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REVIEW OF THE LITERATURE

Spinal Pain Syndromes: Nociceptive, Neuropathic, and Psychologic Mechanisms

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ABSTRACT

Background: Pain continues to be the main symptom reported by patients. Frequently, clinicians incorrectly diagnose patients and resulting treatments are ineffective, which may promote the development of chronic pain. This situation may arise as a result of a lack of clarity in the literature regarding pain syndromes.

Objective: To discuss the differences between nociceptive, neuropathic, and psychologic induction of pain and provide important clinical correlates to aid in diagnosis and treatment.

Data Sources: The data were accumulated over a period of years by reviewing contemporary articles and books and subsequently retrieving relevant papers. Articles also were selected from MEDLINE searches and from manual library searches.

Data Synthesis: Nociceptive pain syndromes are responsible for the majority of pain complaints in clinical practice. Care must be taken to avoid the common mistake of the diagnosis of neuropathic pain, which can lead to inappropriate treatments.

Conclusions: Although the treatment of neuropathic pain is difficult, sufficient evidence in the literature demonstrates that the treatment of nociceptive pain should be multimodal and involve spinal manipulation, muscle lengthening/stretching, trigger point therapy, rehabilitation exercises, electrical modalities, a variety of nutritional factors, and mental/emotional support. (J Manipulative Physiol Ther 1999;22:458-72)

Key Indexing Terms: Pain; Referred Pain; Nociception; Joints

INTRODUCTION

The subject of pain has always been a focus of attention because of its debilitating nature. According to Bonica,

> Pain has been a major concern of humankind since our beginnings, and it has been the object of ubiquitous efforts to understand and to control it. Indeed, it is even older, for there is reason to believe that pain is inherent in any life linked with consciousness.[1]

Melzack stated that "prolonged pain destroys the quality of life. It can erode the will to live, at times driving people to suicide."[2] Albert Schweitzer, quoted by Melzack, provided an even more graphic description, stating that pain is "a more terrible lord of mankind than even death itself."[2] Weinstein quotes Ralph Waldo Emerson: "he has seen but half the universe who has not been shown the house of pain."[3]

Although the topic of pain has always been a focus for researchers and philosophers, much confusion still exists about the pathophysiological nature of pain. Indeed, according to Wall,

> we are faced with a crisis epidemic of painful states where no peripheral pathology has been discovered. . . these conditions now include tension headaches, migraine, temporomandibular joint syndrome, trigeminal neuralgia, the majority of neck and back pains, fibromyalgia, interstitial cystitis, etc.[4]

The crisis is obvious. If we cannot determine the cause of the pain, it will be impossible to provide a treatment program that has any chance of offering short- or long-term relief.

In orthopedic surgeon Vert Mooney's 1986 presidential address, "Where is the pain coming from," for the International Society for the Study of the Lumbar Spine, he stated

> In the case of low-back disease, although we are aware of it, the depth of our ignorance must be emphasized. In the United States in the decade from 1971 to 1981, the numbers of those individuals disabled from low-back pain grew at a rate 14 times that of the population growth. This is a greater growth of medical disability than any other. Yet this growth occurred in the very decade when there was an explosion of ergonomic knowledge, labor-saving mechanical assistance devices, and improved diagnostic equipment. We apparently could not find the source of the pain.[5]

Using this as an example, we must ask where the pain comes from. Some say pain comes from the zygapophyseal joints, some from the muscles, others from the nerve root compression from the intervertebral foramen or disk, and finally, others from the disk itself. Ultimately, the theory that we should support one opinion over another is foolish. Each patient is different, and we need to do our best to determine the cause of pain for every patient. To make an appropriate diagnosis, clinicians must understand the nature of pain

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itself and the various mechanisms by which pain can be evoked. This knowledge will permit the doctor to narrow the potential causes and allow the development of an appropriate diagnosis and treatment program.

DISCUSSION

The Nature of Pain

What is pain? Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage."[6,7] It should be emphasized that pain is always subjective.[6,7] Indeed, Mooney has referred to pain as the perception of unhappiness.[5]

LaRocca,[8] in his Presidential Address at the annual meeting of the Cervical Spine Research Society quoted Wyke's commentary on pain:

> Contrary to long-standing traditional views, it is now clear that pain as a phenomenon of human experience is not a primary sensation in the sense that vision, hearing, smell, taste, touch, pressure, thermal sensibility and kinaesthesis are. On the contrary, it is an abnormal affective state, ie, an emotional disturbance, that is called into being by the development of mechanical and/or chemical changes in the tissues of the body whose nature and magnitude are such that they give rise to activity in afferent systems within the neuraxis that are normally quiescent.[9]

The emotional/psychologic experience of pain and the realization of its bodily location occur in different parts of the brain. Whereas the emotional component of pain (the "hurt") occurs in the limbic sectors of the cerebral cortex, the sensory component of pain (where it hurts, but not the hurt itself) occurs in the sensory strip of the parietal lobe.[10]

Categories of pain syndromes. Discussions about pain syndromes often can be confusing unless consistent terms are used. From a pathogenic perspective, pain can be induced through injury of either nonneural or neural tissues. Pain caused by nonneural tissue injury, such as joint/muscle injury or visceral pathology, is referred to as nociceptive pain. Pain caused by neural tissue injury is referred to as neuropathic pain. Psychologic mechanisms can be involved in the promotion of pain. Bonica[11] and Portenoy[12] have indicated that pain syndromes are either nociceptive, neuropathic, psychogenic/psychologic in nature, or a combination of the three.

Nociceptive Pain

Pain induced by nociceptive mechanisms is the most common variety seen in clinical practice.[13-15] Terminology problems with nociceptive pain are common for students and practitioners. For example, the inaccurate term "pain receptor" often is used in the place of nociceptor when discussing the topics of nociception and pain.[16] "Pain receptor" suggests that tissue receptors can encode the experience of pain. However, tissue nociceptors are physiologically incapable of encoding the emotional experience of pain. Indeed, "activity induced in the nociceptor and nociceptive pathways by a noxious stimulus is not pain, which is always a psychologic state, even though pain most often has a proximate physical cause."[6] Clearly, pain occurs in the brain and not at the level of the tissue receptor. Thus the so-called pain receptors and pain pathways cannot exist, and terms like these should be avoided.[6]

Nociceptor activity. Contemporary researchers agree that nociceptors can be found in paraspinal tissues including skin, subcutaneous and adipose tissue, walls of intramuscular arteries, walls of blood vessels supplying the spinal joints, sacroiliac joints, the vertebral cancellous bone, walls of epidural and paravertebral veins, fibrous capsules of apophyseal and sacroiliac joints, spinal ligaments, periosteum covering vertebral bodies and arches (and attached fascia, tendons and aponeurosis), at least the outer third of the annulus fibrosis, dura mater, and epidural fibro-adipose tissue.[13-15,17-22] The same authors explain that nociceptors are excited by noxious mechanical and chemical stimuli that typically are associated with tissue injury. Tissue injury disrupts the integrity of local structures, creating noxious mechanical irritation and permitting the release of the various chemical mediators of inflammation and nociception, such as histamine, 5-hydroxytryptamine, prostaglandin E_2, and bradykinin.

Many of the various endogenous chemicals are capable of stimulating and sensitizing tissue nociceptors.[23,24] The mechanism by which the chemical mediators depolarize and/or sensitize a nociceptor is thought to occur through the interaction of the chemical mediators with chemosensitive receptors on the membrane of the nociceptor. This process results in the entry of sodium or calcium ions and/or the exit of potassium ions.[25,26] Whereas some of the chemical mediators have receptors linked directly to ion channels, the receptors for other mediators are linked to second messenger systems that modulate ion channels.[25,26] Rang et al[25,26] provide details regarding this interesting aspect of nociceptor function.

As mentioned above, nociceptors can be sensitized by the chemical mediators released after tissue injury. The term peripheral sensitization is used when referring to tissue-nociceptor sensitization.[24] "Sensitization" is defined as the lowering of nociceptor thresholds.[27] Normally, nociceptors have very high thresholds of activation; however, sensitized nociceptors can be stimulated by innocuous stimuli, such as touch and normal movements.[24] Sensitized nociceptors may also discharge spontaneously.[28,29]

The abnormal, intense nociceptive barrage created by sensitized nociceptors can stimulate and sensitize neurons in the dorsal horn, intermediate region, and ventral horn of the spinal cord.[30] The sensitization of such central nervous system neurons, ie central neurons, is called central sensitization.[24] Most authors now agree that central sensitization manifests in CNS neurons as increased spontaneous activity, reduced thresholds or increased responsitivity to afferent inputs, prolonged after discharges to repeated stimulation, and the expansion of the receptive fields of dorsal horn neurons.[31]

The typical outcome of nociceptive activity is pain. However, the peripheral and central sensitization of the nociceptive system can lead to exaggerated forms of pain, such as

Table 1. *Negative effects of immobilization*

Joints	
	Shrinks joint capsules
	Increases compressive loading
	Leads to joint contracture
	Increases synthesis rate of glycosaminoglycans
	Increase in periarticular fibrosis
	Irreversible changes post-8-wk immobilization
Ligament	
	Lowers failure or yield point
	Decreased thickness of collagen fibers
Disc biochemistry	
	Decreases oxygen
	Decreases glucose
	Decreases sulfate
	Increases lactate concentration
	Decreases proteoglycan content
Bone	
	Decreases bone density
	Eburnation
Muscle	
	Decreased thickening of collagen fibers
	Decreased oxidative potential
	Decreased muscle mass
	Decreases sarcomeres
	Decreases cross-sectional area
	Decreased mitochondrial content
	Type 1 muscular atrophy
	Type 2 muscular atrophy
	20% loss of muscle strength per week
Cardiopulmonary	
	Increased maximal heart rate
	Decreased Vo_{2max}
	Decreased plasma volume

From Liebenson C. Pathogenesis of chronic back pain. J Manipulative Physiol Ther 1992;15:299-308.

allodynia and hyperalgesia. Allodynia is defined as "pain produced by a stimulus that is normally not painful,"[27] such as with normal joint movement or upon spinal palpation. When a patient has pain from innocuous palpation, the clinician may have encountered a sensitized nociceptive system.

Hyperalgesia was originally defined by Hardy et al as "a state of increased pain sensation induced by either noxious or ordinarily nonnoxious stimulation of peripheral tissue."[32] In the early 1980s, hyperalgesia was redefined by the International Association for the Study of Pain as an "increase in the pain produced by a stimulus that is normally painful."[32] The clinical perspective is that it is not necessary to examine for hyperalgesia. In other words, when innocuous palpation causes pain, ie allodynia, the doctor knows that the nociceptive system is sensitized. Therefore, it is not necessary to palpate the area by applying increased or noxious pressure so that the patient has increased pain.

Nociceptive pain syndromes. Not surprisingly, nociceptive pain can be defined as "pain that is believed to be commensurate with the presumed degree of ongoing activation of peripheral nociceptors."[33] Nociceptive pain may result from injury of somatic and visceral structures. The commonly used terms "somatic pain" and "visceral pain" actually refer to nociceptive pain syndromes.[33] "Arthritis and some types of cancer pain (eg, bone pain) exemplify somatic nociceptive pains."[33] In fact, numerous terms to describe pains thought to be of nociceptive origin such as myofascial pain, muscle pain, fibromyalgia, trigger points, joint pain, cervicogenic headaches, referred pain, sclerotomal pain, sclerotogenous pain, deep pain, diffuse pain, primary disk pain, mechanical low-back pain, neck pain, simple backache, somatic pain, and somatic-referred pain exist. Clearly, most patients who enter a clinician's office have pain that is nociceptive in nature.

Nociceptive pain often is more devastating than the perceived severity of the inciting lesion. However, researchers and clinicians continue to be preoccupied with the idea that the severity of the pathology should be the same as the severity of pain. Overt structural changes, ie, disk herniation, fracture, tumors, or spondylosis, are not the only changes associated with tissue pathology; nor do structural changes need to be present for a pathology to exist. Thus, we must ask: what is pathology?

In 1984, Robbins et al stated that "pathology literally is the study (logos) of suffering (pathos)."[34] On a more practical level, "pathology deals with the study of deviations from normal structure, physiology, biochemistry, and cellular and molecular biology."[34] Clearly, structural changes do not need to be present for a peripheral pathology to exist. Therefore, it is surprising that contemporary pain researchers/authors believe that structural changes must be present for a peripheral pathology to exist. The first edition of *Pathologic Basis of Disease*, published in 1974, states

> All injuries, whether mild or lethal, ultimately occur at a biochemical level beyond our present range of detection. For this reason, it has not been possible to determine the precise biochemical site of action of injurious agents or the extent of cellular injury compatible with reversibility or irreversibility. Four intracellular systems are thought to be particularly vulnerable: (1) aerobic respiration involving oxidative phosphorylation and production of ATP, (2) synthesis of enzymatic and structural proteins, (3) maintenance of the integrity of cellular membranes on which the ionic and osmotic homeostasis of the cell and its organelles are dependent, and (4) preservation of the integrity of the cell's genetic apparatus.[35]

Robbins discusses overt structural pathologies, stating that "morphologic changes become apparent only after some critical biochemical system within the cell has been deranged for some time."[35] Clearly, a peripheral pathology can exist without the presence of overt structural changes. Research suggests that tissue injury leads to inflammation, nociception, and pain, all of which can reduce joint mobility and promote pathologic changes in joint complex structures through various mechanisms.[36] Table 1 lists the pathologic changes that occur as a result of immobilization. In addition, muscle imbalances, such as tightening/shortening and myofascial trigger points, often are associated with joint hypomobility/immobility.[36] Seaman has suggested that the term "joint complex dysfunction" refers to the negative effects of immobilization, inflammation, and the aforementioned muscle imbalances.[36]

Joint complex dysfunction is often accompanied by a reduction in cardiovascular fitness (Table 1) and pain, collectively referred to as the deconditioning syndrome.[37,38] Clearly, the somatic component of low-back pain can be devastating, even when no structural pathology exists, such as disk prolapse or nerve root compression. The great majority of neck and back pains existing without overt structural pathologies may be caused by joint complex dysfunction and the deconditioning syndrome, which involve nociceptive processes rather than nerve injury. It is time that medical and chiropractic doctors focus on pathophysiological changes involving nociceptive processes as the cause of most spinal pain syndromes instead of the pathoanatomical changes involving neuropathic processes.[39]

The quality of the pain associated with somatic tissue injury generally is related to the nature of the causative stimuli such that nociceptive pain can be described as sharp, aching, dull, throbbing, knife-like, crampy, and crushing.[40] The common presentation of spinal nociceptive pain is a deep, tender, dull, aching, and diffuse variety which makes it hard to localize.[13]

Frequently, the presence of so-called referred pain can lead a clinician to believe incorrectly that a patient's pain is caused by a neuropathic lesion, such as nerve root compression. Although nerve root compression can generate referred pain, nociceptive input from joint structures and muscles is also capable of generating a variety of referred pain patterns,[13,15,41,42] some of which resemble that of neurocompression.[43] In fact, referred pain as a result of nociceptive processes is more common than referred pain from a nerve lesion.[41,42,44]

Nociceptive referred pain. Nociceptive input can generate local and referred pain. The term "nociceptive referred pain" is used to distinguish it from local pain induced by nociceptive processes.

Most of the best research available to examine nociceptive-induced local and referred pain was performed prior to 1960. Several authors injected hypertonic saline, which acts as a noxious chemical irritant, into musculoskeletal tissues for the purpose of studying pain patterns.[45-50] Such a procedure permitted researchers to examine the extent to which symptoms can manifest in response to a controlled noxious stimulus that seemed to resemble actual tissue injury. Feinstein et al,[46] Inman and Saunders,[47] and Kellgren[48] observed pain patterns associated with noxious irritation of posterior spinal structures innervated by the dorsal ramus or posterior primary division of the spinal nerve. Each discovered that an injection of hypertonic saline into paravertebral muscles or interspinous structures caused both local and referred pain. The referred pain did not resemble the dermatomal patterns seen with neurocompression. Inman and Saunders suggested that this nondermatomal pattern of referred pain followed a sclerotomal distribution.

Inman and Saunders[47] explained that the sclerotome is the periosteum, ligamentous structures, and muscle attachments that are innervated by a specific spinal segment. A sclerotome is the connective-tissue structures innervated by a specific spinal level, a dermatome is a specific area of skin, and a myotome consists of the specific muscles that are innervated by a specific spinal level. Sclerotomes are more diffuse in their arrangement compared with dermatomes and myotomes, and frequently extend the entire length of an extremity. Kessler provides a succinct description of the differences between sclerotomes, dermatomes, and myotomes.[51]

Nociceptive referred pain follows a sclerotomal pattern of distribution. However, in clinical practice, patients do not always fit the pain maps that have been put forth by various authors. Thus the terms sclerotomal/sclerotogenous pain are technically inaccurate. Given the existence of semantic limitations, "nociceptive referred pain" is the most accurate term available.

When a specific spinal level is irritated, the pain can be local and may also extend partially or throughout the entire length of the extremity. The volume of saline injected accounts for both the intensity of pain and the extent of pain referral.[43,46]

The mechanisms by which nociceptive referral patterns develop is a major source of confusion. Many practitioners are under the erroneous perception that pain travels down the extremity. Lynch and Kessler provide an excellent explanation:

> When a tissue of a particular sclerotome is irritated, the patient may perceive the resulting pain as arising from any or all of the tissues innervated by the same segmental nerve. This is a result of the lack of precision in central neural connections and is not related to abnormal impulses spreading down a nerve; in other words, the problem is central, not peripheral, and nothing is wrong with most of the area from which the pain seems to arise.[52]

Gillette et al[53,54] offer a more detailed explanation of the central nociceptive connections that give rise to the illusion that pain is traveling down an extremity. Central nociceptive projection neurons, ie, second order neurons, in the dorsal horn have receptive fields. The receptive field of central neurons is related to the peripheral structures that are capable of generating an action potential in the central projection neuron. For example, a projection neuron for the fifth lumbar nerve may receive input from structures in the low-back, hip, thigh, leg, and foot. The term "hyperconvergent" describes the receptive field of such a projection neuron, which receives input from multiple peripheral structures.[53,54]

Nociceptive input of a sufficient magnitude from an injured facet joint or spinal muscle can activate such a projection neuron. Although the noxious input has been generated in spinal structures alone, the contralateral somatosensory cortex can receive information in this case via second order neurons, which indicates that the nociceptive input has come from the spine and the extremity. The so-called referred pain in the leg is an illusion; it arises as a result of the presence of a projection neuron with hyperconvergent receptive fields and not from the extremity.

Projection neurons throughout the spinal cord contain hyperconvergent receptive fields. This is especially evident in the cervical spine. The spinal nucleus of the trigeminal nerve, which contains projection neurons for the face and head, extends to approximately the third cervical segment.[55]

The receptive fields of such trigeminal projection neurons for the face and head also receive nociceptive input from cervical spine-innervated structures[55] and can create the illusion that pain is being generated in the head and face. Nociceptive input from structures innervated by C-1 through C-3, in particular, commonly give rise to head and face pain.[41,55,56] This can often be demonstrated in the clinical setting by applying mechanical pressure to the upper cervical zygapophyseal joints and suboccipital muscles and the middle trapezius, which often causes or exacerbates ipsilateral head and face pain.

Although a detailed explanation of the central mechanisms of pain referral is new, research by Feinstein et al[46] in 1954 demonstrated that the central nervous system could generate referred pain. To demonstrate that so-called referred pain does not require peripheral nerve input, Feinstein et al conducted an experiment in which "a complete acute blockade of peripheral input from an upper extremity was achieved by a brachial plexus block with local anesthesia for all sensory modalities."[46] Even injections of hypertonic saline into the extremity could not evoke pain. However, an injection of hypertonic saline into the interspinous tissues of the lower cervical vertebrae produced the characteristic pattern of perceived pain into the arm. In a later paper, Feinstein[57] further demonstrated that CNS mechanisms promote referred pain. The interspinous tissues of amputees were injected with hypertonic saline which resulted in the experience of pain and other sensations in extremities that did not exist.[57]

Nonnociceptive/mechanoreceptive pain. Many authors have suggested that pain can be induced by nonnociceptive afferents, more commonly referred to as mechanoreceptor afferents.[24,58-61] This can occur experimentally; however, the clinical situations in which this arises are not clear.

Experimental observations of cutaneous injury suggest that pain may be a result of A-β mechanoreceptor afferent activity.[24] Cutaneous injury produces two so-called zones of hyperalgesia—the primary and secondary zones. The terms primary and secondary hyperalgesia are misleading. As stated earlier, hyperalgesia is defined as an "increase in the pain produced by a stimulus that is normally painful."[32] However, the zones of primary and secondary hyperalgesia are usually discussed by researchers in the context of pain produced by innocuous input (ie, allodynia). Thus it would be more accurate to describe such regions of tissue injury and pain as zones of primary and secondary allodynia.

Primary hyperalgesia is found at the site of injury; secondary hyperalgesia develops in the uninjured tissues surrounding the area of injury. Although considerable mechanosensitivity exists in the zone of secondary hyperalgesia, research has yet to demonstrate changes in nociceptor activity in this uninjured region. Woolf states that "clinical pain involves a transformation from a situation where only nociceptors can drive the nervous system to produce pain to one where A-beta afferents can."[24] This transformation is thought to develop as a consequence of central nociceptive sensitization. As mentioned earlier, sensitized nociceptors promote a state of central sensitization. Sensitized central projection neurons develop the capability to be depolarized by A-beta mechanoreceptor afferents, resulting in the experience of pain.[24] Recent papers have advanced this hypothesis, particularly as it relates to the central mechanism by which A-beta mechanoreceptor afferents gain access to nociceptive projection neurons.[59,60] Although the theories behind these mechanisms are still in their developmental stages, some researchers suggest that nonnociceptive pain can often be intractable and an important component in conditions such as fibromyalgia and idiopathic low-back pain.[59]

The great majority of evidence that suggests the involvement of nonnociceptive/mechanoreceptor afferents in pain generation has been gleaned from the study of nerve injury models, ie, neuropathic models, rather than somatic tissue injury.[58,61-65] Therefore, the theory that nonnociceptive/mechanoreceptor afferents is responsible for the somatic pain associated with fibromyalgia and back pain seems unreasonable.

Whether mechanoreceptor afferents are involved in the generation of somatic pain can be discovered by the use of therapies that would activate mechanoreceptors and their A-beta afferents, such as vibratory stimuli (vibration therapy) and transcutaneous electrical nerve stimulation (TENS). In this case, research has clearly demonstrated that vibration and TENS therapy are effective in reducing nociceptive and neuropathic pain.[66,67] Therefore, mechanoreceptor afferent fibers likely are not involved in the promotion of most pain. However, there are exceptions. For example, in the case of causalgia, a classical neuropathic pain syndrome, "transcutaneous electrical stimulation of the nerve supply to the affected area resulted in pain at stimulus strengths sufficient to activate A but not C fibers."[58]

Several possible reasons why the stimulation of mechanoreceptor afferents may cause pain in the presence of nerve injury, ie, neuropathic pain, exist. For example, peripheral nerve injury causes the central processes of mechanoreceptor afferents to develop new connections. Normally, mechanoreceptor axons synapse with second-order neurons located deep in the dorsal horn. However, nerve injury causes the central connections of mechanoreceptor afferents to sprout into the superficial layers of the dorsal horn, ie, lamina II and perhaps lamina I, and create synaptic connections with projection neurons that normally receive input exclusively from nociceptive afferents.[68-70] In this situation, lightly stroking the skin can cause severe pain, ie, allodynia, which is also described as intractable touch-evoked pain,[69] a condition typically associated with postherpetic neuralgia, partial nerve trauma, and metabolic and inflammatory neuropathies.[70] These are not a very common clinical presentation, particularly in chiropractic offices.

As mentioned earlier, in clinical practice, innocuous palpation of spinal muscles results in pain whereas light stroking of the skin does not. The allodynia related to innocuous palpation may involve the stimulation of sensitized C-fibers within the spinal muscles, ie, nociceptive pain. In contrast, the allodynia related to light stroking of the skin probably involves mechanoreceptor stimulation and the subsequent activation of nociceptive projection neurons as a result of dorsal horn reorganization in response to nerve injury, ie, neuropathic pain.

Neuropathic Pain

A great deal of confusion exists regarding the nature of neuropathic pain. Authors commonly define and discuss neuropathic pain in different fashions, which leads to confusion. Usually, we are provided with either an injury-based or a physiologic description of neuropathic pain.

1. The injury-based definition states that "neuropathic pain refers to pain arising as a result of damage to any part of the sensory system, either peripheral or central. Sensitization of C fibers is excluded."[71]
2. The physiologic definition states that "the term neuropathic pain is applied to any acute or chronic pain syndrome in which the sustaining mechanism for the pain is inferred to involve aberrant somatosensory processing in the peripheral or central nervous system."[72]

Notice that the first definition clearly states that neuropathic pain arises from injury to the nervous system. This injury-based definition also indicates that nociceptive C-fiber sensitization is not neuropathic pain. This is most likely because nociceptor sensitization is typically associated with injury of nonneural structures, particularly somatic tissues.

The second definition of neuropathic pain creates confusion. This is because neuropathic pain in this definition is described in physiologic terms, rather than injury-based terms. We are told that any pain can be defined as "neuropathic" so long as aberrant somatosensory processing exists. This is enormously confusing because both neural and somatic tissue injury can result in abnormal somatosensory processing, known as central sensitization.[72] Thus the physiologic definition states that C-fiber induced nociceptive pain also can be neuropathic pain, if central sensitization develops after somatic tissue injury. This is inconsistent with the injury-based definition and also can lead to diagnostic confusion. For example, the physiologic definition can lead researchers and clinicians to inaccurately assign the diagnosis of neuropathic pain to all chronic pain patients. This is hardly reasonable, considering it has been estimated that only 1% of pain patients aged <65 years have neuropathic pain.[73] It should be mentioned that numerous authors describe neuropathic pain in relation to the injury-based definition, ie, pain as a result of nerve injury.[71,73-82]

The inconsistency and inaccuracy of the physiologic definition of neuropathic pain is exemplified by the fact that certain authors provide detailed reasons for why neuropathic pain necessarily involves injured nerve fibers. For example, Devor states that, "the acquisition by injured nerve fibers of ectopic pacemaker capability is among the fundamental pathophysiologic changes that underlie the emergence of neuropathic pain."[81] Neuromas, regenerating sprouts, and demyelination are thought to be responsible for the ectopic discharge of injured nerves.[73,81,82]

The quality of pain associated with neuropathic lesions is different from nociceptive pain. Areas of severe pain may be associated with some sensory deficit. Intermittent bouts of sharp, shooting, jabbing, and/or lancinating pain are common, as are steady burning and tingling sensations.[40,73,77,80] In contrast to nociceptive pain, these neuropathic pain sensations, referred to as paresthesias, dysesthesias, and hyperpathia, often are entirely new and different to the patient.[77,80]

Neuropathic lesions can occur in the peripheral and central nervous systems, each of which will be discussed in separate sections. Two types of nociceptive pain often are mistaken for neuropathic pain: discal and nerve root sheath nociceptive pain.

Discal and nerve root sheath nociceptive pain. According to Bogduk and Twomey[83]: "In contradistinction to pain caused by the compression of spinal nerves by herniated intervertebral discs, primary disc pain is pain that stems directly from the disc itself, and is caused by the stimulation of the nerve endings with the anulus fibrosus [sic]." Mechanical strain/injury to the anulus leads to chemical mediator release, which leads to inflammation and nociception.[83] This type of disk injury is similar to that of a sprained ligament[83] and does not involve a neuropathic process.

Most authors credit Ashbury and Fields[84] for determining that the nerve root sheath can be a source of nociceptive input and cause so-called nerve trunk pain.[3,40,61,72,85-87] The term "nervi nervorum" describes the nerve fibers which innervate the nerve sheaths, and they serve a nociceptive function.[86] An injured disk, for example, releases chemical mediators of inflammation, which may activate nerve sheath nociceptors,[15] and cause symptoms similar to those produced by nociceptive input from somatic tissues. However, mechanical trauma could injure the nervi nervorum and lead to the development of pain. Such injury-induced nerve pain would be considered neuropathic pain rather than nociceptive.[88] The extent to which this type of neuropathic pain exists is unknown; however, it may explain the presence of intractable pain in patients with no objective signs of injury to the nerve root or peripheral nerve.

Peripheral neuropathy. Several types of pathologies can cause neuropathic pain: nerve root compression, dorsal root ganglia compression, peripheral nerve entrapment (peripheral neuropathies), post herpetic neuralgia, avulsion injuries, tumor invasion, diabetic neuropathy and other metabolic neuropathies, and toxic and nutritional neuropathies.[73,77,80,81,87,89] Several conditions can develop as a result of nerve injury, including trigeminal neuralgia, complex regional pain syndromes, phantom pain, deafferentation pain, and Tinel's sign.[81,89,90]

The severity of neuropathic pain must be emphasized. Once neuropathic pain develops, it rarely goes away.[61,71,73,91] Fortunately, neuropathic pain is uncommon compared with nociceptive pain. For this reason, we strongly recommend that doctors avoid telling patients that they have pinched nerves, ie, a neuropathic process, unless objective diagnostic evidence shows that a neuropathic process exists. The following evidence supports our proposal.

As mentioned earlier, it has been estimated that about 1% of pain patients have neuropathic pain.[73] However, this percentage may rise as high as 50% in patients aged >65 years.[73] This increase is probably as a result of the fact that cancer, skeletal injuries, metabolic diseases, neurologic diseases, and degenerative changes are far more common in senior citizens.

Mooney discusses spinal neuropathic pain, stating that "depending on what country and what series, perhaps 1% have a disk injury that is "noncontained" and presses upon the nerve root creating irritation sufficient enough that sciatica is unremitting and needs to be resolved by surgical removal."[5] In these cases, the nerve root likely has been damaged by stretching, compression, friction, or inflammation. Stimulation of such damaged nerve roots evokes pain, whereas stimulation of undamaged nerve roots usually does not.[92]

Bogduk is specific in his assertion that neuropathic lesions, such as nerve root compression, which cause radicular (neuropathic) pain, are extraordinarily uncommon in the spine:

> Somatic mechanisms have remained largely overlooked as explanations for cervical pain syndromes, and nerve root compression has remained accepted as the principle if not the only mechanism for cervical pain. However, as a mechanism, nerve root compression is inconsistent with the clinical features of the majority of cervical pain syndromes, and in fact accounts for only a very specific proportion of cases.[13]

Bogduk further states,

> Given that various structures in the lumbar spine have been shown to be capable of producing low-back pain, it is important to realize that in each case the mechanism involved is the stimulation of nerve endings in the affected structure. Lumbar nerve-root compression is in no way involved . . . For root compression to be deemed the cause, radicular pain must be accompanied by other features of nerve compression: numbness, weakness, or paresthesia. In the absence of such accompanying features, it is very difficult to maintain that root compression is the cause of any pain.[15]

Nociceptive pain is a spinal pain syndrome that patients frequently bring to their doctor's office. Unfortunately, despite the availability of this information, members of the chiropractic and medical professions continue to promote the theory that the neuropathic lesion is most common.

Central neuropathy. The term central pain is used to describe the pain associated with lesions of the central nervous system. These lesions typically involve the anterolateral pathways and may be located at any level of the neuraxis from the dorsal horn to the cerebral cortex.[93]

Many types of conditions can cause central pain, including vascular lesions in the brain and spinal cord, multiple sclerosis (MS), inflammatory lesions other than MS, myelitis caused by viruses and syphilis, epilepsy, Parkinson's disease, traumatic brain and spinal cord injury, cordotomy, syringomyelia and syringobulbia, tumors, and abscesses.[93] The occurrence of central pain varies among each cause of central neuropathy. For example, the occurrence is 30% in patients with spinal cord injury, 23% in patients with multiple sclerosis, 1.5% in patients with stroke, 2.8% in patients with epilepsy, and 10% in patients with Parkinson's disease.[93]

Tasker[94] indicates that spinal cord injury is the most common cause of central pain. Trauma is the most common cause of injury; however, spinal cord lesions also can be caused by neoplasm, myelitis, infarction, and surgical procedures such as cordotomy.[94]

Central neuropathic pain can also be caused by supraspinal lesions. Although the most common lesion results from a supratentorial stroke, lateral medullary syndrome, hemorrhage, neoplasm, and surgical procedures such as tractotomy also can cause central neuropathic pain.[94] When central pain is caused by supraspinal lesions, related neurological signs often develop, such as tremor, dystonia, cerebellar nystagmus and ataxia, hemiparesis, and abnormalities in cognition, speech, vision, and cranial nerve function.[94] Because of the devastating nature of central pain syndromes, it is fortunate that patients with central neuropathic pain make up a relatively small percentage of the total chronic pain population.[11]

The precise mechanisms associated with central pain have yet to be defined. Research suggests that nociceptive neurons in certain thalamic nuclei are involved. Increased burst activity has been found in the ventroposterior region of the thalamus.[94,95] Central lesions may reduce descending inhibitory output, which would result in a disinhibition of nociceptive projection neurons in the spinal cord.[96]

Sympathetically maintained pain. Because there is confusion about the relationship of the sympathetic nervous system to the experience of pain, a separate section is devoted to the topic of sympathetically maintained pain (SMP). SMP is most commonly discussed in relationship to neuropathic pain; however, research has demonstrated that sympathetic efferents also promote nociceptive pain by enhancing tissue inflammation. Each topic will be discussed individually.

Texts and articles that attempt to discuss the sympathetic nervous system in a clinical fashion have stated that back pain can be of sympathetic origin.[97,98] Such assertions simplify a problem that is quite complex.[99-101] In fact, the spinal pain of sympathetic origin is not seen in the typical medical or chiropractic practice. Indeed, researchers maintain that normal activity in the sympathetic nervous system rarely, if ever, causes pain.[102] Even when pain is maintained by sympathetic activity, the face and torso/spine are rarely affected.[100]

In an effort to properly characterize sympathetically maintained pain, a new system of terminology has been accepted by the International Association for the Study of Pain.[100] The umbrella term, complex regional pain syndrome (CRPS), is now used when discussing sympathetically maintained pain. Two types of CRPS are currently recognized. CRPS I corresponds to reflex sympathetic dystrophy (RSD) and CRPS II corresponds with causalgia. The difference between the two types of CRPS is straightforward. Whereas CRPS I (RSD) is a syndrome that develops after an initiating noxious event (apparently to either somatic tissue or nerve), CRPS II (causalgia) is a syndrome that develops after obvious nerve injury and traditionally involves large nerves such as the median or

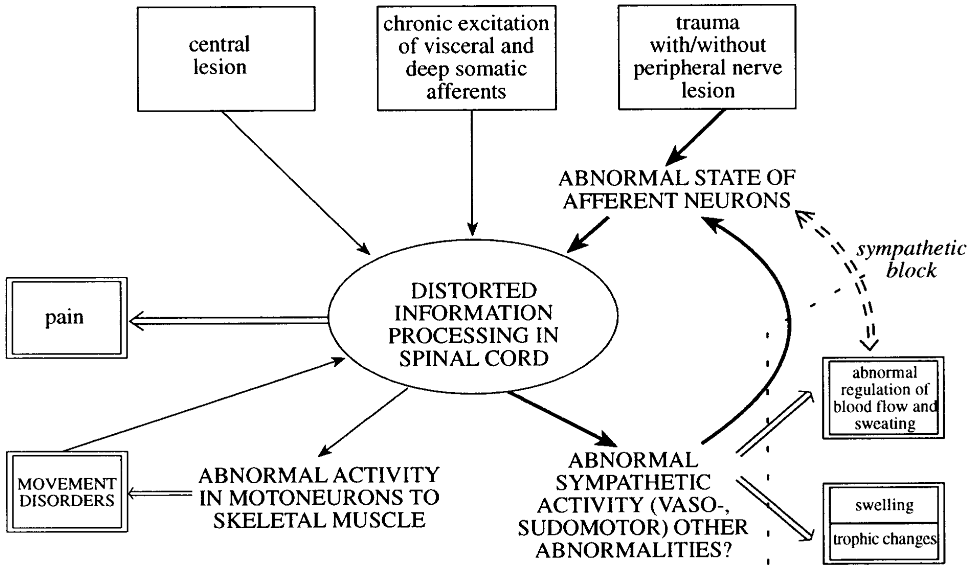

Fig 1. *General hypothesis about the neural mechanisms of generation of CRPS I and II after peripheral trauma with and without nerve lesions, chronic stimulation of visceral afferents (eg, myocardial infarction), deep somatic afferents, and rarely, central trauma. The clinical observations are double-framed. Note the vicious circle* (bold arrows). *An important component of this circle is the excitatory influence of postganglionic sympathetic axons on primary afferent fibers in the periphery. From Jänig and Stanton-Hicks, editors. Reflex sympathetic dystrophy: a reappraisal. Seattle: IASP Press; 1996.*

sciatic nerve.[100] CRPS is characterized by pain, evidence of edema, skin blood flow abnormalities, and/or abnormal sudomotor activity.[100]

Figure 1 outlines a proposed mechanism by which sympathetically maintained pain develops. Nerve and nonneural tissue injury, as illustrated by the bold arrows, results in enhanced nociceptive input to the spinal cord, which can excite segmental sympathetic neurons. Sympathetic hyperactivity can cause abnormal regulation of blood flow and sweating and trophic changes; in addition, it can promote nociceptive input that maintains the experience of pain. Janig[101] and Blumberg[103] provide detailed discussions of each component in this image.

The exact mechanism by which sympathetic efferents and nociceptive afferents interact is not understood precisely because of the complexity of interactions that occur among sympathetic terminals, nociceptors, and local tissue mediators. Research has demonstrated that sympathetic efferent activity is known to contribute to joint inflammation and injury in experimental arthritis.[104] Sympathetic terminals release substances that are pro-inflammatory and contribute to development, severity, and possibly the prolongation of tissue injury.[105] Accordingly, research suggests that sympathetic postganglionic fiber activity is necessary for bradykinin and other inflammatory mediators to fully express their inflammatory and nociceptor-sensitizing properties.[106] Such research indicates that for pain and inflammation to persist in any tissue, a contribution from the sympathetic nervous system is required.[107]

Sympathetic terminals release numerous mediators, including norepinephrine, neuropeptide Y, adenosine triphosphate (ATP), adenosine, prostaglandin E_2, prostacyclin, 5-HETE, 12-HETE, and endothelium-derived relaxing factor.[108] The membrane of sympathetic terminals also has receptors for numerous mediators such as bradykinin, epinephrine, opiate peptides, serotonin, histamine, prostaglandins, and substance P.[108] As mentioned earlier, nociceptor membranes also have receptors for the various inflammatory mediators released by injured tissues, inflammatory cells, and sympathetic terminals. Nociceptors have α_1-adrenergic receptors, the production of which become upregulated during nociceptor activation and sensitization.[109] In this situation, norepinephrine from sympathetic terminals may activate nociceptors via the alpha$_1$-adrenergic receptor.[109] Several articles discuss this relationship.[27,104,106,109,110]

The receptors on sympathetic terminals, such as the β_2-receptor, indicate that systemic endocrine functions also can influence local sympathetic functions. Epinephrine release from the adrenal medulla can stimulate the β_2-receptor and ignite a proinflammatory cascade of events.[105,108,111] Epinephrine exacerbates arthritis by acting on the β_2-receptor.[111]

Psychologic Pain

Psychologic pain is the least understood of the three mechanisms of pain induction. This is probably because the psychologic contribution to pain is very difficult to quantify. It should be mentioned that the term "psychogenic pain" is often used when discussing the psychologic component of pain, which suggests that pain develops as a consequence of psychologic factors alone. This is highly unlikely in the clinical setting, where most patients have pain that is initiated by somatic tissue injury and nociceptive processes. For this reason, the term "psychologic pain" is used instead of "psychogenic pain."

Because pain is defined as a psychologic state, a psychologic component will always be associated with both nociceptive and neuropathic pain. However, practitioners who focus on treating somatic structures, such as chiropractors, orthopedists, and neurosurgeons, tend to minimize the importance of psychologic factors in the promotion of pain.[112-114]

The pain is usually chronic in nature in syndromes involving psychosomatic mechanisms.[112-114] The definition of chronic pain is somewhat arbitrary. Originally, chronic pain referred to pains that persisted for more than 3 or 6 months. A more contemporary definition explains that, "pain is chronic if it persists for a month beyond that usual course of an acute illness or a reasonable duration for an injury to heal, if it is associated with a chronic pathologic process, or if it recurs at intervals for months or years."[33] If a patient's pain syndrome fits the parameters of this definition, clinicians recommend assessment of psychologic factors involved in pain promotion before discussing such a possible relationship with a patient.

Pain can develop as a consequence of psychologic illness and also as a result of certain emotional factors.[115] Anxiety and depression are specific emotional factors that are known to enhance the experience of pain.[115] A recent clinically-oriented paper demonstrated that psychologic/mental distress can promote low-back pain.[116] A group of 1638 subjects without back pain were observed to determine the relationship between psychologic distress and low-back pain. The results indicated that symptoms of psychologic distress can predict the onset of new episodes of back pain. The authors stated that psychologic factors, such as anxiety and depression, are involved in 16% of new episodes of low-back pain in the general population.[116]

The precise mechanisms by which anxiety and depression can promote or enhance pain are not fully understood although several possible mechanisms have been proposed. Despite the fact that precise mechanisms have yet to be elucidated, a reduction in anxiety[115] and depression[117] can lead to a considerable reduction in pain. Although anxiety and depression will be discussed separately, in the clinical setting, anxiety and depression often occur simultaneously.[118]

Anxiety. Patients with anxiety experience much greater pain from a lesion/injury than patients without anxiety.[115] Anxiety may influence the activity of the reticular activating system (RAS) and enhance the supraspinal transmission of nociceptive impulses.

The RAS is located in the midbrain and rostral pons, and projects excitatory input (such as that from nociceptors) to nonspecific thalamic nuclei such as the intralaminar nuclei.[119,120] Nonspecific thalamic nuclei transmit such nociceptive input to widespread areas throughout the cerebral cortex.[119,120] Brodal indicates that adrenaline and carbon dioxide increase RAS activity[120] and, therefore, the transmission of nociceptive input to the thalamus and cerebral cortex. Because anxiety results in increased catecholamine release,[30] a possible outcome would be increased pain sensations.

Anxiety also may influence the function of peripheral tissues, such as blood vessels and muscles, and promote nociceptive input. Kirkaldy-Willis[121] explains that emotional factors, such as tension, anxiety, fear, resentment, and depression, can promote low-back pain. He hypothesizes that such emotions affect the autonomic nervous system and result in local areas of vasoconstriction in muscle which can promote muscle injury. Travell and Simons[122] suggest that anxiety can be expressed as increased muscle tension, which can result in the development of myofascial trigger points. The central nervous system is involved in the control of muscular and vascular function; thus anxiety may influence such peripheral structures via the central nervous system.[123] It is also possible that increased levels of circulating catecholamines may directly enhance muscle tension.[124]

Anxiety also may directly influence nociception in somatic tissues. As mentioned earlier, epinephrine release from the adrenal medulla can stimulate the β_2-receptor and ignite a pro-inflammatory cascade of events and exacerbate the pain of arthritis.[111] This suggests that stress management is an important consideration for those in pain because epinephrine release is increased during anxiety and stressful periods.[125]

Additional symptoms are often associated with anxiety which may add to diagnostic confusion. Hyperventilation syndrome (HVS) is a condition that is associated with qualitative and quantitative augmentation of normal reactions to anxiety.[126] Several organic diseases can cause HVS as well as conditions such as pain, hypoglycemia, and mental stressors which promote anxiety and fear.[126] An example of symptoms associated with HVS include apprehension, faintness, fatigue, headache, impaired concentration, irritability, seizure, weakness, visual disturbances, diaphoresis, perioral numbness, dyspnea, palpations, tachycardia, abdominal discomfort, chest pain, air swallowing, tetany, and distal paresthesias.[126] Additional symptoms include numbness and tingling in the hands, feet, and face, and muscle tightening and stiffness.

HVS is a condition that receives little attention from medical and chiropractic doctors. In 1950, Rice explained that, although the existence of HVS has been known for many years, "medical students as well as practitioners frequently state that they have never heard of this condition."[127] To this day, popular medical diagnostic texts do not list HVS in their indexes, and no discussions can be found in the body of the texts[128-131] despite Rice's assertion that the incidence of HVS is surprisingly common. Most reports suggest an incidence of 6% to 11%, although a few studies estimate that HVS may contribute to some 40% of symptoms in the general medical clinic.[126]

Several articles discuss mechanisms and diagnostic considerations associated with HVS.[126,127,132-134] This syndrome should be considered as a possible diagnosis when pain patients present with additional and seemingly unrelated symptoms that would otherwise confuse and complicate basic diagnostic efforts.

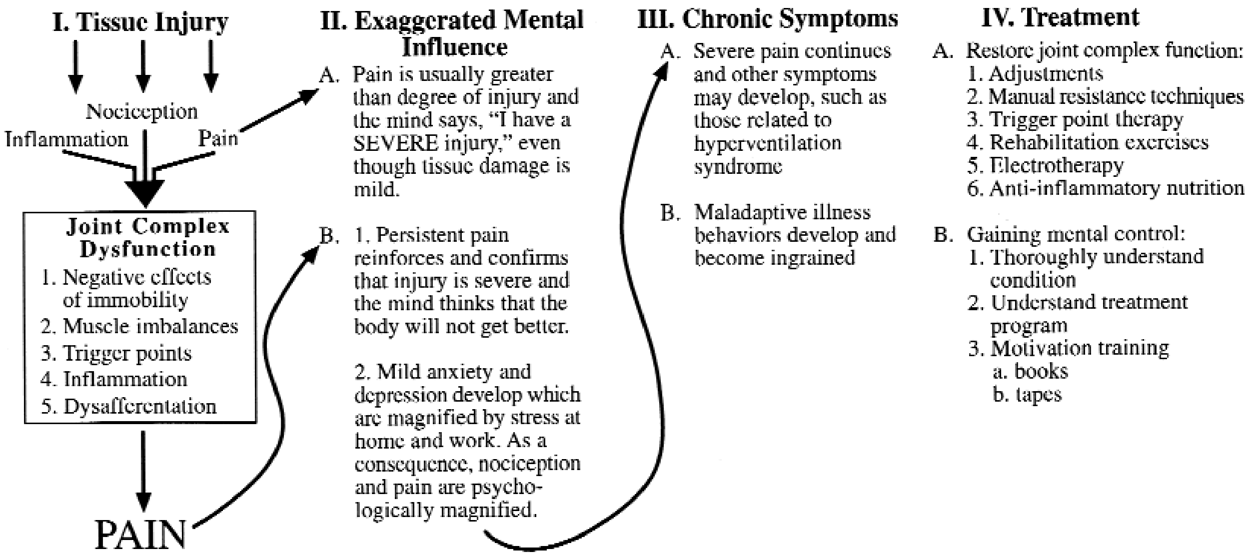

Fig 2. *Patient education: A key to treatment.*

Depression. As mentioned above, depression is also a specific emotional factor that is capable of enhancing the experience of pain. Depression may influence nociception by reduction of the activity of powerful descending inhibitory pathways that emanate from the brainstem. Serotonergic nuclei, such as the nucleus raphae magnus of the medulla, and various catecholamine nuclei located in the pons descend into the spinal cord via the dorsolateral funiculus. The activity of these pathways inhibits nociception at the level of the dorsal horn.

Depression may enhance nociceptive transmission by reduction of descending inhibition. Conversely, mentally engaging attitudes can facilitate the activation of these descending antinociceptive pathways.[96,135-137]

The following section, devoted to the topic of psychosomatic back pain, discusses some of the original work by Sargent[112] and Sarno[113,114] that relates anxiety and depression to back pain. Unfortunately, their work and this subject in general are not given adequate attention in contemporary chiropractic or medical education.

Tension myositis and psychosomatic back pain. At least as early as 1978, Sarno recognized that overt structural pathologies are uncommon causes of low-back pain:

> What pervades the entire spectrum of diagnostic possibilities in low back pain is the concept that the pain must be attributed to a structural disorder of the lumbosacral elements. It is a bias which is deeply ingrained in medical practice and teaching but, unfortunately, largely unsupported by objective data.[114]

Sarno stated that overt structural pathologies do not exist in >90% of patients who present with low-back pain and proposed that this great majority of patients have tension myositis, described as a psychosomatic disorder initiated by injury to spinal muscles. Tension myositis is a painful state associated with a focal muscle spasm and caused by tissue injury that occurs during lifting, bending, twisting, or stretching. Frequently, the pain is caused by an innocent twist or bend of the trunk, which led Sarno to believe that the somatic component of the lesion was minor compared to the psychosomatic component, a painful state perpetuated long after the initial injury.

Sarno credits Sargent[112] for developing this thesis. In 1946 Sargent discussed how 96% of patients with back pain, in an Army Air Forces convalescence hospital, had no structural pathology and instead had psychosomatic backache.[112] Both Sarno and Sargent concede that tissue injury may have initiated the painful state; however, they assert that the pain long outlasts the injury as a result of psychosomatic mechanisms. Indeed, the great majority of subjects in their respective trials became pain-free after psychologic issues were resolved.

Most of Sarno's patients did not require consultation with a psychologist or psychiatrist.[114] Of 52 patients diagnosed with tension myositis, only 3 required psychotherapy. The physical treatment involved heat, electrical therapy, massage, and exercise, which might lead one to believe that these physical therapeutics were responsible for the success in pain reduction. However, he states that, "patients with tension myositis must both understand and accept the psychosomatic diagnosis before they can hope to be free of pain, regardless of the physical therapy program."[114]

Sarno states that the nonpsychiatric clinician can have a profound impact on the treatment of physical disorders with psychic cause: patients are more inclined to believe a nonpsychiatric clinician primarily because he/she is not a psychiatrist, and the diagnosis does not bear the stigma of mental illness. It is more acceptable to the patient when the psychologic problem is described in relation to personality characteristics versus psychopathology. In the case of the chiropractor, neurologist, or orthopedist, the primary goal is to educate the patient about the relationship between mental states, such as anxiety, depression, fear, and anger, and physical disorders, such as back pain.[114]

Table 2. *Assumptions of cognitive-behavioral treatment*

Subjects are active processors of information.
Thoughts can elicit or modulate affect and physiology and can serve as impetuses for behavior. Conversely, affect, physiology, and behavior can instigate or influence thoughts
Behavior is reciprocally determined by the subject and the environment
Clients or patients can learn more adaptive ways of thinking, feeling, and behaving
Clients or patients are capable of and should be involved as active agents in change of their maladaptive thoughts, feelings, and behaviors

From Turk D, Rudy T. A cognitive-behavioral perspective on chronic pain: beyond the scalpel and syringe. In: Tollison C, Satterthwaite J, Tollison J, editors. Handbook on pain management. 2nd ed. Baltimore: Williams and Wilkins; 1994. p. 136-51.

Table 3. *Objectives of cognitive-behavioral treatment*

Reconceptualize clients' or patients' views of their problems from overwhelming to manageable (combat demoralization)
Convince clients or patients that skills necessary for responding to problems more adaptively will be included in treatment (enhance outcome efficacy)
Reconceptualize clients' or patients' views of themselves from passive, reactive, and helpless to active, resourceful, and competent (foster self-efficacy)
Ensure that clients or patients learn how to monitor thoughts, feelings, and behaviors and learn the interrelationship among these (break up automatic, maladaptive patterns)
Teach clients or patients how to use and when to execute the necessary overt and covert behaviors required for adaptive response to problems (skills training)
Encourage clients or patients to attribute success to their own efforts
Anticipate problems and discuss these as well as ways to deal with them (facilitate maintenance and generalization)

From Turk D, Rudy T. A cognitive-behavioral perspective on chronic pain: beyond the scalpel and syringe. In: Tollison C, Satterthwaite J, Tollison J, editors. Handbook on pain management. 2nd ed. Baltimore: Williams and Wilkins; 1994. p. 136-51.

The following six factors are considered important components in the treatment program[113]:

1. An intensive physical and occupational therapy program,
2. Appreciating the psychologic value of the physical and occupational therapy,
3. Ensuring confidence in the attending nonpsychiatric clinician,
4. Ensuring confidence in the treating psychotherapist when one is needed,
5. Ensuring that patients understand the precise nature of the physical pathology and psychologic contribution,
6. Patients must actively begin the process of understanding and resolving the pertinent psychologic issues.

The average patient with low-back pain does not have the pathological form of anxiety/depression that is commonly described in psychology texts. They likely have a functional form that ensues as a result of the normally compromising stress of life which is then compounded by painful injury to the spine. These patients need a caring and reassuring doctor who will accurately describe the nature of the somatic and psychosomatic components of the pain syndromes, and also outline an appropriate treatment program (Figure 2).

In more recent years, Waddell has discussed extensively the relationship between spinal pain and psychologic factors.[138-147] Subsequently, psychologic issues, such as illness behavior and various psychosocial factors, have been given more attention by practitioners, including chiropractors and orthopedists who would otherwise adhere primarily to a biomechanical model.

Lessons from cognitive-behavioral therapy. Behavioral treatment approaches are based upon what are thought to be the fundamental processes of learning: classical and operant conditioning.[148] Watson, Thorndike, and Skinner are the modern fathers of behavioristic therapy, which made a strong impact on the field of psychology during the first half of the 20th century. Behavioristic therapy began to replace Freud's psychoanalytic/psychodynamic model, a cognitive approach to psychotherapy.[149] In the second half of the 20th century, there was a resurgence of interest in cognitive psychology and, thus, the birth of cognitive-behavioral therapy.[149]

The cognitive-behavioral approach differs from traditional psychodynamic and behavioral methods in that emphasis is placed on "a broad domain of potentially relevant variables in defining the often deleterious impact of the chronic pain experience and in identifying possible psychosocial contributors to the problems of the individual with chronic pain."[150] Turk et al[151] were the first to apply cognitive-behavioral therapy to chronic pain patients. Table 2 lists five general assumptions that characterize the cognitive-behavioral perspective. Table 3 outlines the objectives of cognitive-behavioral therapy.

Turk et al state that "the cognitive-behavioral approach can be adapted for use with inpatients and outpatients, conducted on an individual or group basis, and used as a total program for treatment of chronic pain patients in a multidisciplinary setting or by a set of solo practitioners from different disciplines."[151] The key to effective care is that the treatment team must share a common philosophy to treat patients consistently, regardless of the disciplines or techniques used during care.[151] Three central questions guide the physician's assessment of patients with pain[151]:

1. What is the extent of injury or disease (physical impairment)?
2. What is the magnitude of the injury or disease? In other words, to what extent is the patient unable to enjoy normal activities of daily living as a result of the injury or disease?
3. Is the illness behavior commensurate with the extent of illness? Are there any psychologic, social or economic purposes that would cause the patient to amplify their symptoms?

Answers to all of these questions can be determined by the first contact clinician, such as a chiropractor, through the use of a multiaxial assessment of pain (MAP).[151] The MAP consists of three components (Table 4). As indicated, *Axis I* of the MAP involves the physical examination, and *Axis II* and *III* involve the assessment of psychosocial and behavioral aspects of pain. In 1985, Kerns and Jacob[150] and Turk and Rudy[151] developed the West Haven-Yale Multidimensional Pain Inventory (MPI) to assess the psychosocial and behavioral axis of the MAP. The results of the MAP guide a treat-

Table 4. *Components of the multiaxial assessment of pain*

Axis I: Medical-physical quantification of
Laboratory and other diagnostic procedures
Physical examination
Functional mobility, strength, and flexibility
Axis II: Psychosocial, including patients' perceptions of
Pain
Affective distress
Interference of pain with domain of life (eg, social, vocational, marital, recreational, physical)
Axis III: Behavioral-functional, including
Observable communications of pain and distress
Pain-related use of health care system
Medication
Activity levels
Responses of significant others

From Turk D, Rudy T. A cognitive-behavioral perspective on chronic pain: beyond the scalpel and syringe. In: Tollison C, Satterthwaite J, Tollison J, editors. Handbook on pain management. 2nd ed. Baltimore: Williams and Wilkins; 1994. p. 136-51.

ment program. For details see Turk and Rudy[151] and Turk and Meichenbaum.[152]

As stated earlier, cognitive-behavioral therapists use an integrated assessment method in the treatment of pain. For this reason, the cognitive-behavioral approach was discussed in some detail. However, numerous methods for assessing pain are available to the clinician.[153]

CONCLUSIONS

Spinal pain can be caused by nociceptive and neuropathic mechanisms and promoted by psychologic mechanisms. Nociceptive pain and neuropathic pain are distinctly different entities. Nociceptive pain occurs when musculoskeletal tissues are injured, whereas neuropathic pain occurs when the peripheral or central nervous system is injured. Clinicians must determine which mechanisms are involved so that appropriate treatment plans can be implemented.

Although neuropathic pain does occur, research suggests that most pain that patients report to private practitioners is nociceptive. Thus, it is important for practitioners to be aware of treatments that can effectively reduce nociceptive pain, including spinal adjusting/manipulation, muscle lengthening/stretching, trigger point therapy, rehabilitation exercises, electrical modalities, and a variety of nutritional factors.[36] To this date, no trials have been performed in which all of these interventions have been used in the treatment of spinal pain. Such a trial is greatly needed.

Unlike nociceptive pain, the neuropathic variety of pain often persists without remission and without responding to any treatment program. Fortunately, neuropathic pain is far less common than nociceptive pain. In the event that a true neuropathic lesion exists, it may be reasonable to use the conservative treatment methods offered by chiropractors. However, true neuropathic lesions typically require pharmacologic and surgical intervention.[67,77] Chiropractic methods may be used along with such medical care for rehabilitative purposes. A research trial is sorely needed to determine the use of such a multidisciplinary approach to the treatment of neuropathic pain.

Because pain is a psychologic state, clinicians should include treatment programs with a mental component. All patients need to be encouraged and reassured, and they need to become active participants in the treatment process, which helps patients become more confident and less prone to anxiety and depression. Doctors also should consider using health-oriented homework, such as inspirational and motivational books and tapes, which are psychologically uplifting.

As this manuscript went to press, a group of pain experts reported the need for and implications of a mechanism-based classification of pain to facilitate research and treatment methods.[154] These basic scientists and clinicians agreed that two mechanisms exist by which pain can be induced—tissue injury and nervous system injury. A workshop devoted to this topic was held August 22-27, 1999, at the 9th World Congress on Pain in Vienna, Austria.

REFERENCES

1. Bonica J. History of pain concepts and therapies. In: Bonica J, editor. The Management of Pain. 2nd ed. Philadelphia: Lea & Febiger;1990. p. 1-17.
2. Melzack R. The tragedy of needless pain. Sci Amer 1990; 262:27-33.
3. Weinstein J. The role of neurogenic and nonneurogenic mediators as they relate to pain and the development of osteoarthritis: a clinical review. Spine 1992;17:S356-61.
4. Wall P. Introduction to the edition after this one. In: Wall P, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 1-7.
5. Mooney V. Where is the pain coming from? Spine 1987; 12:754-9.
6. Bonica J. Definitions and taxonomy of pain. In: Bonica J, editor. The management of pain. 2nd ed. Philadelphia: Lea & Febiger; 1990. p. 18-27.
7. Watson J. Pain and nociception-mechanisms and modulation. In: Grieve G, editor. Modern manual therapy of the vertebral column. New York: Churchill Livingstone; 1986. p. 206-32.
8. LaRocca H. A taxonomy of chronic pain syndromes. 1991 Presidential Address, Cervical Spine Research Society Annual Meeting, December 5, 1991. Spine 1992;17:S344-55.
9. Wyke B. The neurology of low back pain. In: Jayson M, editor. The lumbar spine and back pain. 2nd ed. London: Pitman; 1980. p. 265-339.
10. Grieve G. Common vertebral joint problems. 2nd ed. New York: Churchill Livingstone; 1988. p. 308.
11. Bonica J. Introduction: semantic, epidemiologic, and educational issues. In: Casey K, editor. Pain and central nervous system disease: the central pain syndromes. New York: Raven Press; 1991. p. 13-29.
12. Portenoy R. Mechanisms of clinical pain. Neurol Clin 1989; 7:205-29.
13. Bogduk N. Innervation patterns of the cervical spine. In: Grant R, editor. Physical therapy of the cervical and thoracic spine. 2nd ed. New York: Churchill Livingstone; 1994. p. 65-76.
14. Bogduk N, Valencia F. Innervation patterns of the thoracic spine. In: Grant R, editor. Physical therapy of the cervical and thoracic spine. 2nd ed. New York: Churchill Livingstone; 1994. p. 77-87.
15. Bogduk N. Innervation, pain patterns, and mechanisms of pain production. In: Twomey L, Taylor J, editors. Physical therapy of the low back. 2nd ed. New York: Churchill Livingstone; 1994. p. 93-109.
16. Guyton A. Basic neuroscience. 2nd ed. Philadelphia: WB Saunders; 1991. p. 127-37.

17. Charman R. Pain and nociception: mechanisms and modulation in sensory context. In: Boyling J, Palastanga N, editors. Grieve's modern manual therapy: The vertebral column. 2nd ed. New York: Churchill Livingstone; 1994. p. 253-70.
18. Grieve G. Common vertebral joint problems. 2nd ed. New York: Churchill Livingstone; 1988. p. 51-2.
19. Haldeman S. The neurophysiology of pain. In: Haldeman S, editor. Principles and practice of chiropractic. 2nd ed. Norwalk: Appleton-Century-Crofts; 1992. p. 165-84.
20. Wyke B. The neurological basis of thoracic pain. Rheum Phys Med 1970;10:356-67.
21. Wyke B. Neurological aspects of pain therapy. In: Swerdlow M, editor. The therapy of pain. Philadelphia: Lippincott; 1980. p. 1-30.
22. Konttinen Y, Koski H, Santavirta S, Hukkanen M, Soinila S. Nociception, proprioception, and neurotransmitters. In: Bland J, editor. Disorders of the cervical spine. 2nd ed. Philadelphia: WB Saunders; 1994. p. 339-63.
23. Fields H. Pain. New York: McGraw-Hill; 1987. p. 26-33.
24. Woolf C. Generation of acute pain: Central mechanisms. Brit Med Bull 1991;47:523-33.
25. Rang H, Bevan S, Dray A. Chemical activation of nociceptive peripheral neurones. Brit Med Bull 1991;47:534-48.
26. Rang H, Bevan S, Dray A. Nociceptive peripheral neurons: cellular properties. In: Wall P, Melzack R, editors. New York: Churchill Livingstone; 1994. p. 57-78.
27. Casey K. Nociceptors and their sensitization: overview. In: Willis W, editor. Hyperalgesia and allodynia. New York: Raven Press; 1992. p. 13-5.
28. Light A. The initial processing of pain and its descending control: spinal and trigeminal systems. New York: Karger; 1992. p. 28.
29. Dubner R, Basbaum A. Spinal cord plasticity following tissue or nerve injury. In: Wall R, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 225-41.
30. Bonica J. Clinical importance of hyperalgesia. In: Willis W, editor. Hyperalgesia and allodynia. New York: Raven Press; 1992. p. 17-43.
31. Coderre T, Katz J, Vaccarino A, Melzack R. Contribution of central neuroplastically to pathological pain: review of clinical and experimental evidence. Pain 1993;52:259-85.
32. Willis W. Hyperalgesia and allodynia: Summary and overview. In: Willis W, editor. Hyperalgesia and allodynia. New York: Raven Press; 1992. p. 1-11.
33. Portenoy R, Kanner R. Definition and assessment of pain. Pain management: theory and practice. Philadelphia: FA Davis; 1996. p. 3-18.
34. Robbins S, Cotran R, Kumar V. Pathologic basis of disease. Philadelphia: WB Saunders; 1984. p. 1.
35. Robbins S. Pathologic basis of disease. Philadelphia: WB Saunders; 1974. p. 21-22.
36. Seaman D. Joint complex dysfunction: a novel term to replace subluxation/subluxation complex. Etiologic and treatment considerations. J Manipulative Physiol Ther 1997;20:634-44.
37. Mayer T, Gatchel R. Functional restoration for spinal disorders: the sports medicine approach. Philadelphia: Lea & Febiger; 1988.
38. Liebenson C. Integrating rehabilitation into chiropractic practice (blending active and passive care). In: Liebenson C, editor. Rehabilitation of the spine: a practitioner's manual. Baltimore: Williams & Wilkins; 1996. p. 13-43.
39. Waddell G. Modern management of spinal disorders. J Manipulative Physiol Ther 1995;18:590-6.
40. Tasker R. Management of nociceptive, deafferentation and central pain by surgical intervention. In: Fields H, editor. Pain syndromes in neurology. Oxford: Butterworth-Heinemann; 1990. p. 143-200.
41. Travell J, Simons D. Myofascial pain and dysfunction: the trigger point manual. Baltimore: Williams & Wilkins; 1983.
42. Travell J, Simons D. Myofascial pain and dysfunction: the trigger point manual. The lower extremities. Volume 2. Baltimore: Williams & Wilkins; 1983.
43. Mooney V, Robertson J. The facet syndrome. Clin Orthop 1976;115:149-56.
44. Bogduk N, Twomey L. Clinical anatomy of the lumbar spine. 2nd ed. New York: Churchill Livingstone; 1991. p. 151-9.
45. Campbell D, Parsons C. Referred head pain and its concomitants. J Nerv Ment Dis 1944; 99:544-51.
46. Feinstein B, Langton J, Jameson R, Schiller F. Experiments on pain referred from deep somatic tissues. Br J Bone Joint Surg 1954;36-A:981-97.
47. Inman V, Saunders J. Referred pain from skeletal structures. J Nerv Ment Dis 1944;99:660-7.
48. Kellgren J. Observations on referred pain arising from muscle. Clin Sci 1938;3:175-90.
49. Kellgren J. On the distribution of pain arising from deep somatic structures with charts of segmental pain areas. Clin Sci 1939;4:35-46.
50. Steinbrocker O, Isenberg S, Silver M, Neustadt D, Kuhn R, Schittone M. Observations on pain produced by injection of hypertonic saline into muscle and other supportive tissues. J Clin Invest 1953;32:1045-51.
51. Kessler R. Embryology of the musculoskeletal system. In: Hertling D, Kessler R, editor. Management of common musculoskeletal disorders. 2nd ed. Philadelphia: JB Lippincott; 1990. p. 3-8.
52. Lynch M, Kessler R. Pain. In: Hertling D, Kessler R, editors. Management of common musculoskeletal disorders. 2nd ed. Philadelphia: JB Lippincott; 1990. p. 40-59.
53. Gillette R, Kramis R, Roberts W. Characterization of spinal somatonsensory neurons having receptive fields in lumbar tissues of cats. Pain 1993;54:85-98.
54. Gillette R. Spinal cord mechanisms of referred pain and related neuroplasticity. In: Gatterman M, editor. Foundations of chiropractic: subluxation. St. Louis: Mosby; 1995. p. 288-301.
55. Bogduk N. The anatomical basis for cervicogenic headache. J Manipulative Physiol Ther 1992;15:67-70.
56. Pfaffenrath V, Dandekar R, Pollmann W. Cervicogenic headache—The clinical picture, radiological findings and hypothesis on its pathophysiology. Headache 1987;27:495-9.
57. Feinstein B. Referred pain from parabvertebral structures. In: Buerger A, Tobis J, editors. Approaches to the validation of manipulation therapy. Springfield, (Ill): Charles C Thomas; 1977. p. 139-74.
58. Raja S, Meyer R, Campbell J. Hyperalgesia and sensitization of primary afferent fibers. In: Fields H, editor. Pain syndromes in neurology. Oxford: Butterworth-Heinemann; 1990. p. 9-45.
59. Kramis R, Roberts W, Gillette R. Non-nociceptive aspects of persistent musculoskeletal pain. J Orthop Sports Phys Ther 1996;24:255-67.
60. Cervero F, Laird J. Mechanisms of touch evoked pain (allodynia): a new model. Pain 1996;68:13-23.
61. Bennett G. Neuropathic pain. In: Wall P, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 201-24.
62. Roberts W, Kramis R. Sympathetic nervous system influence on acute and chronic pain. In: Fields H, editor. Pain syndromes in neurology. Oxford: Butterworth-Heinemann; 1990. p. 85-106.
63. Campbell J, Raja S, Meyer R, Mackinnon S. Myelinated afferents signal the hyperalgesia associated with nerve injury. Pain 1988;32:89-94.
64. Gracely R, Lynch S, Bennett G. Painful neuropathy: Altered central processing maintained dynamically by peripheral input. Pain 1992;51:175-94.
65. Kramis R, Roberts W, Gillette R. Postsympathectomy neuralgia: hypothesis on peripheral and central neuronal mechanisms. Pain 1996;64:1-9.

66. Woolf C. Segmental afferent fibre-induced analgesia: transcutaneous electrical nerve stimulation (TENS) and vibration. In: Wall P, Melzack R, editors. Textbook of pain. 2nd ed. New York: Churchill Livingstone; 1989. p. 884-96.
67. Woolf C, Thompson J. Stimulation-induced analgesia: transcutaneous electrical nerve stimulation (TENS) and vibration. In: Wall P, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 1191-1208.
68. Woolf CJ, Doubell TP. The pathophysiology of chronic pain-increased sensitivity to low threshold A-beta fiber inputs. Curr Opin Neurobiol 1994;4:525-34.
69. Woolf CJ, Shortland P, Reynolds M, Doubell RT, Coggeshall RE. Reorganization of central terminals of myelinated primary afferents in the rat dorsal horn following peripheral nerve injury. J Comp Neurol 1995;360:121-34.
70. Woolf CJ. Molecular signals responsible for the reorganization of the synaptic circuitry of the dorsal horn after peripheral nerve injury: the mechanisms of tactile allodynia. In: Borsook D, editor. Progress in pain research and management. vol. 9. Seattle: IASP Press; 1997. p. 171-200.
71. Scadding J. Neuropathic pain. In: Asbury A, McKhann G, McDonald W, editor. Diseases of the nervous system: clinical neurobiology. 2nd ed. Philadelphia: WB Saunders; 1992. p. 858-72.
72. Portenoy R. Neuropathic pain. In: Portenoy R, Kanner R, editors. Pain management: theory and practice. Philadelphia: FA Davis; 1996. p. 83-125.
73. MacFarlane BV, Wright A, Callaghan JO, Benson AE. Chronic neuropathic pain and its control by drugs. Pharmacol Ther 1997;5:1-19.
74. Bowsher D. Pain syndromes and their treatment. Curr Opin Neurol Neurosurg 1993;6:257-63.
75. Tracey DJ, Walker JS. Pain due to nerve damage: are inflammatory mediators involved? Inflamm Res 1995;44:407-11.
76. Alexander J, Black A. Pain mechanisms and the management of neuropathic pain. Curr Opin Neurol Neurosurg 1992; 5:228-34.
77. Elliott KJ. Taxonomy and mechanisms of neuropathic pain. Sem Neurol 1994;14:195-205.
78. Galer BS. Neuropathic pain of peripheral origin: advances in pharmacologic treatment. Neurology 1995;45:S1-S25.
79. Kenner DJ. Pain forum. Part 2. Neuropathic pain. Aust Fam Physician 1994;23:1279-83.
80. Garcia J, Altman RD. Chronic pain states: pathophysiology and medical therapy. Semin Arthritis Rheum 1997;27:1-16.
81. Devor M, Rappaport Z. Pain and the pathophysiology of damaged nerve. In: Fields H, editor. Pain syndromes in neurology. Oxford: Butterworth-Heinemann; 1990. p. 47-83.
82. Devor M. The pathophysiology of damaged peripheral nerves. In: Wall R, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 79-100.
83. Bogduk N, Twomey L. Clinical anatomy of the lumbar spine. 2nd ed. New York: Churchill Livingstone; 1991. p. 153-65.
84. Ashbury A, Fields H. Pain due to peripheral nerve damage: an hypothesis. Neurology 1984;34:1587-90.
85. Fields H. Peripheral neuropathic pain: an approach to management. In: Wall R, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 991-6.
86. Bove G, Light A. Unmyelinated nociceptors of rat paraspinal tissues. J Neurophysiol 1995;73:1752-62.
87. Asbury A. Pain in generalized neuropathies. In: Fields H, editor. Pain syndromes in neurology. Oxford: Butterworth-Heinemann; 1990. p. 131-41.
88. Bove GM, Light AR. The nervi nervorum: Missing link for neuropathic pain? Pain Forum 1997;6:181-90.
89. Fields H. Introduction. In: Fields H, editor. Pain syndromes in neurology. Oxford: Butterworth-Heinemann; 1990. p. 1-18.
90. Payne R. Reflex sympathetic dystrophy syndrome: diagnosis and treatment. In: Fields H, editor. Pain syndromes in neurology. Oxford: Butterworth-Heinemann; 1990. p. 107-29.
91. Bennett GJ. Neuropathic pain: an overview. Molecular neurobiology of pain. In: Borsook D, editor. Progress in pain research and management. Volume 9. Seattle: IASP Press; 1997. p. 109-113.
92. Howe JF, Loeser JD, Calvin WH. Mechanosensitivity of dorsal root ganglia and chronically injured axons: a physiological bases for the radicular pain of nerve root compression. Pain 1977;3:25-41.
93. Boivie J. Central pain. In: Wall P, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 871-902.
94. Tasker R, de Carvalho G, Dostrovsky J. The history of central pain syndromes, with observations concerning pathophysiology and treatment. In: Casey K, editor. Pain and central system disease: the central pain syndromes. New York: Raven Press; 1991. p. 31-58.
95. Lenz F. The thalamus and central pain syndromes: Human and animal studies. In: Casey K, editor. Pain and central system disease: The central pain syndromes. New York: Raven Press; 1991. p. 171-82.
96. Woolf C. The dorsal horn: state-dependent sensory processing and the generation of pain. In: Wall P, Melzack R, editors. Textbook of Pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 101-2.
97. Kirkadly-Willis W. The mediation of pain. In: Kirkaldy-Willis W. Managing low back pain. 2nd ed. New York: Churchill Livingstone; 1988. p. 77-81.
98. Cramer G, Darby S. Clinical anatomy related to low back pain. Topics Clin Chiro 1996;3:1-8.
99. Stanton-Hicks M. editor. Pain and the sympathetic nervous system. Boston: Kluwer; 1990.
100. Stanton-Hicks M, Janig W, Hassenbusch S, Haddox J, Boas R, Wilson P. Reflex sympathetic dystrophy: changing concepts and taxonomy. Pain 1995;63:127-33.
101. Janig W. The puzzle of "reflex sympathetic dystrophy": mechanisms, hypotheses, open questions. In: Janig W, Stanton-Hicks M, editors. Reflex sympathetic dystrophy: a reappraisal. Seattle: IASP Press; 1996.
102. Levine J, Taiwo Y. Inflammatory pain. In: Wall P, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 45-56.
103. Blumberg H, Janig W. Clinical manifestations of reflex sympathetic dystrophy and sympathetically maintained pain. In: Wall P, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 685-98.
104. Levine J, Coderre T, Basbaum A. The peripheral nervous system and the inflammatory process. In: Dubner R, Gebhart G, Bond M, editors. Proceedings of the Vth World Congress on Pain. New York: Elsevier; 1987. p. 33-43.
105. Basbaum AI, Levine JD. The contribution of the nervous system to inflammation and inflammatory disease. Can J Physiol Pharmacol 1991;69:647-51.
106. Levine J, Taiwo Y, Heller P. Hyperalgesic pain: inflammatory and neuropathic. In: Willis W, editor. Hyperalgesia and allodynia. New York: Raven Press; 1992. p. 117-23.
107. Green PG, Miao FJ, Strausbaugh H, Heller P, Janig W, Levine JD. Endocrine and vagal controls of sympathetically dependent neurogenic inflammation. Ann N Y Acad Sci 1998;840:282-8.
108. Heller PH, Green PG, Tanner KD, Miao FJP, Levine JD. Peripheral neural contributions to inflammation. In: Fields HL, Liebeskind JC, editors. Pharmacological approaches to the treatment of chronic pain: new concepts and critical issues. Prog Pain Res Management, vol. 1; 1994. p. 31-42.
109. Campbell J, Meyer R, Davis K, Raja S. Sympathetically maintained pain: a unifying hypothesis. In: Willis W, editor. Hyperalgesia and allodynia. New York: Raven Press; 1992. p. 141-9.

110. Janig W, Levine JD, Michaelis M. Interactions of sympathetic and primary afferent neurons following nerve injury and tissue trauma. Prog Brain Res 1996;113:161-84.
111. Coderre TJ, Bashaum AI, Dallman MF, Helms C, Levine JD. Epinephrine exacerbates arthritis by an action at presynaptic β_2-adrenoceptors. Neuroscience 1990;34:521-3.
112. Sargent M. Psychosomatic backache. N Engl J Med 1946; 234:521-3.
113. Sarno J. Therapeutic exercise for back pain. In: Basmajian J, editor. Therapeutic Exercise. 3rd ed. Baltimore: Williams & Wilkins; 1978. p. 409-29.
114. Sarno J. Therapeutic exercise for back pain. In: Basmajian J, editor. Therapeutic exercise. 3rd ed. Baltimore: Williams & Wilkins; 1978. p. 409-29.
115. Merskey H. Pain and psychological medicine. In: Wall P, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 903-20.
116. Croft P, Papageorgiou A, Ferry S, Thomas E, Jayson M, Silman A. Psychologic distress and low back pain. Spine 1996; 20:2731-7.
117. Sternbach R. The psychologists role in the diagnosis and treatment of pain patients. In: Barber J, Adrian C, editors. Psychological approaches to the management of pain. New York: Brunner/Mazel; 1982. p. 3-20.
118. Carson R, Butcher J, Coleman J. Abnormal psychology and modern life. 8th ed. New York: HarperCollins; 1988. p. 193.
119. Nolte J. The human brain. 3rd ed. St. Louis: Mosby; 1993. p. 259-60.
120. Brodal A. Neurological anatomy. 3rd ed. New York: University Press; 1981. p. 428-9.
121. Kirkadly-Willis W. Pathology and pathogenesis of low back. In: Kirkaldy-Willis W, Burton C, editors. Managing low back pain. 3rd ed. New York: Churchill Livingstone; 1992. p. 49-79.
122. Travell J, Simons D. Myofascial pain and dysfunction: the trigger point manual. Baltimore: Williams & Wilkins; 1983. p. 149.
123. Jay G. Pathophysiology of tension-type headache. In: Tollison C, Kunkel R, editors. Headache: diagnosis and treatment. Baltimore: Williams & Wilkins; 1993. p. 129-41.
124. Hubbard D, Berkoff G. Myofascial trigger points show spontaneous needle EMG activity. Spine 1993;18:1803-7.
125. McEwen BS. Protective and damaging effects of stress mediators. N Engl J Med 1998;338:171-9.
126. Duncan S, Raffin T. Handling hyperventilation syndrome. Hosp Med 1992;28:58-67.
127. Rice R. Symptom patterns of the hyperventilation syndrome. Am J Med 1950;8:691-700.
128. Rakel R. editor. Conn's current therapy. Philadelphia: WB Saunders; 1993.
129. Griffith H, Dambro M. The 5 minute clinical consult. Philadelphia: Lea & Febiger; 1993.
130. Wyngarden J, Smith L, Bennett J. editors. Cecil textbook of medicine. 19th ed. Philadelphia: WB Saunders; 1992.
131. Isselbacher K, Braunwald E, Wilson J, Martin J, Fauci A, Kasper D. Harrison's principles of internal medicine. New York: McGraw-Hill; 1994.
132. Gardner W, Bass C. Hyperventilation in clinical practice. BMJ 1989;41:73-81.
133. van den Hout MA, Griez E. Peripheral panic symptoms occur during changes in alveolar carbon dioxide. Compr Psychiatry 1985;26:381-7.
134. Roll M, Zetterquist S. Acute chest pain without obvious organic cause before the age of 40 years: response to force hyperventilation. J Intern Med 1990;288:223-8.
135. Fields H, Bausbaum A. Central nervous system mechanisms of pain modulation. In: Wall P, Melzack R, editors. The textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 243-57.
136. Pert C. The wisdom of the receptors: neuropeptides, the emotions, and bodymind. Advances 1986;3:8-16.
137. Price D. Psychological and neural mechanisms of pain. New York: Raven Press; 1988. p. 181-211.
138. Waddell G, McCulloch FA, Kummel E, Venenr RM. Nonorganic physical signs in low-back pain. Spine 1980;5:117-25.
139. Waddell G, Main CJ, Morris EW, Di Paola MP, Gray ICM. Chronic low-back pain, psychologic distress, and illness behavior. Spine 1984;9:209-13.
140. Waddell G, Bircher M, Finalyson D, Main CJ. Symptoms and signs: physical disease or illness behavior? BMJ 1984; 289:739-41.
141. Gray ICM, Main CJ, Waddell G. Psychological assessment in general orthopedic practice. Clin Orthop 1985;194:258-63.
142. Waddell G, Morris EW, Di Paola MP, Bircher M, Finalyson D. A concept of illness tested as an improved basis for surgical decisions in low-back disorders. Spine 1986;11:712-9.
143. Waddell G. A new clinical model for the treatment of low-back pain. Spine 1987;12:632-44.
144. Waddell G, Pilowsky I, Bond MR. Clinical assessment and interpretation of abnormal illness behavior in low back pain. Pain 1989;39:41-53.
145. Waddell G. Biopsychosocial analysis of low back pain. Baillieres Clin Rheumatol 1992;6:523-57.
146. Waddell G, Newton M, Henderson I, Somerville D, Main CJ. Pain 1993;52:157-68.
147. Waddell G. Low back pain: a twentieth century health care enigma. Spine 1996;21:2820-5.
148. Feldman R. Understanding psychology. 2nd ed. New York: McGraw-Hill; 1990. p. 589-622.
149. Carson R, Butcher J, Coleman J. Abnormal psychology and modern life. 8th ed. New York: HarperCollins; 1988. p. 67-73.
150. Kerns R, Jacob M. Assessment of the psychosocial context of the experience of chronic pain. In: Turk D, Melzack R, editors. Handbook of pain assessment. New York: Guilford Press; 1992. p. 235-53.
151. Turk D, Rudy T. A cognitive-behavioral perspective on chronic pain: beyond the scalpel and syringe. In: Tollison C, Satterthwaite J, Tollison J, editors. Handbook on pain management. 2nd ed. Baltimore: Williams & Wilkins; 1994. p. 136-51.
152. Turk D, Meichenbaum D. A cognitive-behavorial approach to pain management. In: Wall P, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 1337-48.
153. Turk D, Melzack R. editors. Handbook of pain assessment. New York: Guilford; 1992.
154. Woolf CJ, Bennett GJ, Doherty M, Dubner R, Kidd B, Koltzenburg M et al. Towards a mechanism-based classification of pain? Pain 1998;77:227-9.