

# CAN ELECTROACUPUNCTURE OR TRANSCUTANEOUS NERVE STIMULATION INFLUENCE COGNITIVE AND EMOTIONAL OUTCOME AFTER STROKE?

Ia Rorsman<sup>1</sup> and Barbro Johansson<sup>2</sup>

From the <sup>1</sup>Department of Neurology, Lund University Hospital, Lund and <sup>2</sup>Division for Experimental Brain Research, Wallenberg Neuroscience Center, Lund, Sweden

**Objective:** The authors know of no controlled randomized studies on the cognitive effects of acupuncture following stroke. The aim of this study is to assess the effects of acupuncture combined with electroacupuncture and transcutaneous electrical nerve stimulation on emotional and cognitive functioning.

**Methods:** Five to 10 days after stroke, 54 patients with moderate or severe functional impairment were randomized to 1 of 3 interventions: (i) acupuncture, including electroacupuncture; (ii) sensory stimulation with high-intensity, low-frequency transcutaneous electrical nerve stimulation that induced muscle contractions; and (iii) low-intensity (subliminal) high-frequency transcutaneous electrical nerve stimulation (control group). Twenty treatment sessions were performed over 10 weeks. Outcome measures included cognitive performance and emotional functioning. Measures were obtained prior to any stimulation treatment and at 3 and 12 months.

**Results:** At baseline, groups were comparable with regard to demographic, medical, emotional and functional status. The control group demonstrated lower cognitive performances, but this difference did not remain at 3 or 12 months. There were no treatment effects on emotional status. When pooling treatment groups, there were significant cognitive and emotional improvements.

**Conclusion:** Although patients from all 3 groups demonstrated cognitive and emotional improvements, the present study does not suggest any treatment effects on emotional status or cognitive functioning.

**Key words:** acupuncture, transcutaneous electric nerve stimulation, neuropsychology, rehabilitation, cerebrovascular disorders.

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Correspondence address: Ia Rorsman, Department of Neurology, Lund University Hospital, SE-221 85 Lund, Sweden. E-mail: Ia.Rorsman@skane.se

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## INTRODUCTION

During recent years, acupuncture has been used increasingly in patients with stroke in Western society (1). A meta-analysis of 14 randomized controlled trials concluded that acupuncture has no additional effect on motor recovery, but a possible

small beneficial effect on disability (2). Motor function and disability have been the focus of investigation, whereas possible effects of acupuncture on cognitive function have received little attention. To the knowledge of the authors, there have been no previous studies on the cognitive effects of acupuncture in humans although the effect of transcutaneous electrical nerve stimulation (TENS) on human cognitive function has been investigated with promising results by one team (3, 4). Available research on acupuncture and psychological wellbeing has suggested beneficial effects on depression (5, 6) although specific effects of needling defined acupuncture points have been questioned (6).

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 (7–9). Electro-physiologically, both acupuncture and electroacupuncture stimulate skin and muscle afferents. Theoretically, other types of deep-muscle stimulation (for instance, high intensity, low-frequency TENS) that induces muscle contraction could have the same effect as electroacupuncture with needles.

The purpose of the present study was to test the effects of sensory stimulation by acupuncture combined with electroacupuncture and high-intensity low-frequency TENS on emotional and cognitive functioning. Due to similar electro-physiological mechanisms in electroacupuncture and TENS, any beneficial effects on cognitive and emotional recovery may be comparable in these treatment groups. The present study was part of a previously published multicentre investigation on electroacupuncture and TENS in stroke rehabilitation (10). One of the centres had the resources to conduct neuropsychological investigations. To determine possible effects on cognitive function, recruitment of patients was therefore extended at this site.

## METHODS

### Subjects

Fifty-four patients were included in the study after providing informed consent. Thirty-eight patients were included as part of a multicentre randomized controlled trial (10). Patients at all ages were eligible if they had had an acute stroke between 5 and 10 days prior to randomization. Criteria for the qualifying event were according to World Health Organization criteria for acute cerebrovascular disease (11). If the stroke was a recurrent one, the patient was not functionally impaired from the previous events.

Patients with moderate or severe functional impairment at randomization were included. Impairment was defined as inability to perform the Nine Hole Peg test (12) within 60 seconds (impaired fine-motor function of the hand) or inability to walk 10 metres without mechanical or personal support. Exclusion criteria were: (i) previous neurological, psychiatric, or other disorder making it difficult to pursue the treatment or evaluations; (ii) inability to comprehend information about the trial; (iii) concurrent participation in another trial of interventions supposed to affect long-term neurological and functional outcome; and (iv) failure to obtain informed consent.

Computerized tomography (CT) was performed on all patients at an early stage of hospitalization to exclude haemorrhages, but too early to confirm location of lesions.

### Treatment

Eligible patients were randomized into 3 treatment groups: (i) acupuncture combined with electroacupuncture; (ii) high-intensity low-frequency TENS (TENS group); and (iii) low-intensity high-frequency subliminal TENS (control group). The study co-ordinator and evaluators did not have access to information on allocation. Treatments were started 5–10 days after onset of stroke. Each treatment session was 30 minutes and took place twice a week for 10 weeks. The study was approved by the medical ethics committee.

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. The chosen treatment points had been used in an earlier study at our centre (1). Two modes of treatment (13) were alternated (with either 10 or 9 acupuncture points). In the first mode, 2 needles were inserted on the non-paretic side: 1 in the thenar muscle (LI4) and the other in the muscle of tibialis anterior (ST 36). The letters and numbers in parentheses denote the points for acupuncture according to the standard international nomenclature for meridians (14). 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 of the vertex of the head was kept. On the non-paretic 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 LI11 and LI 4 in the upper limb and GB 34 and ST 40 in the lower limb. Frequency was pre-set 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 non-electrostimulated 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 the acupuncture-treated patients, namely LI 4, LI 11, ST 36, and ST 40/GB 34. Frequency was pre-set 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 pre-setting 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. All therapists performed all 3 treatment modalities. All patients, irrespective of group, received conventional physiotherapy, occupational therapy, and speech therapy if needed. Drug therapy was not pre-specified, except that experimental drugs in stroke trials were not allowed. Antiplatelet agents and anticoagulants were allowed at the discretion of the attending physician.

### Evaluations

Baseline variables included activities of daily living (ADL) function as assessed by Barthel Index (15), overall motor function by the Rivermead Mobility Index (16), and walking ability defined by the ability to walk 10 metres (with or without mechanical support). Baseline and outcome measures included the patient's subjective emotional status on the Hospital Anxiety and Depression Scale (HADS) (17) and the clinician's ratings of depressive symptoms on the Comprehensive Psychiatric Rating Scale (CPRS-Dep) (18). Treatment with benzodiazepines and/or antidepressant medication was registered. Cognitive functioning was assessed by 8 neuropsychological variables intended to measure Global cognitive functioning (Mini Mental State Inventory (MMSE)) (19), Verbal learning and Verbal memory (Rey Auditory Verbal Learning Test (RAVLT)) (20), Visual memory (Facial Recognition Memory) (21), Visual attention (Star Cancellation Test) (22), Visual perception (Time perception) (22), Receptive language (Token test) (23) and Word fluency (FAS) (24).

All outcome variables were recorded in the hospital at randomization (baseline) and at follow-up, 3 and 12 months after onset of stroke. One psychologist (IR) administered all neuropsychological tests on all occasions. Activities of daily living (ADL) and motor function data from the first 38 patients have been presented in a previously published multicentre trial (10).

To compare expectations, all patients were given a simple credibility/expectancy scale based on more extensive questionnaires (25, 26). After the first and the fifth treatment sessions, patients were asked the question: "Do you think that his treatment will help you?" Five response alternatives were provided: "yes", "probably", "I have no opinion", "probably not" or "no."

Independent clinicians, unaware of the treatment group to which the patient had been assigned, performed the outcome investigations and recordings. However, treatment-related adverse reactions were registered by the therapists. Patients and therapists were instructed not to discuss the treatment with the independent clinicians.

### Statistical analyses

Intention-to-treat analyses were conducted on all cognitive measures. Missing data were recorded as zero (inability to complete/understand the task). Missing data were also recorded as zero when a patient had died. The last recorded value was carried forward for patients that discontinued the study for other reasons. Variables assessing emotional functioning were not assessed with intention-to-treat analyses, and missing data were not converted.

Between-group-comparisons were conducted with Kruskal-Wallis or  $\chi^2$  analyses (nominal data). Significant *p*-values were further analysed with pairwise comparisons using the Mann-Whitney *U* test. Within-group comparisons were assessed with Friedman analyses or  $\chi^2$  (nominal data) and *post-hoc* analyses were conducted with Wilcoxon signed rank tests. Two-tailed tests were used in all applicable analyses.

## RESULTS

A total of 54 stroke patients were randomized. Patient characteristics at randomization are presented in Table I. Between baseline and 12 months, 1 control patient withdrew at his own request (no adverse reaction) and 2 patients (1 control and 1 from the electroacupuncture group) deceased. Thus, 51 patients received all 3 neuropsychological evaluations.

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 significantly higher in the TENS group (83%) than in the electroacupuncture (42%) and control groups (53%),  $\chi^2=10.9$ ,  $p<0.005$ . When the question was repeated after the fifth treatment session, there were no significant differences between the 3 groups. The proportion

Table I. Baseline characteristics of patients randomized to electroacupuncture; high-intensity low-frequency transcutaneous electrical nerve stimulation (TENS); and subliminal TENS (control group): demographic, medical, motor and activities of daily living (ADL) variables

Characteristics	Electroacupuncture <i>n</i> = 18	TENS <i>n</i> = 19	Control <i>n</i> = 17
Age (years), Mean (SD)	75 (8)	74 (9)	78 (5)
Education (years), Mean (SD)	9 (3)	9 (3)	8 (2)
Females ( <i>n</i> )	8	10	10
Medical history: patients ( <i>n</i> ) with:			
Previous stroke	3	3	2
Ischaemic heart disease	7	6	5
Atrial fibrillation	2	4	3
Hypertension	5	9	6
Diabetes	2	5	4
Side of lesion: patients ( <i>n</i> ) with:			
Left	6	11	8
Not lateralized (pons)	0	1	0
Patients able to walk 10 metres	10	7	7
Motor function: RMI, Median (interquartile range)	3 (2–6)	2 (1–5)	2 (1–7)
ADL: BI, Median (interquartile range)	40 (25–50)	40 (25–50)	35 (25–60)

SD = standard deviation. Scores on Rivermead Mobility Index (RMI) and Barthel ADL Index (BI) range from 0–15 and 0–100, respectively, with lower score indicating lower function.

of patients with positive expectations remained high in the TENS group (74%) and was comparable to the electroacupuncture (79%) and control groups (76%).

There were no significant differences at randomization between the 3 treatment groups with regard to demographic, medical, motor or ADL characteristics listed in Table I. The 3 groups were also well balanced on variables measuring overall motor function on the Rivermead Mobility Index, walking ability and ADL on the Barthel Index.

#### Cognitive functioning

Table II illustrates cognitive test performances in the 3 treatment groups. On 4 of the 8 variables there were significant differences between groups with inferior performances in the control group at baseline, prior to any treatment (Visual memory:  $\chi^2 = 9.9$ ,  $p < 0.01$ ; Visual attention:  $\chi^2 = 8.0$ ,  $p < 0.05$ ; Visual perception:  $\chi^2 = 8.8$ ,  $p < 0.05$ ; Receptive language:  $\chi^2 = 8.3$ ,  $p < 0.05$ ). There were no significant differences between groups on any cognitive variables at 3 or 12 months.

Changes over time within each treatment group are presented in Table II. The electroacupuncture group demonstrated significant improvements on Visual memory ( $\chi^2 = 6.2$ ,  $p < 0.05$ ) and Word fluency ( $\chi^2 = 9.3$ ,  $p < 0.01$ ). The TENS group demonstrated significant changes in Verbal learning ( $\chi^2 = 12.9$ ,  $p < 0.01$ ), Verbal memory ( $\chi^2 = 12.2$ ,  $p < 0.01$ ), Visual memory ( $\chi^2 = 14.1$ ,  $p < 0.001$ ), Visual attention ( $\chi^2 = 6.0$ ,  $p < 0.05$ ) and Visual perception ( $\chi^2 = 6.9$ ,  $p < 0.05$ ). The control group showed changes in Visual Memory ( $\chi^2 = 16.0$ ,  $p < 0.001$ ), Visual attention ( $\chi^2 = 13.6$ ,  $p < 0.001$ ), Visual perception ( $\chi^2 = 7.7$ ,  $p < 0.05$ ), Receptive language ( $\chi^2 = 8.1$ ,  $p < 0.05$ ) and Word fluency ( $\chi^2 = 11.4$ ,  $p < 0.01$ ). Significant findings were further analysed with *post-hoc* tests.

Results for the whole pooled patient group, irrespective of treatment, showed significant improvements on all cognitive

measures: Global cognitive function:  $\chi^2 = 10.9$ ,  $p < 0.01$ ; Verbal learning:  $\chi^2 = 17.9$ ,  $p < 0.001$ ; Verbal memory:  $\chi^2 = 19.7$ ,  $p < 0.001$ ; Visual memory:  $\chi^2 = 32.7$ ,  $p < 0.001$ ; Visual attention:  $\chi^2 = 29.6$ ,  $p < 0.001$ ; Visual perception  $\chi^2 = 15.5$ ,  $p < 0.001$ ; Receptive language:  $\chi^2 = 9.0$ ,  $p < 0.05$ ; Word fluency  $\chi^2 = 18.7$ ,  $p < 0.001$ .

Table III demonstrates the number of patients with significant cognitive impairment at baseline and the number of patients showing significant changes over time. The table includes patients assessed all 3 times (51 patients). Cognitive impairment at baseline was defined by scores  $> 2$  standard deviations below normative age-appropriate means and significant change was indicated by a discrepancy of  $> 2$  standard deviations between 2 testing occasions. For measures with no normal distribution, significant change was indicated by a difference at least twice the size of the norm cut-off error. That is, the normative cut-off score for Visual attention (Star cancellation) is 3 errors (22). Thus, a change from one test occasion to another was indicated by an improvement or deterioration of at least 6 scores.

Most patients improved on the measure of Visual attention (14 patients, from baseline to 12 months) whereas the Word fluency measure showed the least change (2 patients).

#### Emotional functioning

As demonstrated in Table IV, there were no differences between groups at any time on the HADS scales, CPRS-Dep or number of patients receiving benzodiazepines or antidepressants. When treatment groups were pooled, all 3 emotional measures improved significantly from baseline to 12 months: HADS Anxiety:  $\chi^2 = 6.2$ ,  $p < 0.05$ ; HADS Depression  $\chi^2 = 5.5$ ,  $p < 0.05$ ; CPRS-Dep:  $\chi^2 = 8.9$ ,  $p < 0.05$ . However, *post-hoc* analyses demonstrated no differences between baseline and 3 months.

Table II. Cognitive outcome measures: comparisons between and within treatment groups

	A, electroacupuncture <i>n</i> = 18			B, TENS <i>n</i> = 19			C, control <i>n</i> = 17			<i>p</i> between groups
	Med	IQR	<i>n</i>	Med	IQR	<i>n</i>	Med	IQR	<i>n</i>	
Global cognition										
Baseline	26	24–28	17	25	16–27	17	22	16–26	16	ns
3 months	28	22–29	18	27	21–28	18	24	21–27	16	ns
12 months	27	25–28	16	26	23–28	17	24	19–26	16	ns
Verbal learning										
Baseline	26	20–40	16	22*** <sup>3,12</sup>	0–31	13	17	5–32	13	ns
3 months	32	20–45	17	24* <sup>12</sup>	18–32	15	19	15–32	15	ns
12 months	35	24–48	16	30	21–38	16	19	13–38	15	ns
Verbal memory										
Baseline	4	1–7	16	3*** <sup>3,12</sup>	0–5	13	0	0–6	13	ns
3 months	6	1–9	17	5* <sup>12</sup>	2–7	15	0	0–6	15	ns
12 months	6	0–8	16	6	3–9	16	2	0–7	15	ns
Visual memory										
Baseline	33* <sup>12</sup>	29–43	16	32*** <sup>3,12</sup>	0–38	12	0*** <sup>12</sup>	0–30	8	C vs A** & B*
3 months	34	29–45	17	38* <sup>12</sup>	28–41	15	31*** <sup>12</sup>	25–38	14	ns
12 months	39	29–45	17	39	33–44	15	32	26–37	15	ns
Visual attention										
Baseline	52	42–53	17	50* <sup>3,12</sup>	0–54	13	37* <sup>3,12</sup>	0–48	12	A vs C**
3 months	54	52–54	17	52	50–54	16	50	47–54	16	ns
12 months	53	49–54	16	53	50–54	16	50	44–53	16	ns
Visual perception										
Baseline	9	7–9	17	8* <sup>3</sup>	5–9	15	5* <sup>3,12</sup>	1–8	13	A vs C**
3 months	9	8–9	17	9	8–9	16	8	7–9	17	ns
12 months	9	8–9	16	9	8–9	16	9	7–9	16	ns
Receptive language										
Baseline	14	13–15	17	13	11–13	13	12* <sup>3,12</sup>	5–13	2	A vs C**
3 months	13	13–15	18	13	11–15	16	13	10–15	16	ns
12 months	14	12–15	16	13	10–15	16	13	10–14	16	ns
Fluency										
Baseline	19* <sup>3,12</sup>	9–27	17	13	7–22	14	14*** <sup>3,12</sup>	2–20	13	ns
3 months	26	8–35	17	16	7–28	15	22	10–28	15	ns
12 months	26	10–34	16	18	9–30	17	17	8–26	14	ns

TENS = transcutaneous electrical nerve stimulation; Med = median; IQR = interquartile range; *n* = number of patients able to complete test. Lower scores indicate lower performances. \**p* ≤ 0.05; \*\**p* ≤ 0.01; \*\*\**p* ≤ 0.001; ns = not significant.

<sup>3</sup> and <sup>12</sup> indicate significant pairwise within-group differences between baseline, 3 and 12 months.

## DISCUSSION

Patients from all 3 treatment groups improved significantly with regard to emotional functioning and cognitive status from inclusion to 12-month follow-up. However, the present investigation provides no support for the hypothesis that electroacupuncture or TENS with muscle contractions may have favourable cognitive or emotional effects in stroke recovery. There were no treatment-related effects on cognitive measures and no differential effects on symptoms of depression or anxiety as rated by patients or clinician.

Cognitive differences between groups at inclusion, prior to any treatment, is suggested by the control group's significantly lower scores on 4 of the 8 cognitive variables. These initial differences were apparently subtle as the groups were not significantly unbalanced on variables measuring overall motor function, walking ability and ADL. Randomization was conducted strictly and leaves no explanation to the observed baseline differences in cognition. At 3 and 12 months there

were no differences in cognitive functioning between treatment groups. The fact that the control group "caught up" from their comparatively inferior cognitive status makes it further unlikely that electroacupuncture and high-intensity low-frequency TENS had considerable impact on cognitive recovery.

A high proportion of the patients demonstrated impaired cognitive performances on the different measures at baseline, with 14–37 patients scoring >2 SD below the norm mean. Statistical analyses demonstrated significant improvements on all cognitive variables from inclusion to 3-month follow-up and recovery was maintained at 12 months. Using pre-defined criteria for significant clinical difference, the number of improved patients varied considerably between the different measures, ranging from 2 patients (Fluency) to 18 patients (Visual attention) at 12 months. The majority of patients did not show significant change in cognitive functioning. A small number (up to 4 patients) showed deteriorated performances over time.

Table III. Number of patients with significant cognitive impairment\* at baseline and number of patients with significant changes\*\* in test results (deteriorated or improved) after 3 and 12 months

Outcome variable	Patients impaired at baseline (n = 51)	Patients deteriorated (n = 51)	Patients improved (n = 51)
Global Cognitive	23		
Function (0–30)			
Baseline-3 months		3	11
Baseline-12 months		3	14
Verbal learning (0–75)	14		
Baseline-3 months		0	7
Baseline-12 months		1	6
Verbal memory (0–15)	18		
Baseline-3 months		0	4
Baseline-12 months		2	7
Visual memory (0–50)	29		
Baseline-3 months		1	12
Baseline-12 months		0	14
Visual attention (0–54)	26		
Baseline-3 months		4	20
Baseline-12 months		1	18
Visual perception (0–9)	19		
Baseline-3 months		0	13
Baseline-12 months		3	15
Receptive language (0–16)	19		
Baseline-3 months		1	6
Baseline-12 months		4	8
Word fluency	37		
Baseline-3 months		0	2
Baseline-12 months		0	2

\*Impairment defined by scores >2 standard deviations below normative age-appropriate means. For measures with no normal distribution (Receptive language, Visual attention, and Visual perception) impairment is indicated by a performance below the norm cut-off score.

\*\*Significant change (improvement or deterioration) indicated by a discrepancy of >2 standard deviations between 2 test occasions. For measures with no normal distribution (Receptive language, Visual attention and Visual perception) change is indicated by a difference at least twice the size of the norm cut-off error.

Considerable functional and cognitive recovery is common within the first days, weeks and months following stroke (27, 28). Studies suggest continued, but less dramatic, progress from 3 months and onward (27, 29). Our findings are consistent with previous reports on stroke recovery showing significant cognitive improvements across time and where a subset of

patients seem to account for these improvements (29, 30). Desmond et al. (29) found cognitive improvement in 19 of 151 stroke patients (12.6%) 3 months and 1 year after stroke. Hochstenbach et al. (30) obtained similar results when re-testing 65 stroke patients 2 years after stroke. They concluded that despite . . . “these improvements, we should not forget that most patients showed no improvement or even declined, which leaves a vast number of stroke patients with considerable cognitive impairments”. Hochstenbach et al. found significant decline in 0–18% of the patients. Although direct comparisons between the present investigation and previous studies are not possible, current data suggest comparable, and possibly better, outcome among the patients in the present investigation.

Whereas cognitive recovery was most notable between baseline and 3 months, emotional improvement was slower, with a significant change to the better at 12-month follow-up. Patients on antidepressant medication increased from 2 at inclusion to 16 at 3-month and 18 at 12-month follow-up. The high number antidepressant prescriptions probably reflects the general increase in antidepressant prescriptions as well as the current awareness of post-stroke depression among treating physicians. The effect of medication from natural recovery/adaptation can not be discerned in this material.

The results of this investigation are not consistent with some previous studies reporting beneficial effects of TENS on cognition in ageing (3, 4). The mean age of the patients in our study was 76 years. However, patient age does not appear to be a factor that distinguishes positive from negative outcome in this area of research (1, 3).

The rationale underlying our study was that electroacupuncture and high-intensity low-frequency TENS could have circulatory and biochemical effects in common with physical exercise (31). Stroke patients are often limited in their ability to gain natural exercise and sensory stimulation may be perceived as another method of activating multiple pathways that can lead to altered activity in neural systems. However, conventional rehabilitation in stroke units provides important beneficial non-specific effects (32) along with regular physiotherapy and occupational therapy. The patients, including treatment controls, received considerable attention, physical contact and training. Patients in relatively therapist-dense stroke-unit settings may receive an appropriate amount of training, making it difficult to identify any additional treatment effects from sensory stimulation through electroacupuncture or TENS.

Table IV. Emotional outcome measures and number of patients receiving benzodiazepines and antidepressants

	HADS – Anxiety			HADS – Depression			CPRS – Depression			Benzodiazepines	Antidepressants
	Med	IQR	n	Med	IQR	n	Med	IQR	n	n	n
Baseline	4	1–8	44	5	1–9	44	4	2–7	44	1	2
3 months	4	2–6	48	5	2–8	48	4	2–7	49	4	16
12 months	2	0–6	49	4	2–7	49	3	1–6	49	5	18

Med = Median. IQR = Interquartile range. More severe problems are indicated by higher scores. HADS = Hospital Anxiety and Depression Scale: 0–21 point scales. CPRS = Comprehensive Psychiatric Rating Scale: 0–30.

Consequently, some of the contradictory outcomes in acupuncture studies may be influenced by various background factors where specific treatment effects can't be distinguished from the non-specific effects.

Patients in all 3 modes of treatment reported high expectations of the treatment and received considerable attention both from the therapist and the clinicians conducting the assessments. Expectations play an important role in treatment and can result in clinical responses that are indistinguishable from those seen in active interventions. Current neuroimaging data suggest that expectancy effects can lead to biochemical and neurobiological processes related to the medical problem that is the focus of treatment (33). Given this, it seems certainly possible that treatment-independent factors such as high expectations could have had beneficial effects on the patients in this study.

As discussed in the multicentre study, it may be argued that the control group received some degree of sensory input although the stimulation was below the perception threshold. Placement of electrodes on the skin are likely to stimulate mechanosensitive fibres (34) and subthreshold stimulation can affect brain activation (35). Therefore, future studies may provide additional information if including another control group with no intervention beyond conventional rehabilitation. However, a trial design from the multicentre study did not yield any differences in outcome when using 2 control groups: sham acupuncture and no intervention except conventional rehabilitation.

There are no previous randomized controlled studies on acupuncture and cognitive functioning in stroke. The purpose of the present investigation was to assess the effects of different types of sensory stimulation and should not be considered a study on acupuncture consistent with traditional Chinese medicine. Treatment was standardized and electrostimulation was used with the purpose of producing broad physiological changes (31). The chosen outcome measures are behavioural and activity-oriented, rather than organic.

The statistical power was not sufficient to permit subgroup analyses. The study was aimed to detect a large effect size. The improvements among acupuncture patients in a previous study from our centre (1) gave reason to expect this possibility. The results from the present investigation suggest that if, indeed, there are cognitive and emotional effects from electroacupuncture or TENS, these effect sizes are probably small and would require large samples to be detected. The data were collected at a stroke unit with 20 beds serving an area of 280,000 inhabitants. With the inclusion criteria presented earlier, subjects were included consecutively over 4 years. It is thus recommended that future studies draw from a larger population pool.

The present results are consistent with those obtained from the larger multicentre trial (10). Both studies differ from most investigations in the field by inclusion of a placebo treatment with subliminal sensory input and by controlling for expectancy levels. Although it is not excluded that a subgroup of patients

may have benefited from TENS or electroacupuncture, the overall findings do not suggest different treatment effects between sensory stimulation with or without muscle contractions. These findings strengthen our conclusion that routine treatment with electroacupuncture or TENS is not merited in the purpose of enhancing cognitive functions in the subacute phase of stroke.

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## REFERENCES

- Johansson K, Lindgren I, Widner H, Wiklund I, Johansson BB. Can sensory stimulation improve the functional outcome in stroke patients? *Neurology* 1993; 43: 2189–2192.
- Sze FK, Wong E, Or KK, Lau J, Woo J. Does acupuncture improve motor recovery after stroke? A meta-analysis of randomized controlled trials. *Stroke* 2002; 33: 2604–2619.
- Scherder EJ, Van Someren EJ, Bouma A, v d Berg M. Effects of transcutaneous electrical nerve stimulation (TENS) on cognition and behaviour in aging. *Behav Brain Res* 2000; 111: 223–225.
- Scherder EJ, Bouma A, Steen L. Influence of transcutaneous electrical nerve stimulation on memory in patients with dementia of the Alzheimer type. *J Clin Exp Neuropsychol* 1992; 14: 951–960.
- Manber R, Schnyer RN, Allen JJ, Rush AJ, Blasey CM. Acupuncture: a promising treatment for depression during pregnancy. *J Affect Disord* 2004; 83: 89–95.
- Röschke J, Wolf C, Müller MJ, Wagner P, Mann K, Grözinger M, Bech S. The benefit from whole body acupuncture in major depression. *J Affect Disord* 2000; 57: 73–81.
- Pan B, Castro-Lopes JM, Coimbra A. Activation of anterior lobe corticotrophs by electroacupuncture or noxious stimulation in the anaesthetized rat, as shown by colocalization of Fos protein with ACTH and beta-endorphin and increased hormone release. *Brain Res Bull* 1996; 40: 175–182.
- Wyon Y, Hammar M, Theodorsson E, Lundeberg T. Effects of physical activity and acupuncture on calcitonin gene-related peptide immunoreactivity in different parts of the rat brain and in cerebrospinal fluid serum and urine. *Acta Physiol Scand* 1998; 162: 517–522.
- Bucinskaite V, Lundeberg T, Stenfors C, Ekblom A, Dahlin L, Theodorsson E. Effects of electro-acupuncture and physical exercise on regional concentrations of neuropeptides in rat brain. *Brain Res* 1994; 666: 128–132.
- Johansson BB, Haker E, von Arbin M, Britton M, Långström G, Terent A, Ursing D, Asplund K. Acupuncture and transcutaneous nerve stimulation in stroke rehabilitation: a randomized, controlled trial. *Stroke* 2001; 32: 707–713.
- Asplund K, Tuomilehto J, Stegmayr B, Wester PO, Tunstall-Pedoe H. Diagnostic criteria and quality control of the registration of stroke events in the MONICA project. *Acta Med Scand Suppl* 1988; 728: 26–39.
- Sunderland A, Tinson D, Bradley L, Hewer RL. Arm function after stroke. An evaluation of grip strength as a measure of recovery and a prognostic indicator. *J Neurol Neurosurg Psychiatry* 1989; 52: 1267–1272.
- Beijing College of Traditional Chinese Medicine. *Essentials of chinese acupuncture*. Beijing: Foreign Language Press; 1993.

14. A standard international acupuncture nomenclature: memorandum from a WHO meeting. *Bull World Health Organ* 1990; 68: 165–169.
15. Mahoney FI, Barthel DW. Functional Evaluation: The Barthel Index. *Md State Med J* 1965; 14: 61–65
16. Collen FM, Wade DT, Robb GF, Bradshaw CM. The Rivermead Mobility Index: a further development of the Rivermead Motor Assessment. *Int Disabil Stud* 1991; 13: 50–54
17. Zigmond SS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983; 67: 361–370.
18. Montgomery SA, Åsberg M. A new depression scale designed to be sensitive to change. *Br J Psychiatry* 1979; 134: 382–389.
19. Folstein MF, Folstein SE, McHugh PR. Mini Mental State. *J Psych Research* 1975; 12: 189–198.
20. Lezak MD. Neuropsychological assessment. New York: Oxford University Press; 1976.
21. Warrington EK. Recognition Memory Test. Windsor UK: NFER-Nelson; 1984.
22. Wilson B, Cockburn J, Halligan PW. Behavioral Inattention Test. Suffolk, UK: Thames Valley Test Company; 1987.
23. Spellacy FJ, Spreen OA. A short form of the token test. *Cortex* 1969; 5: 390–397.
24. Benton AL, Hamsher K, Sivan AB. Multilingual aphasia examination. Iowa City, IA: AJA Associates; 1976
25. Borkovec TD, Nau SD. Credibility of analogue therapy rationales. *J Behav Ther Exp Psychiatry* 1971; 3: 257–260
26. Petrie J, Hazleman B. Credibility of placebo transcutaneous nerve stimulation and acupuncture. *Clin Exp Rheumatol* 1985; 3: 151–153.
27. Kotila M, Waltimo O, Niemi ML, Laaksonen R, Lempinen M. The profile of recovery from stroke and factors influencing outcome. *Stroke* 1984; 15: 1039–1044.
28. Wade DT, Skilbeck C, Hewer RL. Selected cognitive losses after stroke. Frequency, recovery and prognostic importance. *Int Disabil Stud* 1989; 11: 34–39.
29. Desmond DW, Moroney JT, Sano M, Stern Y. Recovery of cognitive function after stroke. *Stroke* 1996; 27: 1798–1803.
30. Hochstenbach JB, den Otter R, Mulder TW. Cognitive recovery after stroke: a 2-year follow-up. *Arch Phys Med Rehabil* 2003; 84: 1499–1504.
31. Andersson S, Lundeberg T. Acupuncture – from empiricism to science: functional background to acupuncture effects in pain and disease. *Med Hypotheses* 1995; 45: 271–281.
32. Langhorne P, Dennis M. Stroke units: an evidence based approach. London: BMJ Books; 1998.
33. Wager TD, Rilling JK, Smith EE, Sokolik A, Casey KL, Davidson RJ, Kosslyn SM, Rose RM, Cohen JD. Placebo-induced changes in fMRI in the anticipation and experience of pain. *Science* 2004; 303: 1162–1167.
34. Vallbo AB, Olausson H, Wessberg J. Unmyelinated afferents constitute a second system coding tactile stimuli of the human hairy skin. *J Neurophysiol* 1999; 81: 2753–2763.
35. Golaszewski S, Kremser C, Wagner M, Felber S, Aichner F, Dimitrijevic MM. Functional magnetic resonance imaging of the human motor cortex before and after whole-hand afferent electrical stimulation. *Scand J Rehabil Med* 1999; 31: 165–173.