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Sensory Electrical Stimulation for Recovery of Hand and Arm Function in Stroke Patients: A Review of the Literature

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Abstract

Background: Sensory amplitude electrical stimulation has been reported to induce changes in corticospinal excitability. The aim of this review is to evaluate the effects of sensory electrical stimulation on hand and arm function in stroke patients.

Methods: A literature search was undertaken to locate papers that used sensory electrical stimulation in stroke patients. The methodological quality of each study was assessed using the Physiotherapy Evidence Database (PEDro) score.

Results: Ten studies were considered suitable for inclusion in this review. Six of the 10 studies provided the PEDro score, with the mean (standard deviation) score being 5.7 (1.0). There were no adverse effects in any of the studies. In only one study, the patients with acute stroke were included. There was much study of patients with mild arm hemiparesis. Most studies reported that sensory electrical stimulation was delivered at 10 Hz with pulse duration of 1 millisecond for 2 hours at the paretic wrist (median and/or ulnar nerve). Five studies reported sensory stimulation should not be used in isolation, but rather in combination with task training, to improve arm and hand function.

Conclusions: Sensory electrical stimulation may improve hand and arm function if it combines with functional task training in patients with mild arm paresis but there are no studies with high methodological quality. In addition, it is uncertain whether sensory electrical stimulation would be of benefit for patients with severe paresis and be effective in the acute phase. Therefore, the results of this review remain inconclusive due to a lack of suitable randomized controlled trials.

Keywords: Electrical stimulation; Sensory stimulation; Arm function; Upper-limb; Stroke

Introduction

Stroke causes motor and sensory impairments that downgrade quality of life [1]. Impaired movement of the arm is a common result of stroke, and it is often the most troublesome problem experienced by stroke survivors. Six months after a stroke, about 65% of patients cannot incorporate the affected hand into their usual activities [2].

As reported in a recent review, the most promising interventions for restoring function of the arm seem to be high-repetition doses of task-oriented training, such as constraint-induced movement therapy [3]. However, constraint-induced movement therapy requires considerable clinical staff input and a long treatment time, which makes clinical introduction impractical [4]. In fact, the reality of stroke rehabilitation is that at present patients receive only limited task-oriented training [5]. Novel concepts beyond the current strategies such as combinations of cortical stimulation and robotic training [6] for hand and arm motor rehabilitation are therefore needed for the treatment of stroke patients [7].

Neuromuscular electrical stimulation (NMES) is commonly used as a treatment to improve motor recovery, reduce pain and spasticity, and strengthen muscles in stroke rehabilitation. There is growing evidence that NMES has a positive effect on upper extremity motor recovery in patients with stroke [8]. When NMES is used to improve muscle strength and induce neuromuscular reeducation, the current amplitude is increased to produce a contraction level within the patient's tolerance but doing so has a risk of causing pain, muscle fatigue and skin irritation.

Meanwhile, sensory amplitude electrical stimulation has been reported to induce changes in the corticospinal excitability of the hand area in healthy subjects [9]. Based on that report, sensory electrical stimulation has been proposed as a possible supplemental therapy to facilitate motor functions such as pinching [10], swallowing [11], and performing hand tasks in patients with stroke [12]. This new method has several advantages. Firstly, the method is safer than motor amplitude NMES, and there is no pain. Secondly, it can be implemented in any neurorehabilitation setting, and the stimulation parameters are easy to control. Thirdly, the method permits researchers not only to perform therapeutic trials in clinical settings but also to carry out basic studies of the underlying neurophysiological mechanisms. Recently, Laufer and Elboim-Gabyzon [13] reported the effects of sensory transcutaneous electrical stimulation on motor recovery after stroke. Most recently, several studies which aimed to improve arm motor function which have been reported. In this review article, we will update including the recent studies and discuss the clinical application of this method, focusing on clinical which aimed to improve arm motor function.

Materials and Methods

In previous studies, sensory amplitude electrical stimulation

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has been referred to using various terms (i.e., peripheral nerve stimulation, repetitive sensory nerve stimulation, peripheral sensory electrical stimulation and somatosensory stimulation). A literature search was undertaken to locate papers that used sensory amplitude electrical stimulation in stroke patients. The search terms 'peripheral nerve stimulation/electrical stimulation/sensory stimulation/somatosensory stimulation', 'stroke/hemiplegia/hemiparesis' and 'hand/arm/upper limb' were used in various combinations. The databases searched were Pubmed, MEDline, EcscoHost and the Physiotherapy Evidence Database (PEDro). Articles appearing in these databases ahead of print were also included. In this review, we included the clinical studies in which the sensory amplitude electrical stimulation was delivered at the peripheral nerve or muscle in humans. We excluded studies that involved the delivery of motor amplitude electrical stimulation, including stimuli that produce muscle contraction even when the muscle contraction is slight. In addition, we excluded the studies that combined sensory amplitude electrical stimulation with one or more other treatments, such as repetitive transcranial magnetic stimulation and transcranial direct current stimulation, but we permitted studies that combined it with therapeutic exercise.

The methodological quality of individual randomized controlled trials (RCTs) was assessed using the PEDro score [14]. Studies included in this review using a non-experimental or uncontrolled design could not be assigned a PEDro score and were given no score designation. The PEDro Scale consists of 10 quality ratings that each receive either a yes or no; the maximum score (number of "yes" designations) was 10. Studies scoring 9 to 10 were considered to be methodologically "excellent", those ranging from 6 to 8 were considered to be of "good"

							Parameter			
Author / PEDro score	Study design	n	Time since stroke	Intervention	Treatment period	Pulse width (u sec)	Frequency (Hz)	Duty cycle (on/off)	Stimulation time (min)	Outcome measures Results
Peurala et al. [22] No score	Controlled study	54	3.3 (0.6 - 14) years	Cutaneous stimulation by glove or sock electrode + Rehabilitation vs. placebo stimulation + rehabilitation	3 weeks	not described	50	-	20×2	Modified Motor Assessment Scale (+) 10-metre walking test (+) Somatosensory evoked potential (+) Paretic upper limb function (+) Paretic upper limb skin sensation (+)
Conforto et al. [18] 6	Randomized, crossover design	8	5.5 (1.2 - 7) years	Median nerve stimulation vs. subsensory stimulation	1 day	1000	10	-	120	Pinch strength (+)
Wu et al. [12] 4	Randomized, crossover design	9	6.5 (1.0) years	Median, ulnar and radial stimulation vs. no stimulation vs. leg stimulation	1 day	1000	10	500 ms/500 ms	120	Jebsen-Taylor Hand Function Test (+)
Conforto et al. [18] 6	Quasi-randomized, crossover design	11	4.3 (0.7) years	Sensory median nerve stimulation + task-specific training vs. subsensory median nerve stimulation task-specific training	1 day	1000	10	-	120	Jebsen-Taylor Hand Function Test (+)
Celnik et al. [16] 6	Randomized, crossover design	9	3.2 (1.6) years	Synchronous peripheral nerve stimulation + task-specific training vs. no stimulation + task-specific training vs. asynchronous peripheral nerve stimulation + task-specific training	1 day	1000	10	-	120	Jebsen-Taylor Hand Function Test (+) short intracortical inhibition (+) Intracortical facilitation (-)
Klaiput et al. [15] 7	Randomized, Sham-controlled trial	20	25.4 (32.3) days	Median and ulnar nerve stimulation (below motor threshold) vs. control stimulation (just sensory threshold)	1 day	1000	10	500 ms/500 ms	120	Pinch strength (+) Action Research Arm Test (-)
Koesler et al. [21] No score	Quasi-randomized, crossover design	12	15.7 (4.2) months	Median nerve stimulation vs. sham stimulation	1 day	1000	10	-	120	Index finger tapping frequency (+) Hand tapping frequency (+) Reach-to-grasp movements (+)
Conforto et al. [18] 5	Quasi-randomized Sham-controlled trial	22	61.8 (2.6) days	Suprasensory stimulation + task-specific training vs. subsensory stimulation+ task-specific training	3 times per week, for 1 month	1000	10	-	120	Jebsen-Taylor Hand Function Test (+) Pinch strength (-) FIM (-)
Ikuno et al. [19] Ahead of print	Randomized crossover design with a between-group comparison	22	100.7 (45.9) days	Peripheral sensory nerve electrical stimulation + task-oriented training vs. task-oriented training alone	6 times a week for 2 weeks inpatient rehabilitation program	1000	10	500 ms/500 ms	60	Wolf Motor Function Test (-), but within group comparison (+) Box and Block Test (-) but within group comparison (+) Pinch strength (-) Grip Strength (-)
Sullivan et al. [20] Ahead of print	Randomized Sham-controlled trial	38	7.2 (1-29) years	Sensory electrical stimulation using glove electrode + task-based home exercise vs. subsensory (sham) stimulation + task-based home exercise	5 days per week, 4 weeks	250	35	10 sec/10 sec	30×2	Arm Motor Ability Test (-), but within group comparison (+) Fugl-Meyer Assessment (-) Motor Activity Log-14 (-) Nottingham Stereognosis Assessment (-) Stroke Impact Scale-16 (-)

Table 1: Sensory electrical stimulation in the treatment of reduced arm function.

quality, and studies scoring 4 to 5 were of "fair" quality. Studies that scored below 4 were considered to be of "poor" quality.

Results

The literature search resulted in the identification of 178 studies. Of these, 10 were considered suitable for inclusion in this review. The excluded articles were related to functional electrical stimulation, neuromuscular stimulation, transcutaneous electrical stimulation with motor amplitude, acupuncture stimulation and paired associative stimulation (n=168).

Study quality and design

Quality rating scores based on the PEDro scale of each study are summarized in table 1. Six of 10 studies provided the PEDro score, with the mean (SD) score being 5.7 (1.0). The PEDro score was not included in two recent studies because the studies had not yet gone to print [15,16]. No studies were graded as "excellent"; four of the six studies were graded as "good" (score range from 6 to 8) [8,12-14]. Two studies were graded as "fair" [10,17]. In study design, five studies used a repeated measure crossover design [10,12,18-20], and three studies used a randomized controlled design [16,17,21]. Only four studies among the RCTs and randomized crossover trials conducted a between-group comparison [15,17,21].

Participants

The number of patients per study receiving sensory electrical stimulation treatment ranged between 7 and 20, and the number receiving sham or control treatment ranged between 7 and 18. However, six of 10 studies were crossover repeated measure designs, and both interventions were performed in each patient [10,12,18-20]. The range of the time since onset was an average of 11.9 to 2372 days. In one study, patients were in the acute or subacute phase (<30 days) [12], and patients were in the subacute phase (30<180 days) in two studies [15,21]. In seven studies, patients were in the chronic phase (>180 days) [10,12,16,18-20,22]. On the whole, there was much study of patients with mild arm hemiparesis (Fugl-Meyer Assessment Upper Extremity Item>80%). Patients with severe to moderate upper limb hemiparesis participated in only one study (Fugl-Meyer Assessment Upper Extremity Item score is 15-46) [16].

Intervention

No adverse effects were reported in any of the studies. These studies were conducted using a variety of electrical stimulation parameters including waveform, frequency, site, and treatment time. In each study reviewed, the electrical stimulation was administered at different intensities at the sensory level, such as intensities that elicited strong or mild paresthesia, intensities just below the motor threshold, intensities at the sensory threshold, and subsensory stimulation.

Waveform

All 10 studies provided information on the waveform used. In eight studies, monophasic square pulses were used [10,12,17-19,21]. In one study, monophasic constant current twin pulses were used [22]. In one study, asymmetrical biphasic waveform was used [16].

Stimulation frequency

In eight studies, the pulse frequency was 10 Hz with or without a 50% duty cycle (500 ms on/500 ms off) [10,12,17-19,21]. This parameter was employed in the neurophysiological research that Kaelin-Lang et al. [9] reported. In one study, the frequency was 50 Hz, and continuous stimulation was applied [22]. In one study, the frequency was 35 Hz with duty cycle of 10 seconds ON: 10 seconds OFF [16].

Stimulation site

Most authors located the electrodes over the peripheral nerve at the wrist. In three studies, the stimulation site overlaid both the median and ulnar nerves at the wrist of the paretic arm [17,18,21]. In four studies, only the median nerve was stimulated, but the site of the stimulus was the wrist of the paretic arm [10,19,21,20]. In one study, the median, ulnar and radial nerves were stimulated by three pairs of electrodes [12]. In two studies, the stimulation was given with a glove electrode [16,22]. This unique electrode was connected as a common anode while a surface carbon electrode (diameter 6 cm), placed 2.5 cm proximal to the wrist, served as a cathode. Thus, this method of stimulation might provide somatosensory input via a cutaneous sense organ in the median, ulnar and radial nerve territories.

Treatment type

In three studies, the sensory electrical stimulation was performed alone [10,12,17,20]. In one study, the sensory electrical stimulation was used together with a regular inpatient rehabilitation program, but the details of the program were not described [22]. In three studies, the patients underwent the sensory electrical stimulation followed by task-specific training using the Jebsen-Taylor Hand Function Test [18,19,21]. Two studies simultaneously conducted sensory electrical stimulation and task training [15,16]. Many studies reported positive effects in which the sensory electrical stimulation was better than sham or no-stimulation conditions, and the sensory electrical stimulation combined with task training was better than task training alone.

Stimulation time

In seven studies, sensory electrical stimulation was delivered for 2 hours [10,12,17-21]. The reasons for applying it for 2 hours were probably based on the previous studies [9]. However, these studies with the exception of the study by Conforto et al. [19] involved a single session. The study by Conforto et al. [21] investigated the influence of the sensory electrical stimulation over multiple sessions, as sensory electrical stimulation plus task-specific training was performed three times per week, for one month (a total of 12 sessions). In one study, sensory electrical stimulation was delivered for 20 minutes twice per day during 3-week inpatient rehabilitation periods [22]. In one study, sensory electrical stimulation was delivered for 60 minutes per day, six times a week (a total of six sessions) [15]. In one study, sensory electrical stimulation was delivered for 30 minutes twice per day, five times per week for four weeks (a total of 40 sessions) [16].

Outcome measures

There were only three studies with follow-up assessment [16,18,19]. Almost all studies were assessed at pre- and post-intervention. The range of the follow-up period was from 24 hours to 2-3 months. Among the impairment level measures, pinch strength was assessed in most studies. In one study, sensory function was assessed using a visual analog scale [22]. Sullivan et al. [16] assessed sensory function using the Perceptual Threshold Test Using Electrical Stimulation, which is a reliable and clinically feasible test with the potential to identify sensory capacity in stroke survivors with substantial sensory loss [23]. Only one study assessed arm and hand movement kinematics [20]. The arm and hand function measure most commonly used was the Jebsen-Taylor Hand Function Test. The Action Research Arm Test was used in one study [17]. The Wolf Motor Function Test was used in one

study [15]. The Arm Motor Ability Test was used in one study [16]. Only one study assessed quality of life and real-life activity assessment using the Stroke Impact Scale-16 and Motor Activity Log [16].

Two studies included neurophysiological assessment. Peurala et al. [22] measured somatosensory evoked potentials (SEPs) delivered to the median nerve at the wrist. Celnik et al. [18] measured the motor evoked potentials of the first dorsal interosseus delivered to the ipsilesional motor cortex using transcranial magnetic stimulation. In addition, the study measured short intracortical inhibition and intracortical facilitation.

Treatment effect

Pinch strength was found to be affected positively in two of four studies [10,17]. Each study which showed a positive effect had investigated the immediate effect. Another study which showed a negative effect investigated the effect of the multiple sessions [15,21]. Koesler et al. [20] reported that 2-hour sensory electrical stimulation enhanced the frequency of index-finger and hand-tapping movements and improved the kinematics of reach-to-grasp movements in the paretic hand.

The Jebsen-Taylor Hand Function Test was found to show a positive effect in all of these studies including pre-post, follow-up and multiple session studies. However, the one study which evaluated the Action Research Arm Test showed a negative result [17]. Unfortunately, two recent studies showed no significant between-group differences in functional outcomes. However, there were significant within-group differences [15,16].

Peurala et al. [22] reported that the somatosensory evoked potential normality classification of the paretic hand improved significantly in the treatment group ($p<0.01$). Celnik et al. [18] reported that sensory electrical stimulation plus training significantly decreased short intracortical inhibition in the absence of change with no stimulation. In addition, intracortical facilitation increased after both interventions. The treatment effect was summarized in table 1.

Discussion

Ten RCTs or controlled trials investigating the effects of sensory electrical stimulation on upper-limb function in stroke patients were found in the literature databases. Two RCTs were added as compared with the previous review. However, there were still few high-quality clinical studies, and their sample sizes were small. Therefore, the evidence needed to determine whether sensory electrical stimulation is effective for upper-limb motor impairments is lacking. Experimental studies in the laboratory setting that were designed relatively well reported positive effects of sensory electrical stimulation. However, the studies largely looked at a small group of patients who had slight-mild upper-limb hemiparesis, many of whom would not normally have been admitted to most stroke rehabilitation units. Only one study conducted sensory electrical stimulation in patients with severe to moderate upper-limb hemiparesis [16]. Unfortunately, although the study did not show a significant effect on the functional outcome of the upper limbs, it found a tendency to improve. It is uncertain whether sensory electrical stimulation would be of benefit for patients with severe paresis. In patients with severe stroke, several RCTs have reported motor amplitude electrical stimulation such as NMES is more effective as compared with conventional physical therapy [24-26]. It seems that motor amplitude electrical stimulation is beneficial to recovery of motor impairment in patients with severe stroke although there is no study which compared the effect of sensory electrical stimulation versus motor amplitude electrical stimulation directly. In addition, the result of present review could not show that sensory electrical stimulation would be effective in the acute phase. In the VECTORS study [27], the surprising result was that at 90 days, affected arm motor outcomes, measured with the upper-extremity Fugl-Meyer score, were worse for the more intensive CIMT (constraint-induced movement therapy) group. In contrast, Hsu et al. [25] reported the effects of two different doses of NMES on upper-extremity function in acute stroke patients. Both NMES groups showed significant improvement on Fugl-Meyer and Action Research Arm Test scores compared with the control group at week 4 and follow-up. Although there were the reports which conflicted about the effect of high-intensity training in acute phase, electrical stimulation may lead to a beneficial result in patients with severe arm hemiparesis.

Several small-scale studies suggest that the short-term carry-over effect on hand function was caused by sensory electrical stimulation. Conforto et al. [19] reported that the effect of motor training was still present up to 30 days after sensory electrical stimulation. The authors found in a later study that the effect continued for 2 to 3 months when patients received 1-month task training plus sensory electrical stimulation [21]. In addition, these studies suggest that sensory electrical stimulation should not be used alone, but rather combined with active task training in order to enhance the effects of physical training. Stroke studies as well as several studies in patients with spinal cord injury suggest that sensory electrical stimulation can enhance the effect of massed motor training [28,29]. The task training increases the excitability of the motor cortex and induces persistent plastic change [30,31]. Sensory electrical stimulation may enhance persistent plastic changes by involving a long-term potentiation-like mechanism [32]. In order to acquire the carry-over effect, it may be an important factor to combine sensory electrical stimulation and active task training.

In sensory electrical stimulation therapy, the parameter of the electrical stimulation seems to have an important role. Clinically, frequencies between 30 and 50 Hz are most commonly used to achieve a titanic muscle contraction in NMES therapy. However, 10 Hz was also used for sensory electrical stimulation on the basis of a previous study [9]. These studies seem to show positive effects. Two studies conducted using the commonly used frequencies of 35 or 50 Hz [16,22] reported conflicting results, but their study designs differed greatly. High-frequency peripheral mixed median nerve stimulation of 150 Hz reduced the excitability of the motor cortex [33]. In addition, Mima et al. [34] reported that short-term high frequency electric somatosensory stimulation at 90 Hz transiently reduces corticospinal excitability. For the pharyngeal muscles, sensory electrical stimulation at 5 Hz induced an increase in motor cortex excitability [35], whereas the stimulation at 20–40 Hz reduced the cortical excitability. Mang et al. [36] demonstrated a frequency-dependent effect of NMES on corticospinal excitability in the tibialis anterior and showed that 100-Hz stimulation was more effective than 10, 50, and 200 Hz. These results suggest that the optimal frequency may change depending on the site at which the sensory electrical stimulation is delivered. Further studies are needed to determine the optimal frequency every therapeutic targets.

The stimulation time of the electrical stimulation is also important. Many studies conducted sensory electrical stimulation for 2 hours. The 2-hour stimulation showed positive effects on pinch strength and arm function outcomes. However, the protocol did not appear to be practical to implement in a clinical rehabilitation setting [15]. Therefore, we investigated the effects of 1-hour pragmatic electrical

stimulation plus task training during inpatient rehabilitation. There was no significant difference in the level of fatigue, and there were no adverse events. In addition, within-group comparison showed significant improvements in the hand and arm outcomes. Mckay et al. [37] reported that increases in cortical excitability peaked 45-60 minutes after the electrical stimulation. Accordingly, in order to produce the maximum effect of the electrical stimulation, stimulation for at least 30 minutes or more may be needed.

There was a contradictory result in terms of stimulation intensity. Conforto et al. [21] reported that subsensory stimulation better facilitated the trained Jebsen-Taylor Hand Function Test task than suprasensory stimulation at one month. This result seemed to differ from the author's hypothesis. Although there was a significant difference, both groups improved similarly on the Jebsen-Taylor Hand Function Test. Further studies are needed to determine the optimized intensity of electrical stimulation in a randomized sham-controlled clinical trial. Based on previous studies [3,8], the effectiveness of motor amplitude electrical stimulation such as NMES or functional electrical stimulation may be greater than that of sensory amplitude stimulation. However, sensory amplitude electrical stimulation has the advantage of not producing fatigue or pain, which may be caused by motor amplitude electrical stimulation. In addition, sensory electrical stimulation permits prolonged stimulation and the performance of massed task-oriented training simultaneously. As indicated in several studies, sensory electrical stimulation may be useful as a supplementary tool that enhances the effect of upper limb rehabilitation in stroke patients who need constraint-induced movement therapy treatment [15,16,21,28,29].

Sensory electrical stimulation may improve hand and arm function if it combines with functional task training in patients with mild arm paresis but the results of this review remain inconclusive due to a lack of suitable randomized controlled trials. Further research should specifically address what frequency, duration and intensity of electrical stimulation would be most effective and at what time interval after a stroke. In addition, a large, randomized, multicenter trial with long-term follow-up is needed to determine the effectiveness of sensory electrical stimulation in stroke patients. On the other hand, the advantage of this intervention seems to be safe and easy to use in clinical and home settings.

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