

Sensory barrage stimulation in the treatment of elbow spasticity: a crossover double blind randomized pilot trial

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ABSTRACT

Objective: To assess the feasibility of using a novel form of multi-channel electrical stimulation, termed Sensory Barrage Stimulation (SBS) for the treatment of spasticity affecting the elbow flexor muscles and to compare this with conventional single-channel TENS stimulation.

Materials and methods: altogether 10 participants with spasticity of the flexor muscles of the elbow of grade 2 or above on the Modified Ashworth Scale (MAS) were recruited to this crossover double blind randomized trial. The participants received two intervention sessions (SBS and TENS), one week apart in a randomised order. Both interventions were applied over the triceps brachii on the affected arm for a duration of 60 minutes. Spasticity was measured using the MAS. Secondary outcome measures were self-reported change in spasticity, measured on a Visual Analogue Scale (VAS, 0-100), and therapist-rated strength of elbow extension (SEE) and strength of elbow flexion (SEF). Measurements were taken immediately before each intervention was applied, immediately after the intervention, and one hour after the intervention.

Results: Immediately after stimulation spasticity showed a significant reduction for both TENS and SBS groups assessed by MAS -0.9 ± 0.2 vs. -1.1 ± 0.2 and by VAS -15 ± 3 vs. -31 ± 8 . For SBS this improvement in MAS was still present

at one hour after the stimulation, but not for TENS. Altogether seven SBS responders and four TENS responders were identified.

Conclusions: This study demonstrates the feasibility and practicality of applying the new concept of Sensory Barrage Stimulation. Promising results indicate it causes a reduction in spasticity.

Introduction

Spasticity is a disorder of sensorimotor control, resulting from an upper motor neurone (UMN) lesion and presenting as the intermittent or sustained involuntary activation of muscles [1]. It can interfere with functional recovery and lead to contractures, which may impact significantly on patients' everyday living activities. Botulinum toxin, Intrathecal Baclofen Therapy and commonly used pharmacological agents such as Baclofen, Tizanidine, Dantrolene, or Diazepam are used for the treatment of spasticity [2]. However, in some patients spasticity might be resistant to oral treatment or the therapy might not be well tolerated due to side effects such as weakness, dizziness and drowsiness. In particular use of oral pharmacological in focal limb spasticity seems to be ineffective [3]. Non-pharmacological approaches such as muscle vibration, extracorporeal shock wave therapy and various forms of magnetic or electrical stimulation have been tried for the treatment of spasticity [2], but there is insufficient evidence to justify using these modalities routinely [4]. This paper focuses on the use of two different types of electrical stimulation: a conventional type of transcutaneous electrical nerve stimulation (TENS) and a novel concept of Sensory Barrage Stimulation (SBS) as described below.

TENS typically uses a single pair of electrodes placed on the skin over the affected site and delivers a continuous stream of repeated electrical stimuli at an amplitude below that which causes muscle contraction. TENS applied to the sural nerve was reported to reduce spasticity in patients with hemiplegia [5]. Similar effects were noted in patients with spinal cord injury immediately after 60 min of 100 Hz stimulation using TENS [6]. Several long term studies showed promising results [7, 8], but a study with multiple sclerosis patients did not demonstrate a reduction in spasticity [9] although TENS did help to reduce pain.

It has been proposed that applying TENS to peripheral sensory nerves reduces spasticity by modulating either spinal inhibitory circuits or those of the central nervous system [6].

We hypothesise that the effects of TENS on spasticity can be enhanced with a new form of stimulus that has two distinct features. Firstly, we hypothesise that it would be beneficial to stimulate a larger area of skin and hence stimulate more sensory fibres. This could be achieved by using larger electrodes. However, the stimulus current density would not be guaranteed to be distributed evenly over the electrode and, in particular, would be expected to be greater at the edges of the electrode [10]. Instead therefore, we used a modified 64-channel, constant current, programmable electrical stimulator,

previously developed for use in foot drop therapy [11], which allowed us to deliver the stimuli evenly over a larger area compared to TENS. Our second hypothesis was that participants may become habituated to the constant stimulation delivered by TENS between two fixed sites, and thus the stimulus becomes less effective over time. The mechanisms underlying recovery after neural injury, such as stroke, presumably involve a 'rewiring' plasticity processes [12]. Areas of the cortex can take over functionality in response to an injury or as a natural process following learning. It has been shown that attention plays an important role in learning and hence in plasticity [13]. Therefore stimulation capable of producing 'interesting' (or 'salient') sensations, delivered via multiple electrodes (as opposed to a single electrode with a monotonic stimulus delivery) may improve neuroplasticity effects due to the direction of attention to the salient stimulus. Further, reciprocal inhibition of antagonist muscle groups plays an important role in voluntary movement in healthy subjects. A deficiency in these mechanisms is likely to contribute to spasticity and has been the focus of some studies [14, 15]. It has been noted that patterned sensory stimulation is more effective in inducing plasticity in this reciprocal 1a sensory inhibition in comparison to monotone stimulation [16]. Therefore to further enhance the effects of multi-electrode stimulation we have employed an intermittent pattern of stimuli which mimics a sensation of

movement (stroking) [17] over the electrode array. We have termed this generic type of stimulation “Sensory Barrage Stimulation” (SBS).

The aim of this pilot trial was to assess the feasibility of using SBS for the treatment of spasticity affecting the elbow flexor muscles and to compare this with conventional TENS stimulation applied between two electrodes.

Methodology

The study was approved by the regional ethics committee. Ten participants with spasticity of the flexor muscles of the elbow were recruited from neurology clinics at the Royal Hallamshire Hospital, Sheffield.

The study was designed as a crossover double-blind randomized trial. Potential participants were provided with an information sheet and contacted two weeks later. If they decided to participate in the study they were invited to attend two study visits, spaced one week apart. At the first visit the participants were screened for inclusion and exclusion criteria and gave their informed consent. The inclusion criteria were: (1) male or female, age ≥ 18 ; (2) spasticity of the flexor muscles of the elbow (of Grade 2 or more on the Modified Ashworth Scale (MAS) [18]); (3) neurologically stable for at least 6 months. The exclusion criteria were (1) a cognitive impairment that would interfere with their ability to comply with the experimental protocol or provide informed consent; (2)

any dermatological, rheumatologic or orthopaedic complications that might interfere with the stimulation of the affected arm; (3) pre-existing severe cardiovascular disease; active cancer or renal disease; end stage pulmonary or cardiovascular disease; psychiatric illness including severe alcohol or drug abuse and depression; (4) severe tactile hypersensitivity as assessed by a non-stimulation approach; and (5) those who had participated in other spasticity-related studies.

The eligible participants were randomised into one of two groups using computer-generated random numbers provided by a colleague who was not involved in the data collection or analyses. Group 1 underwent SBS at their first study visit and TENS one week later. Group 2 underwent the same interventions in the opposite order, TENS first and SBS one week later. Only the experimenter who applied the stimulation, and who was not involved in data collection, knew the allocation sequence and thus knew which group each participant was allocated to and what intervention was delivered. Both interventions were applied for 60 minutes at a stimulus level just below the threshold for motor contraction. The intensity was gradually increased until a visible motor contraction was observed and then decreased to a level when it just ceased. If this level could not be achieved due to discomfort, then the strongest comfortable intensity was used.

SBS was delivered using a modified 64-channel, constant current, programmable electrical stimulator. During the stimulation, the 64-channel stimulator was connected to a laptop and controlled via software produced in-house. The electrodes consisted of an 8x8 array of 8x8 mm square electrodes (with a 3 mm gap between each electrode) on a flexible printed circuit board. The overall dimension of the electrode array was 91x91 mm. An adhesive hydrogel sheet (ST GEL-high impedance grade SCBZAB-05M, Sekisui Plastics, Japan) with a resistivity of 1.3 k Ω *m and a thickness of 0.5 mm was adhered to the surface of the electrode array to act as the interface between the electrodes and the skin [19]. The design of the moving SBS pattern is shown in Figure 1. The electrode array was divided virtually into eight strips (each eight electrodes long). Each individual strip was activated for approximately 0.3 s with a burst of fifteen 250 μ s current pulses at 50 Hz applied simultaneously to all electrodes in the strip. The next strip was then activated while the previous one was deactivated and this cycle was repeated until the last strip had completed its sequence of stimulation pulses. This was followed by a pause of approximately 2.5 s, when no current was delivered. In combination this provided a pattern mimicking stroking from the proximal to the distal part of the arm. The pulse repetition rate of 50 Hz and the on/off periods were chosen because they gave the most convincing subjective sensation of stroking in pilot studies. All

electrodes delivered the same current and this was globally adjusted by the operator according to each individual participant's motor threshold.

TENS intervention was delivered using a commercial stimulator (Multi-TENS, NeuroTrac, VerityMedical Ltd., UK). The parameters of the stimulation were set as a pattern of stimulation with pulse repetition of 100 Hz according to previous studies [6, 9, 16] and 250 μ s pulse width with an "on phase" of 6 s including a 1 s rising edge ramp, a 1 s falling edge ramp, and a 4 s "off phase" in which no current was delivered. To mimic the physical setup of SBS and to blind participants to which system was being applied, the cathode electrode (50x50 mm, VS50, VerityMedical Ltd., UK) was placed centrally underneath the array setup used for SBS stimulation, which was not activated during the TENS stimulation. This single electrode was connected to the TENS stimulator and the participant was not aware that was being applied. The setup visually identical for both interventions.

The arrays (both for SBS and TENS) were placed on the middle of the triceps brachii on the dorsal aspect of the affected arm and strapped with a cohesive bandage to ensure consistent contact between the electrode and the skin (Figure 2). An anode electrode (100x50 mm, VS10050, VerityMedical Ltd.,

UK) was placed proximally on the deltoid muscle of the shoulder on the same arm for both types of stimulation.

The assessment protocol was the same for both the SBS and TENS study visits. Participants were assessed before the stimulation was applied, immediately after the stimulation finished, and a further one hour after the stimulation finished. The clinical assessments described below were performed by the same clinician throughout the study. The clinician was blinded as to the intervention applied. This was achieved by removing the electrodes and equipment before the clinician was invited into the room to perform the assessments. The clinician recorded the assessment data in the participant's study file. The participants were informed that the study was investigating two different techniques for stimulating sensory nerves. The primary outcome measure was the MAS at the elbow, as assessed by the clinician as follows. The participant laid in a supine position with the arm supported, in a neutral position and the forearm in supination. The arm was passively flexed and then extended over a period of one second. This was repeated several times and the resistance to the extension was scored according to the MAS [20]. The secondary outcome measures used were 1. strength of elbow extension (SEE) and flexion (SEF) based on Medical Research Council (MRC) grades [21] and 2. a Visual Analogue Scale (VAS) of the perceived effect on spasticity rated by

the participant on a 13 cm line with the left end being the worst imaginable spasticity and right end being no spasticity. The VAS was subsequently normalised to a percentage where 0% represented the participant experiencing no spasticity and 100% represented the worst spasticity they could envisage. The participants who had a reduction in spasticity of at least one grade on the MAS when combined with a 30% decrease of spasticity relative to the baseline value on the VAS were considered to be responders.

Analyses of the data were performed by a researcher not involved in the data collection. Baseline data were compared with those immediately after and one hour after the interventions using the Wilcoxon Signed Rank test (chosen because of the non-parametric nature of the outcome measures). TENS and SBS were compared using the Mann-Whitney U test at each assessment period. GraphPad Prism version 6.00 for Windows (GraphPad Software, San Diego California USA) was used for the analyses. All analyses were performed using intention to treat.

Results

We approached 17 patients, of whom 10 consented to take part in the study. Four others did not wish to participate: two were not able to participate due to problems with transport and one had an implanted device - an exclusion

criteria for the study . The study flow diagram is shown on Figure 3. Among the 10 recruited participants there were five men and five women. Their age ranged from 18 to 65 years (40 ± 17 years, mean \pm SD). The aetiology of spasticity was: cerebral palsy (4), stroke (3), traumatic brain injury (2) and multiple sclerosis (1). The duration of spasticity symptoms varied from six to 38 years. All tolerated the interventions well and completed the study, giving a 100% retention rate.

Across all participants, the average current during a pulse was in the range of 8 to 16 mA with a mean of 10.9 ± 2.2 mA (mean \pm SD) for TENS (excluding the ramp period) and the average total current from the eight simultaneously activated SBS electrodes was in the range of 7.2 to 15.2 mA with a mean of 12.9 ± 2.5 mA.

Individual clinical outcome measures in each participant for spasticity, MAS and VAS are shown in Figure 4. Immediately after TENS there were 2/10 responders and after SBS 6/10 responders, as defined in the methodology (Table 1). One hour after the interventions, these effects persisted in both of the TENS responders and in four of the SBS responders. However two additional TENS and one additional SBS participants fulfilled the criteria of clinically

significant improvement at this point and were therefore also considered as responders .

The overall comparison of both interventions is summarised in Table 2. Immediately after stimulation the MAS showed a significant reduction for both TENS ($p = 0.016$) and SBS ($p = 0.0039$). There was a reduction of at least one MAS grade in seven TENS participants and nine SBS participants at the end of stimulation (Figure 4). The VAS also reduced significantly for both TENS ($p = 0.027$) and SBS ($p = 0.0059$). At one hour after the stimulation with TENS, there was no significant change in MAS compared to baseline. However, the patients' perception as recorded with VAS continued to show a significant change (Table 2). One hour after SBS a significant reduction in spasticity both on the MAS and VAS was noted. There was no statistically significant difference between the interventions in any of the outcomes (Table 2). However, a trend was noted for a better response with SBS at one hour after the stimulation compared to TENS and this was close to significance ($p = 0.063$). The order of interventions was randomised and no significant difference was found between Group 1 (SBS first) and Group 2 (TENS first) in baseline results for either MAS or VAS, with the exception of participant #7 (Group 1, SBS responder). There were no significant changes in the MRC grades of elbow flexion and extension with TENS and SBS (Table 2). The adverse events reported after SBS were

one case of muscle spasm and one of an ache localised over the triceps muscle. One participant reported experiencing a sensation of pins and needles over his little finger after TENS.

Discussion

Among 17 potentially eligible subjects, 10 participated in this study and all completed the trial protocol. All participants tolerated the interventions well and there were no significant adverse events. This study demonstrated the feasibility and practicality of using SBS; a new type of electrical stimulation.

TENS stimulation below motor threshold, has been reported to have positive effects on spasticity in spinal cord injury [6], in chronic hemiplegia after stroke [5, 22] and in multiple sclerosis [8]. Although optimal TENS stimulation parameters have not been determined, 100Hz seems to be effective [5, 8]. In our study TENS significantly reduced spasticity as measured on MAS immediately after 60 minutes of stimulation. Although the effect seems to have persisted in some of the participants after one hour, this did not achieve significance ($p>0.063$) in this small sample size group ($n=10$).

To try to enhance the effects of conventional TENS we have created the novel concept of Sensory Barrage Stimulation, which allows us to deliver

stimuli at multiple sites and with spatio-temporal patterns which give the sensation that the stimuli are moving over the skin, both of which may aid in producing a greater subjective sensory input. In this study, SBS continued to show a significant response both immediately after and one hour after stimulation (Table 2).

A combination of improvement in both MAS and in the participants' VAS outcome measures was assumed to be a clinically robust way of evaluating the effects of stimulation and this identified seven SBS responders compared to four in the TENS group (Table 1). Although the Wilcoxon Signed Rank test showed significant differences in MAS and VAS immediately after TENS, SBS showed greater differences in mean values and 95% CI (Table 2) compared to baseline with a that persisted for at least one hour after stimulation. These results are not definitive, but are suggestive of our hypothesis that SBS is better than TENS in reducing spasticity.

Extension and flexion strength did not show a significant improvement, although this could possibly be explained by already high grades, indicating a low severity in muscle weakness, with 6 out of 10 participants displaying normal extension strength (MRC grade of 5) throughout the full test procedure with both TENS and SBS.

SBS might also be beneficial in rehabilitation techniques where peripheral electrical nerve stimulation has been proposed as a method to enhance motor or tactile sensation deficits [7, 22] as well as in combination with standard rehabilitation programmes [23, 24]. Support for TENS over Baclofen was also noted previously with similar marginal decrease in MAS [25], although decrease of about 1 unit maybe of only minor clinical significance. This study investigated only the short-term effects of stimulation. However, since the effects of SBS lasted at least an hour after the intervention, this could potentially be an opportunity for occupational therapists and physiotherapists to provide further therapy and assessments of other contractures. Thus this enhanced transient effect could be the major benefit of SBS, specifically for focal spasticity when other treatments could not be used or are not effective... If patients are more likely to benefit from several sessions it may be preferable if they are managed at home, as this would be both more cost-effective and convenient for the patient. We think that this should be practical both for SBS and TENS. Although patients tolerated SBS well and there are no know side effects of this type of therapies, further investigations would be required to assess the tolerability and acceptability of several sessions of stimulation. Future studies on TENS and SBS need to use more patient-reported outcome measures and

functional goals and also investigate its use in spasticity involving multiple muscle groups.

TENS is cost effective treatment option when delivered via commercially available stimulators. Although the initial cost of SBS would be higher than TENS we anticipate that it may be comparable in the long term as the stimulator and the electrode array are reusable (the hydrogel sheet is single patient use).

Study limitations

The limitations of this study are a small sample size and very short follow up period. Further randomised control trials should investigate long term application in order to evaluate any sustained effects on participants' upper limb function. Participants should also be stratified based on different pathology and severity of symptoms, which was not practical with the limited size of this pilot study.

Conclusions

SBS results indicate a reduction in spasticity immediately after stimulation that persists for at least one hour. Further investigation of optimal stimulation parameters followed by larger and longer-term placebo controlled trials are

required before firm conclusions can be made about the clinical value of the technique.

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