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Task-Related Training Combined with Transcutaneous Electrical Nerve Stimulation Promotes Upper Limb Functions in Patients with Chronic Stroke

Tae Hoon Kim,[1,*] Tae Sung In[2,*] and Hwi-young Cho[3]

[1]The Post-Professional DPT Program, The Richard Stockton College of New Jersey, NJ, USA
[2]Department of Physical Therapy, Shin-Hwa Rehabilitation Hospital, Seoul, South Korea
[3]Department of Physical Therapy, College of Health Science, Gachon University, Inchon, South Korea

Severe upper limb paresis is a major contributor to disability after stroke. This study investigated the efficacy of task-related training (TRT) with transcutaneous electrical nerve stimulation (TENS) on recovery of upper limb motor function in chronic-stroke survivors. Thirty patients with chronic stroke were randomly allocated two groups: the TRT+TENS group (n = 15) and the TRT+placebo (TRT+PLBO) group (n = 15). Patients in the TRT+TENS group received TENS stimulation (two to three times the sensory threshold), while subjects in the TRT+PLBO group received TENS without real electrical stimulation. TENS was applied to muscle belly of triceps and wrist extensors, while placebo (PLBO) stimulation was administrated without real electrical stimulation. Both interventions were given for 30 minutes per day, 5 days per week, for a period of 4 weeks. The primary outcomes were assessed with Fugl-Meyer assessment scores (FMA), Manual function test (MFT), Box and block test (BBT), and Modified Ashworth scale (MAS), each of which was performed one day before and one day after intervention. Both groups showed significant improvements in FMA, MFT, and BBT after intervention. When compared with the TRT+PLBO group, the TRT+TENS group showed significantly greater improvements in FMA (p = 0.034), MFT (p = 0.037), and BBT (p = 0.042). In MAS score, significant improvement was observed only in the TRT+TENS group (p = 0.011). Our findings indicate that TRT with TENS can reduce motor impairment and improve motor activity in stroke survivors with chronic upper limb paresis, highlighting the benefits of somatosensory stimulation from TENS.

Keywords: spasticity; stroke; task-related training; transcutaneous electrical nerve stimulation; upper limb motor function
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Introduction

Decrease of voluntary arm motor function is a common impairment after stroke (Smith et al. 1985). A number of intervention studies on stroke rehabilitation for improvement of arm function of stoke survivors have been reported, however, understanding the relationship between the intensity of arm rehabilitation and functional improvement of the upper limb is difficult (Kwakkel et al. 1997, 1999). A growing number of studies have demonstrated that task-oriented or task-related training (TRT) promotes upper limb recovery (Van Peppen et al. 2004; Barker et al. 2008), because the training is a rehabilitational method involving goal-directed practice and functional movements in a natural environment for alleviation of limited movement (Carr and Shepherd 1998; Ng and Hui-Chan 2007). However, for stroke survivors with upper limb paresis, participation in task-related training is difficult because they do not have adequate potential to work with the training (Barker et al. 2007).

More recent interventions, such as electrical stimulation, have been found to reduce arm impairment in stroke survivors by enhancing neural excitability within motor cortical areas (Kaelin-Lang et al. 2002; Wu et al. 2006; Conforto et al. 2007). Association of somatosensory stimulation from electrical stimulation with increased signals in a variety of cortical areas, including somatosensory area (S1), primary motor area (M1), and supplementary motor area has been reported (Wu et al. 2005, 2006). In addition, direct connections between S1 and M1 could provide the

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*These authors are equally contributed to this study.
Correspondence: Hwi-young Cho, Department of Physical Therapy, College of Health Science, Gachon University, 191, Hambangmoe-ro, Yeonsu-gu, Incheon 406-799, South Korea.
e-mail address: hwiyoung@gachon.ac.kr

influence of electrical somatosensory stimulation on motor cortical reorganization (Floel et al. 2008). Therefore, it appears that electrical somatosensory stimulation is sufficient for modulation of reorganization of the motor cortex during performance of the required motor task, which may be beneficial to improvement of motor function in stroke rehabilitation (Golaszewski et al. 1999; Ridding et al. 2000; Ng and Hui-Chan 2007). There are a variety of electrical stimulators; however, unlike functional electrical stimulator, neuromuscular electrical stimulation, or interferential current therapy, transcutaneous electrical nerve stimulation (TENS) is relatively easy to apply and control, readily available, risk free, and inexpensive, particularly if the stimulation is applied at a pleasant sensory level (Laufer and Elboim-Gabyzon 2011; Tyson et al. 2013). Based on previous studies, we hypothesized that additional benefit could be attained if task-related training was used with TENS in upper arm rehabilitation.

Thus, the purpose of this study was to determine whether TRT combined with TENS plays a positive role in facilitating functional recovery of the paretic upper arm of chronic stroke patients.

Methods

Participants

This study was designed as a single-blind, randomized clinical trial. Thirty inpatients with a first-time stroke participated in the study conducted at a local rehabilitation center in Seoul. All patients met the following inclusion criteria: (1) hemiparesis caused by stroke, (2) chronic phase at least six months post stroke, (3) presentation with mild to moderate motor and/or sensory deficits at the upper arm, (4) unimpaired visual and vestibular functions, (5) Mini-Mental State Examination scores ranged from 26 to 30, (6) the ability to complete the experimental protocol using the affected arm, and (7) no experience with TENS stimulation in their lives. The exclusion criteria were: (1) severe aphasia, apraxia, or visuospatial disorder, (2) any pre-existing neurological disorders, (3) severe spasticity (modified Ashworth scale (MAS) ≥ 3), (4) severe heart or lung disease, and (5) unable to tolerate electric stimulation. Data for the study were collected from October 2012 to June, 30, 2013. Prior to data collection, patients signed a written informed consent explaining the protocol, and experimental procedures were performed in compliance with the ethical committee of Gachon University. We used the G-Power 3.1.7 for calculation of the sample size. Sample size was determined on the basis of ability to detect a clinically significant improvement in the primary outcome measures, as described below (see *Outcome measurements*).

We set the effects size as 0.8 and the alpha error as 0.05. According to the analysis, at least 14 subjects were needed in order to make an adequate group size. In this study, we randomly allocated 20 subjects to each group considering inclusion criteria at the beginning, and finally selected 15 subjects per group.

Experimental procedure and intervention

Thirty-eight patients with chronic stroke volunteered for this study. Eight patients were not included for the following reasons:

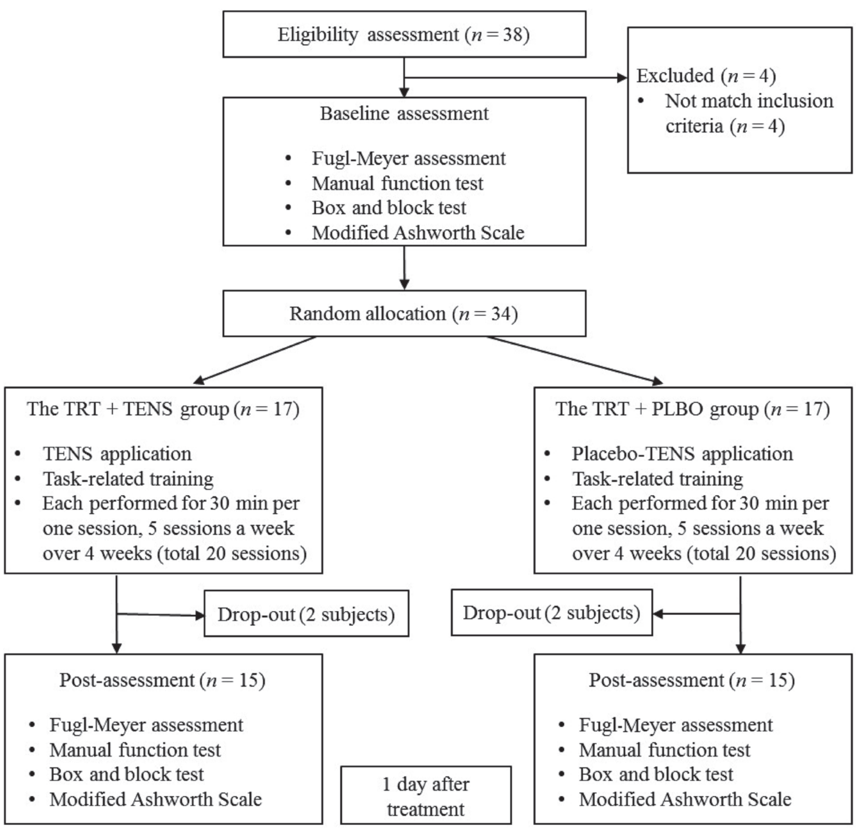

Fig. 1. Flow-chart through this study.

four patients did not satisfy selective criteria, and four patients failed to comply with the intervention for personal reasons. All experimental processes are shown in Fig. 1.

All patients were randomly assigned to two groups using tables of random numbers: (1) the TRT+TENS group (n = 15) and (2) the TRT+placebo (TRT+PLBO) group (n = 15). All subjects participated in TRT delivered by the same physical therapists, and they received 20 sessions of 30 minutes per one session, five sessions per week over a four-week period. One trained physical therapist supervised all interventions according to a standardized set of instructions. All sessions began with a 5-minute warm-up period. TRT included arm or hand tasks related to functional movements needed in their daily lives. Each task became increasingly difficult (starting with active flexion of the affected shoulder to throw a soft ball, active rotation of the affected wrist to turn off a water tap, followed by performance of more complex movements, such as selective flexion of the affected fingers to tighten shoe laces, etc.). The physical therapist instructed them to perform all exercises 20 times by minimizing compensatory movements and by checking their progression during a 30-minute period.

The TRT+TENS group received 30 minutes of TRT followed by TENS stimulation for 30 minutes. Electrical stimulation (two to three times the sensory threshold, 100 Hz, 200 us) was applied to muscle belly of triceps and wrist extensors using a two channel TENS machine (TENS-7000, Koalaty Products Inc., USA). Applied stimulation usually evoked the occurrence of visual muscle contraction. While electrodes were attached at the same location, real electrical stimulation was not applied in the TRT+PLBO group.

Outcome measurements

Patients were assessed one day before and after treatment each time by the same blinded raters using these measurements. Fugl-Meyer assessment (FMA), comprised of 18 items dealing with shoulder, elbow, wrist, and forearm: five with wrist, seven with hand, and three with coordination, was used for testing upper extremity motor recovery (Fugl-Meyer et al. 1975). The maximum score for upper-limb section of FMA was 66. Inter-rater reliability of upper-extremity scale of FMA was r = 0.99 with test-retest reliability at r = 0.99 (Duncan et al. 1983).

For evaluation of the motor function of the upper limb in stroke patients, we used the manual function test (MFT), which consists of “arm motion” and “manipulative activities”. The arm motion was performed using four tasks: forward elevation and lateral elevation of the upper limb, touch the occiput and touch the dorsum with the palm. The manipulative activities included four tasks: grip, pinch, carry cubes, and peg board. The total score of MFT for eight tasks is 32: 0 indicates severe impairment and 32 indicates full function in the upper limb function. Test-retest reliability and inter-rater reliability of MFT are r = 0.99 and r = 0.99, respectively (Miyamoto et al. 2009).

Box and block test (BBT) was used to measure promptness in the upper limbs and hand coordination. In general, this test has been used to assess unilateral gross manual dexterity of the upper limbs. BBT verified the ability to reach for and grasp wooden regular hexahedrons (2.54 cm × 2.54 cm × 2.54 cm), and to transport them to the other side of a wooden box (53.7 cm × 8.5 cm × 27.4 cm) with a separation in the middle, releasing regular hexahedrons. The test measured the number of hexahedrons transferred to the other side for 60 seconds. Test-retest reliability and inter-rater reliability of BBT are r = 0.99 and r = 0.99, respectively (Trombly 1989).

MAS have been used to assess the degree of spasticity. This is a subjective assessment and has verified validity for testing spasticity of the upper extremity in stroke patients (Pizzi et al. 2005). MAS is a 6-point scale (0, 1, 2, 3, 4, 5), with a score of 0 indicating no resistance and 5 indicating rigidity. We measured spasticity three times, and then averaged the values. Inter-rater reliability of MAS was r = 0.92 with intra-rater reliability at r = 0.86 (Gregson et al. 1999).

Data analysis

Statistical analysis was performed using SPSS version 15.0. The normal distributions of the results were tested with Kolmogorov-Smirnov or Shapiro-Wilk test. Differences between tests before and after treatment were compared using paired samples t-test or nonparametric Wilcoxon and marginal homogenity test, and the differences between two groups were compared using independent samples t-test or Mann-Whitney U test. Pearson correlation coefficient was used to measure the relationship between spasticity and motor function improvement in the TRT+TENS group. Results were accepted as statistically significant at $P < 0.05$.

Results

The general characteristics of the participants are shown in Table 1.

Fifteen patients with chronic stroke received TRT+TENS and 15 received TRT+PLBO in the paretic arm. There were no drop-outs in the study during the four-week intervention period and no statistical difference in the baseline between the groups (P = 0.554 for FMA, P = 0.507 for MFT, P = 0.571 for BBT, and P = 0.717 for MAS). The main findings of this study were that (a) performance of TRT in both groups resulted in significantly enhanced upper limb motor

Table 1. General characteristics of participants.

	TENS+TRT group (n = 15)	PLBO+TRT group (n = 15)	X^2/t	P
Gender (Male/Female)	9 / 6	8 / 7	0.714	0.481
Age (years)	63.3 ± 8.30	61.3 ± 9.97	0.577	0.568
Height (cm)	163.1 ± 9.26	161.5 ± 7.91	0.488	0.630
Weight (kg)	62.4 ± 12.74	60.9 ± 10.64	0.358	0.723
Onset time (month)	13.6 ± 4.36	12.3 ± 5.26	0.718	0.478
Involved side (Lt / Rt)	8 / 7	6 / 9	0.714	0.481

Values are expressed as mean ± standard deviation (S.D.).

Table 2. Chances of the Fugl-Meyer assessment (FMA).

		TENS+TRT group	PLBO+TRT group	*t*	*P*
Total	Baseline	42.9 ± 7.81	41.0 ± 9.21	0.599	0.554
	Post	50.1 ± 5.73	44.6 ± 7.71	2.231	0.034
	t	9.738	7.407		
	P	0.000	0.000		
Shoulder/Elbow/ Forearm	Baseline	28.3 ± 3.68	27.8 ± 4.28	0.366	0.717
	Post	31.3 ± 2.02	28.9 ± 3.83	2.090	0.046
	t	5.275	5.264		
	P	0.000	0.000		
Wrist	Baseline	4.7 ± 2.19	4.4 ± 1.92	0.444	0.661
	Post	6.8 ± 1.78	5.2 ± 2.01	2.309	0.029
	t	7.750	4.583		
	P	0.000	0.000		
Hand	Baseline	6.8 ± 2.27	6.4 ± 2.77	0.432	0.669
	Post	7.7 ± 2.60	7.3 ± 2.69	0.414	0.682
	t	2.432	4.525		
	P	0.029	0.000		
Coordination	Baseline	3.0 ± 1.25	2.4 ± 1.18	1.348	0.188
	Post	4.3 ± 1.29	3.1 ± 1.25	2.590	0.015
	t	6.325	2.219		
	P	0.000	0.044		

Values are expressed as mean ± standard deviation (S.D.).

Table 3. Chances of the manual function test (MFT).

		TENS+TRT group	PLBO+TRT group	*t*	*P*
Total	Baseline	19.3 ± 3.13	18.5 ± 3.89	0.672	0.507
	Post	22.5 ± 3.18	19.9 ± 3.31	2.192	0.037
	t	8.622	5.137		
	P	0.000	0.000		
Arm motion	Baseline	17.1 ± 2.95	16.5 ± 3.40	0.574	0.571
	Post	19.3 ± 2.43	17.5 ± 2.88	1.782	0.086
	t	5.670	5.172		
	P	0.000	0.000		
Manipulative activities	Baseline	2.2 ± 0.41	2.0 ± 0.65	1.000	0.326
	Post	3.2 ± 1.01	2.3 ± 0.72	2.694	0.012
	t	4.583	2.092		
	P	0.000	0.055		

Values are expressed as mean ± standard deviation (S.D.).

Table 4. Chances of the Box and block test (BBT).

		TENS+TRT group	PLBO+TRT group	*t*	*P*
Box and block test	Baseline	18.2 ± 5.12	17.1 ± 5.07	0.574	0.571
	Post	22.0 ± 4.39	18.4 ± 4.84	2.134	0.042
	t	12.192	5.551		
	P	0.000	0.000		

Values are expressed as mean ± standard deviation (S.D.).

Table 5. Chances of the modified Ashworth scale (MAS).

		TENS group	Placebo-TENS group	z	*P*
MAS scores	Baseline	1.4 ± 0.51	1.5 ± 0.52	0.362	0.717
	Post	0.9 ± 0.74	1.3 ± 0.70	1.782	0.075
	z	2.530	1.732		
	P	0.011	0.083		

Values are expressed as mean ± standard deviation (S.D.).

Table 6. The correlation between spasticity and motor function recovery of the upper extremity.

	Correlation Coefficient	*P*
MAS VS FMA total	−0.712	0.000
MAS VS FMA-shoulder/elbow/forearm	−0.637	0.000
MAS VS FMA-wrist	−0.639	0.000
MAS VS FMA-hand	−0.518	0.003
MAS VS FMA-coordination	−0.486	0.006
MAS VS MFT total	−0.688	0.000
MAS VS MFT-arm motion	−0.700	0.000
MAS VS MFT-manipulative activities	−0.265	0.156
MAS VS BBT	−0.463	0.010

Values are expressed as mean ± standard deviation (S.D.).
MAS, the modified Ashworth scale; FMA, the Fugl-Meyer assessment; MFT, the manual function test; BBT, the Box and block test.

function (Tables 2, 3, and 4), (b) a significantly greater increase in upper limb motor function was observed in the TRT+TENS group than in the TRT+PLBO group (Tables 2, 3, and 4), (c) spasticity in the paretic arm showed a significant decrease only in the TRT+TENS group (Table 5).

When comparing the differences of outcomes between before and after treatment within each group, the three primary arm function outcome measures (FMA, MFT, and BBT) showed a significant increase in both groups ($P < 0.001$). By independent samples *t*-test, significant differences in three outcome measures were observed between the two groups at the end of the four-week intervention period ($P = 0.034$ for FMA, $P = 0.037$ for MFT and $P = 0.042$ for BBT). In MAS score, significant improvement was observed only in the TRT+TENS group ($P = 0.011$).

Table 6 presents the correlation between spasticity and motor function improvement in the upper limb. FMA total and other FMA subcategories (shoulder/elbow/forearm, wrist, hand, and coordination) show a statistical significance of negative correlations with MAS. Also, a significant negative correlation was found between MAS and MFT total, MFT-arm motion and BBT. However, there was no significant correlation between MAS and MFT-manipulative activities.

Discussion

In this study, combining 30 minutes of TENS with TRT is generally more effective than placebo-TENS with TRT in improving the functional ability of the affected arm. Although the combined TENS with the training group showed significantly greater scores in the three primary arm function measures (FMA, MFT, and BBT), scores in placebo-TENS with the training group also showed a significant increased. This result indicates that TRT has a positive influence on paretic arm function, and supports the results of previous studies showing that TRT is effective for improvement of complicated motor learning and promotion of the upper limb motor recovery, and motor improvements of the upper limb by TRT can continue well into the phase of chronic stroke (Barreca et al. 2003; Thielman et al. 2004; Higgins et al. 2005; Michaelsen et al. 2006; O'Dell et al. 2009).

In this study, differences in FMA, MFT, and BBT between the TRT+TENS group and the TRT+PLBO group demonstrated that application of TENS has therapeutic effects on improving motor function of the affected arm. Possible underlying mechanisms of the improvement may include the possibility that sensory input facilitates sensorimotor integration in the alternative motor areas that control the paretic hand after cortical lesions (Calautti and Baron 2003; Conforto et al. 2007), since somatosensory stimulation activates skin receptors and proprioceptors, and leads to plastic change in S1, M1, and premotor cortex (Wu et al. 2005). Meesen et al. demonstrated the long-term effect of somatosensory stimulation with TENS on reorganization of the motor cortex, and determined the representation of the corticospinal projection to the finger and forearm muscles before and after a three-week intervention period by calculating map area and volume, and topographical overlaps between the cortical motor representations of these muscles. They found a significant increase in cortical motor representation of all muscles in the TENS group from pre-test to post-test, and suggested the potential of sensory training by application of TENS in neurorehabilitation (Meesen et al. 2011). A recent study by Tyson et al. (2013) reported that application of TENS had positive effects on strength, proprioception, balance, and mobility in stroke survivors by providing supplementary sensory stimulation. In a randomized controlled study, Tekeoğlu et al. (1998) reported on the effectiveness of TENS on the level of activities of daily living (ADL) of stroke patients after an eight-week intervention period, and suggested that TENS can be an effective additional method in regaining motor functions and improving ADL in hemiplegic patients.

When compared with the TRT+PLBO group, the TRT+TENS group showed significantly improved scores in MAS. This result indicates that TENS may be effective for reduction of muscle spasticity. A growing number of studies have reported on the relationship between electrical stimulation and spasticity (Ozer et al. 2006; Miller et al. 2007; Bakhtiary and Fatemy 2008; Cho et al. 2013). In this study, the reduction in spasticity was comparable to that reported by Bakhtiary and Fatemy. They investigated the effect of electrical stimulation on plantarflexor spasticity in patients with stroke, and suggested that electrical stimulation may effectively reduce spasticity and improve motor performance (Bakhtiary and Fatemy 2008). In addition, Cho et al. (2013) demonstrated that TENS effectively induced a decrease in spasticity in TENS-applied muscle and increased postural balance in patients with chronic stroke. They observed a positive correlation between spasticity and postural balance, supporting that decreasing spasticity plays an important role in improvement of balance function or motor performance. Their results are in agreement with our findings showing significant correlation between spasticity and various variables related to motor function such as FMA, MFT, and BBT (Table 6). Therefore, our result indicates that decreasing spasticity may be an important factor in improvement of motor function. However, one additional important and novel finding in our study is that application of TENS on weakened antagonist muscles had a positive effect on agonists involved in spasticity. This result differed from findings from previous studies reporting decreased spasticity by application of TENS to agonist muscles involved in spasticity (Tekeoğlu et al. 1998; Calautti and Baron 2003; Ng and Hui-Chan 2007). Two mechanisms may underpin these improvements. First, application of TENS leads to increased expression or release of the inhibitory neurotransmitter GABA at the dorsal horn of the spinal cord (Maeda et al. 2007). Spasticity is induced in hyper-excitable status of the central nervous system (Mukherjee and Chakravarty 2010). Although we applied TENS to the peripheral nerve system, it may reduce spasticity by decreasing hyper-excitability of the central nervous system. Second, activation of reciprocal inhibition may lead to decreased spasticity.

A previous study reported that TENS changed neuromuscular activity of antagonist muscle through reciprocal inhibition (Tinazzi et al. 2005). In addition, in this study, application of TENS contributed to the effect of TRT since TENS may increase the applied muscle strength by reducing spasticity through reciprocal inhibition.

Reciprocal inhibition technique of Proprioceptive Neuromuscular Facilitation (PNF) is a therapeutic technique that decreases the activation level of target muscles by increasing voluntary contraction of opposing muscles (Sharman et al. 2006). Although we could not determine muscle strength of elbow extensors, it may be supposed that the reciprocal inhibition originated by increasing muscle activation of elbow extensors decreases spasticity.

Information on the details underlying the beneficial effects of TENS in performance of dextrous arm movements after stroke may enrich the development of innovative behavioral concepts in rehabilitation. However, we have not performed testing to determine how long the effects of TENS on arm motor function persist after intervention has ceased. Conduct of future studies with longer treatment periods and larger samples of stroke survivors may result in larger improvements by determining the assisting role of TENS application to improvement of impaired motor function of the upper limb in daily life after stroke. Intensity of applied electrical stimulation (two to three times the sensory threshold) sometimes gave an unpleasant feeling to the participants. Therefore, further study is required to identify the optimal intensity to improve motor recovery of upper limb with comfortable sense. The finding of this study is that TENS allowed retention of training effects, suggesting that the combination of TENS with motor training may contribute to consolidation of the positive effects of rehabilitative treatments based on practice of motor tasks.

Conclusion

Based on the results of this study, combination of TENS with TRT may be more effective than placebo-TENS with TRT in improving the functional ability of the affected arm. TENS with TRT may play a positive role in reducing motor impairment and improving motor activity in stroke survivors with chronic upper limb paresis. This supports the notion of using TENS in neurorehabilitation during performance of everyday activity. Future research might include dose-response experiments to establish the amount and duration of TENS needed to produce sustained change.

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Conflict of Interest

The authors declare no conflict of interest.

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