaired before the present event. No records were kept of clinical characteristics of patients considered for study but not included. The 4 regional ethical committees concerned approved the study.

Only patients with moderate or severe functional impairment at randomization were included. This was defined as a Barthel ADL Index²¹ of ≤ 70 points in combination with inability to perform the Nine Hole Peg test²² within 60 seconds (impaired fine motor function of the hand) or inability to walk 10 meters without mechanical or personal support. Exclusion criteria were (a) previous neurological, psychiatric, or other disorder making it difficult to pursue the treatment or evaluations, (b) inability to comprehend information about the trial, (c) concurrent participation in another trial of interventions supposed to affect long-term neurological and functional outcome, and (d) failure to obtain informed consent.

With the use of closed envelopes and stratified by center, eligible patients were randomized in blocks of 6 to 1 of 3 treatment groups: acupuncture; high-intensity, low-frequency TENS, and subliminal high-frequency transcutaneous electrostimulation (control group). Opaque randomization envelopes, numbered consecutively, were produced centrally by computer-generated random allocation and distributed to the participating centers. The therapist opened the randomization envelope, and the local study coordinator and evaluators did not have access to information on allocation. In all 3 groups, treatments were started 5 to 10 days after onset of stroke. Each treatment session was 30 minutes and took place twice a week for 10 weeks (20 treatment sessions total).

Interventions

All patients were treated while they were in the supine position. Hwato sterile disposable acupuncture needles, 15 and 30 mm with tube, and the Cefar Acus stimulator were used. Two modes of treatment¹ were alternated (with either 10 or 9 acupuncture points). In the first mode, 2 needles were inserted on the nonparetic side: 1 in the thenar muscle (LI4) and the other in the muscle of tibialis anterior (ST 36). A third needle was inserted on the vertex of the head (GV 20). Seven needles were inserted on the hemiparetic side at 3 acupuncture points along the upper limb (LI 11, LI 4, and EX 28:2) and 4 points along the lower limb ("the mobility point," ST 36, ST 40, and EX 36:1). Low-frequency electrostimulation was applied to the paretic side (at LI 11 and LI 4 in the upper limb and ST 36 and ST 40 in the lower limb). In the second mode, the point on the vertex of the head was kept. On the nonparetic side, the point in the thenar muscle was replaced by a needle in the elbow region (LI 11) and that in the muscle of tibialis anterior (ST 36) by a needle in the muscle of tibialis posterior (GB 34). On the hemiparetic side, points on the upper limb were kept, whereas the mobility point above the knee was omitted and ST 36 was replaced by GB 34. Low-frequency electrostimulation was used on LI 11 and LI 4 in the upper limb and GB 34 and ST 40 in the lower limb. Frequency was preset to 2 Hz and amplitude was adjusted to be strong enough to elicit visible muscle contractions. The special needle sensation, called "de Chi," was evoked at every point except GV 20 on the top of the head. The nonelectrostimulated needles were manipulated, and needle sensation was evoked every 10 minutes for 30 minutes.

For high-intensity, low-frequency TENS, the Cefar dual TENS stimulator and adhesive electrodes were used. Only the affected side was stimulated. Two pairs of electrodes were placed over areas that corresponded to the stimulated points used in acupuncture-treated patients, namely LI 4, LI 11, ST 36, and ST 40/GB 34. Frequency was preset to 2 Hz, and the amplitude was strong enough to elicit visible muscle contractions.

For subliminal stimulation (control group), the same equipment and identical placements of electrodes were used as in the TENS group. High-frequency, low-intensity stimulation was achieved by presetting the frequency to 80 Hz and using a fixed amplitude (0.4 mA) below the perception threshold (no skin sensation and no visible muscle contractions).

Before onset of the study, the therapists received training that ensured uniformity in the treatment procedures between centers. Each therapist performed all 3 treatment modalities. In addition, all patients, irrespective of the group they had been allocated to, received conventional physiotherapy, occupational therapy, and speech therapy if needed. Drug therapy was not prespecified, except that experimental drugs in stroke trials were not allowed after inclusion into the study. Antiplatelet agents and anticoagulants were allowed at the discretion of the attending physician.

Evaluations

Adverse reactions that occurred during the treatment sessions were monitored. Outcome variables were recorded in the hospital at randomization and at follow-up at 3 and 12 months after onset of stroke. ADL function was assessed by the Barthel Index,²¹ overall motor function by the Rivermead Mobility Index,²³ fine motor function by the Nine Hole Peg Test,²² walking ability by the time

needed to walk 10 meters (with or without mechanical support), and quality of life by the Nottingham Health Profile.²⁴

To compare expectations of the patients in the 3 groups, we designed a simple credibility/expectancy scale based on more extensive questionnaires used to assess patients' expectation of effectiveness in studies on acupuncture in chronic pain.^{25,26} After the first and the fifth treatment sessions, patients were asked 2 questions: "Do you think that this treatment will help you?" and "Would you recommend this treatment for others with the same problem as you have?". For each question, patients were asked to choose 1 of 5 alternatives: "yes," "probably," "I have no opinion," "probably not," or "no."

An independent observer unaware of the group to which the patient had been assigned performed all investigations and recordings except monitoring of adverse reactions during treatment. Patients and observers were instructed not to discuss the treatment sessions. Causes of death and other reasons for withdrawal were assessed by an experienced internist (1 of the authors of this article) before disclosing the group to which the patient had been allocated.

Statistics

The present study was designed to provide an 80% power to detect a 20% difference in the number of patients with severe ADL dependency (≤ 70 points in the Barthel Index) at follow-up. Intention-to-treat analyses were performed to test the hypotheses. Missing data in the assessment of ADL function were recorded as zero if the patient had died, whereas the last recorded value was carried forward if data were missing for other reasons. Efficacy analyses that included only patients who completed the 10-week treatment sessions were done to possibly generate new hypotheses. The Wilcoxon rank sum test, Fisher's Exact Test, and the Cochran-Maentel-Haenszel test (as specified below and in the tables) were used in comparisons between groups. Possible prognostic factors for of ADL performance at 12 months (Barthel score ≥ 70 versus < 70 points) were assessed by logistic regression analysis. Factors included in the analysis were age (≥ 77 versus < 77 years, median age), sex, marital status, hypertension, ischemic heart disease, atrial fibrillation, diabetes, Barthel's Index at baseline (≥ 35 versus < 35 ; median score), and center.

Results

A total of 150 stroke patients were randomized. Patient characteristics at randomization were similar in the 3 comparison groups (Table 1). Of these patients, 138 (92%) remained in the trial at 3-month follow-up and 126 (84%) at 12-month follow-up.

At baseline, patients were asked about expectations of treatment. The proportion of patients with a positive response ("yes" or "probably") to the question "Do you think that this treatment will help you?" was high in all 3 groups but significantly higher in the TENS (43 of 48 respondents; 90%) than in the acupuncture (29 of 41 respondents; 71%; $P=0.031$) and control (31 of 46 respondents; 67%; $P=0.011$ by Fisher's Exact Test) groups. When the question was repeated at the fifth treatment session, the proportion of patients with positive expectations remained high in the TENS (34 of 40 respondents; 85%) and increased somewhat in the acupuncture (30 of 35 respondents; 86%) and control (27 of 37 respondents; 73%) groups. Changes from sessions 1 to 5 or the differences between the 3 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).

Withdrawal before completion of the 20 treatment sessions occurred in 4 patients in the acupuncture, 3 in the TENS, and

TABLE 1. Baseline Characteristics of Patients Randomized to Acupuncture; High-Intensity, Low-Frequency TENS; and Subliminal Stimulation

Characteristic	Acupuncture (n=48)	TENS (n=51)	Subliminal (n=51)
Age, y (mean \pm SD)	76 \pm 9	77 \pm 9	76 \pm 11
Sex, % women	40	45	51
Marital status, %			
Married/cohabitant	56	45	41
Living alone	44	55	59
Community support for outdoor transportation before stroke, %	8	10	6
Medical history, %			
Previous stroke	10	20	12
Ischemic heart disease	31	31	18
Atrial fibrillation	29	16	14
Hypertension	42	37	31
Diabetes	21	18	18
CT findings, %*			
Normal	27	14	27
Subcortical infarct	35	37	31
Cortical infarct	19	24	25
Other	19	24	16
Information missing	0	2	0

*Usually only 1 investigation, in the majority of instances performed within the first hours of hospital admission; data missing in 0 to 2 patients per group.

5 in the control groups. Reasons for early termination are shown in Table 2. During the 3-month intervention period, 2 patients treated with acupuncture died from recurrent ischemic stroke (Figure 1). In the TENS group, 1 patient died from an unknown cause, and in the control group, 2 died from myocardial infarction and 1 from pancreatic cancer. In the 3- to 12-month follow-up interval, another 4 patients died in the acupuncture group (from subarachnoid hemorrhage, recurrent brain infarction, progressing general deterioration after the index stroke, and unknown cause), and 3 died in the control group (gall duct cancer, colon cancer, and recurrent unspecified stroke). No patients in the TENS group died during this interval (Figure 1).

The only adverse reaction that caused early termination of treatment occurred in the TENS group, in which 1 patient was too bothered by fasciculations to continue. Other reported adverse effects were all trivial and did not differ between the groups. No bleeding complication was observed in the acupuncture group, despite 6 patients being on warfarin treatment (during a total of 120 treatment sessions) and another 30 on antiplatelet agents during the treatment period.

At baseline, the 3 groups were well balanced in the predefined outcome variables measuring motor function and ADL proficiency (Figure 2 and Table 3). In intention-to-treat analyses, no clinically meaningful or statistically significant differences existed in overall motor function measured by the Rivermead Mobility Index or in walking ability (Table 3). Most patients in all groups were unable to score more than zero in the Nine Hole Peg Test, which was used to assess fine

TABLE 2. Reasons for Withdrawal From Trial Among Patients Randomized to Acupuncture; High-Intensity, Low-Frequency TENS; and Subliminal Stimulation

Reason	0–3 mo			0–12 mo		
	Acupuncture (n=48)	TENS (n=51)	Subliminal (n=51)	Acupuncture (n=48)	TENS (n=51)	Subliminal (n=51)
Death during the follow-up period	2	1	3	6	1	6
Adverse reactions	0	1	0	0	1	0
Other						
Comorbidity	2	0	1	2	0	1
At patient's own request	0	0	1	2	0	1
Unknown	0	1	0	1	2	1
Total	4	3	5	11	4	9

Values indicate Nos. of patients.

motor function of the affected hand; this was true both at inclusion into the study and at 3 months' follow-up (data not shown).

Neither at 3- or 12-month follow-up did any statistically significant differences occur between the 3 intervention groups in Barthel's ADL Index (Figure 2). Excluding fatal cases and including values for survivors with missing values in explanatory analyses produced essentially the same results in motor and ADL functions, with no statistically significant differences in outcome (data not shown). In a logistic regression model, determinants of ADL outcome at 12 months (score >70 versus ≤70 points) were assessed. Older age ($P=0.001$), female sex ($P=0.009$), and presence of atrial fibrillation ($P=0.018$) were all significant predictors of poor ADL function at late follow-up. Participating center or treatment group to which the patients had been assigned did not predict ADL function.

Quality-of-life items in the Nottingham Health Profile were similar in all groups at 3- as well as the 12-month follow-up (Table 4). On both occasions, the score on energy was more favorable in the acupuncture group than in the 2 other groups, but the differences did not reach statistical significance. Items in the Nottingham Health Profile that reflected social well being (return to work, household work, social life, family life, sexuality, and leisure time activities)

did not differ between groups at 3 or 12 months (data not shown).

During the treatment period, benzodiazepines were used somewhat less by patients undergoing acupuncture (6%) than by TENS (20%) and control patients (15%). Similar proportions of patients in the 3 groups (9 to 13%) were on antidepressants during the first 3 months. Later during the first year after stroke, consumption of tranquilizers and antidepressant agents followed a similar pattern among groups (data not presented).

Discussion

Patients in all 3 groups improved markedly in motor and ADL functions from inclusion to 3-month follow-up. However, no differences in the extent of improvement between the groups were observed for any of the outcome measures (ie, ADL proficiency, mobility, walking speed, and quality of life). Thus, our data do not support the hypothesis that, when compared with subliminal stimulation, muscle afferent stimulation by manual acupuncture combined with electroacupuncture or low-frequency, high-intensity TENS starting in the subacute phase (5 to 10 days) after stroke onset has a beneficial effect in patients with moderate or severe hemiparesis.

All but 1²⁷ of 5 previous randomized controlled trials of acupuncture after stroke have reported beneficial results in ≥1 outcome measure.^{5,6,9,10} The reasons for the discrepant results between our trial and previous studies are not immediately evident. The acupuncture procedure usually has been similar to the present one, with a combination of manual acupuncture and electroacupuncture. Duration of the treatment period was the same or even longer in the present trial compared with previous studies, in which the duration varied from 2¹¹ to 10 weeks.^{5,27} Reports from several of the former trials do not state whether outcome measures were recorded by observers blinded as to which experimental group the patients had been assigned.

All trials have been small, with poor statistical power. Therefore, the possibility exists of type I errors in the positive trials. The heterogeneity of stroke patients has probably caused, in some trials in which <50 patients were randomized, reports of statistically significant differences in favor of acupuncture.^{6,9,10} The previous dominance of positive reports

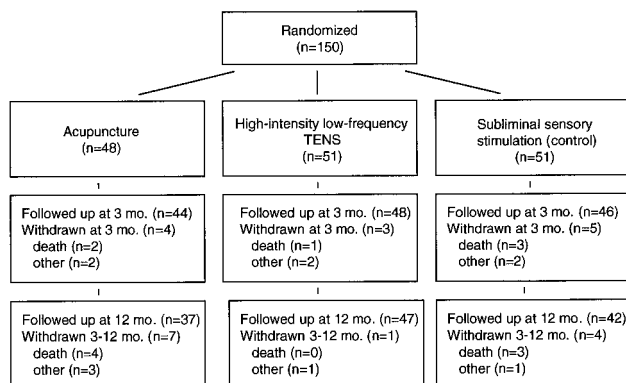


Figure 1. Patients randomized, allocated to 1 of 3 treatment groups, and withdrawn from the study after randomization. All randomized patients started treatment as allocated.

TABLE 3. Case Fatality and Motor Function in Patients Randomized to Acupuncture; High-Intensity, Low-Frequency TENS; and Subliminal Stimulation

Outcome Variable	A, Acupuncture (n=48)	B, TENS (n=51)	C, Subliminal (n=51)	P* for Differences at 12 mo
Case fatality, %				
3 mo	4	2	6	A vs B: 0.06
12 mo	13	2	12	A vs C: 1.00 B vs C: 0.11
Motor function, Rivermead Mobility Index, median points (interquartile range)*				
Baseline	2 (1–5)	2 (1–5)	2 (1–5)	A vs B: 0.55
3 mo	7 (3–13)	7 (4–12)	7 (4–13)	A vs C: 0.44
12 mo	11 (7–14)	9 (6–13)	11 (4–13)	B vs C: 0.83
Ability to walk 10 m, %*				
Baseline	31	25	29	A vs B: 0.42
3 mo	67	67	71	A vs C: 0.63
12 mo	63	73	67	B vs C: 0.74
Walking speed, m/s, median (interquartile range)*				
Baseline	0 (0–0.22)	0 (0–0.14)	0 (0–0.33)	A vs B: 0.75
3 mo	0.20 (0.00–0.84)	0.33 (0–0.63)	0.42 (0.09–0.77)	A vs C: 0.91
12 mo	0.56 (0.12–0.83)	0.23 (0.08–0.71)	0.38 (0.11–0.83)	B vs C: 0.96

*Based on intention-to-treat analyses; analyses by Fisher’s Exact Test (case fatality), Wilcoxon rank sum test (change in motor function and walking speed), and Cochran-Mantel-Haenszel test (walking ability). Data based on 46–51 observations in each group at baseline, 44–48 observations per group at 3 months, and 37–47 observations at 12 months.

may reflect a publication bias, given that the results of small negative trials may not have been reported in the scientific literature. Similarly, a type II error is possible in the present study and the previous negative one.²⁷ Our study, albeit the largest performed so far on sensory stimulation after stroke, was not designed to detect small differences in outcome that would have been of doubtful clinical relevance in view of the extensive resources used.

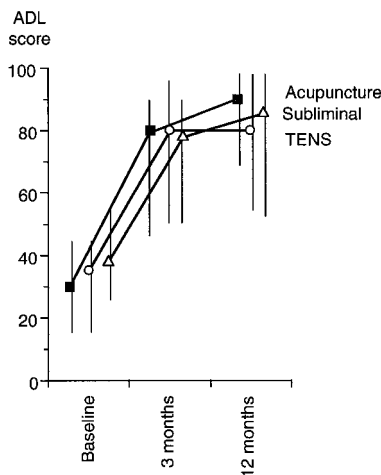


Figure 2. Median scores of the Barthel ADL Index in patients randomized to acupuncture (n=48); high-intensity, low-frequency transcutaneous electrical nerve stimulation (TENS; n=51); or control group (subliminal stimulation; n=51); intention-to-treat analysis. See Methods on entering of data in patients with missing values because of death or other reasons. Vertical lines denote interquartile ranges.

Apart from stroke severity, inclusion criteria were not restrictive. The patient sample included seems to be representative of patients with moderate or severe stroke in an aging society, with a high mean age (77 years), many patients living alone before their stroke, and extensive comorbidity (Table 1). Patients included in the present study had more severe neurological deficits than those included in many earlier studies. For instance, mean Barthel Index ADL score at inclusion was 33 in the present trial versus 45 in a previous Swedish acupuncture study with positive outcome.⁵ Clearly, the outcome after stroke is dependent on stroke severity in the acute phase,²⁸ and the possibility remains that an effect of sensory stimulation may have occurred in patients with mild strokes. The statistical power was not sufficient to permit subgroup analyses. The potential to improve function in patients with severe neurological deficits even late after stroke is illustrated by the apparent beneficial effects of constraint-induced movement therapy.^{29,30}

The mean age of our study patients was high (77 years), as it was in the other negative trial.²⁷ Comparably, mean age was 76 and 57 years, respectively, in the 2 Scandinavian trials that reported beneficial results of acupuncture.^{5,9} Patient age does not seem to be the only factor that distinguishes trials with positive versus negative outcome.

Timing of the intervention may also be of importance. One trial with mean start of acupuncture therapy at 40 days after stroke reported beneficial results in a small group of patients.⁹ In other trials reporting positive^{5,6} or negative²⁷ results, acupuncture treatment was started in the acute⁶ or subacute phase (first few weeks). Thus, the studies reported so far

TABLE 4. Quality-of-Life Domains in the Nottingham Health Profile in Patients Randomized to Acupuncture; High-Intensity, Low-Frequency TENS; and Subliminal Stimulation

Domain	3 mo			12 mo		
	Acupuncture (n=40)	TENS (n=45)	Subliminal (n=41)	Acupuncture (n=34)	TENS (n=41)	Subliminal (n=37)
Emotional reactions	16 (0–39)	8 (0–31)	20 (0–44)	8 (0–39)	16 (0–45)	11 (0–47)
Sleep disturbances	11 (0–34)	20 (0–34)	23 (11–55)	11 (0–43)	11 (0–34)	23 (0–48)
Lack of energy	24 (0–63)	61 (24–100)	61 (24–100)	24 (0–100)	39 (24–76)	39 (0–100)
Pain	0 (0–19)	8 (0–17)	11 (0–29)	0 (0–22)	9 (0–21)	17 (0–29)
Physical mobility	55 (18–82)	57 (35–82)	68 (38–86)	40 (10–71)	56 (30–86)	67 (35–82)
Social isolation	0 (0–42)	0 (0–27)	24 (0–36)	24 (0–25)	11 (0–25)	24 (0–49)
Total score	27 (16–39)	30 (17–46)	34 (18–50)	28 (8–42)	34 (16–47)	32 (24–47)

Median points (interquartile range). 0–100 point scales with 0 as best and 100 as worst outcome.

provide no clear pattern as to the timing of treatment versus outcome.

Apart from the size of the trial, the most evident difference in our trial design compared with several previous studies of acupuncture after stroke with positive outcomes is the choice of control group. In most other trials, the control group received “conventional rehabilitation” but no other attention.^{5,6,9,10} In the present study, the control patients received the same extent of attention as the intervention groups by the same therapists during 20 sessions over a 3-month period. The 3 groups had similar expectations at onset and halfway through the course of treatment. This is, to our knowledge, the first time an expectancy scale has been applied in stroke patients. The therapists’ enthusiasm, drive, and empathy may well have profoundly affected outcome in an unspecific manner by as yet unexplained mechanisms. By analogy, studies have suggested that much of the beneficial effects of stroke unit care are nonspecific and that general support and enthusiasm of staff particularly knowledgeable and devoted to stroke care are of prime importance to patient outcome (see discussion in Langhorne and Dennis³¹). If this is so, a control group receiving the same attention as the active treatment group seems essential in trials of specific rehabilitation interventions such as sensory stimulation.

The improvement in motor and ADL performance was pronounced in all 3 groups. The other 2 Swedish trials, 1 with a positive⁵ and 1 with a negative²⁷ outcome, were designed similarly to the present study. The extent of improvement in ADL score in the control groups of the present study and of the other trial with negative outcome was similar to that observed in acupuncture group and more pronounced than in the control group in the early positive trial.⁵ This suggests that a general unspecific improvement in stroke outcome has occurred during the years since the first study was published. Although the amount of specific rehabilitation was similar in the intervention and control groups in the early Swedish trial,⁵ the patients were not cared for in a stroke unit.

We are unable to conclude whether patients in the control group with subliminal stimulation did better than they would have if not given special attention. In the only other negative trial on acupuncture after stroke reported until now, no difference was seen in ADL or quality of life at follow up

whether the patients were treated by acupuncture/electroacupuncture or sham acupuncture or received no treatment.²⁷ This result would speak against a major effect on outcome by unspecific attention during repeated therapy sessions.

Although stimulation in the control group was subliminal (ie, of too low of an intensity to evoke any skin sensation), it could be argued that the control group received some degree of sensory input. Placement of electrodes on the skin are likely to stimulate mechanosensitive nerve fibers.³² Even if the electrical stimulation was below the perception threshold, we cannot rule out some degree of brain activation. Research with functional magnetic resonance imaging has demonstrated that whole-hand stimulation at the subthreshold level for sensation may to some extent affect regional blood flow in the primary and secondary motor and somatosensory areas of the brain.³³ Therefore, in designing future trials of acupuncture after stroke, adding another control group with no intervention except conventional rehabilitation could provide supplementary information. However, such a trial design was used in the Gothenburg acupuncture trial, in which no difference in outcome was observed between the 2 control groups, of which 1 received sham acupuncture and 1 conventional rehabilitation.

Current data on plasticity indicate that various types of training, sensory stimulation, and activation can influence rehabilitation.¹⁹ Acupuncture and electroacupuncture have physiological effects that theoretically could influence brain plasticity and, thus, the rehabilitation process.¹⁵ If present, to find such effects would probably need more homogeneous patient groups, both as disability and lesion site. We conclude that acupuncture combined with electroacupuncture or TENS-induced muscle contraction cannot be recommended as a standard treatment in the subacute phase for patients with moderate or severe stroke.

Appendix

Participating Centers and Key Personnel

Numbers of patients included in the trial are shown in parentheses.

Department of Medicine, Uppsala University Hospital (n=39): Anna-Lena Berggren, Elisabet Degerman, Brita Flemström, Anna Fondelius, Karin Gissen, Lisbeth Lindqvist, Ann-Charlotte Ljunglöf,

Ragnhild Nylund, Carina Sandström, Mona Stålhandske, Andreas Terént (coordinator), Annika Ternér, and Susanna Tuvemo-Johnson.

Department of Neurology, Lund University Hospital (n=38): Helen Åkerlund, Ingrid Dahlman, Annika Felländer, Katarina Johansson (coordinator), Marie Malmqvist, Bengt Mattsson, Ia Rorsman, Lena Tegård, and Monika Thornton.

St Göran Hospital, Stockholm (n=24): Jan Bakke, Mona Britton (coordinator), Margareta Hammar, Eva Holmström, Rolf Jönsson, Anneli Norevik, Birgitta Tryberg, Elisabeth Wahlberg, Sigun Wendel Hansen, and Lotta Ytterberg (coordinator).

Department of Medicine, Danderyd Hospital, Stockholm (n=18): Magnus von Arbin (coordinator), Elsy Eek, Kerstin Ekdahl, Silja Hermansson, Gunilla Östlund, and Disa Sommerfeld (coordinator).

Departments of Medicine and Neurology, Umeå University Hospital (n=14): Katarina Gustavsson, Anna Olofsson, Anne Olofsson, Bert-Ove Olofsson (coordinator), Marie Omgren, and Kerstin Westman.

Department of Medicine, Ängelholm Hospital (n=11): Peter Kamme, Helena Löfqvist, Ia Theander, Dag Ursing (coordinator), and Karin Ursing.

Department of Medicine, Gällivare Hospital (n=6): Ronnie Are-spong, Christer Åström, Ann-Christin Gramner, Bo Henriksson, Sara Lennestål, Stig Nordqvist (coordinator), and Lisbeth Törne.

Steering and Publication Committee: Barbro Johansson (chair), Magnus von Arbin, Kjell Asplund, Mona Britton, Eva Haker, Göran Långström (biostatistician), Andreas Terént, and Dag Ursing.

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