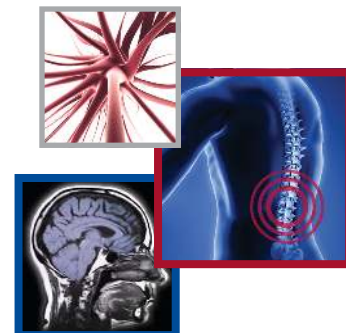


# Using TENS for pain control: the state of the evidence



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### Practice points

- High frequency (HF) and low frequency (LF) transcutaneous electrical nerve stimulation (TENS) activate different opioid receptors. Both applications have been shown to provide analgesia specifically when applied at a strong, nonpainful intensity. HF TENS may be more effective for people taking opioids.
- Effective analgesia for chronic pain conditions may be limited by the development of tolerance to TENS if repeated application of either LF or HF TENS at the same frequency and intensity is used daily (i.e., same dose). Strategies to prolong analgesia may include varying these parameters.
- Application of TENS electrodes at acupoint sites may increase analgesia.
- Targeting the use of TENS during movement or activity may be most beneficial.
- Systematic reviews suggest that TENS, when applied at adequate intensities, is effective for postoperative pain, osteoarthritis, painful diabetic neuropathy and some acute pain conditions.
- Emerging evidence suggests TENS may be helpful for people with fibromyalgia and spinal cord injury.
- TENS may be effective in restoration of central pain modulation, a measure of central inhibition.
- A clearer picture of TENS effectiveness will emerge as trials with attention to optimal dosing and appropriate outcome measures increase in numbers.

**SUMMARY:** Transcutaneous electrical nerve stimulation (TENS) is a nonpharmacological intervention that activates a complex neuronal network to reduce pain by activating descending inhibitory systems in the central nervous system to reduce hyperalgesia. The evidence for TENS efficacy is conflicting and requires not only description but also critique. Population-specific systemic reviews and meta-analyses are emerging, indicating both HF and LF TENS being shown to provide analgesia, specifically when applied at a strong, nonpainful intensity. The purpose of this article is to provide a critical review of the latest basic science and clinical evidence for TENS. Additional research is necessary to determine if TENS has effects specific to mechanical stimuli and/or beyond reduction of pain and will improve activity levels, function and quality of life.

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## Background

Transcutaneous electrical nerve stimulation (TENS) is an inexpensive nonpharmacological intervention used in the treatment of acute and chronic pain conditions. These small battery-powered devices deliver alternating current via cutaneous electrodes positioned near the painful area. The parameters of pulse frequency, and pulse intensity are adjustable and linked to TENS efficacy. This article will provide a critical review of the latest basic science and clinical evidence for TENS. We will summarize mechanisms of action, factors that influence TENS efficacy, and describe and critique the use of TENS for pain control in a variety of patient populations. Findings of systematic reviews of TENS for pain management in the last 7 years will be presented. We will also highlight advances from Randomized Controlled Trials (RCT) published in the last 5–7 years, which are not included in the systematic reviews. This article offers a concise review of the basic science mechanisms for TENS as well as an up to date critique of current clinical research for TENS.

## Mechanisms of TENS reduction on analgesia

TENS activates a complex neuronal network to result in a reduction in pain. At frequencies and intensities used clinically, TENS activates large diameter afferent fibers [1,2]. This afferent input is sent to the central nervous system to activate descending inhibitory systems to reduce hyperalgesia. Specifically, blockade of neuronal activity in the periaqueductal gray (PAG), rostral ventromedial medulla (RVM) and spinal cord inhibit the analgesic effects of TENS showing that TENS analgesia is maintained through these pathways [3–5]. In parallel, studies in people with fibromyalgia show that TENS can restore central pain modulation, a measure of central inhibition [6]. Therefore, TENS reduces hyperalgesia through both peripheral and central mechanisms.

### • Neurotransmitters & receptors that mediate TENS analgesia

HF TENS increases the concentration of  $\beta$ -endorphins in the bloodstream and cerebrospinal fluid, and methionine-enkephalin in the cerebrospinal fluid, in human subjects [7,8]. The analgesia produced reduction in hyperalgesia by HF TENS is prevented by blockade of opioid receptors in the RVM or spinal cord, or

synaptic transmission in the ventrolateral PAG [4–5,9]. This opioid-mediated analgesia produced by HF TENS has been confirmed in human subjects [10]. Furthermore, the reduction in hyperalgesia produced by HF TENS is prevented by blockade of muscarinic receptors (M1 and M3) and GABA<sub>A</sub> receptors in the spinal cord [11,12]. However, blockade of serotonin or noradrenergic receptors in the spinal cord has no effect on the reversal of hyperalgesia produced by HF TENS [13]. Thus, HF TENS produces analgesia by activating endogenous inhibitory mechanisms in the central nervous system involving opioid GABA, and muscarinic receptors.

The reduction in hyperalgesia by LF TENS is prevented by blockade of  $\mu$  opioid receptors in the spinal cord or the RVM or spinal cord, and by synaptic transmission in the ventrolateral PAG [4,5,9]. Further, the reduction in hyperalgesia by LF TENS is prevented by blockade of GABA<sub>A</sub>, serotonin 5-HT<sub>2A</sub> and 5-HT<sub>3</sub>, and muscarinic M1 and M3 receptors in the spinal cord [11–13], and is associated with increased release of serotonin [14]. This opioid mediated effect of LF TENS has been confirmed in human subjects [15]. In addition, LF TENS does not produce analgesia in opioid tolerant people and animals but HF TENS does [16,17]. Thus, LF TENS uses classical descending inhibitory pathways involving the PAG-RVM pathway activating opioid, GABA, serotonin and muscarinic receptors to reduce dorsal horn neuron activity and the consequent pain.

### • Reduction in central excitability

In animals without tissue injury, both LF and HF TENS reduce dorsal horn neuron activity [18–22]. In animals with peripheral inflammation or neuropathic pain, enhanced activity of dorsal horn neurons (i.e., central sensitization) to both noxious and innocuous stimuli is reduced by both HF and LF TENS [23–26]. In parallel, there is a reduction in both primary and secondary hyperalgesia by both LF and HF TENS [23,25–31]. Furthermore, in people with fibromyalgia and osteoarthritis, there is a reduction in pressure pain thresholds not only at the site of stimulation, but also at sites outside the area of application [6,32], implicating a reduction in central excitability.

HF TENS also reduces central neuron sensitization [24], and release of the excitatory neurotransmitters glutamate and substance P in the spinal cord dorsal horn in animals with

inflammation [33,34]. The reduction in glutamate is prevented by blockade of  $\delta$ -opioid receptors. Thus, one consequence of activation of inhibitory pathways by TENS is to reduce excitation and consequent neuron sensitization in the spinal cord.

#### • Peripheral mechanisms of TENS

Both HF and LF TENS have effects at the site of stimulation. HF TENS reduces substance P, which is increased in dorsal root ganglia neurons in animals after tissue injury [33]. Blockade of peripheral opioid receptors prevents the analgesia produced by LF, but not HF TENS [35,36]. Thus, TENS may also alter excitability of peripheral nociceptors to reduce afferent input to the central nervous system.

In  $\alpha$ -2a adrenergic knockout mice, analgesia by LF and HF TENS does not occur [37]. Blockade of peripheral, but not spinal or supraspinal,  $\alpha$ -2 receptors prevents the analgesia produced by TENS [37] suggesting a role for peripheral  $\alpha$ -2a-adrenergic receptors in analgesia produced by TENS. Further, the reduction in cold allodynia by LF TENS is reduced by administration of systemic phentolamine to block  $\alpha$ -adrenergic receptors [25]. This adrenergic effect may alter the autonomic system. There are increases in blood flow with LF TENS at intensities that produce motor contractions; greater than 25% above motor threshold [38–42]. Thus, some of the analgesic effects of TENS are mediated through peripheral adrenergic receptors.

#### Factors that directly affect TENS efficacy

The factors affecting TENS efficacy include the population and the outcome assessed, timing of the outcome measures, negative interaction of opioid use and the parameters of the TENS dose. Three important factors for TENS efficacy are tolerance to repeated TENS, intensity of the stimulation and electrode placement. A recent article by Sluka *et al.* [43] provides an extensive review of variables that can affect the clinical use of TENS.

#### • Tolerance to repeated TENS

Repeated application of either LF or HF TENS at the same frequency, intensity and pulse duration daily (i.e., same dose), produces analgesic tolerance in animals [17] and humans [44]. The analgesic tolerance by LF TENS results in cross-tolerance at  $\mu$ -opioid receptors in the spinal cord,

and the analgesic tolerance by HF TENS results in cross-tolerance at  $\delta$ -opioid receptors in the spinal cord in animals [17]. Prevention of analgesic tolerance occurs with pharmacological modulation of pathways involved in opioid tolerance. Specifically blockade of NMDA-glutamate receptors or CCK receptors in the spinal cord prevents analgesic tolerance to both LF and HF TENS [45,46]. Analgesic tolerance can also be prevented by modulating between LF and HF TENS within a treatment session [47], or by increasing intensity of TENS daily [48]. Thus, animal studies suggest TENS tolerance can be delayed with pharmacological methods as well as with non-pharmacological modulation of TENS parameters.

#### • Intensity of TENS established as a critical factor in efficacy

The intensity of stimulation utilized is critical with TENS application. Using the strongest intensity that remains comfortable produces hypoalgesia in healthy subjects; lower intensities are ineffective [49–56]. In addition to activation of greater numbers of sensory afferents, higher pulse amplitudes are proposed to activate deeper tissue afferents allowing for greater analgesia [2]. High intensity TENS decreases post-operative opioid requirements and negative opioid-side effects [57,58]. Even as researchers demonstrate the importance of intensity in TENS delivery, TENS systematic reviews continue to include studies with wide ranging intensity settings. In fact, as outlined below, application of TENS at inadequate intensities is one of the primary factors attributed to conflicting reports of TENS efficacy. Therefore, clinicians should strive to apply TENS at the maximally tolerated intensity for each individual person.

#### • Electrode site placement

The intersection of acupuncture and TENS is receiving increasing attention in research. Numerous studies have examined both electroacupuncture and traditional TENS pad electrodes applied over acupuncture sites [59–67]. Clinically, application of TENS at these acupoints reduces pain and may be more effective than when applied over non-acupoint sites when measuring pain and pain thresholds to heat and pressure in normal subjects [59–63], as well as in patient populations [64–67] when compared with sham TENS. In post-operative hysterectomy subjects, TENS at acupoint sites reduced opioid

intake, nausea and dizziness when compared with TENS at non-acupoint sites [64].

### Evidence of TENS for pain management

#### • Systematic reviews/meta-analyses

In the last 7 years, there have been a number of systematic reviews/meta-analyses that have examined efficacy of TENS for pain reduction in people with neck pain [68], postoperative pain [69], cancer pain [70,71], labor pain [72], acute pain [73], low back pain [74,75] and osteoarthritis pain [58,76]. There have also been systematic reviews on the methodology of TENS [77,78]. As a whole, these reviews are conflicting with some showing efficacy and some showing no efficacy for the use of TENS. The challenge is often a lack of high quality studies or a lack of consistency between high-quality studies included in the systematic reviews with respect to clinical population homogeneity, dose of TENS (i.e., location of TENS electrodes, frequency and intensity of TENS stimulation, and frequency and duration of TENS delivery), description of blinding and the influence of analgesic medication. **Table 1** represents a summary of these systematic reviews. Below we address the evidence on postoperative pain, acute non-postoperative pain, low back pain, osteoarthritis pain and painful diabetic neuropathy as examples.

#### Postoperative pain

There have been reviews of TENS efficacy in the last 7 years on management of postoperative pain which present differing results. A systematic review shows inconclusive results, [86] and a subsequent review shows positive effects [87]. The review by Bjordal and colleagues grouped trials into those with adequate TENS parameters (adequate frequency: 1-8 Hz for LF -TENS or 25-150 Hz for HF TENS; adequate intensity: strong sub noxious, maximal tolerable, or  $\geq 15$  mA) and those that did not meet these criteria. They show that those with adequate TENS parameters (n = 11) showed a 36% reduction in analgesic intake compared with those with inadequate TENS parameters (n = 10) that showed a 4% reduction. In contrast, the Cochrane review [86] did not consider dosing. Additionally, TENS has been found to reduce movement (walking and vital capacity maneuvers), but not resting, pain postoperatively [88]. Since the above systematic reviews focused on TENS for resting or overall pain, this factor may have also contributed to the conflicting results.

#### Acute nonpostoperative pain

A Cochrane review addressing acute pain (i.e., pain less than 12 weeks duration associated with procedures such as cervical laser, venipuncture, sigmoidoscopy screen, postpartum uterine contraction and rib fractures) in adults used a minimum stimulation intensity of 'strong but comfortable' as an inclusion factor. However, with 12 studies included, the authors were unable to make any conclusions due to insufficient evidence [73]. Four studies were included in a separate meta-analysis of RCTs where TENS was utilized in a pre-hospital setting for acute pain, (defined as moderate to severe) with TENS delivered by emergency service personnel. All studies found TENS lead to a clinically significant reduction in pain severity as compared with placebo TENS [89]. This review only included studies where TENS was used short term in ambulance responses. These studies were excluded from the Cochrane review of TENS and acute pain [73] due to low stimulation intensity. Thus, short-term use of TENS in ambulance responses the required intensity may be less than that required for chronic or other types of acute conditions. Recent randomized controlled trials for TENS show significant reductions in postpartum pain [90] and pain during wound-care procedures [91]. Interestingly, the mechanical triggers of wound-care procedures are similar to movement pain, supporting the effect of TENS for pain caused by mechanical stimulation, such as muscle movement, pressure, or force.

#### Low back pain

Systematic reviews [74,80] and a meta-analysis [75] have examined the efficacy of TENS for low back pain with conflicting results from not recommended [80], inconclusive [74], and effective [75]. All analyses used different inclusion and exclusion criteria, all examined effects on pain at rest, several used a mixed patient population, and none used dosing or timing of outcome, or examined potential interactions with pharmacological agents.

For example, the systematic review by Dubinsky and Miyasaki [80] was based on only two studies with differing patient populations - one for chronic, non-specific low back pain [92] and the other for low back pain in people with multiple sclerosis. The pain of MS is related to direct injury and permanent damage to the central nervous system [93]; while chronic musculoskeletal pain is generally due to modifiable

**Table 1. TENS systematic reviews 2007–2013.**

Year	Topic	Author	Review type	Studies (n)	Subjects (n)	Results	Ref.
2013	Neck pain	Kroeling	Systematic review	20	1239	Update on 2009 and 2005 systematic review. Authors were unable to determine effect of TENS in neck pain due to limited quality of evidence, but suggest active TENS may be more effective than placebo TENS. Limited number of studies with standardization and description of treatment characteristics.	[68]
2012	Thoracic surgery	Sbruzzi	Meta-analysis	11	545	Use of random effects models to assess TENS effect s/p thoracic surgery. In thoracotomy and sternotomy, TENS associated with pharmacological analgesia improved pain relief compared with placebo TENS. With sternotomy, TENS was more effective than pharmacological analgesia for pain relief. No change in pulmonary function.	[69]
2012	Cancer pain adults	Hurlow	Systematic review	3	176	Update of 2008 Robb article in cancer pain. Addition of one RCT suggesting TENS may improve bone pain on movement in a cancer population. Results remained inconclusive due to a limited number of RCTs for review.	[71]
2011	Methodological Quality TENS and pain	Bennett	Systematic review	38	2268	Review of three Cochrane systematic reviews: acute pain, chronic pain and cancer pain. Authors identified sources of potential bias related to study design including less than optimal dosing of TENS, outcome assessment and timing as well as blinding and application of TENS. Proposal of criteria for future studies to enhance fidelity.	[77]
2011	Pain in labor	Bedwell	Systematic review	14	1256	Update to 2009 Dowsell article. Limited evidence that TENS reduces pain in labor. TENS does not appear to have effect on other outcomes for mothers and infants.	[72]
2010	Phantom limb pain	Mulvey	Cochrane systematic review	0	0	No RCTs have been completed to examine decreased pain in amputees. Further investigation is needed.	[79]

CLBP: Chronic low back pain; DPN: Diabetic peripheral neuropathy; IFC: Interferential current; LBP: Low back pain; OA: Osteoarthritis; QOL: Quality of life; RA: Rheumatoid arthritis; RCT: Randomized controlled trials; TENS: Transcutaneous electrical nerve stimulation.

Table 1. TENS systematic reviews 2007–2013 (cont.).

Year	Topic	Author	Review type	Studies (n)	Subjects (n)	Results	Ref.
2008	TENS dose response for chronic pain	Claydon	Review of systematic reviews	6	Hand RA: 78 cLBP: 175 Knee OA: 294 Chronic musculoskeletal pain: 984 Chronic pain: 1227 Total: 2758	Two of six reviews of TENS and chronic pain reported high intensity TENS applications were more effective compared with placebo than low intensity. Reviewed confounding variables of inadequate design, low statistical power and different TENS protocols – single treatment versus repeated treatments of TENS.	[78]
2010	Neurological disorders (LBP and DPN)	Dubinsky	Systematic review	11		Inconsistent evidence for pain reduction in cLBP; probable evidence for pain reduction with diabetic peripheral neuropathy.	[80]
2010	Diabetic Peripheral Neuropathy	Jin	Meta-analysis	3	78	Pain reduction significantly greater than placebo following 4–6 weeks of treatment. Reduced hyperalgesia and numbness and increased QOL also significantly improved with active TENS.	[81]
2010	Hand RA	Brouseau	Cochrane systematic review	3	78	Update of 2003 review; Acupuncture like TENS has benefit for reducing pain intensity and increasing grip over placebo while conventional TENS no benefit compared with placebo.	[82]
2009	Pain in labor	Dowswell	Cochrane systematic review	17	1466	Limited evidence that TENS reduces pain in labor. Little difference between TENS groups and control groups. Those women receiving TENS to acupuncture points were less likely to report severe pain.	[83]
2009	Non-specific low back pain	Machado	Meta-analysis	4	178	Random effects statistical model demonstrated moderate effect for TENS in acute and chronic LBP	[75]
2009/2011	Acute pain	Walsh	Cochrane systematic review	12	919	Insufficient evidence to draw any conclusions about the effectiveness of TENS for the treatment of acute pain in adults.	[73]
2008	Chronic low back pain	Khadilkar	Cochrane systematic review	4	585	Conflicting evidence about TENS benefit in reducing back pain intensity. Acupuncture like TENS responded similar to conventional TENS, two of four studies lacked adequate stimulation intensity.	[74]

cLBP: Chronic low back pain; DPN: Diabetic peripheral neuropathy; IFC: Interferential current; LBP: Low back pain; OA: Osteoarthritis; QOL: Quality of life; RA: Rheumatoid arthritis; RCT: Randomized controlled trials; TENS: Transcutaneous electrical nerve stimulation.

**Table 1. TENS systematic reviews 2007–2013 (cont.).**

Year	Topic	Author	Review type	Studies (n)	Subjects (n)	Results	Ref.
2008	Cancer pain adults	Robb	Cochrane systematic review	2	64	Due to small number of subjects and studies, there is insufficient evidence to determine the effectiveness of TENS and cancer pain. One RCT no significant difference in TENS and placebo TENS; one RCT no significant difference in acupuncture-like TENS and sham TENS.	[70]
2008	OA of knee	Rutjes	Cochrane systematic review	18	813	Mixed review of trials for TENS, IFC and pulsed electrical stimulation. Inconclusive for the results of TENS for pain and function of the knee due to small trials and inadequate design and power.	[76]
2008	Chronic pain	Nnoahm	Cochrane systematic review	25	1281	13/22 inactive control studies demonstrate a positive analgesic outcome for active TENS treatments. For multiple treatment comparison studies 8/15 were in favor of active TENS. 7/9 active controlled studies found no difference in analgesic efficacy between high frequency TENS and low frequency TENS.	[84]
2007	Knee OA	Bjordal	Systematic review and meta-analysis	11	425	Seven of 11 studies had optimal TENS dosing and demonstrated clinically relevant pain relief compared with placebo control. These studies included IFC, electro acupuncture and low level laser therapy.	[58]
2007	Chronic low back pain; skeletal pain	Johnson	Meta-analysis	38	1227	With resting pain as main outcome measure, the overall random effects meta-analysis model showed a decrease in pain with electrical nerve stimulation.	[85]

cLBP: Chronic low back pain; DPN: Diabetic peripheral neuropathy; IFC: Interferential current; LBP: Low back pain; OA: Osteoarthritis; QOL: Quality of life; RA: Rheumatoid arthritis; RCT: Randomized controlled trials; TENS: Transcutaneous electrical nerve stimulation.

'plastic' changes in both the peripheral and central pain pathways (sensitization) [94–96]. Machado [75] used people with non-specific low back pain with positive results – however, they combined acute and chronic low back pain, which likely have different underlying mechanisms.

None of the reviews considered adequate dosing of TENS and there were studies included in each review that did not describe TENS parameters or used inadequate doses. For example, the study by Deyo and colleagues [92], comparing TENS with and without exercise to placebo TENS with and without exercise in people with chronic low back pain, was included in two systematic reviews [74,80] and is rated as a well-designed clinical trial using appropriate blinding, randomization and good description of withdrawal and dropouts. However there are significant weaknesses in the application of TENS, some of which have been discovered since the trial was conducted 23 years ago. Intensity was applied by having subjects set the amplitude to a pre-designated setting on the machine which corresponded to 15 mA as obtained from the manufacturer. Patient response to stimulation was not stated. In our preliminary data, application of TENS to the spine that results in a strong but comfortable intensity requires at least 30 mA and, thus, the amplitude used was likely below an effective dose. Thus, it is not clear if TENS is effective for low back pain. Future studies should design clinical trials with adequate dosing and appropriate outcome measures. Future systematic reviews need to use patient populations with similar pain physiology and adequate use of TENS parameters as inclusion criteria.

#### Osteoarthritis pain

Similar to the reviews of acute pain and low back pain, a recent Cochrane systematic review showed that TENS was not effective for knee osteoarthritis(OA) pain [97], and is in direct contrast to a prior systematic review by the same group that concluded TENS was effective for knee OA pain [98] and a meta-analysis that showed a significant reduction in knee OA pain with TENS [58]. Intensities in the included studies varied widely. For example in the recent Cochrane review [97], 12 included trials used adequate intensities, five trials used inadequate intensities (HF-TENS at sensory threshold or below [99–103] and two trials did not report TENS intensity [104,105]. To address dosing, Bjordal and colleagues performed

a systematic review on TENS for osteoarthritis pain and show that when given at adequate intensities and frequencies TENS produces a clinically significant reduction in pain when compared with studies of inadequate dosing [58]. Therefore TENS works for OA pain if used at adequate intensities. A recent randomized controlled trial applied TENS in people with knee OA as an adjunct to primary care and showed no added benefit. However, parameters were not standardized and, participants were allowed to self-select from eight different TENS protocols in the 6 week trial making interpretation of findings challenging [106].

#### Diabetic peripheral neuropathy (DPN)

In people with painful DPN, TENS may also provide benefit. A meta-analysis including three RCTs (n = 78) reported reduction of pain that was significantly greater than placebo TENS following 4–6 weeks of treatment [81] In addition, secondary outcomes of overall improvement in DPN symptoms (hyperalgesia, numbness, and quality of life) were significantly greater for active TENS groups when compared with placebo [107–109] Therefore, there is support for the use of TENS in reducing pain and improving quality of life in people with painful DPN.

#### • TENS interventions: emerging evidence from recent clinical trials

##### Fibromyalgia (FM)

Recent evidence suggests that TENS can be effective for people with fibromyalgia. Although there have been several randomized controlled-trials [6,110–113], no systematic reviews have been published and the quality of these studies and the intervention have varied significantly. Two trials compared TENS to a placebo and used an adequate dose. Dailey *et al.* [6] showed a one-time session of TENS (using a maximum tolerable intensity) significantly decreased movement pain and hyperalgesia. No changes were observed in resting pain [6] Lauretti *et al.* [111] showed TENS using a strong intensity (60 mA) at two sites and at one site produced a significant decrease in pain at rest compared with placebo when applied over a seven day period. Two additional studies show reductions in pain with strong but comfortable intensity HF TENS compared with warmth therapy and to a no TENS group [110,112.] Thus, when used at a strong but comfortable sensation, TENS may be effective for both resting and movement pain in people with fibromyalgia.



### Neuropathic pain

TENS may offer relief to people with neuropathic pain and complex regional pain syndrome. A crossover design trial investigating neuropathic pain in people with spinal cord injury, [114] found a favorable effect of both LF and HF TENS (LF TENS 38%; HF TENS 29%) on a global relief scale and 25% of subjects requested a unit for further treatment. However, this study did not compare against a placebo or control group, intensity was not reported, and there were a low number of study participants (n = 24). A more recent study reports LF TENS provided significant reduction in pain when compared with placebo TENS in people with spinal cord injury. Here the parameters of 4 Hz and 200  $\mu$ s were applied at sites below the level of injury at a set intensity of 50 mA [115]. Thus, LF TENS may be most effective for pain in people with spinal cord injury.

### Other pain conditions

A recent randomized controlled trial of TENS as an adjunct treatment in the management of lateral epicondylalgia concludes that TENS does not provide additional benefit when used as an adjunct to primary care (education and therapeutic exercise) [116]. In review, while an appropriate intensity was used, the intervention was not monitored for dosing and low adherence was reported. Further, outcome measures were assessed through questionnaires and not necessarily while wearing the TENS device. Additional TENS reports are favorable for relief of chronic pelvic pain syndrome [117] and pain associated with latent upper trapezius trigger points [118]. Overall, the evidence suggests, TENS may be useful for a variety of pain conditions.

### Summary & conclusion

Because no single profession holds all the keys to successful management of pain, further investigation is warranted to ensure optimal use of this safe, noninvasive, inexpensive and patient friendly intervention. The advantages of

obtaining pain relief without the negative side effects of many pharmaceutical interventions is welcomed and desired by certain patients. Both HF and LF TENS been shown to provide analgesia specifically when applied at a strong, non-painful intensity and HF TENS may be more effective for people taking opioids. Effective analgesia for chronic pain conditions may be limited by the development of tolerance to TENS if repeated application of either HF or LF TENS at the same frequency, intensity and pulse duration is used daily. Application of TENS electrodes at acupoint sites may increase analgesia and targeting the use of TENS during movement or required activity may provide the most benefit.

Experiments investigating the concept of TENS responders will enable clinicians to select this modality for the correct population. Additional investigation in the area of TENS tolerance is necessary to determine methods to decrease tolerance and to establish if a wash out period is required to determine when tolerance would no longer be a factor in the application of TENS in patient care. Although parameter selection is becoming clearer, investigating the parameters of electrode site selection, daily treatment duration, and long-term usage will further clarify appropriate dosing so that TENS may be given in the most effective manner. Further, examining a variety of outcomes, beyond resting pain, will determine if TENS has effects specific to mechanical stimuli and/or beyond reduction of pain and will improve activity levels, function and quality of life.

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### References

Papers of special note have been highlighted as:

• of interest; •• of considerable interest

- 1 Levin MF, Hui-Chan CW. Conventional and acupuncture-like transcutaneous electrical nerve stimulation excite similar afferent fibers. *Arch. Phys. Med. Rehabil.* 74, 54–60 (1993).
- 2 Radhakrishnan R, Sluka KA. Deep tissue afferents, but not cutaneous afferents, mediate

TENS-induced antihyperalgesia. *J. Pain* 6, 673–680 (2005).

- **‘Transcutaneous’ may be a misnomer as transcutaneous electrical nerve stimulation (TENS) induced anti-hyperalgesia is mediated by deep tissue afferents. Animal study showing that anesthetic applied to the skin has no effect on the analgesia produced by TENS while anesthetic within the knee**

**joint prevents the analgesia produced by TENS.**

- 3 Desantana JM, Da Silva LF, De Resende MA, Sluka KA. Transcutaneous electrical nerve stimulation at both high and low frequencies activates ventrolateral periaqueductal grey to decrease mechanical hyperalgesia in arthritic rats. *Neuroscience* 163(4), 1233–1241 (2009).

- 4 Kalra A, Urban MO, Sluka KA. Blockade of opioid receptors in rostral ventral medulla prevents antihyperalgesia produced by transcutaneous electrical nerve stimulation (TENS). *J. Pharmacol. Exp. Ther.* 298, 257–263 (2001).
- 5 Sluka KA, Deacon M, Stibal A *et al.* Spinal blockade of opioid receptors prevents the analgesia produced by TENS in arthritic rats. *J. Pharmacol. Exp. Ther.* 289, 840–846 (1999).
- 6 Dailey DL, Rakel BA, Vance CG *et al.* Transcutaneous electrical nerve stimulation reduces pain, fatigue and hyperalgesia while restoring central inhibition in primary fibromyalgia. *Pain* 154, 2554–2562 (2013).
- **A single TENS treatment in people with fibromyalgia reduces movement pain and restores conditioned pain modulation (CPM).**
- 7 Salar G, Job I, Mingrino S *et al.* Effect of transcutaneous electrotherapy on CSF beta-endorphin content in patients without pain problems. *Pain* 10, 169–172 (1981).
- 8 Han JS, Chen XH, Sun SL *et al.* Effect of low and high frequency TENS on met-enkephalin-arg-phe and dynorphin A immunoreactivity in human lumbar CSF. *Pain* 47, 295–298 (1991).
- 9 DeSantana JM, da Silva LF, De Resende MA, Sluka KA. Transcutaneous electrical nerve stimulation at both high and low frequencies activates ventrolateral periaqueductal grey to decrease mechanical hyperalgesia in arthritic rats. *Neuroscience* 163, 1233–1241 (2009).
- 10 Leonard G, Goffaux P, Marchand S. Deciphering the role of endogenous opioids in high-frequency TENS using low and high doses of naloxone. *Pain* 151, 215–219 (2010).
- **Opioid-mediated analgesia by of high frequency TENS confirmed in human subjects. High frequency TENS analgesia is blocked by high, but not low, dose of naloxone.**
- 11 Radhakrishnan R, Sluka KA. Spinal muscarinic receptors are activated during low or high frequency TENS-induced antihyperalgesia in rats. *Neuropharm* 45, 1111–1119 (2003).
- 12 Maeda Y, Lisi TL, Vance CG, Sluka KA. Release of GABA and activation of GABA<sub>A</sub> receptors in the spinal cord mediates the effects of TENS in rats. *Brain Res.* 1136, 43–50 (2007).
- 13 Radhakrishnan R, King EW, Dickman J *et al.* Blockade of spinal 5-HT receptor subtypes prevents low, but not high, frequency TENS-induced antihyperalgesia in rats. *Pain* 105, 205–213 (2003).
- 14 Sluka KA, Lisi TL, Westlund KN. Increased release of serotonin in the spinal cord during low, but not high, frequency TENS in rats with joint inflammation. *Arch. Phys. Med. Rehab* 87, 1137–1140 (2006).
- 15 Sjolund BH, Eriksson MBE. The influence of naloxone on analgesia produced by peripheral conditioning stimulation. *Brain Res.* 173, 295–301 (1979).
- 16 Léonard G, Cloutier C, Marchand S. Reduced analgesic effect of acupuncture-like TENS but not conventional TENS in opioid-treated patients. *J. Pain* 12(2), 213–221 (2011).
- **Translates prior work from animal studies and shows cross-tolerance between low frequency TENS and opioid-tolerant individuals.**
- 17 Chandran P, Sluka KA. Development of opioid tolerance with repeated transcutaneous electrical nerve stimulation administration. *Pain* 102, 195–201 (2003).
- 18 Lee KH, Chung JM, Willis WD. Inhibition of primate spinothalamic tract cells by TENS. *J. Neurosurg.* 62, 276–287 (1985).
- 19 Sjolund BH. Peripheral nerve stimulation suppression of C-fiber evoked flexion reflex in rats. Part 1: parameters of continuous stimulation. *J. Neurosurg.* 63, 612–616 (1985).
- 20 Sjolund BH. Peripheral nerve stimulation suppression of C-fiber evoked flexion reflex in rats. Part 2. Parameters of low rat train stimulation of skin and muscle afferent nerves. *J. Neurosurg.* 68, 279–283 (1988).
- 21 Garrison DW, Foreman RD. Decreased activity of spontaneous and noxiously evoked dorsal horn cells during transcutaneous electrical nerve stimulation (TENS). *Pain* 58, 309–315 (1994).
- 22 Garrison DW, Foreman RD. Effects of prolonged transcutaneous electrical nerve stimulation (TENS) and variation of stimulation variables on dorsal horn cell activity. *Eur. J. Phys. Med. Rehabil.* 6, 87–94 (1997).
- 23 Somers DL, Clemente FR. High-frequency transcutaneous electrical nerve stimulation alters thermal but not mechanical allodynia following chronic constriction injury of the rat sciatic nerve. *Arch. Phys. Med. Rehabil.* 79, 1370–1376 (1998).
- 24 Ma YT, Sluka KA. Reduction in inflammation-induced sensitization of dorsal horn neurons by transcutaneous electrical nerve stimulation in anesthetized rats. *Exp. Brain Res.* 137, 94–102 (2001).
- 25 Nam TS, Choi Y, Yeon DS *et al.* Differential antinociceptive effect of transcutaneous electrical stimulation on pain behavior sensitive or insensitive to phentolamine in neuropathic rats. *Neurosci. Lett.* 301, 17–20 (2001).
- 26 Leem JW, Park ES, Paik KS. Electrophysiological evidence for the antinociceptive effect of transcutaneous electrical nerve stimulation on mechanically evoked responsiveness of dorsal horn neurons in neuropathic rats. *Neurosci. Lett.* 192, 197–200 (1995).
- 27 Sluka KA, Bailey K, Bogush J *et al.* Treatment with either high or low frequency TENS reduces the secondary hyperalgesia observed after injection of kaolin and carrageenan into the knee joint. *Pain* 77, 97–102 (1998).
- 28 Vance CG, Radhakrishnan R, Skyba DA, Sluka KA. Transcutaneous electrical nerve stimulation at both high and low frequencies reduces primary hyperalgesia in rats with joint inflammation in a time-dependent manner. *Phys. Ther.* 87(1), 44–51 (2006).
- 29 Ainsworth L, Budelier K, Clinesmith M *et al.* Transcutaneous electrical nerve stimulation (TENS) reduces chronic hyperalgesia induced by muscle inflammation. *Pain* 120, 182–187 (2006).
- 30 Gopalkrishnan P, Sluka KA. Effect of varying frequency, intensity and pulse duration of TENS on primary hyperalgesia in inflamed rats. *Arch. Phys. Med. Rehabil.* 81, 984–990 (2000).
- 31 Resende MA, Sabino GG, Candido CRM *et al.* Transcutaneous electrical stimulation (TENS) effects in experimental inflammatory edema and pain. *Eur. J. Pharmacol.* 504, 217–222 (2004).
- 32 Vance CG, Rakel BA, Blodgett NP *et al.* Effects of transcutaneous electrical nerve stimulation on pain, pain sensitivity, and function in people with knee osteoarthritis: a randomized controlled trial. *Phys. Ther.* 92(7), 898–910 (2012).
- 33 Rokugo T, Takeuchi T, Ito H. A histochemical study of substance P in the rat spinal cord: effect of transcutaneous electrical nerve stimulation. *J. Nippon Med. Sch.* 69, 428–433 (2002).
- 34 Sluka KA, Vance CGT, Lisi TL. High-frequency, but not low-frequency, transcutaneous electrical nerve stimulation reduces aspartate and glutamate release in the spinal cord dorsal horn. *J. Neurochem.* 95, 1794–1801 (2005).
- 35 Sabino GS, Santos CM, Francischi JN, de Resende MA. Release of endogenous opioids following transcutaneous electric nerve stimulation in an experimental model of acute inflammatory pain. *J. Pain* 9, 157–163 (2008).

- 36 Santos CM, Francischi JN, Lima-Paiva P, Sluka KA, Resende MA. Effect of transcutaneous electrical stimulation on nociception and edema induced by peripheral serotonin. *Int. J. Neurosci.* 123(7), 507–515 (2013).
- 37 King EW, Audette K, Athman GA *et al.* Transcutaneous electrical nerve stimulation activates peripherally located alpha-2A adrenergic receptors. *Pain* 115, 364–373 (2005).
- 38 Sherry JE, Oehrlein KM, Hegge KS, Morgan BJ. Effect of burst-mode transcutaneous electrical nerve stimulation on peripheral vascular resistance. *Phys. Ther.* 81, 1183–1191 (2001).
- 39 Cramp FL, McCullough GR, Lowe AS, Walsh DM. Transcutaneous electric nerve stimulation: the effect of intensity on local and distal cutaneous blood flow and skin temperature in healthy subjects. *Arch. Phys. Med. Rehabil.* 83, 5–9 (2002).
- 40 Cramp AF, Gilson C, Lowe AS, Walsh DM. The effect of high- and low-frequency transcutaneous electrical nerve stimulation upon cutaneous blood flow and skin temperature in healthy subjects. *Clin. Physiol.* 20, 150–157 (2000).
- 41 Chen CC, Johnson MI, McDonough S, Cramp F. The effect of transcutaneous electrical nerve stimulation on local and distal cutaneous blood flow following a prolonged heat stimulus in healthy subjects. *Clin. Physiol. Funct. Imaging* 27, 154–161 (2007).
- 42 Sandberg ML, Sandberg MK, Dahl J. Blood flow changes in the trapezius muscle and overlying skin following transcutaneous electrical nerve stimulation. *Phys. Ther.* 87, 1047–1055 (2007).
- 43 Sluka KA, Bjordal JM, Marchand S, Rakel BA. What makes transcutaneous electrical nerve stimulation work? Making sense of the mixed results in the clinical literature. *Phys. Ther.* 93(10), 1397–1402 (2013).
- 44 Liebano R, Rakel B, Vance C *et al.* An investigation of the development of analgesic tolerance to transcutaneous electrical nerve stimulation (TENS) in humans. *Pain* 152, 335–342 (2011).
- 45 Hingne PM, Sluka KA. Blockade of NMDA receptors prevents analgesic tolerance to repeated transcutaneous electrical nerve stimulation (TENS) in rats. *J. Pain* 9, 217–225 (2008).
- 46 DeSantana JM, da Silva LF, Sluka KA. Cholecystokinin receptors mediate tolerance to the analgesic effect of TENS in arthritic rats. *Pain* 148, 84–93 (2010).
- 47 DeSantana JM, Santana-Filho VJ, Sluka KA. Modulation between high- and low-frequency transcutaneous electric nerve stimulation delays the development of analgesic tolerance in arthritic rats. *Arch. Phys. Med. Rehabil.* 89, 754–780 (2008).
- 48 Sato KL, Sanada LS, Rakel BA, Sluka KA. Increasing intensity of TENS prevents analgesic tolerance in rats. *J. Pain* 13, 884–890 (2012).
- **Describes a nonpharmacological approach to prevention of analgesic tolerance to TENS by increasing intensity 10% per day.**
- 49 Aarskog R, Johnson MI, Demmink JH *et al.* Is mechanical pain threshold after transcutaneous electrical nerve stimulation (TENS) increased locally and unilaterally? A randomized placebo-controlled trial in healthy subjects. *Physiother. Res. Int.* 12, 251–263 (2007).
- 50 Chesterton LS, Barlas P, Foster NE, Lundeberg T, Wright CC, Baxter GD. Sensory stimulation (TENS): effects of parameter manipulation on mechanical pain thresholds in healthy human subjects. *Pain* 99, 253–262 (2002).
- 51 Chesterton LS, Foster NE, Wright CC, Baxter GD, Barlas P. Effects of TENS frequency, intensity and stimulation site parameter manipulation on pressure pain thresholds in healthy human subjects. *Pain* 106, 73–80 (2003).
- 52 Claydon LS, Chesterton LS. Does transcutaneous electrical nerve stimulation (TENS) produce ‘dose-responses’? A review of systematic reviews on chronic pain. *Phys. Ther. Rev.* 13, 450–463 (2008).
- 53 Cowan S, McKenna J, McCrum-Gardner E, Johnson MI, Sluka KA, Walsh DM. An investigation of the hypoalgesic effects of TENS delivered by a glove electrode. *J. Pain* 10, 694–701 (2009).
- 54 Pantaleo MA, Laurino MF, Gallego NL *et al.* Adjusting pulse amplitude during TENS application produces greater hypoalgesia. *J. Pain* 12(5), 581–590 (2011).
- 55 Moran F, Leonard T, Hawthorne S *et al.* Hypoalgesia in response to transcutaneous electrical nerve stimulation (TENS) depends on stimulation intensity. *J. Pain* 12(8), 929–935 (2011).
- 56 Rakel B, Cooper N, Adams HJ *et al.* A new transient sham TENS device allows for investigator blinding while delivering a true placebo treatment. *J. Pain* 11, 230–238 (2010).
- 57 Wang B, Tang J, White PF *et al.* Effect of the intensity of transcutaneous acupoint electrical stimulation on the postoperative analgesic requirement. *Anesth. Analg.* 85, 406–413 (1997).
- 58 Bjordal JM, Johnson MI, Lopes-Martins RA, Bogen B, Chow R, Ljunggren AE. Short-term efficacy of physical interventions in osteoarthritic knee pain. A systematic review and meta-analysis of randomised placebo-controlled trials. *BMC Musculoskelet. Disord.* 8, 51 (2007).
- **When given at adequate intensity and frequency, TENS produces a clinically significant reduction in pain in individuals with osteoarthritic pain.**
- 59 Barlas P, Ting SL, Chesterton LS, Jones PW, Sim J. Effects of intensity of electroacupuncture upon experimental pain in healthy human volunteers: a randomized, double-blind, placebo-controlled study. *Pain* 122, 81–89 (2006).
- 60 Cheing GL, Chan WW. Influence of choice of electrical stimulation site on peripheral neurophysiological and hypoalgesic effects. *J. Rehabil. Med.* 41, 412–417 (2009).
- 61 Lang PM, Stoer J, Schober GM, Audette JF, Irnich D. Bilateral acupuncture analgesia observed by quantitative sensory testing in healthy volunteers. *Anesth. Analg.* 110, 1448–1456 (2010).
- 62 Schliessbach J, van der Klift E, Arendt-Nielsen L, Curatolo M, Streitberger K. The effect of brief electrical and manual acupuncture stimulation on mechanical experimental pain. *Pain Med.* 12, 268–275 (2011).
- 63 Wang N, Hui-Chan C. Effects of acupoints TENS on heat pain threshold in normal subjects. *Chin. Med. J. (Engl)* 116, 1864–1868 (2003).
- 64 Chen L, Tang J, White PF *et al.* The effect of location of transcutaneous electrical nerve stimulation on postoperative opioid analgesic requirement: acupoint versus nonacupoint stimulation. *Anesth. Analg.* 87, 1129–1134 (1998).
- 65 Lan F, Ma YH, Xue JX, Wang TL, Ma DQ. Transcutaneous electrical nerve stimulation on acupoints reduces fentanyl requirement for postoperative pain relief after total hip arthroplasty in elderly patients. *Minerva Anesthesiol.* 78, 887–895 (2012).
- 66 Liu YY, Duan SE, Cai MX, Zou P, Lai Y, Li YL. Evaluation of transcutaneous electroacupoint stimulation with the train-of-four mode for preventing nausea and vomiting after laparoscopic cholecystectomy. *Chin. J. Integr. Med.* 14, 94–97 (2008).

- 67 Ma YX, Ma LX, Liu XL *et al.* A comparative study on the immediate effects of electroacupuncture at Sanyinjiao (SP6), Xuanzhong (GB39) and a non-meridian point, on menstrual pain and uterine arterial blood flow, in primary dysmenorrhea patients. *Pain Med.* 11, 1564–1575 (2010).
- 68 Kroeling P, Gross A, Graham N *et al.* Electrotherapy for neck pain. *Cochrane Database Syst. Rev.* 8, CD004251 (2013).
- 69 Sbruzzi G, Silveira SA, Silva DV, Coronel CC, Plentz RD. Transcutaneous electrical nerve stimulation after thoracic surgery: systematic review and meta-analysis of 11 randomized trials. *Rev. Bras. Cir. Cardiovasc.* 27, 75–87 (2012).
- 70 Robb KA, Bennett MI, Johnson MI, Simpson KJ, Oxberry SG. Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. *Cochrane Database Syst. Rev.* 3, CD006276(2008).
- 71 Hurlow A, Bennett MI, Robb KA, Johnson MI, Simpson KH, Oxberry SG. Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. *Cochrane Database Syst. Rev.* 3, CD006276 (2012).
- 72 Bedwell C, Dowswell T, Neilson JP, Lavender T. The use of transcutaneous electrical nerve stimulation (TENS) for pain relief in labour: a review of the evidence. *Midwifery* 27, e141–148 (2011).
- 73 Walsh DM, Howe TE, Johnson MI, Sluka KA. Transcutaneous electrical nerve stimulation for acute pain. *Cochrane Database Syst. Rev.* 2, CD006142 (2009).
- 74 Khadilkar A, Odebiyi DO, Brosseau L, Wells GA. Transcutaneous electrical nerve stimulation (TENS) versus placebo for chronic low-back pain. *Cochrane Database Syst. Rev.* 4, CD003008 (2008).
- 75 Machado LA, Kamper SJ, Herbert RD, Maher CG, McAuley JH. Analgesic effects of treatments for non-specific low back pain: a meta-analysis of placebo-controlled randomized trials. *Rheumatology (Oxford)* 48, 520–527 (2009).
- 76 Rutjes AW, Nuesch E, Sterchi R *et al.* Transcutaneous electrostimulation for osteoarthritis of the knee. *Cochrane Database Syst. Rev.* 4, CD002823 (2009).
- 77 Bennett MI, Hughes N, Johnson MI. Methodological quality in randomised controlled trials of transcutaneous electric nerve stimulation for pain: low fidelity may explain negative findings. *Pain* 152, 1226–1232 (2011).
- **Addresses current points of interest with regard to TENS investigation and proposes criteria for future studies to enhance fidelity.**
- 78 Claydon LS, Chesterton LS. Does transcutaneous electrical stimulation (TENS) produce ‘dose-response’? A review of systematic reviews on chronic pain. *Phys. Ther. Rev.* 13(6), 450–463 (2008).
- **A systematic review of TENS trials in multiple chronic pain conditions with attention to TENS dose, protocol differences, and statistical power.**
- 79 Mulvey MR, Bagnall AM, Johnson MI, Marchant PR. Transcutaneous electrical nerve stimulation (TENS) for phantom pain and stump pain following amputation in adults. *Cochrane Database Syst. Rev.* 5, CD007264 (2010).
- 80 Dubinsky RM, Miyasaki J. Assessment: efficacy of transcutaneous electric nerve stimulation in the treatment of pain in neurologic disorders (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 74, 173–176 (2010).
- 81 Jin DM, Xu Y, Geng DF, Yan TB. Effect of transcutaneous electrical nerve stimulation on symptomatic diabetic peripheral neuropathy: a meta-analysis of randomized controlled trials. *Diabetes Res. Clin. Pract.* 89(1), 10–15 (2010).
- **Meta-analysis indicates TENS reduces pain, hyperalgesia, numbness and improves quality of life in individuals with painful diabetic peripheral neuropathy (DPN).**
- 82 Brosseau L, Judd MG, Marchand S *et al.* Transcutaneous electrical nerve stimulation (TENS) for the treatment of rheumatoid arthritis in the hand. *Cochrane Database Syst. Rev.* 3, CD004377 (2003).
- 83 Dowswell T, Bedwell C, Lavender T, Neilson JP. Transcutaneous electrical nerve stimulation (TENS) for pain relief in labour. *Cochrane Database Syst. Rev.* 2, CD007214 (2009).
- 84 Nnoaham KE, Kumbang J. Transcutaneous electrical nerve stimulation (TENS) for chronic pain. *Cochrane Database Syst. Rev.* 3, CD003222 (2008).
- 85 Johnson M, Martinson M. Efficacy of electrical nerve stimulation for chronic musculoskeletal pain: a meta-analysis of randomized controlled trials. *Pain* 130, 157–165 (2007).
- 86 Carroll D, Tramer M, McQuay H, Nye B, Moore A. Randomization is important in studies with pain outcomes: systematic review of transcutaneous electrical nerve stimulation in acute postoperative pain. *Br. J. Anaesth.* 77, 798–803 (1996).
- 87 Bjordal JM, Johnson MI, Ljunggreen AE. Transcutaneous electrical nerve stimulation (TENS) can reduce postoperative analgesic consumption. A meta-analysis with assessment of optimal treatment parameters for postoperative pain. *Eur. J. Pain* 7, 181–188 (2003).
- 88 Rakel B, Frantz R. Effectiveness of transcutaneous electrical nerve stimulation on postoperative pain with movement. *J. Pain* 4, 455–464 (2003).
- 89 Barker R, Lang T, Steinlechner B *et al.* Transcutaneous electrical nerve stimulation as prehospital emergency interventional care. *Neuromodulation* 9(2), 136–142 (2006).
- 90 Kayman-Kose S, Arioz DT, Toktas H *et al.* Transcutaneous electrical nerve stimulation (TENS) for pain control after vaginal delivery and cesarean section. *J. Matern. Fetal Neonatal Med.* doi:10.3109/14767058.2013.870549 (2014) (Epub ahead of print).
- 91 Gardner SE, Blodgett NP, Hillis SL *et al.* HI-TENS reduces moderate-to-severe pain associated with most wound care procedures: a pilot study. *Biol. Res. Nurs.* doi:10.1177/1099800413498639 (2013). (Epub ahead of print).
- 92 Deyo RA, Walsh NE, Martin DC, Schoenfeld LS, Ramamurthy S. A controlled trial of transcutaneous electrical nerve stimulation (TENS) and exercise for chronic low back pain. *N. Engl. J. Med.* 322, 1627–1634 (1990).
- 93 Kerns RD, Kassirer M, Otis J. Pain in multiple sclerosis: a biopsychosocial perspective. *J. Rehabil. Res. Dev.* 39, 225–232 (2002).
- 94 DeSantana JM, Sluka KA. Central mechanisms in the maintenance of chronic widespread noninflammatory muscle pain. *Curr. Pain Headache Rep.* 12, 338–343 (2008).
- 95 Sluka KA. Central mechanisms involved in pain processing. In: *Pain Mechanisms and Management for the Physical Therapist*. Sluka KA (Ed.) IASP Press, Washington, DC, USA, 41–72 (2009).
- 96 Sluka KA. Peripheral mechanisms involved in pain processing. In: *Pain Mechanisms and Management of Pain for the Physical Therapist*. Sluka KA (Ed.) IASP Press, Washington, DC, USA, 19–40 (2009).
- 97 Rutjes AW, Nuesch E, Sterchi R *et al.* Transcutaneous electrostimulation for osteoarthritis of the knee. *Cochrane Database Syst. Rev.* 4, CD002823 (2009).

- 98 Osiri M, Welch V, Brosseau L *et al.* Transcutaneous electrical nerve stimulation for knee osteoarthritis. *Cochrane Database Syst. Rev.* 4, CD002823 (2000).
- 99 Adedoyin RA, Olaogun MO, Fagbeja OO. Effect of interferential current stimulation in management of osteo-arthritic knee pain. *Physiotherapy* 88, 493–499 (2002).
- 100 Bal S, Turan Y, Gurgan A. The effectiveness of transcutaneous electrical nerve stimulation in patients with knee osteoarthritis. *J. Rheum. Med. Rehab.* 1–5 (2007).
- 101 Garland D, Holt P, Harrington JT, Caldwell J, Zizic T, Cholewczynski J. A 3-month, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of a highly optimized, capacitively coupled, pulsed electrical stimulator in patients with osteoarthritis of the knee. *Osteoarthr. Cartil.* 15, 630–637 (2007).
- 102 Itoh K, Hirota S, Katsumi Y, Ochi H, Kitakoji H. A pilot study on using acupuncture and transcutaneous electrical nerve stimulation (TENS) to treat knee osteoarthritis (OA). *Chin. Med.* 3, 2 (2008).
- 103 Ng MM, Leung MC, Poon DM. The effects of electro-acupuncture and transcutaneous electrical nerve stimulation on patients with painful osteoarthritic knees: a randomized controlled trial with follow-up evaluation. *J. Altern. Complement. Med.* 9, 641–649 (2003).
- 104 Quirk AS, Newman RJ, Newman KJ. An evaluation of interferential therapy, shortwave diathermy, and exercise in the treatment of osteoarthritis of the knee. *Physiotherapy* 71, 55–57 (1985).
- 105 Smith CR, Lewith GT, Machin D. TNS and osteo-arthritic pain. Preliminary study to establish a controlled method of assessing transcutaneous nerve stimulation as a treatment for the pain caused by osteo-arthritis of the knee. *Physiotherapy* 69, 266–268 (1983).
- 106 Palmer S, Domaille M, Cramp F *et al.* Transcutaneous electrical nerve stimulation as an adjunct to education and exercise for knee osteoarthritis: a randomised controlled trial. *Arthritis Care Res. (Hoboken)* 66(3), 387–394 (2013).
- 107 Kumar D, Marshall HJ. Diabetic peripheral neuropathy: amelioration of pain with transcutaneous electrostimulation. *Diabetes Care* 20(11), 1702–1705 (1997).
- 108 Julka IS, Alvaro M, Kumar D. Beneficial effects of electrical stimulation on neuropathic symptoms in diabetes patients. *J. Foot Ankle Surg.* 37(3), 191–194 (1998).
- 109 Forst T, Nguyen M, Forst S, Disselhoff B, Pohlmann T, Pfützner A. Impact of low frequency transcutaneous electrical nerve stimulation on symptomatic diabetic neuropathy using the new Salutaris device. *Diabetes Nutr. Metab.* 17(3), 163–168 (2004).
- 110 Carbonario F, Matsutani LA, Yuan SL, Marques AP. Effectiveness of high-frequency transcutaneous electrical nerve stimulation at tender points as adjuvant therapy for patients with fibromyalgia. *Eur. J. Phys. Rehabil. Med.* 49, 197–204 (2013).
- 111 Lauretti GR, Chubaci EF, Mattos AL. Efficacy of the use of two simultaneously TENS devices for fibromyalgia pain. *Rheumatol. Int.* 33, 2117–2122 (2013).
- 112 Lofgren M, Norrbrink C. Pain relief in women with fibromyalgia: a cross-over study of superficial warmth stimulation and transcutaneous electrical nerve stimulation. *J. Rehabil. Med.* 41, 557–562 (2009).
- 113 Mutlu B, Paker N, Bugdayci D, Tekdos D, Kesiktas N. Efficacy of supervised exercise combined with transcutaneous electrical nerve stimulation in women with fibromyalgia: a prospective controlled study. *Rheumatol. Int.* 33, 649–655 (2013).
- 114 Norrbrink C. Transcutaneous electrical nerve stimulation for treatment of spinal cord injury neuropathic pain. *J. Rehabil. Res. Dev.* 46(1), 85–93 (2009).
- 115 Celik EC, Erhan B, Gunduz B, Lakse E. The effect of low-frequency TENS in the treatment of neuropathic pain in patients with spinal cord injury. *Spinal Cord* 51(4), 334–337 (2013).
- 116 Chesterton LS, Lewis AM, Sim J *et al.* Transcutaneous electrical nerve stimulation as adjunct to primary care management for tennis elbow: pragmatic randomised controlled trial (TATE trial). *BMJ* 347, f5160 (2013).
- 117 Schneider MP, Tellenbach M, Mordasini L, Thalmann GN, Kessler TM. Refractory chronic pelvic pain syndrome in men: can transcutaneous electrical nerve stimulation help? *BJU Int.* 112(2), E159–E163 (2013).
- 118 Gemmell H, Hilland A. Immediate effect of electric point stimulation (TENS) in treating latent upper trapezius trigger points: a double blind randomised placebo-controlled trial. *J. Bodyw Mov. Ther.* 15(3), 348–354 (2011).