

Stimulation-produced analgesia: acupuncture, TENS and related techniques

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Abstract

Stimulation-produced analgesia (SPA) is a term that describes many techniques, both non-invasive and invasive. These techniques relieve pain via both peripheral and central mechanisms. Simple antidromic conduction of non-painful stimuli (electrical or physical) and gate control of noxious impulses typically produce rapid analgesia of short duration. Longer-term effects are dependent on production of endogenous opioids at spinal cord and brain level and activation of non-opioid transmitter systems in the limbic system and at the spinal gate. There is no scientific evidence that metaphysical (without form or substance) energy pathways play any role in SPA. Methods of producing analgesia by nerve stimulation include non-invasive or minimally invasive techniques such as acupuncture, transcutaneous electrical nerve stimulation (TENS) and acupressure. Good evidence indicates that they are useful as a sole or supplementary analgesic technique for many painful conditions, both acute and chronic. Electronic stimulators may also be permanently implanted at peripheral nerves, into the epidural space or into the brain. These invasive techniques are useful for refractory pain conditions, mostly of neuropathic origin.

Keywords acupuncture; analgesia; electrical stimulation therapy; opioid peptides; pain

Relieving pain by stimulation of nerves is not a new concept; 'rubbing a pain better' is instinctive. The use of needling is another well-established analgesic technique; the first textbook on acupuncture by the Yellow Emperor was written before 100 BC.¹ Electrical analgesia was documented even earlier by Aristotle who described the use of electric fish as a treatment for the pain of gout.²

Neurophysiology of stimulation-produced analgesia (Figure 1)

It is likely that analgesia after stimulation of nerves is produced via multiple mechanisms at peripheral and central sites. Although

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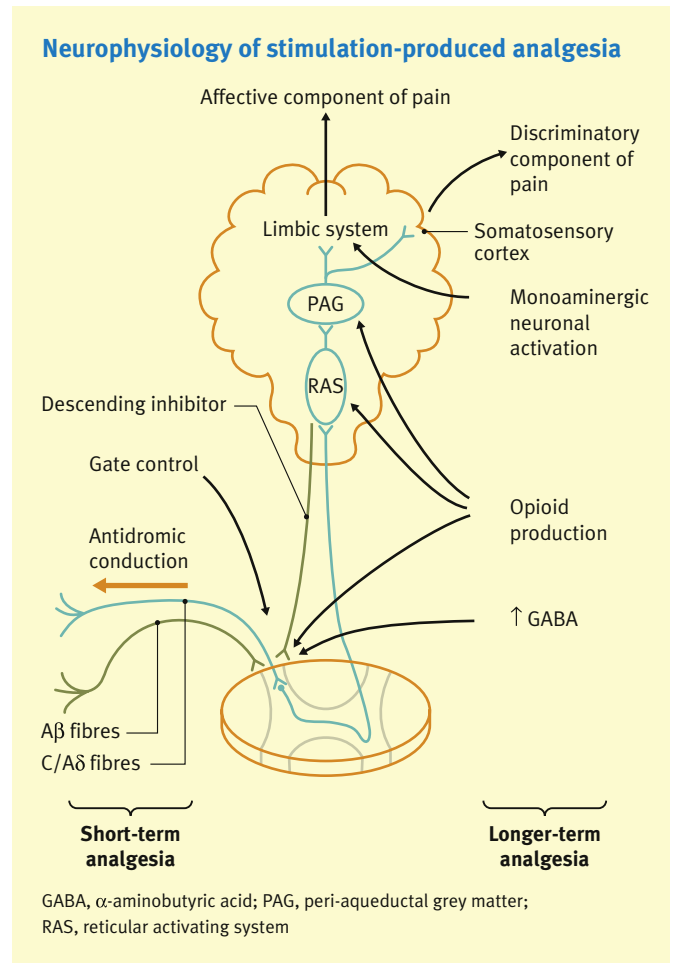


Figure 1

the gate theory was a convenient explanation for stimulation-produced analgesia, Patrick Wall, one of the theory's proponents, was aware that the situation was more plastic than the theory suggests. Mechanisms that are involved may include the factors listed below.

For short-term effects (e.g. whilst transcutaneous electrical nerve stimulation is on or needles are in the patient):

- Gate control. Stimulation of Aβ fibres activates inhibitory neurons in the substantia gelatinosa (lamina II) of dorsal horn. This causes release of non-opioid inhibitory neurotransmitters, leading to inhibition of upward transmission of painful C-fibre impulses.²
- Intense non-painful stimulation proximal to a site of tissue injury leads to antidromic conduction along nerve fibres. This directly interferes with impulse propagation of noxious stimuli (the 'busy-line' effect).²

For longer-term effects (e.g. analgesia a few days after acupuncture):

- Production of endogenous opioids (e.g. enkephalin, endorphin and dynorphin) at the peri-aqueductal grey and reticular activating systems and at the spinal 'gate'.³ Several studies support this mechanism: CSF transfusion from acupuncture-treated animals to non-treated ones leads to analgesia in the recipients^{1,2}; acupuncture and TENS (transcutaneous electrical nerve stimulation) are partially reversed by naloxone; cross-tolerance develops between

opioids and regular TENS; and cholecystokinin (an anti-opioid) antagonizes acupuncture analgesia in animals.⁴

- Monoaminergic neurons in the thalamus, hypothalamus and brainstem are also activated by needle acupuncture.⁵
 - Functional MRI and PET studies show considerable overlap in brain regions activated by true acupuncture or placebo needling (using telescopic needles of Von Frey filaments). However, blinded volunteers showed more extensive activation in limbic areas with true acupuncture than with sham. In particular, the reticular activating system seems to be involved in both acupuncture and placebo effects, whereas activation in the amygdala and hypothalamus seems to be specific to acupuncture analgesia.⁵
- Spinal cord stimulation (SCS) has several putative mechanisms:
- SCS would be successful for nociceptive pain if simple spinal gating was the mechanism involved. However, it is mainly used for various forms of neuralgia, and therefore probably does not work at a spinal level.⁶
 - Activation of second-order neurons in the dorsal horn, selective inhibition of abnormally hypersensitive neurons in the dorsal horn and increased release of γ -aminobutyric acid (GABA) in spinal neurons are observed in animal models of SCS.⁶
 - SCS analgesia is probably not mediated by endogenous opioids.⁶
 - Descending inhibition from supra-spinal centres via the pre-tectal zone and posterior columns may also play an important role.

Types of stimulation analgesia (Figure 2)

TENS

- Definition: pulsed electrical current passed across intact skin via adhesive, conductive electrodes. There are many different modalities and devices available (Figure 3).
- High-frequency stimulation selectively activates A β fibres; the predominant analgesic effect is probably via spinal gating. Analgesia is typically fast in onset and of short duration (Table 1).²
- The commonest mode is 'standard TENS', which involves high-frequency (50–200 Hz), low-amplitude pulses delivered at or close to the painful area via adhesive electrodes.² The user typically increases intensity until stimulation is felt as a strong, non-painful paraesthesia covering the area of pain.⁷
- Other modes include acupuncture-like TENS (AL-TENS), intense TENS, transcranial TENS and many TENS-like devices, each with its own 'unique' electrical output characteristics. There are many claims made by manufacturers of the benefit of these devices. None are well studied, and standard TENS is indicated in the first instance.⁷
- To be maximally effective, the TENS electrodes must be placed on healthy skin with normal sensation, as close to the painful area as possible. If this is impossible, alternatives include stimulation proximal to the area of pain, or stimulation of the corresponding position on the contralateral side.
- TENS is a low-risk therapy. Its risks usually compare favourably with the risks of other treatments, including drug therapy. Nevertheless, relative contraindications include the presence of a pacemaker or implantable defibrillator, cardiac arrhythmias and epilepsy.
- Inappropriate electrode sites include the anterior neck (risk of stimulating the carotid body or laryngeal nerves), across a pregnant uterus (risk of causing inappropriate uterine contraction)

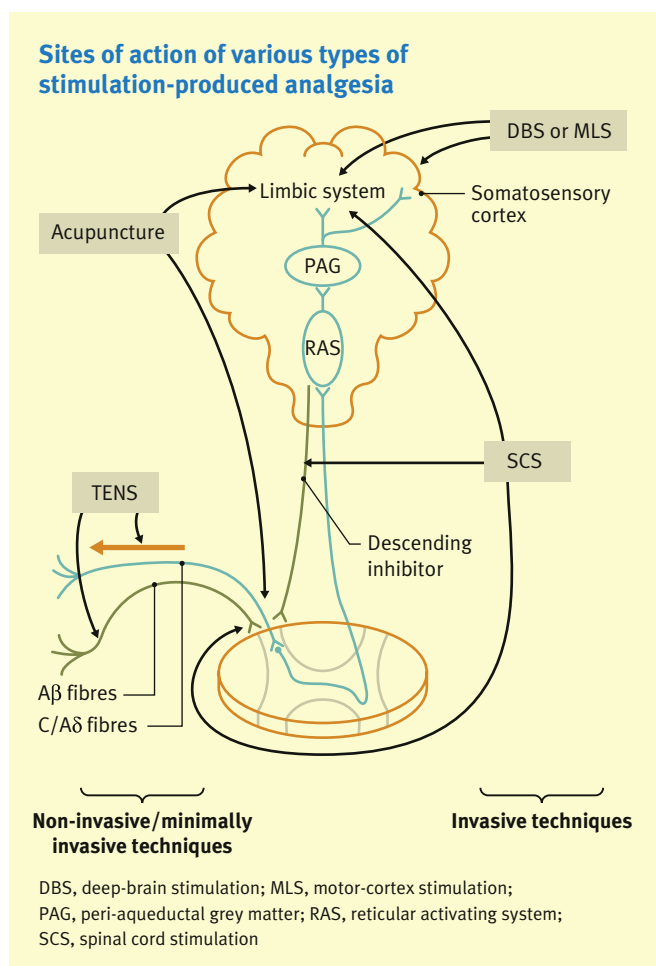


Figure 2

or anteroposterior stimulation across the chest (risk of cardiac arrhythmias or interference with respiration).

Acupuncture

- The term acupuncture derives from the Latin *acus* (needle) and *punctura* (pricking); it refers to insertion of solid needles into specific acupuncture points.
- Traditional Chinese medicine (TCM) theory behind acupuncture is that the needles rebalance the flow of vital energy (*qi*) through non-physical pathways (*meridians*) in the body and organs (as defined by TCM rather than Western medicine), so curing disease. There is little evidence that knowledge of TCM is needed to provide effective acupuncture.
- The modern understanding is quite different from the traditional metaphysical theories of TCM. Acupuncture points are likely to be functional areas rather than anatomical structures, no different from surrounding tissue on microscopy, but with lowered electrical resistance.⁸
- In practice, acupuncture points are located on the basis of anatomical landmarks, reference to meridians and at points which will elicit a specific needling sensation (*de qi*, typically a dull ache or sensation of heaviness) when a point is located.
- The needles are typically made of stainless steel, solid, and fine gauge (0.15–0.3 mm diameter).

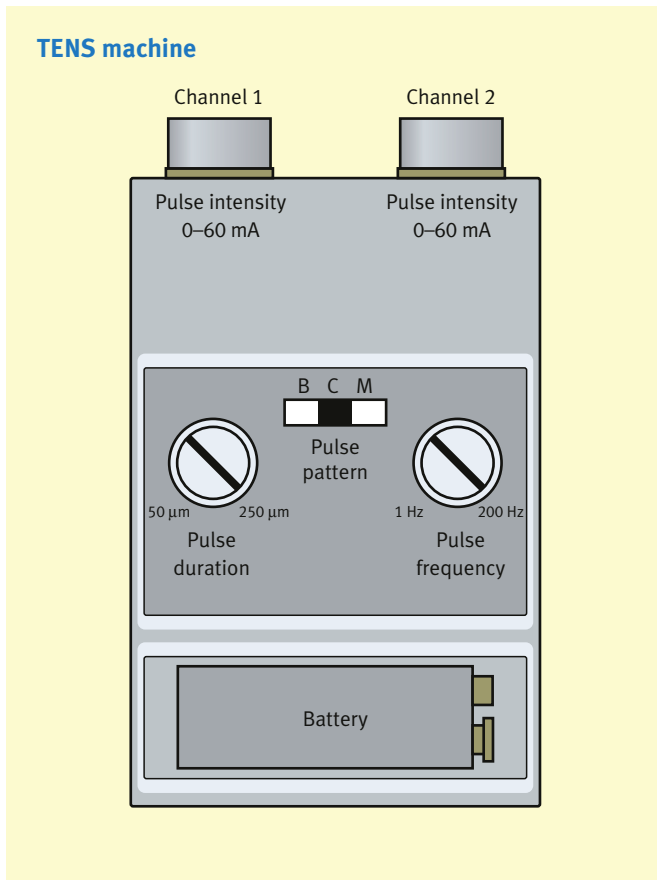


Figure 3

- The acupuncture points used may be close to the painful structure (local needling), or distant but innervated by the same spinal cord segment (segmental needling). Certain traditional points are also used for their systemic effects (e.g. pericardium 6 for anti-emesis).
- Needles may be inserted and left in place for a short period, or may be manually manipulated to increase needling sensation and thus titrate the 'dose' of acupuncture. Heating of needles may also be used to increase the 'dose' given.
- Stimulation of both deep polymodal receptors and A β and A δ fibres by the needles forms the afferent path of a neural circuit.⁴

High- versus low-frequency stimulation with TENS

	Low-frequency stimulation (2–4 Hz)	High-frequency stimulation (>50 Hz)
Employed during	Electroacupuncture ALTENS	Standard TENS
Mechanism of action	β -endorphin release at dorsal horn	Spinal gating Antidromic conduction Dynorphin release at dorsal horn
Onset	Delayed (hours–days)	Immediate
Duration of action	Prolonged	Short

Table 1

- Gate control seems to be less important than the production of endogenous opioids at spinal cord and in the limbic system.^{8,9}
- Needling often also produces demonstrable changes in blood flow to skin, muscle and nerve tissue, and autonomic tone.
- The immunomodulation shown after acupuncture in animal models⁸ has not been replicated in humans.¹⁰
- Further systemic effects comprise: anti-emesis after chemotherapy and anaesthesia, during pregnancy,¹¹ and anxiolysis.¹

Electroacupuncture (EA)

- Electroacupuncture is a passage of weak pulsed electric current through acupuncture needles.
- This technique produces a slowly developing (maximal over weeks) analgesia of long duration.⁹ It was originally developed as a substitute for manual manipulation of acupuncture needles.
- Opioid production is central to the mechanism of action of electroacupuncture. The type of opioid is dependent on the frequency of current pulses: β -endorphin, enkephalin and dynorphin are released selectively by 2, 15/30 and 100 Hz, respectively (Table 1).⁴

Other methods of acupuncture point stimulation

Acupuncture points can be stimulated without piercing the skin in several ways. Acupressure (digitally or with studs) and TENS applied to acupuncture points have not been as well studied as needling. These are generally thought of as 'low-dose' acustimulation techniques. Red or infrared laser beams can reach subdermal tissues, and laser acupuncture has been shown to produce analgesia in both animal and humans. The technique shows promise, but has not been well studied.¹²

SCS

- For this technique single or dual leads with variable numbers of electrodes can be implanted and so programming can be complex.
- The aim is to produce comfortable paraesthesiae covering the area of pain.
- SCS can be placed at all spinal levels, including retrograde stimulation of sacral nerve roots.
- The patient controls the stimulation.

Peripheral nerve stimulation: pain localized to the distribution of a peripheral nerve (e.g. greater occipital, supra-scapular or genito-femoral neuralgia) may be treated by electrical stimulation, usually with implantable subcutaneous electrodes.

Deep-brain stimulation and motor-cortex stimulation techniques involve surgical implantation of stimulating electrodes into the substance of the brain to treat refractory neuropathic pain states (e.g. after stroke).

Indications and evidence of efficacy for stimulation-produced analgesia

Acute, obstetric and peri-operative pain

- There is an obvious analogy for SPA techniques with the WHO analgesic ladder (from less to more invasive: acupressure < TENS < acupuncture < electroacupuncture).
- Acupoint stimulation may be effective for nociceptive and musculoskeletal pain, but less effective for neuropathic pain.

- There are few adverse events with acupuncture or TENS, but this alone cannot justify their routine use without more evidence of efficacy.
- Trials have suffered from problems with blinding of participants. The endpoint of adequate stimulation analgesia is a sensation experienced by the patient (e.g. paraesthesiae with TENS). To blind patients in randomized trials, suboptimal stimulation has often been used.⁷
- Systematic reviews of acupuncture trials have suffered from similar problems.¹³
- Findings from a meta-analysis showed that analgesia was improved with TENS compared with a sham if optimal stimulation was applied.⁷
- More evidence is needed before these modalities can be recommended or discounted. However, their simplicity and inherent safety should prompt more good-quality randomized controlled trials.

Chronic pain

- TENS is used frequently for localized non-malignant pain of nociceptive or neuropathic origin. There is some evidence to support TENS for use in refractory angina pectoris.⁷
- Systematic reviews have concluded that acupuncture is beneficial for myofascial pain, knee osteoarthritis, dysmenorrhoea, mechanical back and neck pain, and idiopathic headache.¹¹ Acupuncture is safe and has few side effects.
- There is good evidence for the use of SCS in complex regional pain syndrome, failed back surgery with radicular pain and some other neuropathic pain states (e.g. visceral and pelvic pain). There is also evidence of improved perfusion and exercise tolerance when used for the pain of refractory angina and peripheral vascular disease.⁶

Summary

Stimulation-produced analgesia covers many techniques that have been tested informally over time (acupuncture) and some more modern innovations (SCS and deep-brain stimulation). These techniques have potential benefits in terms of avoiding the

side effects of drugs that commonly accompany pain management strategies. However, they must be subject to the same rigorous analysis of benefits and burdens as medication, and their use needs to be supported by a sound evidence base. ◆

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