Does the pulse frequency of transcutaneous electrical nerve stimulation (TENS) influence hypoalgesia?
A systematic review of studies using experimental pain and healthy human participants

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Abstract

Objectives To determine the hypoalgesic effect of pulse frequency of transcutaneous electrical nerve stimulation (TENS) when all other TENS parameters are held constant.

Data sources Systematic review of studies using experimentally induced pain on healthy participants where there was a head-to-head comparison of different pulse frequencies. AMED, CINAHL, EMBASE, Inspec, PEDro, Pre-CINAHL, PsycARTICLES, PubMed, SPORTDiscus were searched in September 2006.

Review methods Inclusion criteria were studies that directly compared two or more pulse frequencies head-to-head and recorded outcome as change in pain threshold or pain intensity. Studies were excluded if pulse intensity, pulse pattern, or pulse duration of TENS were not standardized between groups. Two reviewers judged the trial outcome independently. Primary outcome was a report of a statistically significant difference between pulse frequencies for pain threshold or intensity at any time point through the experiment.

Results Twenty studies were identified, of which 13 experimental studies from 12 published reports were included for review. Ten studies found no statistically significant differences in hypoalgesia between pulse frequencies. Of the three studies judged as positive outcome, one reported that 100 pulses per second (pps) was superior to 10 pps; one that 4 pps was superior to 100 pps; and one that 5 pps and 80 pps were superior to 2 pps.

Conclusion Evidence from experimental pain studies suggests that TENS pulse frequency does not influence hypoalgesia when its pulse intensity, pulse pattern, and pulse duration are kept constant. Inadequate sample sizes may have generated false negative findings in some studies.

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Keywords: Transcutaneous electrical nerve stimulation (TENS); Analgesia; Experimental pain; Healthy subjects; Systematic review

Introduction

Transcutaneous electrical nerve stimulation (TENS) is commonly used for the treatment of pain [1–4]. It has long been believed that the electrical characteristics of TENS influence the magnitude of pain relief and as a consequence TENS manufacturers have manipulated the technical specifications of devices in an attempt to improve efficacy [1]. Nowadays TENS devices allow the user to alter pulse amplitude (mA), pulse duration (μs), pulse pattern (continuous, burst, modulation) and pulse frequency ( pulses per second, pps) in order to selectively recruit different populations of nerve fibres. Opinion leaders claim that pulse frequency is a key determinant of TENS outcome [1,3–7]. However, long term users of TENS often select pulse frequency ad hoc and for reasons of comfort [8,9]. The findings of studies using healthy humans exposed to experimental pain, which manipulated TENS parameters under laboratory controlled conditions, are often used to support claims that pulse frequency may be a key determinant of hypoalgesic effect [1,4]. To date there has been
no attempt to assess the published literature in a systematic fashion by comparing pulse frequencies head-to-head when all other parameters are held constant.

TENS interventions tend to be described according to the technical characteristics of TENS as ‘high frequency, low intensity’ (conventional TENS) or ‘low frequency, high intensity’ (acupuncture-like TENS). This has resulted in unclear reporting of TENS interventions because it fails to specify the physiological intention of TENS. In this regard, the physiological intention of conventional TENS is to selectively activate non-noxious skin afferents (Aβ fibres) without simultaneously activating noxious skin afferents (Aδ- and C-fibres) as this leads to segmental anti-nociception [4,10]. Theoretically, high frequency (~10–250 pps), low intensity (non-painful) currents would be most efficient in selectively activating Aβ fibres [3,11]. In practice, Aβ afferent activity is achieved by the user reporting ‘strong but comfortable’ non-painful electrical paraesthesia beneath the electrodes. The physiological intention of acupuncture-like TENS is to activate small diameter non-noxious muscle afferents through the generation of a muscle twitch as this elicits extrasegmental anti-nociceptive mechanisms via descending pain inhibitory pathways [6,12]. This is achieved by delivering TENS at low frequencies at high but non-painful intensities over muscles. Pulsed electrical currents given at low frequency were found to be uncomfortable in producing muscle twitches so low frequency trains of pulsed currents, termed ‘burst mode TENS’, were used instead [3,6,12–14].

It is often written in textbooks [1,5,15,16], chapters [3,4,6,7] and user guides accompanying TENS devices [17–19] that certain pulse frequencies are superior to others for treating particular conditions. Laboratory studies on healthy humans exposed to an external stimulus to create the experience of pain (i.e. experimental pain) are often used to support these claims. Experimental pain studies are used to assess analgesic efficacy because they are relatively safe and they enable investigators to control pain experience and adherence to the treatment intervention. There is no doubt that experimental pain does not reflect biopsychosocial factors that influence pain experience in the clinical setting but it does contribute to knowledge about treatment response for transient pain, which aids understanding of the early processing of clinical pain. Hence, studies on healthy human subjects are often used as a precursor to clinical trials [20,21].

Closer examination of this supporting evidence reveals that inferences about the relative effects of pulse frequency are based on active group comparisons with sham/control group or when more than one TENS parameter has been manipulated simultaneously. However, investigations which compare the hypoalgesic effects of pulse frequencies head-to-head are necessary to determine the differential effects of pulse frequency of TENS. The purpose of this systematic review of studies using experimentally induced pain in healthy human subjects was to determine the hypoalgesic effects of TENS pulse frequency when other TENS parameters are kept constant.

Methods

Search strategy


Inclusion criteria

To be included in this review studies must have:

- Been published as a full experimental report.
- Used experimental pain on healthy human participants.
- Directly compared at least two or more pulse frequencies head-to-head using a continuous pattern of pulse delivery. For experimental reports which did not explicitly state which pulse pattern was used reviewers included studies if they were confident that TENS was not delivered using other pulse patterns (i.e. did not use burst or modulated pulse patterns).
- Recorded pain outcome as change in pain threshold or pain intensity. These are commonly used outcomes to quantify hypoalgesia in such studies. Hypoalgesia is defined as diminished pain in response to a normally painful stimulus including raised threshold [22].
- Delivered TENS using a ‘standard TENS device’ which we have defined as biphasic pulsed current delivered in a repetitive manner with pulse durations between 10 μs and 1000 μs and pulse frequencies between 1 pps and 250 pps [14].
- Intensities that were above sensory perception threshold and described using terms such as ‘strong’ and/or ‘comfortable’ and/or ‘tolerable’ [23].

Studies and/or comparisons were excluded if:

- The effect of pulse frequency could not be isolated because other TENS settings were not standardised.
- TENS intensities were described as ‘barely perceptible’.
- Hypoalgesia using a verbal report of pain was not an outcome measure (e.g. nerve conduction or withdrawal reflex).
- Pulse patterns other than ‘continuous’ (‘normal’) were used.
Data extraction and analysis

Two reviewers (CC and MJ) extracted information and judged trial outcome independently. Outcome was dichotomised as either positive, where one frequency was statistically different to another, or negative, where one frequency was not statistically different to another. A statistically significant reduction in pain at any time point through the experiment was taken as a difference between the groups. Disagreements in judgements were logged and a final decision was made following a discussion between the reviewers in the presence of a third investigator (GT), who had not taken part in the original data extraction and trial judgement process.

Results

Over 2100 articles were identified in the initial search of the electronic databases, although the majority were found to be not relevant during screening of study title and abstract. Twenty full published reports were potentially relevant and retrieved (Fig. 1). Two of these studies were excluded because hypoalgesia was not an outcome measure [24,25]. Six studies were excluded because pulse intensity, pulse duration or stimulation site were not standardised between groups, making direct head-to-head comparisons and subsequent isolation of pulse frequency effects impossible [26–31].

Twelve studies met the inclusion criteria for review (Table 1). The report by Walsh et al. [32] examined pulse frequency on mechanical pain threshold, which was included in the analysis, and also peripheral nerve conduction, which was excluded from the analysis. The reports by Walsh et al. [33] and Cramp et al. [34] examined the effect of pulse frequency on electrical pain using visual analogue scales, which was included in our analysis, and the RIII and H-reflex, which was excluded in our analysis. The report by Foster et al. [35] contained two separate experimental studies and both were included in our analysis. The intervention group receiving
<table>
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<td>CO₂ laser</td>
<td>10</td>
<td>200</td>
<td>SBC</td>
<td>Within site of pain</td>
<td>2 TENS groups</td>
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<td>100 pps &gt; 10 pps in SPR</td>
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<td>125</td>
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<td>SBC</td>
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Table 1 (Continued)

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<th>Reference</th>
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<th>TENS pulse frequency (pps)</th>
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<th>TENS subjective intensity</th>
<th>TENS paraesthesia</th>
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<th>Authors’ conclusion</th>
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<td>50</td>
<td>SBC</td>
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<td>4 TENS groups, placebo, control</td>
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<td>TENS groups &gt; control</td>
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<td>Sphygmomanometer cuff</td>
<td>4</td>
<td>50</td>
<td>SBC</td>
<td>Proximal to site of pain</td>
<td>4 TENS groups, placebo, control</td>
<td>VAS, MPQ</td>
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<td>287</td>
<td>SBC</td>
<td>Proximal to site of pain</td>
<td>2 TENS groups, placebo, control</td>
<td>VAS, MPQ</td>
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<td>4 pps &gt; 110 pps</td>
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<td>Craig et al. [44]</td>
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<td>200</td>
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<td>Within site of pain</td>
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Note: Many studies included control and treatment groups which were excluded from our head-to-head analysis of TENS pulse frequency. Hence, stated study sample size will be larger than the aggregate of groups extracted for analysis (represented by n per group).

Abbreviations: CAP, compound action potentials; DAC, distinct and comfortable; DOMS, delayed onset muscle soreness; EPQ, Eysenck personality questionnaire; IFT, interferential therapy; LEPs, CO2 laser evoked potentials; MPQ, McGill pain questionnaire; MPT, mechanical pain threshold; N/A, not available; ROM, range of motion; SBC, strong but comfortable; SPR, subjective perception (pain) rating; TENS, transcutaneous electrical nerve stimulation; TT, tactile threshold; VAS, visual analogue scale.

a 2000 Hz was excluded because it was delivered using sinusoidal currents rather than biphasic pulsed currents as used in the other groups.

b The authors did not make a direct statistical comparison of 8 pps with 100 pps.
2000 Hz as sinusoidal currents in the study by Chakour et al. [36] was excluded from our analysis because it did not meet our eligibility criteria. Thus, there were 12 reports of 13 experimental studies with usable information by outcome.

Several approaches were used to induce experimental pain, including heat (n = 2), electrical (n = 3, not including Walsh et al. [32]), cold (n = 3), mechanical (n = 2), ischaemia (n = 2) and delayed onset muscle soreness (n = 1) methods. A total of 631 participants recruited in the included studies. Study reports often stated that subjects were randomised into intervention groups although it is more likely that block randomisation had been used because groups often contained equal numbers of subjects. Similarly, study reports often claimed that a double blind approach was used although details about the assessor, participant and person administering TENS were limited. Furthermore, true blinding would be impossible as participants would experience differences in the sensations generated by different frequencies of TENS.

**Studies demonstrating effects for pulse frequency**

Only three studies reported a significant difference in the magnitude of hypoalgesia between pulse frequencies. de Tommaso et al. [37] reported that 100 pps was superior to 10 pps in reducing painful heat administered to 16 participants (n = 8 per group) using a CO2 laser stimulus (10.6 μm wavelength, 2.5 mm beam diameter, 45 ms). TENS was delivered on the ventral surface of the right forearm using electrodes applied to either side of the stimulus at a ‘strong but comfortable’ intensity and a pulse duration of 200 μs. Subjective perception/pain rating and peak-to-peak amplitude of laser evoked potentials were taken before, immediately after and almost 50 minutes after 15 minutes of TENS. A pulse frequency of 100 pps produced a significantly larger decrease in pain rating when compared to 10 pps, although it was not possible to ascertain the magnitude of this difference from the study report.

Chakour et al. [36] using 10 participants per group reported that 5 pps and 80 pps given as biphasic square waves were superior to 2 pps in reducing painful heat administered using a CO2 laser stimulus (10.6 μm wavelength, 1–100 W power, 5 mm beam diameter, 50 ms). This effect was observed when TENS was high enough to produce distinct noxious pricking (maximal intensity), but was not observed when TENS was given at a ‘strong but comfortable non-painful paraesthesia’ (sub-maximal intensity). Pain threshold was taken during a 5-minute TENS intervention period and the results indicated that similar changes were observed for all frequencies except for 2 pps, which was less effective than other frequencies when given at the maximal intensity (i.e. a mean change of 1 W from baseline compared to a change of between 8 W and 12 W in the other groups). We judged this study as being positive outcome based on the finding that 5 pps and 80 pps reduced the threshold to experimental thermal pain when compared to 2 pps when TENS was given at a ‘maximal’ intensity. It is very possible that this finding was
due to an erroneous result for the 2 pps group, and the authors themselves concluded that there were no frequency effects.

The study by Chakour et al. [36] would have been judged as negative outcome if we had used the results obtained when TENS was given at a ‘strong but comfortable’ intensity because there were no differences between pulse frequencies. This differs from de Tommaso et al. [37], who found significantly larger reductions in pain for 100 pps compared to 10 pps. This discrepancy may be due in part to the use of different outcome measures in the studies, with de Tommaso et al. [37] using a 10-point verbal category scale to measure pain intensity and Chakour et al. [36] measuring pain threshold in watts. In their study report Chakour et al. [36] concluded that frequency effects were negligible between the groups.

Walsh et al. [38] reported that 4 pps was superior to 100 pps for reducing ischaemic pain induced by the submaximal effort tourniquet test in 32 female healthy participants who were randomly assigned into one of four groups (n = 8 per group): 110 pps TENS, 4 pps TENS, placebo TENS and no treatment control. TENS was delivered at a ‘strong but comfortable’ intensity via two electrodes placed over the ipsilateral Erb’s point and lateral to C6 and C7 vertebral spines. Ischaemic pain was induced over a 12 minute period and pain intensity measured using visual analogue scales and the McGill Pain Questionnaire respectively. There were significant differences in visual analogue scale but not McGill Pain Questionnaire scores between groups, with the 4 pps TENS group showing a larger hypoalgesic effect than the 100 pps group.

**Studies demonstrating no effects for pulse frequency**

Ten of the 13 experimental studies reported no differences in hypoalgesia between pulse frequencies when all other TENS characteristics were held constant. The findings of Walsh et al. [38] that 4 pps was superior to 100 pps, when pulse duration is 287 μs, for reducing ischaemic pain were not replicated by a follow-up study by the same investigators. Foster et al. [35] reported no differences in visual analogue scales and McGill Pain Questionnaires between 110 pps and 4 pps when pulse durations were 50 and 200 μs. It is noteworthy that Walsh et al. [38] used a pulse duration of 287 μs and Foster et al. [35] used 50 μs and 200 μs, although such differences seem small (especially between 287 μs and 200 μs) and unlikely to have contributed to the discrepancies in study outcome.

Ashton et al. [39], Johnson et al. [40] and Foster et al. [35] used the cold-pressor pain technique to assess the effects of TENS in healthy young participants. Cold-pressor stimulation has been successfully used as a model of experimental pain to investigate analgesic interventions [41]. Ashton et al. [39] found no significant differences between 100 pps and 8 pps on pain threshold or pain tolerance in the hand (n = 10–13 per group) when TENS was administered at a ‘strong but comfortable’ intensity (200 μs pulse duration) via electrodes (8 cm² each) on the ventral surface of the forearm
for 20 minutes. Johnson et al. [40] working with the same
group found no difference in pain threshold or pain tolerance
between 10 pps, 20 pps, 40 pps, 80 pps and 160 pps (n = 12 per
study) when TENS was delivered at a ‘strong but comfortable'
intensity (200 μs pulse duration) to the ventral surface of
the forearm. Most pulse frequencies produced a significant
increase in pain threshold when compared to sham
TENS. Foster et al. [35] reported no significant differences
in cold-induced pain threshold in the hand between 110 pps
and 4 pps (n = 8 per group) when TENS was given at a ‘strong
but comfortable’ intensity (200 μs biphasic pulse) applied to
the ventral surface of the forearm.

Studies using noxious electrical stimulation on healthy
humans failed to demonstrate effects between pulse frequen-
cies. Barr et al. [42] assessed 30 pps, 60 pps or 85 pps given
as either a monophasic or biphasic wave at a ‘distinct and
comfortable’ intensity (n = 28 per group). Noxious electrical
stimulation was induced on the distal phalanx and palm on
the dominant hand just before and after a treatment and each
TENS intervention was delivered on the ventral surface of
the forearm for 4 minutes. No significant differences were found
between different pulse frequencies on pain threshold or pain
tolerance, although pain tolerance increased significantly for
60 pps and decreased significantly for 30 pps and 85 pps when
compared to pre-treatment, but there was no direct compari-
son made between the TENS pulse frequency groups. Using
noxious electrical stimulation lateral to the malleolus over
the course of the sural nerve, Cramp et al. [34] (n = 10 per
group) found no significant difference in the rating of pain
intensity to an electrical stimulus used to elicit an RIH reflex
before, during and 30 minutes following TENS and interfer-
ental therapy given at 5 pps, 100 pps and 300 pps. Walsh et al.
[33] (n = 10 per group) using similar methodology also found
no significant difference between TENS given at a ‘strong but
comfortable’ intensity and 110 pps or 4 pps and either 200 μs
or 50 μs.

Both Walsh et al. [32] (n = 8 per group) and Walsh et al.
[43] (n = 10 per group) reported no difference in the
mechanical pain between 4 pps and 110 pps given at a ‘strong
but comfortable’ intensity using 50 μs or 200 μs pulses. All
active TENS groups produced significant effects compared
to control and placebo groups. Craig et al. [44] (n = 12 per
group) reported no frequency effect for pain intensity rating,
mechanical pain threshold or dimensions measured using the
McGill Pain Questionnaire for induced delayed onset mus-
cle soreness on the elbow flexors. TENS was applied at a
‘strong but comfortable’ intensity (200 μs pulse duration) for
20 minutes on the musculo-tendinous junction of the biceps
brachii at 110 pps and 4 pps.

Discussion

It is often written that TENS outcome is a function of
the site of stimulation and the electrical characteristics
of TENS, including pulse amplitude, duration and frequency.
These claims are based on primary research that fails to iso-
late the effect of individual variables. Often primary research
undertakes comparisons between ‘high intensity, low fre-
cuency’ TENS with ‘low intensity, high frequency’ TENS
and observed outcomes could be due to any combination of
high or low intensity with high or low frequency. Neverthe-
less, study investigators often infer that pulse frequency is a
determinant of outcome. The purpose of our review was
to evaluate, for the first time, primary research that isolated
the effect of pulse frequency while other parameters were
kept constant. We felt it important to try to ascertain the direct
influence of pulse frequency when TENS is administered in
its conventional form, i.e. generating a non-noxious electri-
cal paraesthesia within or immediately proximal to the site
of pain. We only included studies that explicitly standardised
the intensity of stimulation at a level rated by participants
as ‘strong but comfortable’ or ‘non-noxious electrical para-
esthesia’ (i.e. the way that TENS is conventionally given in
clinical practice). The alternative approach of standardising
output according to pulse amplitude (i.e. mA) is fraught with
difficulties because of inter-participant variability in sensory
detection thresholds to TENS. Furthermore, many studies do
not report TENS amplitude, and when they do, they rarely
report it in relation to milliamps above sensory detection
threshold.

Despite much published literature on TENS, only 20
experimental studies on different pulse frequencies of TENS
using healthy participants were found. Of these, 13 experi-
mental studies examined the effects of different pulse
frequencies when all other TENS parameters were kept
constant. Our approach resulted in the exclusion of some
TENS studies that were methodologically robust [30,31].
Ten studies reported no differences in the hypoalgesic effects
of different pulse frequencies of TENS although studies
included multiple group comparisons, multiple outcome
measures and small subject sample sizes. The three stud-
ies that we judged to demonstrate pulse frequency effects
were not convincing. Chakour et al. [36] reported that 5 pps
and 80 pps were superior to 2 pps but only when given at
a ‘maximal intensity’ and not when given at a ‘strong but
comfortable level’, which is the way it is used in clinical
practice. de Tommaso et al. [37] reported that 100 pps was
better than 10 pps and Walsh et al. [38] reported that 4 pps
was better than 110 pps when TENS was delivered at a ‘strong
but comfortable’ intensity. Table 1 highlights that some trials
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threshold.
equally ineffective; (iii) the studies were inadequate to detect a difference between pulse frequencies.

An insight into whether pulse frequencies were or were not effective can be obtained by examining studies that compared active TENS with a no-treatment control and/or a sham TENS control. Four out of 10 studies reported that active TENS was better than a no treatment control [38,43,32,40] and two out of seven studies reported that active TENS was better than a sham (dummy) TENS [38,40]. However, this analysis cannot establish with any degree of certainty that active TENS was not superior to sham TENS because our review has only included studies that compared pulse frequencies head-to-head. A significant number of additional studies that have compared TENS against sham TENS may be available in the literature and therefore a separate review of studies comparing TENS against a sham control is needed.

The failure to detect differences between active and sham TENS, and between TENS pulse frequencies may be due to limitations in study methodologies which reduce the sensitivity (internal validity) of the analgesic assay. Most experimental studies included in this review used inadequate sample sizes and this would increase the likelihood of reporting a type II error (false negative). Experimentally meaningful effect sizes were rarely stated in experimental reports and only a few studies performed a power calculation to establish appropriate sizes. Only one study used more than 20 participants per group [41], most others used fewer than 10 participants per group. A retrospective calculation of the sample size required to achieve 80% power (alpha set at 0.05) for one of our own studies [40] which was included in this review highlights the problem. Our original study used 12 participants per group, although 37 participants per group would be necessary to detect a 10-second difference in cold-pressor pain threshold (standard deviation set at ±15 seconds) and 143 participants necessary to detect a 5-second difference [45]. Whether a change of 5 seconds or 10 seconds is considered experimentally meaningful is open to debate, but the smaller the difference between pulse frequencies the less likely they are to translate into effects that are physiologically and ultimately clinically meaningful. Carroll et al. [46] estimated that randomised controlled clinical trials of TENS would need at least 40 patients in each arm of the trial in order to detect clinically meaningful effects.

Shortcomings in the psychophysical methods used to quantify pain threshold or intensity to an experimental pain stimulus may affect study outcome [21,47]. All techniques rely on a judgment about the presence and/or magnitude of the experimental stimulus. Tools used to measure subjective rating of pain intensity, such as the visual analogue scale, and pain threshold have known validity and reliability [48–50], but judgements are compromised because they are made against a pain stimulus that has changing temporospatial dimensions. Good test-retest reliability has been reported for pain thresholds and pain intensities measured using pressure algometers [51], the cold pressor technique [39], electrical stimuli [52] and a CO₂ laser [53], although all techniques have limitations [21,54,55]. For example, faster rates of application of force can lead to overestimates of pain threshold measured using pressure algometers [56]. Similarly, cold pain intensity rises rapidly within the first minute of the cold pressor test, which can overestimate pain threshold. In the cold pressor pain test pain intensity measurements are compromised by numbness developing in the submerged limb. Repeated application of painful stimuli can also lead to sensitisation and a lowering of thresholds [57]. In addition to these difficulties studies on TENS require participants to make judgements whilst experiencing TENS-induced paraesthesia close to or within the site of experimentally induced pain. The interaction between sensations of TENS paraesthesia and pain has received little attention in the literature, although Woolf et al. [58] reported that TENS effects differ according to the sensory modality of the experimental pain intervention. When these difficulties are taken into account it is likely that the majority of experimental studies included in our review lacked the internal sensitivity necessary to be an effective analgesic assay.

It is also known that many studies on TENS fail to use an adequate TENS technique [23]. TENS effects are maximal when administered at the site of pain to generate a strong but comfortable electrical paraesthesia [3,59,60]. Because of technical difficulties in accessing the site of pain, only three of the 13 included experimental studies generated TENS paraesthesia within the site of pain [36,44,60]. It is not possible to administer TENS directly over the site of experimentally induced cold pain because the hand is immersed in water, although investigators did attempt to direct TENS paraesthesia into the painful hand by careful placement over the median nerve at the wrist. Similarly, in ischaemic pain studies TENS was administered over large nerve bundles immediately proximal to the site of pain, at Erb’s point, because the upper arm was inaccessible due to the sphygmomanometer cuff. Interestingly, two of the three studies that were able to produce TENS paraesthesia within the site of pain were judged as positive outcome [36,61]. However, only de Tommaso et al. [37] were able to demonstrate frequency-dependent effects when TENS was administered at a strong but comfortable intensity and therefore variations in the site of TENS application are unlikely to contribute to the lack of frequency-dependent effects observed in our review. Nevertheless, it is important to recognise that TENS is often given inappropriately in clinical trials and this has led to under-dosing and has influenced the outcomes of randomised controlled trials and systematic reviews [23].

Other methodological issues for TENS studies include difficulties in blinding and randomisation, which have been described in depth elsewhere [61]. Nine of the 13 experimental reports stated that they used a double-blind approach ([33–35] (two studies in one report), [32,36,38,43–44]), although it is unlikely that the subjects were truly blind because they will experience differences in the quality of TENS-induced paraesthesia between the pulse frequency groups. Only one study report did not explicitly state that...
subjects were randomly allocated into groups [42]. However, study reports often lacked detail about operational procedures. It is likely that block randomisation was used in many studies because treatment groups often contained equal numbers of participants. Inadequate blinding and randomisation may exaggerate treatment effects by up to 17% and 40%, respectively [62]. We believe that these shortcomings are likely to have less impact on study outcome than the problems associated with inadequate sample size and assay sensitivity, especially as most studies failed to detect differences between groups.

The relevance of experimental pain to the clinical situation has been challenged [47]. Experimental pain is usually evoked using non-injurious stimuli which activate the nociceptive pathway and can be terminated at the request of the participant. In contrast, clinical pain is a more complex biopsychosocial phenomenon which cannot be terminated at will. Clinical pain may occur in the absence of a clearly defined stimulus and often presents with hyperalgesia and/or allodynia resulting from peripheral and central sensitisation of the nociceptive system. Despite these differences, experimental studies are very useful in solving methodological difficulties often encountered in clinical trials. Analgesic drugs reduce clinical and experimental pain to similar levels, suggesting a role for experimental pain studies to inform dosage, toxicity and adverse event profiles before undertaking clinical studies [63]. However, our review demonstrates the importance of designing experimental studies with the same rigour as seen for randomised controlled clinical trials when they are being used as analgesic assays to evaluate treatment interventions.

In summary, claims about optimal TENS settings are based on studies that often fail to isolate the effects of single TENS parameters. Available evidence from experimental studies on healthy human participants does not support the belief that pulse frequency is a key determinant of outcome when the intensity of TENS is standardised at a strong but comfortable intensity close to the site of pain. This finding is compromised because of major shortcomings in study methodologies, including inadequate sample sizes and concerns about the sensitivities of the analgesic assays. For this reason our review should serve to emphasise the need for better research and should not be used as a review of good studies done to date. We intend, in the future, to conduct a similar review which evaluates the effect of intensity when all other TENS parameters are standardised.

Conflict of interest: None.

References


