
Neuropathic Pain: A New Theory for Chronic Pain of Intrinsic Origin

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Summary

Why is acupuncture accepted in the East, especially for the treatment of chronic pain, but not in the West? One reason is that the modus operandi of acupuncture is not fully understood; another is the enigmatic nature of chronic pain. This article introduces a new concept of chronic pain, and suggests how acupuncture may relieve it.

Chronic pain may arise from sources that are extrinsic to the nervous system (for example, ongoing injury or inflammation), but it can also be intrinsic and the result of abnormal hypersensitivity (supersensitivity) in neuropathic or partially denervated structures. Neuropathic pain typically affects the musculoskeletal system, and a pivotal component of this type of pain is muscle spasm or shortening. Spasm can cause pain localised to muscle, but sustained muscle spasm or shortening mechanically overloads tendons and their attachments, and can produce pain in these structures.

Since neuropathic pain is different from nociception or inflammation, its treatment is also distinct (desensitisation of supersensitivity). Most physical treatment modalities for this type of pain, such as heat, massage or transcutaneous electrical nerve stimulation (TENS), desensitise by reflex stimulation of the affected part via its intact innervation. However these modalities are passive and limited in scope. Stimulation ends when their application is terminated. In contrast, injection techniques, including acupuncture, are more effective and long-lasting, because the tissue injury that they produce can unleash the body's healing source of bio-energy through the current of injury. Tissue injury also releases the platelet-derived growth factor (PDGF), which can promote healing.

KEYWORDS: CHRONIC PAIN, NEUROPATHY, SPONDYLOSIS, MUSCLE SPASM, ACUPUNCTURE, DEGENERATIVE CHANGES, OSTEOARTHRITIS.

Introduction

"The bane of pain is in the brain." The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described by the patient in terms of such damage." The definition

Sommaire

Pourquoi l'acupuncture est-elle acceptée dans les pays de l'Est, surtout pour le traitement de la douleur chronique, mais non dans l'Ouest? Le fait que le modus operandi de l'acupuncture n'est pas pleinement compris en est un; le caractère énigmatique de la douleur chronique en est un autre. Dans son article, l'auteur présente un nouveau concept de la douleur chronique et suggère de quelle façon l'acupuncture peut la soulager.

Les causes de la douleur chronique peuvent être extrinsèques au système nerveux (i.e. lésion persistante ou inflammation), mais aussi intrinsèques suite à une hypersensibilité (supersensitivité) des structures atteintes de neuropathies ou d'énervation partielle.

La douleur neuropathique frappe typiquement le système musculo-squelettique et le spasme, ou le raccourcissement musculaire, est partie intégrante de ce type de douleur. Le spasme peut causer une douleur localisée au muscle, mais le spasme ou le raccourcissement musculaire prolongé peut aussi surcharger mécaniquement les tendons et leurs attaches et produire une douleur dans ces structures.

La douleur neuropathique est différente de la douleur nociceptive ou inflammatoire et son traitement aussi est différent (désensibilisation de la supersensibilité). La plupart des modes de traitement de ces douleurs, comme la chaleur, les massages ou l'électrostimulation périphériques désensibilisent par stimulation réflexe de la partie atteinte, via son innervation intacte. Ces modes de traitement sont toutefois passifs et limités dans leur portée; la stimulation cesse une fois leur application terminée. Par contraste, les techniques par piqûres, dont l'acupuncture, ont un résultat meilleur et de plus longue durée, parce que le traumatisme tissulaire qu'elles produisent peut déclencher, par son courant, une source corporelle de bioénergie curative. La lésion tissulaire libère en plus le facteur de croissance dérivé des plaquettes qui peut favoriser la guérison.

emphasises the subjective nature of pain, and recognises its existence in the absence of a detectable physical cause.

Medical diagnosis traditionally presumes that pain is a signal of tissue injury conveyed to the central nervous system (CNS) via a healthy nervous system. Although

pain may be linked causally to tissue injury, it need not be so. Injury does not always generate pain, nor does pain always signal injury. Also, when there is abnormal function in the nervous system, pain perception can arise from non-noxious input, and spurious pain can even arise from within the body. This article invokes the physiology of the abnormal neural responses that can occur in neuropathy to explain intrinsic pain and to present a rationale for its treatment.

Three Phases

Wall saw pain as a reaction pattern of three sequential behavioural phases: immediate, acute and chronic (1). Each phase may exist independently, or in any combination and proportion with the others.

Wall's immediate phase, or nociception, is the perception of a noxious input. Nociceptive signals are sent to the brain via two main routes. One, the spino-reticulo-thalamic tract, is evolutionarily primitive, has many synaptic relays, and ends at the lower parts of the brain, where it arouses the emotions and switches on the body's response of "fight or flight". Its effects may not diffuse into the conscious brain. For example, nociceptive perception may not occur "in the heat of battle", when there are other pressing distractions. The second tract, the neo-spinothalamic, evolved later, and is more efficient, requiring only three relays to reach the sensory cortex that locates the pain. Thus, pain location can occur before its realisation.

Nociception is usually transient, unless there is tissue injury and damaged cells with the release of allogenic substances (for example, histamine and bradykinin) that induce inflammatory pain, or Wall's acute phase. Anti-inflammatory drugs have their application in this phase, but the abatement of inflammation with drugs can be counter-productive, because inflammation is the pre-

lude to healing.

After injury, most people heal rapidly and become pain-free. In some, pain persists beyond the usual time for the healing process and becomes intractable. This chronic pain, or Wall's third phase, is likely to occur if there are:

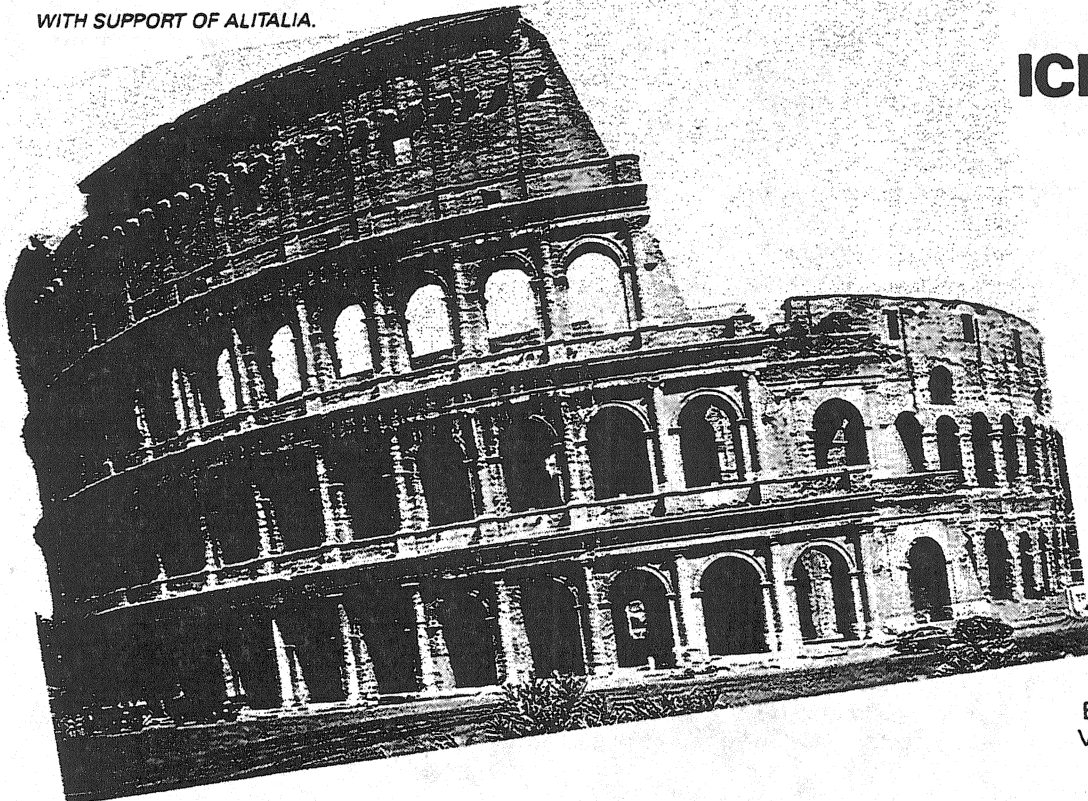
- ongoing nociception and inflammation
- psychological factors such as a somatisation disorder, depression or operant learning processes
- functional or structural disturbances in the nervous system. These generally occur in the peripheral nervous system (for example, peripheral neuropathy), and the term "neuropathic pain" is applied to this category.

Neuropathic Pain

The normal physiological properties of nerve and muscle depend on intact innervation to provide a regulatory or trophic effect. Formerly, it was supposed that the trophic factor was lost with total denervation, leading to "denervation supersensitivity" (2). More recently, it has been shown, that any measure that blocks the flow of motor impulses, and deprives the effector organ of excitatory input for some time, can cause "disuse supersensitivity" in that organ, and in associated spinal reflexes (3). With supersensitivity, nerves and innervated structures become overly sensitive and react abnormally to stimuli, according to Cannon and Rosenblueth's law of denervation (2):

"When in a series of efferent neurons a unit is destroyed, an increased irritability to chemical agents develops in the isolated structure or structures, the effect being maximal in the part directly denervated." Cannon and Rosenblueth recognised four types of increased sensitivity: the amplitude of responses is

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unchanged, but their course is prolonged (superduration of response); the threshold for the stimulating agent is lower than normal (hyper-excitability); lessened stimuli that do not have to exceed a threshold produce responses of normal amplitude (increased susceptibility); and the ability of the tissue to respond is augmented (super-reactivity). They also showed that super-sensitivity can occur in many structures of the body including skeletal muscle, smooth muscle, spinal neurons, sympathetic ganglia, adrenal glands, sweat glands, and brain cells. Furthermore, they showed that denervated structures over-react to many chemical and physical inputs including stretch and pressure.

Probably the most crucial structure to develop super-sensitivity is striated muscle. Apart from the pain and tenderness that may occur in muscle (possibly from the compression of supersensitive nociceptors), neuropathy increases muscle tone (spasm) and concurrent muscle-shortening. Muscle-shortening is a fundamental feature of musculoskeletal pain syndromes and may be palpated as rope bands in muscle. These bands, usually pain-free, may become tender and painful (trigger points) (4). When muscle bands are fibrotic and painful, the condition is known as fibromyositis, fibrositis, or diffuse myofascial pain syndrome (5).

Muscle-shortening puts mechanical stress on tendons and their attachments, and can generate conditions such as tendonitis, tenosynovitis and epicondylitis. Shortening in muscles that act on a joint can increase joint pressure, upset alignment, and cause arthralgia. Muscle-shortening in para-spinal muscles can compress a disc space and narrow the intervertebral foramina. The nerve root may then be irritated through pressure of a bulging disc, or compressed after it emerges. A vicious circle can thus arise: pressure on a nerve root causes neuropathy; neuropathy leads to pain and spasm in target muscles, including paraspinal muscles; spasm in paraspinal muscles compresses the nerve root. Often, pain relief is only possible when spasms in both peripheral and paraspinal muscles are released.

Neuropathy also affects the quality of collagen. The amount of collagen in soft and skeletal tissues may be reduced. Replacement collagen has fewer cross-links and is weaker than normal mature collagen (6). Because collagen gives the strength to ligaments, tendons, cartilage and bone, neuropathy can expedite degeneration in weight-bearing and activity-stressed parts of the body, for example, spondylosis, discogenic disease and osteoarthritis. Such prosaic afflictions are viewed as primary conditions, but are most likely secondary to neuropathy.

In denervation, a muscle can become "twitchy" for many reasons (7). Even at rest, when there is no incoming signal, muscle fibres may generate spontaneous contractions or "fibrillations". This may be the result of a malfunction of the sodium pump and changes in the electrical properties of muscle membrane. Upon arrival of an incoming electric signal, released acetylcholine may act, not only at motor end-plates, but may activate entire muscle fibres at newly formed clusters of receptors, or "hot spots". This abnormal response may be exaggerated, because the amount of available acetylcholine esterase may be reduced. Motor units may be abnormally large. When muscle cells in a motor unit become denervated, the deprived sector may be invaded by surviving axons from adjacent units. These

axons send out sprouts, thus enlarging the territory of the motor unit (territorial invasion). Contraction of these enlarged motor units is seen in electromyography as "giant waves".

Similar abnormalities may also occur in smooth muscle (7). When vascular smooth muscle tone is increased, the result is vasoconstriction. This gives neuropathic pain its cardinal feature — affected parts are colder (as may be shown by thermography). When lymphatic drainage is impaired, there can be local oedema (trophic oedema or trophedema). These can be confirmed by the peau d'orange effect or matchstick test (8). Trophedema is non-pitting to digital pressure, but when a blunt instrument, for example, the end of a matchstick is used, the indentation produced is clear-cut and persists for minutes.

Supersensitivity may likewise affect nerve fibres, which may become sensitive to chemical transmitters at every point along their length instead of only at the terminals (7). Sprouting may also occur in nerves, and denervated neurons may accept contacts from other types of nerves including autonomic and sensory nerve fibres. These possible short circuits between sensory and autonomic (vasomotor) nerves may contribute to reflex sympathetic dystrophy or causalgic pain (7).

Discussion of other possible mechanisms for super-sensitivity and abnormal impulse generation (for example, changes in ion channels, membrane capacitance, voltage-dependent channel gating, current-dependent mechanisms, ephaptic transmission and others) is outside the scope of this article. They were the focus of a meeting of scientists and clinicians, in which many syndromes caused by abnormal discharges were identified (7).

Proposed Theory

Unlike nociception and inflammation, whose noxious sources are extrinsic to a normal nervous system, neuropathic pain may be the result of an abnormally sensitive nervous system distorting non-noxious stimuli into false pain alarms, and spurious pain signals may occur spontaneously.

Peripheral neuropathy can occur from many causes, but probably the most common cause is mechanical irritation, especially of the nerve root (radiculopathy) in spondylosis (the structural disintegration and morphological changes in the intervertebral disc and surrounding structures). Because spondylosis is a consequence of "wear and tear", neuropathic pain is more common in middle-aged individuals.

Neuropathy, and muscle spasm and shortening can account for many musculoskeletal pain syndromes that are now labelled with non-descriptive names often ending in -algia or -itis, for example, metatarsalgia, arthralgia, or lateral epicondylitis. When muscle-shortening is associated with neuropathic degradation of collagen, degenerative changes can occur, for example, osteoarthritis. It is also possible that other unpleasant perceptions not classified as pain, such as tinnitus, vertigo and itch, may be explained by Cannon's law.

Implications

Since the mechanism of neuropathic pain is different from nociception and inflammation, its diagnosis and treatment require different approaches. Diagnosis is

mainly clinical, and can be confirmed by signs of neuropathy (that are different from the well-known ones of outright denervation, such as absent reflexes and loss of sensation). These subtle signs can be found if the clinician knows where to look, and what to look for (8). Laboratory and radiological tests are unhelpful in early neuropathy.

Treatment of neuropathic pain is also different. Super-sensitivity requires desensitisation by the alleviation of neuropathy. Nerve entrapments are usually obvious, and may be surgically released, thereby restoring nerve function. However, neural irritation and neuropathy often occur without entrapment, and surgery is not indicated.

Lomo has shown that supersensitivity, and all the other features of denervation in muscle, can be reversed by stimulating the muscle with electricity. Continuous electrical stimulation substituted for the trophic factor that is deminished or absent in neuropathy (9). In a comparable manner, physical therapy that is used to treat musculoskeletal aches and pain may be likened to electrical stimulation.

All physical and counter-irritational therapies, including acupuncture, may achieve their effect by reflex-stimulation, since they are effective only if the nerve to the painful part is still intact. Their application excites receptors (in skin and muscle) and stimulates their target indirectly. For example, massage and focal pressure activate tactile and pressure receptors; exercise, traction and manipulation stimulate muscle spindles and Golgi organs; heat (including ultrasound) and cold act on thermal receptors. These stimuli are sensed by their specific receptors and relayed to the spinal cord. As with the patellar reflex, stimulation reaches the affected part via a reflex. It is the reflex response in efferent fibres to the affected structure that stimulates the therapeutic target. Even acupuncture is effective only if the nerve to the painful part is still functioning, and its effect can be blocked by a local anesthetic (10).

Unfortunately, all external forms of physical therapy have a drawback. They are passive, and when application is halted, stimulation ceases. Ideally, stimulation should use the body's own bio-energy, which may be recruited in the form of the "current of injury", first described by Galvani in 1797. This current is generated when tissue is damaged by injection techniques including acupuncture. Unlike external forms of stimulation, needle stimulation penetrates into muscle. Injury potentials that are discharged on needle insertion can relax muscle spasm instantly or within minutes. It also induces a sympatholytic effect that spreads throughout the body segment, releasing vasoconstriction. Pain in muscles, tendons and joints caused by muscle tension is eased when the shortened muscles are relaxed. Subjective and objective improvement (which can sometimes occur within minutes) can be confirmed, for example, by an increase in joint range, and minor degrees of joint effusion may resolve. Endogenous opiates, now used to explain acupuncture, cannot account for all its effects (11).

Needle stimulation can last for several days until the miniature wounds heal. Needling may have another unique benefit unavailable to other forms of local therapy. It delivers to the injured area the platelet-derived growth factor (PDGF), which induces deoxyribonucleic acid (DNA) synthesis and stimulates collagen formation (12). Body cells are normally exposed to a filtrate of

plasma (interstitial fluid) and would only see the platelet factor in the presence of injury, hemorrhage and blood coagulation.

Conclusion

The neuropathy pain model has been proposed as an hypothesis to explain chronic musculoskeletal pain problems of obscure origin. It enables many musculoskeletal pain syndromes to be grouped under one etiologic classification (neuropathy). Like all models, however, this one needs refinement.

It is probable that all forms of physical therapy act through one common mechanism (reflex-stimulation). These therapies soothe pain temporarily, but a needle technique is more effective. It stimulates through the current of injury, which may last for days. Needling also releases growth factors that may promote healing. For meaningful results, however, any underlying cause of neuropathy must be eradicated.

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