Sensory stimulation (TENS): effects of parameter manipulation on mechanical pain thresholds in healthy human subjects

Linda S. Chesterton, Panos Barlas, Nadine E. Foster, Thomas Lundeberg, Christine C. Wright, G. David Baxter

Department of Physiotherapy Studies, Keele University, Staffordshire ST5 5BG, UK
Department of Physiology and Pharmacology, Karolinska Institute, Stockholm, Sweden
School of Health and Social Sciences, Coventry University, Coventry, UK
School of Rehabilitation Sciences, University of Ulster, Jordanstown, Northern Ireland, UK

Received 24 September 2001; received in revised form 27 February 2002; accepted 10 April 2002

Abstract

Transcutaneous electrical nerve stimulation (TENS) is a popular form of electrostimulation. Despite an extensive research base, there remains no consensus regarding the parameter selection required to achieve maximal hypoalgesic effects. The aim of this double blind, sham-controlled study was to investigate the relative hypoalgesic effects of different TENS parameters (frequency, intensity and stimulation site) upon experimentally induced mechanical pain.

Two hundred and forty participants were recruited in order to provide statistical analysis with 80% power at $\alpha = 0.05$. Subjects were randomised to one of the six TENS groups, a control, and a sham TENS group ($n = 30$, 15 males, 15 females, per group). TENS groups differed in their combinations of stimulation; frequency (4 or 110 Hz), intensity (‘to tolerance’ or ‘strong but comfortable’) and stimulation site (segmental – over the distribution of the radial nerve or, extrasegmental – over acupuncture point ‘gall bladder 34’, or a combination of both segmental and extrasegmental). Pulse duration was fixed at 200 ms. Stimulation was delivered for 30 min and subjects were then monitored for a further 30 min.

Mechanical pain threshold (MPT) was measured using a pressure algometer and taken from the first dorsal interosseous muscle of the dominant hand, ipsilateral to the stimulation site. MPT measures were taken, at baseline, and at 10-min intervals for 60 min. Difference scores were analysed using repeated measures and one-way ANOVA and relevant post hoc tests.

Low frequency, high intensity, extrasegmental stimulation produced a rapid onset hypoalgesic effect, which increased during the stimulation period ($P < 0.0005$ control and sham) and was sustained for 30 min post-stimulation ($P < 0.0005_{\text{control}}$, $P = 0.024_{\text{sham}}$).Whilst high frequency, ’strong but comfortable’ intensity, segmental stimulation produced comparable hypoalgesic levels during stimulation, this effect was not sustained post-stimulation. Stimulation at a combination of the two sites did not produce any greater hypoalgesic effects. These results may have implications for the clinical use of sensory stimulation. © 2002 International Association for the Study of Pain. Published by Elsevier Science B.V. All rights reserved.

Keywords: Transcutaneous electrical nerve stimulation; Electrostimulation; Parameters; Mechanical pain; Humans

1. Introduction

Transcutaneous electrical nerve stimulation (TENS) is an established form of electrostimulation, which has been used clinically for the treatment of pain for more than 30 years (Ellis, 1998). Despite this clinical popularity and an extensive research base, there is little consensus regarding the optimal stimulation parameters required to induce maximal hypoalgesic effects (Walsh and Baxter, 1996). This lack of consensus is partly due to the diverse nature of the pathologies for which TENS is prescribed, and also to the wide range of stimulation variables which must be considered within the prescription (e.g. stimulation site, electrode size, pulse pattern, patient preference, etc). Rigorous systematic reviews of the available literature suggest that few of the published reports regarding TENS therapy meet acceptable methodological standards to underpin recommendations for clinical practice (Milne et al., 2001; McQuay and Moore 1998; Carroll et al., 1996, 1997a,b; Flowerdew and Gadsby 1997; Reeve et al., 1996). Specific criticisms include: small sample sizes which lead to low statistical power, a lack of adequate blinding, no control

* Corresponding author. Tel.: +44-1782-584251; fax: +44-1782-584255.
E-mail address: p.barlas@keele.ac.uk (P. Barlas).
group and incompatible methodologies, which prevent satisfactory aggregation and replication of results. Milne et al. (2001) specifically identified the lack of experimental data regarding the hypoalgesic effect of manipulating the application site and treatment duration, alongside the selection of optimal frequencies and intensities.

The lack of agreement within the literature regarding the selection of TENS parameters for therapeutic applications, has resulted in the development of standard parameter combinations for clinical use which are referred to as ‘TENS modes’ (Walsh and Baxter, 1996; Walsh, 1997). These modes include ‘conventional TENS’ (high frequency, low intensity), and ‘Acupuncture-like TENS’ (low frequency, high intensity), often called AL-TENS (Johnson, 1998; Walsh, 1997). The pain modulating effect of conventional TENS is traditionally associated with blocked nociceptive transmission in the spinal cord (Garrison and Foreman, 1996; Melzack and Wall, 1965), and the stimulation site for this mode is therefore around the area of pain or within the same dermatomal segment. This generates large diameter afferent barrage to the central nervous system (CNS) via the spinal cord segment associated with the reported pain (Johnson, 1998). AL-TENS pain modulation is associated with endogenous opiates, released via the descending inhibitory pathways in response to afferent activity in the A delta fibres (Chen et al., 1998; Sjolund and Eriksson, 1976). AL-TENS has also been associated with a counter irritation effect proposed by Le Bars et al. (1979a) with inhibition of neural pathways in the dorsal horn being mediated by the rostral ventral medulla (Basbaum and Fields, 1978). To activate this response, stimulation must be at intensities capable of inducing forceful phasic muscle contractions, usually as high as the patient can tolerate (Bushnell et al., 1991). Johnson (1998) proposed that such contractions can be easily achieved by stimulating motor points or the muscle belly, although trigger points, acupuncture points, distant and contralateral areas are also promoted as effective stimulation points (Johnson, 1998; Walsh, 1997). Whilst the evidence to support the hypoalgesic efficacy of each mode is contradictory, studies of long term TENS users have suggested that satisfactory hypoalgesic effects are more likely to be obtained where patients try out different stimulation characteristics and electrode placements (Johnson et al., 1991a; Eriksson et al., 1979). Indeed, Walsh and Baxter (1996) cited ineffective electrode placement as one of the primary factors for poor patient response, and many authors concede that location of stimulation site is the least investigated parameter of TENS (Chen et al., 1998; Danziger et al., 1998; Walsh, 1996, 1997; Johnson et al., 1991b, 1992; Mannheimer, 1978).

With these concerns in mind, the aim of the current study was to investigate the comparative hypoalgesic effects of common clinical TENS modes, using different frequency and intensity settings, applied at different stimulation sites. Acupuncture points were explicitly selected for electrode placement as this represents common clinical practice (the popularity of which may stem from promotional material distributed by manufacturers with TENS equipment) and there is tentative evidence to suggest that stimulation over such points is more effective than just dermatomal/segmental stimulation (Chen et al., 1998; Takeshige et al., 1992a,b).

2. Method

Ethical approval was obtained from the University’s ethical committee, and a randomised, double blind, controlled experiment, with repeated measures was used. The experimental groups included six active TENS groups, a control and a sham TENS group. The stimulation period lasted 30 min, followed by a monitoring period of 30 min. The outcome variable was the mechanical pain threshold (MPT) measured before stimulation and at six further 10-min intervals.

2.1. Subjects

Two hundred and forty volunteers, TENS-naive subjects (120 females, 120 males) were recruited from the University student and staff population. The sample size was calculated according to Cohen (1992), in order to detect an effect size of $\geq 0.5$ for pairwise mean comparisons between active groups and the control, and so that statistical analysis would be supported by 80% power at $\alpha = 0.05$ (Cohen, 1992). The mean age of the sample was 30 years (SD = 7, range 18–57 years). Subjects were screened for relevant contraindications: neuromuscular or cardiac disorders, peripheral neuropathy, history of trauma or surgery to the dominant hand or leg, current medication and pain, history of epilepsy, diabetes, pregnancy or knowledge of TENS treatment. Six subjects were excluded ($n = 1$ epilepsy, $n = 1$ current medication, $n = 1$ pregnancy, $n = 3$ TENS familiarity) and additional subjects were recruited as replacements. The experimental procedure was explained to each subject who then signed a consent form. Subjects were randomly assigned to one of the eight experimental groups using computer generated random number lists. Groups were similar for gender ($n = 30$, 15 males and 15 females) age, and MPT at baseline. This was confirmed by a one-way analysis of variance (ANOVA) for pre-treatment mean MPT ($P = 0.19$) and Kruskal Wallis test for age ($P = 0.59$) showing no significant differences.

2.2. Equipment

Mechanical pain was induced using a pressure algometer\(^1\) with a flat circular metal probe dressed in several layers of lint and measuring 1.1 cm in diameter. Force was displayed

---

\(^1\) Salter Abbey Weighing Machines Ltd, England.
digital in increments of 0.1 N. The algometer was mounted vertically on a purpose-built calibrated iron stand to enable force to be applied at a controlled and steady rate of 5 N/s. The reliability of results obtained using a pressure algometer have been reported elsewhere (Nussbaum and Downes, 1998; Antonaci et al., 1992; Fischer, 1987).

Electrical stimulation was generated via a dual channel, portable TENS unit which was calibrated using an oscilloscope according to Walsh (1997). An asymmetrical biphasic waveform was delivered through 5 cm² self-adhesive carbon rubber electrodes. Frequency was set at 4 or 110 Hz, pulse duration at 200 μs, and intensity was increased to the subjects’ verbal report of ‘strong but comfortable’ or ‘to tolerance’ levels, depending on group allocation. These choices represent intensities traditionally associated with the conventional and AL-TENS modes previously described.

2.3. Subject preparation

Subjects were seated in a comfortable upright position and the stimulation sites were prepared with alcowipes. These sites were termed segmental and extrasegmental to the location of the MPT measurement point. The segmental site was the lateral border of the forearm of the dominant arm over the distribution of the superficial radial nerve, which innervates the MPT measurement site and corresponds to acupoints large intestine 6 (LI6) and lung 7 (Lu 7). This site has been used in previous studies (McDowell et al., 1999; Walsh et al., 1995, 1998) and was chosen for the following reasons: (a) to reflect clinical stimulation of acupoints, (b) allow stimulation within the same dermatome following reasons: (a) to re

<table>
<thead>
<tr>
<th>Group</th>
<th>Frequency (Hz)</th>
<th>Pulse duration (μs)</th>
<th>Stimulation site</th>
<th>Stimulation site identifier</th>
<th>Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>TENS 1</td>
<td>4</td>
<td>200</td>
<td>Radial nerve + GB34</td>
<td>Combination</td>
<td>To tolerance</td>
</tr>
<tr>
<td>TENS 2</td>
<td>4</td>
<td>200</td>
<td>Radial nerve only</td>
<td>Segmental</td>
<td>To tolerance</td>
</tr>
<tr>
<td>TENS 3</td>
<td>4</td>
<td>200</td>
<td>GB34 only</td>
<td>Extrasegmental</td>
<td>To tolerance</td>
</tr>
<tr>
<td>TENS 4</td>
<td>110</td>
<td>200</td>
<td>GB34 only</td>
<td>Extrasegmental</td>
<td>Strong but comfortable</td>
</tr>
<tr>
<td>TENS 5</td>
<td>110</td>
<td>200</td>
<td>Radial nerve only</td>
<td>Segmental</td>
<td>Strong but comfortable</td>
</tr>
<tr>
<td>TENS 6</td>
<td>110</td>
<td>200</td>
<td>Radial nerve + GB34</td>
<td>Combination</td>
<td>Strong but comfortable</td>
</tr>
<tr>
<td>Control</td>
<td>–</td>
<td>–</td>
<td>Both inactive</td>
<td>None</td>
<td>N/A</td>
</tr>
<tr>
<td>Sham</td>
<td>–</td>
<td>–</td>
<td>Both inactive</td>
<td>None</td>
<td>N/A</td>
</tr>
</tbody>
</table>

channel were then attached to the segmental site, (cathode proximal) and with electrodes from the second channel applied such that the cathode was placed directly over GB34, on the dominant leg, with the anode 1 cm distal. All subjects, regardless of group, had electrodes placed at both stimulation sites to maintain blinding.

2.4. TENS procedure

Table 1 provides a summary of the parameter combinations and the active electrode channels for all eight experimental groups. To maintain blinding of the subjects, the small lights on the TENS unit that indicate the active channel were covered with tape. To maintain blinding conditions, two experimenters took part. Experimenter 1 was solely responsible for all aspects of TENS applications. Before stimulation, subjects in TENS groups 1, 2 and 3 (4 Hz/200 μs/‘to tolerance’ intensity) were told that they would feel strong ‘pricking or tapping sensations’ beneath some or all of the electrodes and might experience muscle contractions around their thumb, fingers, knee or leg. The intensity was increased until it reached the maximum tolerable level for the subject, which was described as very strong and uncomfortable. Subjects in TENS groups 4, 5 and 6 (110 Hz/200 μs/‘strong but comfortable’ intensity) were told that they would feel a buzzing or tingling sensation beneath one or both of the electrodes, and this would be increased until it reached a ‘strong but comfortable’ level. Subjects in the sham TENS group, were told that some forms of TENS were imperceptible and, therefore, they may or may not feel a sensation. The battery in the TENS unit was inserted the wrong way round to allow the unit to be visibly switched on and the intensity turned up, but with no current flowing. Subjects in the control group were informed that, although electrodes were attached to maintain blinding of experimenter 1, the machine would not be switched on and no TENS would take place.

The 10-min stimulation periods were timed from the point when the intensity of the TENS had reached the appropriate level for the experimental group. After the first, third, fourth, sixth and eighth minute of stimulation in each 10-min application, subjects were asked if the sensation had faded, if so, the intensity was increased to maintain the specified level. Stimulation was delivered for a total of

---

3 Salter Abbey Weighing Machines Ltd, England.
4 TPN 300, Physio-Med Services, Glossop, Derbyshire, UK.
5 PALS Electrode TPN 40, Physio-Med Services, Glossop, Derbyshire, UK.
30 min, in three blocks of 10 min. Subjects were monitored for a further 30 min after the end of the stimulation period.

2.5. Mechanical pain threshold measurement procedure

The MPT measurement point was marked 3.5 cm distal from the proximal edge of the anatomical snuffbox in the direction of the muscle belly of the first dorsal interosseous muscle, an area innervated by the superficial radial nerve. A 3.5 cm card measure was used to standardise marking of this measurement.

Experimenter 2 was responsible solely for MPT measurements and was blind to the subject’s experimental group allocation. Subjects were instructed in the application of the algometer and given a demonstration by the experimenter. Subjects then underwent two practice MPT measures using their non-dominant hand, during which they were coached in differentiating their report of tactile and painful stimulus. MPT was taken as the amount of pressure required to elicit a sensation of pain distinct from pressure or discomfort (Fischer, 1987). Subjects were asked to say ‘stop’ immediately when a sensation of pain, distinct from pressure or discomfort, was felt. The algometer was applied perpendicularly to the skin and lowered at a rate of approximately 5 N/s until MPT was reached as indicated by the subjects’ verbal report. At this point the experimenter immediately retracted the algometer. Two measures were taken at 10 min intervals over a 60-min period, giving a total of 14 measures. The first MPT measurement was made before switching on the TENS unit and used as a baseline figure. Experimenter 2 left the room after each MPT measurement was completed. The interruption to TENS stimulation at each measurement point lasted approximately 45–60 s.

3. Data analysis

The lower of the two MPT readings at each measurement point was used for analysis. To standardise the data across subjects, MPT difference scores were calculated (MPTdiff = MPTtime(i) – MPTbaseline). A positive difference score indicates a hypoalgesic effect, and negative scores indicate hyperalgesia. These scores were analysed using a two-way ANOVA with repeated measures on the dependent variable of MPT, and one-way ANOVA with post hoc multiple comparisons, to identify differences between groups at each time point. Statistical significance was set at 0.05. Assumptions underlying the tests were checked and did not change the significant findings. Data were analysed using the Statistical Package for Social Scientists (SPSS, Version 10) for Windows.

4. Results

Table 2 summarises the mean MPT difference scores (± standard error of the mean) at each time point for each experimental group. The two-way ANOVA with repeated measures revealed significant differences across the two main effects of group \((P < 0.0005)\), and time \((P < 0.0005)\), and also for the interaction effect \((P < 0.0005)\). Further one-way ANOVA with post hoc multiple comparisons (Bonferroni adjustment) identified the differences, which occurred between groups at each time point. Table 3 summarises the statistically significant results. It is notable that whilst several groups achieved statistically significant differences with both the control and sham TENS groups during stimulation, only TENS group 3 (4 Hz/200 μs/to tolerance intensity/extrasegmental stimulation) achieved significant differences during the post-stimulation period. TENS group 3 also demonstrated significant differences throughout the post-stimulation period compared with TENS group 4 (110 Hz/200 μs/’strong but comfortable’ intensity/extrasegmental).

Fig. 1 summarises MPT difference scores over time for TENS groups 1, 2 and 3 (4 Hz/200 μs/to tolerance intensity), the sham TENS group and the control group. Within the active TENS groups, a rapid and increasing hypoalgesic effect is observed for TENS group 1 (combination site stimulation), and TENS group 3 (extrasegmental stimulation). The maximal mean MPT difference scores were 12.75 N \((P < 0.0005_{\text{control}}, \ P = 0.001_{\text{sham}})\) and 13.72 N \((P < 0.0005_{\text{control}}, \ P < 0.0005_{\text{sham}})\), respectively. During the post-stimulation period, an initial, yet slight, fall in hypoalgesic effect is observed in TENS group 3 (from

---

Table 2

Mean MPT difference scores (standard error of mean) for each group at each time point \((n = 30)\) (all scores are expressed in Newtons)

<table>
<thead>
<tr>
<th>Group</th>
<th>Stimulation</th>
<th>Post-stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10 min</td>
<td>20 min</td>
</tr>
<tr>
<td>TENS 1</td>
<td>5.62 (1.04)</td>
<td>10.20 (1.36)</td>
</tr>
<tr>
<td>TENS 2</td>
<td>2.84 (1.77)</td>
<td>5.14 (1.77)</td>
</tr>
<tr>
<td>TENS 3</td>
<td>8.20 (1.62)</td>
<td>10.71 (1.92)</td>
</tr>
<tr>
<td>TENS 4</td>
<td>3.26 (1.14)</td>
<td>5.41 (1.45)</td>
</tr>
<tr>
<td>TENS 5</td>
<td>5.89 (1.73)</td>
<td>11.50 (1.90)</td>
</tr>
<tr>
<td>TENS 6</td>
<td>6.79 (1.33)</td>
<td>9.60 (1.98)</td>
</tr>
<tr>
<td>Control</td>
<td>−0.40 (1.04)</td>
<td>−0.047 (1.37)</td>
</tr>
<tr>
<td>Sham TENS</td>
<td>3.72 (1.28)</td>
<td>4.02 (1.84)</td>
</tr>
</tbody>
</table>
13.75 N to 12.08 N). For the remainder of the period, a relatively constant and high level of hypoalgesia is maintained (minimum 11.29 N, \( P < 0.0005 \) control, \( P = 0.024 \) sham, \( P = 0.005 \) TENS 4). Conversely, for TENS group 1 (combination site stimulation), when stimulation ceased a rapid and sharp fall in MPT was seen in the first 10-min period (to 7.09 N \( P = 0.19 \) control), which continues to fall, although a level of hypoalgesia above the baseline (6.17 N) was still evident at the 60-min measurement point. Changes in TENS group 2 (segmental stimulation) and the sham TENS group were small and did not achieve statistically significant differences with respect to the control group. Within the control group MPT changed little over the course of the experiment (maximum MPT = 2.02 N) demonstrating the stable, yet sensitive to experimental manipulation, nature of this experimental measure.

Fig. 2 summarises MPT difference scores over time for TENS groups 4, 5 and 6 (110 Hz/200 μs/’strong but comfortable intensity’), the sham TENS group and control groups. A large and rapid hypoalgesic effect for TENS group 5 (segmental stimulation), and TENS group 6 (combination site stimulation) were observed. The maximal mean MPT difference scores measured were 13.27 N (\( P < 0.0005 \) control, \( P < 0.001 \) sham) and 10.2 N (\( P = 0.005 \) control, \( P = 0.042 \) sham), respectively. However, during the post-stimulation monitoring period, a large fall in hypoalgesic effect is observed at the 40-min measurement point for both these groups (TENS 5 MPT = 6.66 N and TENS 6 MPT = 8.11 N) with no significant differences observed between these groups and the sham or control groups. TENS group 4 (extrasegmental stimulation) showed a small rise in MPT (5.41 N maximal) during stimulation which is similar to that of the sham TENS group (4.02 N maximal); TENS group 4 did not show significant differences to the control group.

For comparison, Fig. 3 shows the profiles of each TENS group that achieved statistically significant differences with respect to the control group. Of note is the similar pattern of changes during the stimulation period and the comparable maximal levels of hypoalgesia achieved regardless of different parameter selection (range 10.2–13.73 N). There were no significant differences between active TENS groups shown in this figure (Fig. 3). The important difference between the groups was seen in the post-stimulation period where only TENS group 3 (4 Hz/200 μs/to tolerance intensity/extrasegmental) showed a sustained hypoalgesic effect (\( P < 0.0005 \) control).

5. Discussion

The purpose of this study was to determine the effect of different combinations of TENS frequency, intensity and stimulation site on the MPT in healthy subjects. The results illustrate the hypoalgesic potential of several different TENS parameter combinations and emphasise the impor-

<table>
<thead>
<tr>
<th>Phase</th>
<th>Time (min)</th>
<th>Group</th>
<th>Comparison group</th>
<th>Mean difference between groups</th>
<th>Standard error</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulation</td>
<td>10</td>
<td>Control</td>
<td>TENS 3</td>
<td>-8.60</td>
<td>2.02</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 6</td>
<td>-7.19</td>
<td>2.02</td>
<td>0.013</td>
</tr>
<tr>
<td>Stimulation</td>
<td>20</td>
<td>Control</td>
<td>TENS 1</td>
<td>-10.67</td>
<td>2.42</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 3</td>
<td>-11.18</td>
<td>2.42</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 5</td>
<td>-11.97</td>
<td>2.42</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 6</td>
<td>-10.07</td>
<td>2.42</td>
<td>0.001</td>
</tr>
<tr>
<td>Stimulation</td>
<td>30</td>
<td>Control</td>
<td>TENS 1</td>
<td>-13.08</td>
<td>2.74</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 3</td>
<td>-14.05</td>
<td>2.74</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 5</td>
<td>-13.59</td>
<td>2.74</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 6</td>
<td>-10.52</td>
<td>2.74</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>Sham</td>
<td>TENS 1</td>
<td>-11.37</td>
<td>2.74</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 3</td>
<td>12.34</td>
<td>2.74</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 5</td>
<td>11.89</td>
<td>2.74</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 6</td>
<td>-8.82</td>
<td>2.74</td>
<td>0.042</td>
</tr>
<tr>
<td>Post-stimulation</td>
<td>40</td>
<td>Control</td>
<td>TENS 3</td>
<td>-11.95</td>
<td>2.55</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sham</td>
<td>-10.08</td>
<td>2.55</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 4</td>
<td>-9.96</td>
<td>2.55</td>
<td>0.004</td>
</tr>
<tr>
<td>Post-stimulation</td>
<td>50</td>
<td>Control</td>
<td>TENS 3</td>
<td>-11.92</td>
<td>2.50</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sham</td>
<td>-8.46</td>
<td>2.50</td>
<td>0.024</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 4</td>
<td>-9.58</td>
<td>2.50</td>
<td>0.005</td>
</tr>
<tr>
<td>Post-stimulation</td>
<td>60</td>
<td>Control</td>
<td>TENS 3</td>
<td>-9.36</td>
<td>2.87</td>
<td>0.036</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TENS 4</td>
<td>-9.61</td>
<td>2.87</td>
<td>0.027</td>
</tr>
</tbody>
</table>
Fig. 1. MPT difference scores for 4 Hz/200 ms/noxious intensity intervention groups, sham and control (n = 30 per group). (⊙, significantly different from control group P < 0.05, ◦, significantly different from sham TENS P < 0.05) See text for details.

Fig. 2. MPT difference scores for 110 Hz/200 μs/strong but comfortable intensity intervention groups, sham and control (n = 30 per group) (⊙ Significantly different from control group P < 0.05) – See text for details.
tance of stimulation site in the hypoalgesic effect obtained. Available literature provides directly comparable, albeit limited, experimental evidence with which to evaluate these results; however, a series of studies using large clinical samples from University of Texas provides some comparative data.

Studies by Wang et al. (1997), Chen et al. (1998) and Hamza et al. (1999) have all used a clinical model of acute post-operative pain to investigate the effects of manipulating stimulation intensity, site and frequency. Each study used a similar protocol with 100 women who had undergone lower abdominal surgery. The common design was of a randomised single blind, sham controlled study with experimental groups of 25 subjects. Thirty minutes of stimulation at two-hour intervals (when patients are awake) was applied. Stimulation was used in conjunction with other standardised pharmacological analgesic interventions. The initial study by Wang et al. (1997), reported results for a control group to establish a baseline effect for analgesics alone with no stimulation intervention. In each study, transcutaneous acupoint electrical stimulation (TAES) ‘dense-disperse’ stimulation (an alternating frequency between 2 and 100 Hz every 3 seconds) was used, a combination developed by the reporting authors. The sample size for the initial study was calculated at a power of 80% to identify a 30% reduction in the post-operative opioid analgesic requirements as the dependent variable. This variable is used for discussion here although other dependent variables are reported.

The first study by Wang et al. (1997) investigated the effect of varying intensity whilst stimulating the Hegu acupoint (first interosseous web space – LI4) and the abdominal incision site simultaneously. The results showed that the efficacy of stimulation was dependent upon intensity. This was indicated by a >50% decrease \(P < 0.05\) in the total post-operative analgesic requirement when a stimulation level of 9–12 mA was used as opposed to 4–5 mA. Whilst the effect of the mixed-frequency (2–100 Hz) stimulation does not allow a direct comparison with our results, we also showed that stimulation at a combination of two sites was intensity-dependent, but for very different reasons. High frequency, low intensity stimulation was shown to be just as effective as low frequency, high intensity stimulation. However, in addition we found that there was no additional hypoalgesic benefit from stimulating at two sites over and above the level of hypoalgesia observed at single site stimulation. Indeed the low frequency, high intensity, combined stimulation group showed that the post-stimulation effects of extrasegmental stimulation alone were negated. Nevertheless, some consensus regarding mixed frequencies requiring high intensity stimulation is supplied by Johnson et al. (1992). In a double blind, sham-controlled study, using
an experimental cold pain model, 60 healthy subjects were randomised to five experimental groups. Prolonged post-stimulation hypoalgesia compared with a sham group was only reported when ‘burst’ TENS (frequency of 2.3 Hz with bursts at 80 Hz) was applied for 30 min at a distant, but myotomally-related area stimulating at the highest tolerable intensity. This combination of parameters showed greater hypoalgesic effects than ‘burst’ TENS applied at the same site but at lower intensity levels and also conventional TENS applied segmentally. The authors, however, noted considerable individual variation in this response, which was also previously reported in a study from the same group (Ashton et al., 1984) and in the results presented here. Johnson et al. (1992) did not investigate these reported effects using combined stimulation sites.

The effect of manipulating stimulation site is reported by Chen et al. (1998). Using the clinical model noted above, 100 female subjects were randomly assigned to one of four treatment regimes, including: (1) TENS applied at the level of the surgical incision; (2) bilateral acupoint – TAES at the Zusanli (ST36) acupoints; (3) non-acupoint – TAES at the shoulder, and (4) sham – TAES at acupoint ST36. Mixed-frequency (2/100 Hz) stimulation with intensity between 9 and 12 mA was applied. The total opioid requirements measured in the first 24 h post-surgery in both the dermatomal and acupoint stimulation groups were decreased by between 35 and 39% when compared with the sham group and non-acupoint stimulation groups. Using this and other measured indicators, the authors concluded that dermatomal and acupoint stimulation were equally effective and both of these positions were more effective than the non-acupoint (shoulder) location. The results of our study agree with this to some extent, in so much as the segmental and extrasegmental sites were shown to be equally effective in achieving hypoalgesic effects, but this was dependent upon different combinations frequency and intensity parameters. Results from our study also contrast with Chen et al. (1998) in that segmental stimulation using low frequency/high intensity parameters was shown to be ineffective. Once again, however, the mixed frequency used by Chen et al. (1998) restricts the ability to interpret the role of frequency in the measured outcome. A tentative conclusion that can be reached from the study by Chen et al. (1998) and the current study is that stimulation site is an important determinant to achieve maximal hypoalgesic effects.

Based on the previous results from the same group, Hamza et al. (1999) investigated the effects of stimulation frequency at a segmental site alone. In this case patients were randomly assigned to four groups as follows: low-frequency (2 Hz) TENS; high frequency (100 Hz) TENS; mixed-frequency (2–100 Hz) TENS and sham TENS. Stimulation was given around the surgical incision site at a high intensity of 9–15 mA. The pulse width was reported to alter automatically within a range of 0.2–0.6 ms. The results showed that mixed frequency stimulation reduced opioid requirements by 53% compared with the sham group, with both low (2 Hz) and high (100 Hz) frequencies producing decreases of smaller magnitude (32 and 35%, respectively). Results from our study also showed low frequency (4 Hz) high intensity stimulation to be less effective when applied segmentally, at least when compared with other parameter combinations. Clinically, high frequency, high intensity combinations are rarely used due to patient discomfort, but it is of interest that the mixed frequency, high intensity combination proved most effective. In this instance, however, no comparative low intensity stimulation groups were used and stimulation was only at a segmental non-acupoint site. In making comparisons with these studies, it is important to consider that physiological responses to electrical stimulation in clinical situations of acute pain may not be directly comparable to an experimental model of pain in healthy subjects, and all conclusions must be viewed in this light.

With regard to the results from this study, some physiological support can be suggested. The hypoalgesic effect of high frequency, low intensity segmental parameter combinations, which are not repeated extrasegmentally, is in agreement with the pain modulation effects proposed within the pain gate theory (Melzack and Wall, 1965). Similarly, the prolonged hypoalgesic effects of extrasegmental, low frequency stimulation suggest some form of systemic response in line with the endogenous opioid response. However, the rapid hypoalgesic onset would appear to be inconsistent with the effect of this slow responding system, as suggested by Sjolund and Eriksson (1976). It could be argued that this mechanism may be responsible for the post-stimulation hypoalgesia (Chen and Han, 1992). Alternative mechanisms may also be involved at many levels within the CNS. Whilst it is not clear which systems are involved, or how they are co-ordinated within the individual, possibilities include the ‘diffuse noxious inhibitory control’ system proposed by Le Bars et al. (1979a,b) and the inhibition of the spinthalamic tract cells at a spinal cord level as a response to activation of the Aβ and Aδ fibres, a theory proposed by Chung et al. (1984). Excitation of a sympathetic response may also alter the afferent input to the CNS (Ito et al., 1984) with the autonomic response extending widely to viscera, joints and skin (Shacklock, 1999). Wright and Sluka (2001) have also suggested that motor facilitation and sympathetic excitation are consistent with activation of the lateral periaqueductal grey matter, which may evoke analgesia as part of a defence response (Willis and Westlund, 1997). The initial hypoalgesia, which is not sustained post-stimulation in the low frequency/low intensity, combined site stimulation group (TENS group 1), may suggest a peripheral blocking effect which overrides this systemic response. Although the contribution of altered peripheral nerve activity to the hypoalgesic effect proposed by Ignezli and Nyquist (1976) has been questioned by Janko and Trontelj (1980), other authors strongly suggest a peripheral component to TENS mediated hypoalgesia, which may be regulated by central mechanisms (Walsh et al., 1998;
Levin and Hui-Chan, 1993; Francini et al., 1981). Further studies, which measure such physiological responses, are required to identify the mechanisms involved. Future research is also required to investigate the effects of combining different frequency and intensity parameters.

In summary, the data presented here have confirmed that parameter combinations including stimulation site may play an important role in the maximal hypoalgesic effect attained and in post-stimulation hypoalgesia, within an experimental model of pain. It is therefore possible that popular TENS modes used clinically may not always produce optimal hypoalgesic effects. Further research into stimulation site and intensity levels is therefore required.

Acknowledgements

The authors thank Professor J. Sim for his valuable comments to the final version of the manuscript. Funding for the experiment and equipment was provided by Coventry University School of Health and Social Sciences.

References


Chen X-H, Han JS. All three types of opioid receptors in the spinal cord are important for 2.5 Hz electroacupuncture analgesia. Eur J Pharmacol 1992;211:203–210.


