

ORIGINAL REPORT

TRANSCUTANEOUS ELECTRICAL STIMULATION ON ACUPUNCTURE POINTS IMPROVES MUSCLE FUNCTION IN SUBJECTS AFTER ACUTE STROKE: A RANDOMIZED CONTROLLED TRIAL

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Objective: To investigate whether transcutaneous electrical stimulation, when applied to acupuncture points in patients after acute stroke, decreases spasticity and/or increases muscle strength more effectively than placebo stimulation and standard rehabilitation.

Design: Randomized control trial.

Subjects: Sixty-two patients aged 70.0 (standard deviation 7.4) years and 9.2 (standard deviation 3.4) days post-stroke.

Methods: The patients were randomly assigned to 3 groups receiving transcutaneous electrical stimulation, placebo stimulation, or standard rehabilitation alone. Stimulation was applied to 4 acupuncture points in the affected lower leg for 60 min, 5 days a week for 3 weeks. Plantarflexor spasticity, ankle muscle strength, and functional mobility were measured before treatment, weekly during treatment, and at follow-up at week 8 post-stroke.

Results: No significant difference was found in the outcome measures among groups before treatment. When compared with standard rehabilitation or placebo stimulation, transcutaneous electrical stimulation to acupuncture points significantly increased the percentage of patients with normal tone, increased ankle dorsiflexor strength, and decreased antagonist co-contraction ratio ($p < 0.05$). The patients in the transcutaneous electrical stimulation group also tended to walk 2–4 days earlier than the patients in the other 2 groups.

Conclusions: Three weeks of transcutaneous electrical stimulation to lower leg acupuncture points, given 5 times a week within 10 days post-stroke, significantly decreased ankle plantarflexor spasticity, and increased dorsiflexor strength concomitant with a decrease in antagonist co-contraction.

Key words: transcutaneous electrical stimulation, acupuncture point, stroke, spasticity, randomized controlled trial.

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INTRODUCTION

Neuromuscular electrical stimulation has been used to treat patients after stroke in the last few decades. This included

transcutaneous electrical nerve stimulation (TENS) on the peripheral nerve (1) or acupuncture points (3), and functional electrical stimulation (FES) on the motor points (2). These stimulation protocols were found to improve lower limb motor function of patients after stroke. More specifically, in a randomized control trial, Levin & Hui-Chan (1) assigned spastic hemiparetic subjects who had stroke 26.4–29.2 months previously to 2 groups receiving 60 min of either TENS or placebo stimulation (PS) to the peroneal nerve, 5 times a week for 3 weeks. Results demonstrated that TENS significantly decreased ankle plantarflexor spasticity and increased maximal voluntary contraction of the dorsiflexors.

Subsequently, Tekeolu and co-workers (4) also found that subjects with spasticity 1–8 months following stroke, who received 8 weeks of TENS, but not those receiving PS, had a significant decrease in spasticity and increase in Barthel Index of Activities of Daily Living. Wong and co-workers (5) demonstrated that 2 weeks of transcutaneous electrical stimulation (TES) over 4 acupuncture points each in the affected upper and lower limbs produced a shorter hospital stay and better functional outcome than standard rehabilitation (SR) alone.

However, according to the review by Park and co-workers (6), there was insufficient evidence to support the use of acupuncture for stroke rehabilitation. Needle acupuncture was invasive and skill-based. Besides possible risks of forgotten or broken needles, infection and even transient hypotension had been reported (7).

Many studies had indicated that the most rapid spontaneous recovery of motor function following stroke occurred during the first few weeks (8). Based on modern knowledge about the plastic changes that occur immediately after brain injuries, rehabilitation should be more effective when started soon after brain damage and when given in an intensive manner (9–11). Therefore, this study investigated whether patients after stroke in the acute stage who received TES to acupuncture points in addition to SR experienced earlier and more effective motor recovery than those who received PS + SR or SR alone. Since the acupuncture points are located subcutaneously and intramuscularly, with many closely related to the nerves (12), we hypothesized that early and daily additional TES to the acupuncture points of the affected lower extremity would reduce spasticity development and enhance voluntary ankle dorsiflexor contraction in patients with acute stroke.

METHODS

Study design

This study was a single-blind, stratified randomized control trial. The sample size was calculated according to a meta-analysis (13). Sixty subjects were needed to achieve an 80% chance ($\beta=0.20$) of detecting a 20% difference ($\alpha=0.05$) in improving the maximum voluntary contraction of muscles among the groups.

Subjects

Sixty-two patients, age range 45–85 years, 9.2 (standard deviation (SD) 3.4) days post-stroke, were recruited. Fifty-five had first stroke and 7 had a second onset (Table I). They were diagnosed by computed tomography as having had a unilateral stroke in the carotid artery system. Stratifications included age (45–59, 60–75 and 76–85 years), gender, type of stroke, side of hemiplegia, and muscle strength of affected hip flexors (grade of <2 or of 2–3 according to the manual muscle strength test) (14). Patients were independent in daily activities before stroke. Those with a second stroke were recruited if they were able to walk independently and to look after themselves after the first stroke, with paralysis of the same extremity as the first one. Exclusion criteria were brainstem or cerebellar lesions, medical co-morbidity, receptive dysphasia, or cognitive impairment. This study was approved by the local ethics committees in accordance with the Helsinki Declaration of 1975 as revised in 1983.

After giving informed consent, patients were allocated by a random number produced by a computer to 1 of 3 groups receiving TES + SR, PS + SR, or SR only (control) (15). Fig. 1 illustrates processing of the subjects recruited showing that 6 subjects (2 from each of the 3 groups) dropped out before the follow-up assessment at week 8.

Treatment interventions

All subjects received the same SR including both physiotherapy and occupational therapy, each lasting for 60 min. Neither therapist knew to which group a subject being treated had been assigned.

In the TES group, model 120Z[®] TES stimulator (ITO Co Ltd, Tokyo, Japan) was applied with 0.2 ms pulses, at 100 Hz in the constant mode

Table I. Subject characteristics for each group

	TES (n=19)	PS (n=19)	SR (n=18)
Age, years, mean (SD)	68.4 (9.6)	72.8 (7.4)	70.4 (7.6)
Gender, n (%)			
Men	9 (47.4)	10 (52.6)	9 (50.0)
Women	10 (52.6)	9 (47.4)	9 (50.0)
Type of stroke, n			
Ischaemia	16	16	15
Haemorrhage	3	3	3
Second stroke, n	3	2	2
Paretic side, n (%)			
Left	11 (57.9)	11 (57.9)	11 (61.5)
Right	8 (42.1)	8 (42.1)	7 (38.5)
BMI, kg/m ² , mean (SD)	24.0 (2.7)	23.3 (3.2)	22.8 (2.9)
AMT, score, mean (SD)	8.4 (1.5)	7.7 (2.2)	8.4 (1.2)
CSS, score, median (interquartile)	4.5 (5.8)	4.0 (5.0)	4.0 (5.0)
LOS at acute hospital, days, mean (SD)	6.6 (3.8)	7.2 (3.2)	6.6 (3.3)
Intervention from onset, days, mean (SD)	9.2 (4.4)	9.9 (2.6)	8.7 (3.3)
LOS at sub-acute hospital, days, mean (SD)	35.1 (9.4)	34.3 (10.8)	31.4 (8.7)

AMT: abbreviated mental test; BMI: body mass index; CSS: Composite Spasticity Scale; LOS: length of stay; SR: standard rehabilitation; TES: transcutaneous electrical stimulation + SR; PS: placebo stimulation + SR; SD: standard deviation.

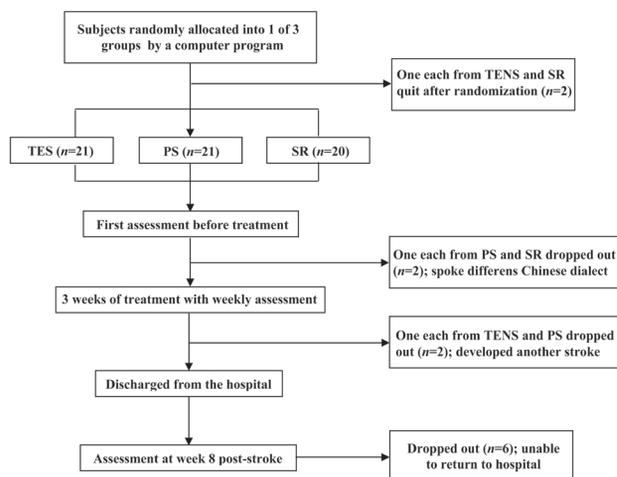


Fig. 1. Flow diagram showing the paths for recruited patients. TES: transcutaneous electrical stimulation; SR: standard rehabilitation; PS: placebo stimulation.

within the subject's tolerance level, via (5 × 3.5 cm) electrodes attached to the following acupuncture points on the affected lower extremity: St 36, Lv 3, GB 34, and BI 60 (Fig. 2). PS was applied using the same electrodes, locations and device, with the circuit disconnected. To ensure similar mental set, subjects were told that they might or might not feel the stimulation. Treatment for both TES and PS lasted 60 min per session, 5 days a week for 3 weeks. Subjects in the control group received only SR.

Outcome measures

Spasticity of the affected ankle plantar-flexors was assessed with Composite Spasticity Scale (CSS) (1–3). Because the Ashworth scale has lower reliability on ankle muscle and does not measure the relatively flaccid muscle tone during acute stroke, we had developed the CSS to register ankle plantarflexor tone more faithfully. Its validity and reliability in evaluating spasticity had been demonstrated in our previous studies (1–3).

Maximum isometric voluntary contraction (MIVC) of the ankle dorsiflexor and plantarflexor muscles was recorded by torque and surface electromyography (EMG) with the subjects supine (2). EMG signals were sampled at 1000 Hz per channel, full-wave rectified then low-pass filtered with the Butterworth method. MIVC value and the corresponding integrated EMG (IEMG) signals (mV.s) of tibialis anterior and medial gastrocnemius muscles were computed. Co-contraction ratio was calculated as the IEMG area of the antagonist over that of the agonist plus antagonist (1–3).

Functional mobility was evaluated with the Timed "Up & Go" (TUG) test when a subject could walk 7–8 m without personal assistance (2–3).

All measurements were carried out by one of our team, who was blinded to the subject allocation. They were recorded before treatment,



Fig. 2. Acupuncture points used in this study in the lower extremities.

weekly during the 3-week treatment in the hospital, and at follow-up 8 weeks after stroke. Details of measurement protocols and reproducibility had been reported in our previous paper (1–3), with intraclass correlation coefficient (ICC) values ranging from 0.73 to 0.99 showing good to excellent repeatability (1, 2).

Statistics

Results were analysed with SPSS (Version 11.0, SPSS, Chicago, IL, USA). Descriptive statistics were used for subjects' relevant characteristics. Repeated measure analysis of variance (ANOVA) was applied to compare the main effects before, during and after treatment, followed by *post-hoc* tests with Bonferroni correction to compare treatment effects among the 3 groups. For categorical variables, a χ^2 test was used. The significance level was set at 5% (2-tailed).

RESULTS

No significant differences were found in relevant subject characteristics (Table I) and baseline values of the outcome measures among the 3 groups (Table II).

Composite spasticity scale

Table II compared the raw CSS scores of the affected plantarflexors. These indices increased progressively in all groups from week 1 to week 8. However, the TES group tended to show less increase in muscle tone than the other 2 groups over time. The percentage of subjects who got a normal resistance sub-score on CSS was analysed with a Chi square test at $\alpha=0.017$ level. There was a significant difference between TES and control groups from week 1 onwards ($p=0.001-0.013$), and between TES and PS groups at week 3 ($p=0.016$). However, no significant differences were found between PS and control groups at any time.

Maximum Isometric Voluntary Contraction (MIVC)

Compared with the control group, the TES group showed a significant increase in the magnitude and percentage increase in ankle dorsiflexion torque and decrease in EMG co-contraction ratio, respectively, from week 2 and 3 onward (Table II and Fig. 3).

Note that, by week 8 post-stroke (5 weeks after TES stopped), the magnitude and percentage increase in MIVC dorsiflexion torque in the TES group was significantly greater than even those of the PS group (Table II, Fig. 3a). This was accompanied by a significantly greater reduction in EMG co-contraction ratio during dorsiflexion (Table II, Fig. 3b).

Walking Performance: Timed "Up & Go" test

The first day when subjects were able to walk in the hospital was 17.2 (SD 6.6), 19.6 (SD 5.8) and 21.2 (SD 8.0) days after stroke, respectively, for the TES, PS and control groups. The percentage of within-group subjects who were able to walk again increased by 37% ((8–1)/19 subjects) at week 1 and by 53% ((11–1)/19 subjects) at week 3 in the TES group, compared with 11% ((4–2)/19 subjects) at week 1 and 47% ((11–2)/19 subjects) in the PS, and 17% ((7–4)/18 subjects) and 28% ((9–4)/18 subjects) in the control group. However, no significant difference was found among the 3 groups using the Chi square test at $p<0.017$.

Table II. Comparison of measurements among the 3 groups

	TES (n=19)	PS (n=19)	SR (n=18)
<i>Composite Spasticity Scale total score (median (interquartile))</i>			
Week 0	4.5 (5.8)	4 (5)	4 (6)
Week 1	7.0 (4)	8 (2)	10 (6.8)
Week 2	7.0 (5)	8 (3)	10 (2)
Week 3	7.0 (2)	10 (3)	11 (3)
Week 8	7.5 (6.2)	10 (11)	11 (8)
<i>Percentage of subjects with normal resistance sub-score</i>			
Week 0	2.0	0.0	1.0
Week 1	42.1	31.6	5.9*
Week 2	57.9	26.3	17.6*
Week 3	52.6	15.8*	5.9*
Week 8	50.0	17.6	0.0*
<i>Maximum Isometric Voluntary Contraction torque, Nm, during dorsiflexion (mean (SD))</i>			
Week 0	1.9 (2.4)	2.1 (2.2)	1.9 (1.8)
Week 1	3.8 (4.6)	3.6 (3.3)	3.0 (3.5)
Week 2	5.2 (5.3)	4.6 (3.9)	3.2 (3.8)*
Week 3	6.4 (5.9)	4.5 (3.2)	4.0 (4.8)*
Week 8	8.2 (5.3)	6.0 (3.8)*	6.1 (6.4)*
<i>Electromyography co-contraction ratio, % (mean (SD))</i>			
Week 0	37.4 (16.7)	34.7 (20.4)	38.7 (15.3)
Week 1	33.1 (20.4)	31.2 (21.2)	40.7 (17.7)
Week 2	29.7 (18.8)	29.8 (23.9)	30.6 (18.4)
Week 3	22.6 (18.6)	26.9 (26.9)	32.1 (20.1)*
Week 8	20.1 (18.5)	26.6 (18.4)*	31.2 (17.9)†
<i>Timed "Up & Go" scores, sec (mean (SD))</i>			
Week 1	67.5 (13.7)	55.5 (14.8)	46.4 (19.6)
Week 2	46.3 (20.4)	34.3 (4.9)	42.0 (42.8)
Week 3	30.0 (13.5)	41.1 (27.9)	55.4 (47.1)
Week 8	15.2 (8.4)	34.5 (28.5)	36.3 (25.3)
<i>Number of subjects able to walk within 3 weeks of treatment</i>			
Week 0	1	2	4
Week 1	8	4	7
Week 2	11	9	9
Week 3	11	11	9

* $p<0.05$, † $p<0.01$, when compared with the TES group.

SR: standard rehabilitation; TES: transcutaneous electrical stimulation + SR; PS: placebo stimulation + SR; SD: standard deviation.

DISCUSSION

Early TES intervention on muscle tone and strength

During the last decade, the effects of TES on motor recovery in patients after stroke were examined mainly during the chronic stage (1, 3, 16). Our previous findings showed that TES applied to the peripheral nerve and acupuncture points decreased spasticity and enhanced dorsiflexion force production (1, 3). Similarly in this study, TES to the acupuncture points produced a significant increase in the percentage of subjects with normal tone, compared with the control group, indicating that the treatment protocol also normalized muscle tone when applied to the acupuncture points in subjects with stroke during the acute stage. The percentage increase in dorsiflexion torque and decrease in EMG co-contraction ratio were also significantly more than those of the control group. In a previous study on subjects with chronic stroke, we also found a significant decrease in spasticity but less significant increase in MIVC of ankle dorsiflexors when 4 weeks of TES

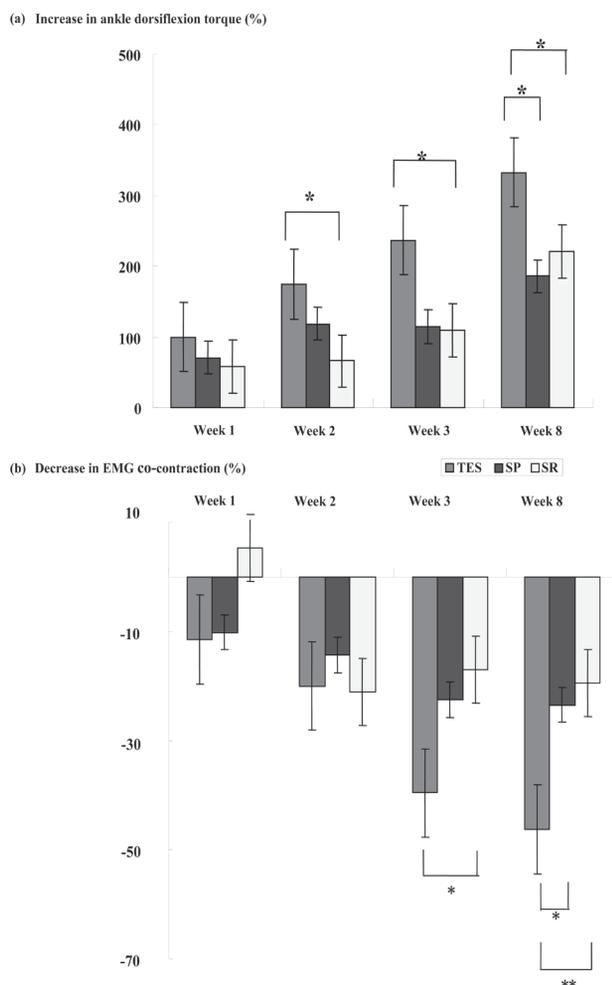


Fig. 3. Comparison among the 3 groups: (a) percentage increases in ankle dorsiflexion torque, and (b) percentage decrease in electromyography (EMG) co-contraction ratio during dorsiflexion of the affected ankle. * $p < 0.05$ and ** $p < 0.01$.

was applied to the same acupuncture points (3). Moreover, no carry-over effects were observed in patients with chronic stroke (3). In contrast, significant improvements were observed at 5 weeks, after TES ended in the present study, when it was applied to patients after stroke during the acute stage. The combined findings from the 3 studies during acute and chronic stages suggested that TES, when given early during acute stroke, may have even greater and longer lasting effects than when given during chronic stroke.

Note that when TES electrodes were applied to the acupuncture points, the areas stimulated were much larger than those of acupuncture needles. Therefore, the effects could have included stimulation of the nerves and/or muscles located along the current flow between the electrodes attached over the acupuncture points. In our previous study, we also found significant improvement in motor function in subjects with acute stroke when the electrodes were placed over the motor points (2). Thus, there had been no concrete evidence hitherto to demonstrate which stimulation protocol including: stimulation sequence, stimulation intensity and frequency, and

electrode location (whether applied to the skin overlying the nerve, motor point or acupuncture points) will produce significantly greater improvement in motor function in subjects with stroke.

TUG test scores and the first day when subjects were able to walk did not show significant differences among groups. This could be due to the relatively small sample size. Because there were always new additional subjects who were able to walk at subsequent assessment session, it made direct data comparison among groups difficult or invalid. Furthermore, this study looked mainly at the efficacy of TES on acupuncture points and did not focus on gait training. There could be improvement in walking speed if specific gait training were applied in this study, or when TES were combined with gait-related training, as demonstrated in our previous study (3) and by other investigators (17,18). Moreover, the tendency for the TES group to walk 2–4 days earlier than the placebo and control groups is interesting, and warrants further investigations using a larger sample size.

Placebo effects

Interestingly, when comparing the results between TES and control groups, significant differences appeared after only one week of treatment for the improvement in percentage of subjects with normal tone as denoted by CSS scores, and after 2–3 weeks of treatment for the improvements in dorsiflexion torque and EMG co-contraction ratio. When comparing between TES and PS groups, percentage improvements in dorsiflexion torque and EMG co-contraction ratio showed significances only at week 8 after stroke, indicating the presence of certain placebo effects. Recently, placebo effects have been suggested to have a biological basis, perhaps involving specialized nerve cells that respond to the expectation of treatment (19). One should caution that in studies designed without placebo control, whether the treatment effect was due to electrical stimulation rather than PS is thus open to question.

Possible mechanisms of TES on motor recovery of subjects after acute stroke

TES applied repetitively to the peripheral nerve or acupuncture points for 3–4 weeks has been found to reduce clinical spasticity and improve motor functions in chronic hemiplegic stroke (1, 3). Possible mechanisms could be partly attributable to an enhancement of presynaptic inhibition of the hyperactive stretch reflexes in spastic muscles, disinhibition of descending voluntary commands to the motoneurons of the paretic muscles, and decrease in co-contraction of the spastic antagonist (1). Our present study found that TES slowed the development of resistance to passive stretch of the plantarflexors and increased voluntary ankle dorsiflexion with a decrease in antagonist co-contraction. The effects and mechanisms thus appeared to be similar to our previous study on patients with chronic stroke (1, 3).

It has been postulated that electrically stimulated sensory inputs could enhance brain plasticity (20, 21). For example, the primary somatosensory area is extremely plastic and could demonstrate considerable reorganization after sensory

stimulation (22, 23). Buonomano & Merzenich (24) noted that repeated natural stimulation of a skin surface resulted in an expansion of its cortical representation. In this context, the increased afferent signals triggered by repeated TES in our study might produce long-term potentiation and induce neural plasticity (20, 24). The sensorimotor cortices are intimately involved with receiving and transmitting sensory information to the other cortical areas including the pre-motor and motor cortices (20, 24). This could explain the carry-over effect seen at week 8 post-stroke in the TES group.

In conclusion, the results of this study demonstrated that 3 weeks of daily TES, applied to acupuncture points of the affected lower leg of acute patients within 10 days post-stroke, significantly reduced the percentage of patients with spasticity and strengthened their ankle dorsiflexor, when compared with PS and/or SR given alone. The underlying mechanism for the present improvement appeared to be similar to what we had demonstrated with TES applied to the peripheral nerve in chronic stroke, in that the increase in ankle dorsiflexor strength was accompanied by a significant decrease in EMG co-contraction (1, 3). Another important finding of the present study is that these improvements in muscle tone and function were carried over to 5 weeks after the 3-week treatment ended. Because TES could be taught easily, it represents a low-cost treatment modality that could be readily applied to patients during the acute stage. However, due to the restrictive sample size in the present study, extension to a larger patient population incorporating a multi-centre trial should be conducted before widespread promotion of this treatment.

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