Article from"Australasian Musculoskeletal Medicine", Vol.7, May 2002, pp. 6-15

The Physiology of Deep, Somatic Pain

by Nikolai Bogduk, Newcastle Bone and Joint Institute

Contemporary knowledge about pain physiology is dominated by cutaneous pain, neuroma pain and neuropathic pain. The reason for this is understandable. The skin provides a target that can be stimulated in a controlled manner using a variety of stimuli – touch, pin-prick, heat, and applications of chemicals, both in experimental animals and in human volunteers. Cutaneous pain can be studied without invading the organism. Neuromas and nerve injuries can be induced at selected and desired sites and provide a known and isolatable source of nociception. Phenomena such as cutaneous hyperalgesia and receptive fields can be readily mapped because they are distributed across only a two-dimensional surface.

The irony is that epidemiologically, cutaneous pain, neuroma, and neuropathic pain are relatively uncommon. Far more common is deep, somatic pain, otherwise referred to as musculoskeletal pain for the reason that, to the patient, the pain seems to arise in muscles, bones or joints; it is felt deeply and definitely not in the skin.

For something as common as musculoskeletal pain, knowledge of its physiology is meagre compared to that of cutaneous pain. Although research into cutaneous pain has been critical in elucidating nociceptive pathways and control mechanisms, and although these principles might be applied to musculoskeletal pain, unless they have been explicitly demonstrated to apply, the possibility remains that different and distinctive processes might apply to musculoskeletal pain.

Certain obvious differences are immediately evident. Skin is exteroceptive, designed to respond to external physical stimuli such as heat and touch. Teleologically, there is no reason for deep somatic structures to be heat nociceptive in the same way as skin. It can be construed that the purpose of cutaneous nociception is to avoid or escape external, threatening stimuli; deep somatic pain cannot be escaped. Since deep tissues lack touch transduction, there is no reason to expect they exhibit Aβ allodynia.

The Legacy

The history of research into musculoskeletal pain can be depicted graphically in three time lines (Figure 1). The earliest studies can be classified as clinical experimental studies, in which pain phenomena were studied in normal, human volunteers. These were then followed by anatomical studies, which pursued the histological substrates of deep, somatic pain. The youngest style of research has been animal experiments in which nociception from musculoskeletal tissues, as opposed to skin, has been studied. Each of these streams of research commenced at various times during the twentieth century, and has continued into the present time.

Another dimension of musculoskeletal pain research has been the target structure. Clinical studies have focused largely on pain stemming from the

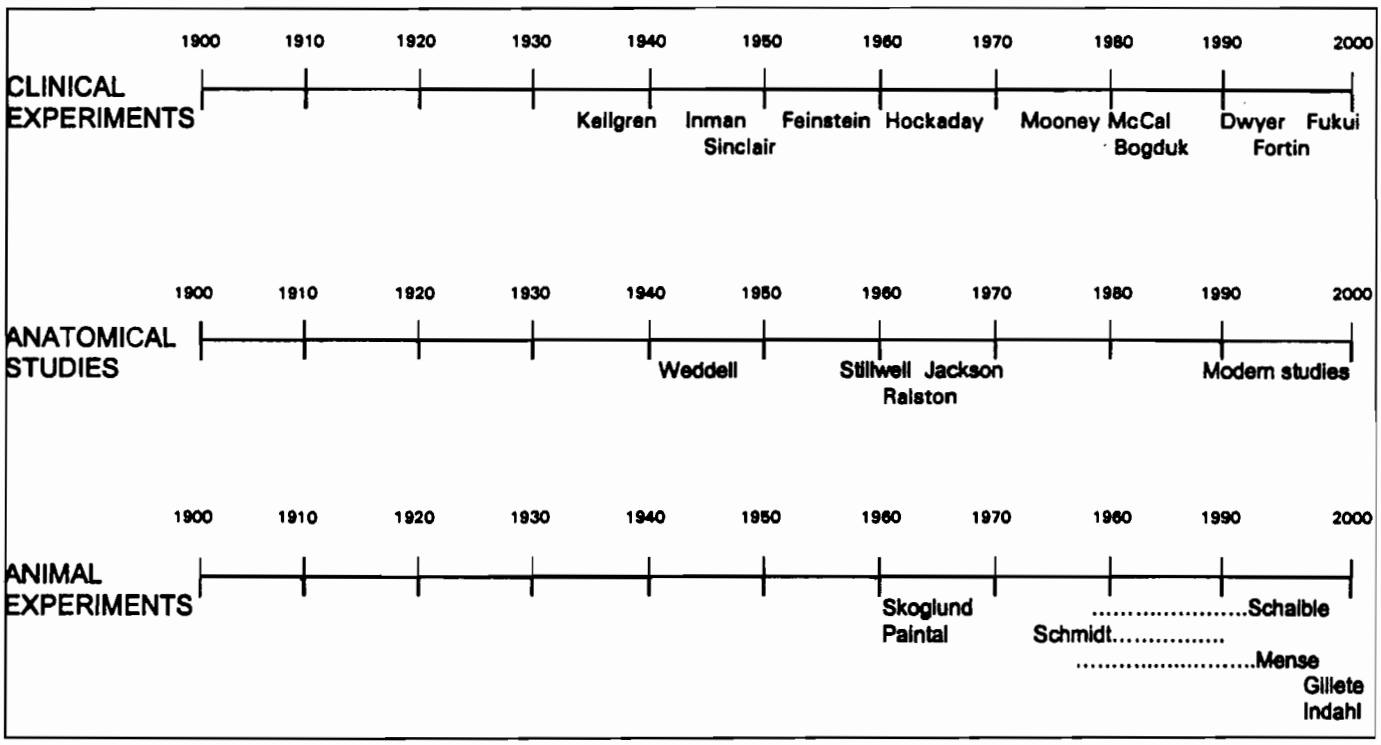

Figure 1. Time lines indicated the occasion, by principal author, of cardinal studies on the mechanisms of deep, somatic pain, in the categories of clinical experiments, anatomical studies in humans, and animal experiments.

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joints and muscles of the vertebral column, largely perhaps because of all the musculoskeletal pains, spinal pain has remained the most poorly understood or rather the one least able to be ascribed, conveniently and dismissively, to "arthritis". Meanwhile, animal experiments have focussed on the knee joint because this joint is the most accessible joint whose behaviour can be controlled and studied in perfect isolation. To a lesser extent, animal experiments have used the ankle joint, again ostensibly because it can be isolated and controlled.

Clinical Experiments

Much of our present understanding of the phenomenology of musculoskeletal pain can be traced to work of Kellgren in the late 1930s. In an effort to understand musculoskeletal pain in patients he explored how deep somatic pain might be elicited in normal volunteers, where it was perceived, what it felt like, and what other features were associated with it.

Kellgren's first study[1] was on referred pain from muscle. He demonstrated that noxious stimulation of muscle, with injections of hypertonic saline, produced pain that was diffuse and perceived remote from the site of stimulation. Moreover, in the limbs, muscle pain tended to be perceived towards the joint upon which the muscle acted. Stimulation of axial and paraxial muscles produced pain anteriorly in the trunk or abdomen or into the upper or lower limb.

Kellgren's most lasting and penetrating contribution, however, was in the study of spinal referred pain.

In an era when disc prolapse had just been discovered and spinal pain was ascribed to nerve root compression, Kellgren[2] ventured a competing paradigm. He showed that noxious stimulation of the interspinous ligaments, by injection of hypertonic saline, could produce referred pain in remote areas.[2] Stimulation of thoracic ligaments produced pain in the posterior and anterior chest wall. Stimulation of cervical and lumbar ligaments produced pain in the respective limbs.

Kellgren's experiment was not intended to demonstrate that interspinous ligaments were the source of back pain and neck pain. Rather, they established several principles:

1. Spinal pain could arise from noxious stimulation of intrinsic structures of the vertebral column.
2. Such stimulation produced referred pain in the trunk and limbs.
3. Referred pain could be produced by mechanisms other than nerve root irritation.
4. This referred pain was not neuralgic in nature, in that it was not shooting, burning or stabbing in quality, and not associated with numbness or paraesthesiae in the skin; rather, it was dull and aching in quality, diffuse and hard to localise in distribution, and perceived deeply, in which respects it resembled the complaints of many patients.
5. In order to distinguish this type of referred pain from pain caused by nerve root irritation or pain arising from viscera, it could be referred to as somatic referred pain. That term specified that the source of pain was in the somatic tissues of the body as opposed to viscera or nerves.
6. Somatic referred pain followed a segmental distribution that was not dermatomal in nature (Figure 2). Stimulation of successively lower spinal segments produced pain in successively more caudal regions of the body wall or limbs, but these regions did not correspond to the known dermatomes of the body. Kellgren believed this pattern to reflect a segmental pattern of innervation of deep tissues.

Kellgren's report and interpretation were not well accepted, because they ran contrary to prevailing wisdom that

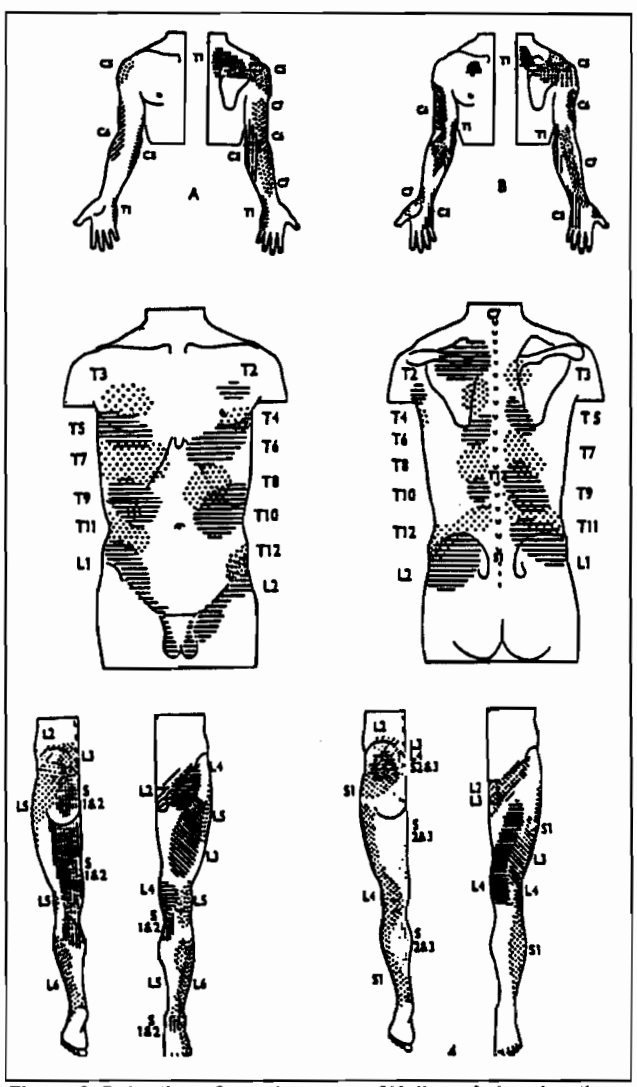

Figure 2. Selections from the maps of Kellgren[2] showing the distribution of referred pain following the noxious stimulation of interspinous ligaments in normal volunteers, at the segments indicated.

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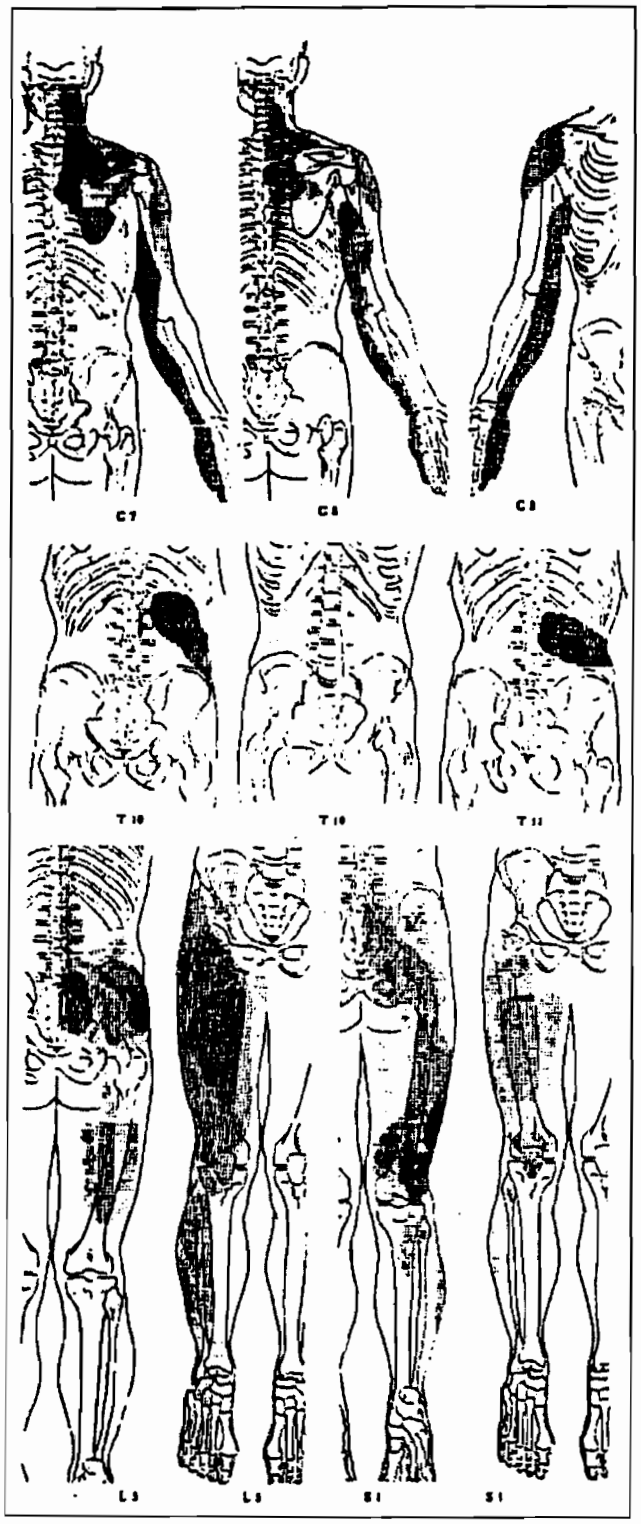

Figure 3. A selection from the maps of Feinstein et al[7] showing the distribution of referred pain following the noxious stimulation of interspinous tissues in normal volunteers, at the segments indicated.

referred pain must be causal by root irritation. Sinclair et al[3] tried to reproduce Kellgren's experiment and failed to produce referred pain to the limbs. They argued against his interpretations and submitted that his injections must have inadvertently stimulated nerve roots. In a contemporary essay on referred pain Sinclair and associates[4] argued that referred pain was due to axonal branching in the periphery, and involved antidromic propagation of impulses to the referred zone, which then triggered pain in that zone, which was then propagated orthodromically back along the same nerve.

However, Kellgren's observations were subsequently reproduced by Hockaday and Whitty[5] and by Whitty and Willison,[6] although the frequency and extent of referred pain to the limbs that they encountered was not as dramatic as that reported by Kellgren. Full corroboration was provided by Feinstein et al[7] who published maps of referred pain that resembled those of Kellgren in extent but not in exact location (Figure 3).

In a short but inordinately influential paper Inman and Saunders[8] firmly consolidated the concept of deep, somatic referred pain. The paper presented little information on methods beyond stating that deep somatic tissues – periosteum, ligaments, bone, joints and muscles, throughout the body were noxiously stimulated by scratching with a needle, drilling with a wire, or by injections of formic acid or 6% saline; it presented no quantitative data; but it assertively declared profound results. The sensitivity of deep somatic tissues was ranked in the order – periosteum > ligament > joint capsule > tendon > fascia > muscle. Most influentially, the paper depicted maps of the dermatomes, the myotomes, and the sclerotomes of the body, in order to contrast their patterns. Dermatomes are the regions of skin innervated by individual spinal nerves, and myotomes are the regions of muscle innervated by a given spinal nerve. Sclerotomes were presented as the regions of bones, joints and ligaments purportedly innervated by the same spinal cord segment. The latter were declared to be the basis for somatic referred pain, and have been repeatedly quoted in the literature since. This paper was influential because it declared an attractive concept but its influence was inordinate because the maps of sclerotomes that it provided were idealised and not based on published quantitative data. The consistency of patterns of referred pain was not stipulated.

In 1950, Kellgren left the spine, and together with Samuel[9] studied the knee joint. In normal volunteers they explored the sensitivity of different structures in the knee with a needle introduced through anaesthetised skin; in patients undergoing arthrotomy they studied the sensitivity of synovium; but in a dramatic experiment they opened the knee of Samuel in order to explore the sensitivity of the synovial membrane across its entire extent. They found the fibrous structures: ligaments and capsule to be nociceptive to me-

chanical and chemical stimulation, but the synovial membrane was largely insensitive to pin-prick, crushing with forceps, and chemical stimulation, except on a few occasions in isolated areas near the upper border of the patella and towards the sides of the joint.

The tradition of Kellgren was resurrected after 1976 when investigators ventured to determine referred pain patterns from specific structures that might be more likely sources of spinal pain than the interspinous ligaments.

Using injections of hypertonic saline, Mooney and Robertson[10] showed in normal volunteers that the lower lumbar zygapophysial joints could be sources of low back pain and referred pain in the lower limbs. They complemented their study with observations of relief of similar patterns of pain in patients following anaesthetisation of the lumbar zygapophysial joints.

This work was corroborated by McCall et al[11] who confirmed that local and referred pain could be evoked in normal volunteers by stimulating the lumbar zygapophysial joints, but the patterns of referred pain that these investigators encountered were not as extensive as those reported by Mooney and Robertson.[10] Moreover, McCall et al demonstrated that the areas of referral from upper lumbar joints overlapped those from lower joints. Consequently, the location of referred pain could not be used to identify the segmental location of a painful joint.

In their experiments, Hockaday and Whitty[5] and Feinstein et al[7] had noted that somatic referred pain could be associated with muscle spasm in the zone of referred pain; and Mooney and Robertson[10] mentioned that referred pain from the lumbar zygapophysial joints was associated with activity in the hamstring muscles, which they demonstrated by EMG. This phenomenon was explored by Bogduk[12] who reproduced Kellgren's experiments but also showed that referred pain from the lower lumbar interspinous ligaments and muscles was accompanied by involuntary activity in the multifidus muscles, tensor fasciae latae and gluteus medius. This activity started shortly after the onset of pain and dissipated as the pain eased over the next few minutes.

The work of Mooney and Robertson[10] was reproduced in the neck by Dwyer et al[13] who stimulated the cervical zygapophysial joints in normal volunteers by distending the joint with injections of contrast medium. The evoked pain was perceived in distinctive, segmental locations (Figure4). In a companion study, the same workers showed how these maps could be used to guide diagnostic investigations.[14]

The sacroiliac joint was the next target in the study of spinal pain. Fortin et al [15] stimulated the sacroiliac joints of normal volunteers with injections of contrast medium and found that the induced pain was perceived over the sacral and gluteal region.

Most recently a pair of Japanese studies[16,17] revisited the lumbar and the cervical zygapophysial joints. The investigators used injections of contrast medium to stimulate individual joints, and electrical stimulation of the nerves that supplied them. They provided quantitative data on the incidence of pain in selected regions following stimulation of a given joint or a given nerve, which was the first time that such data were provided in the history of study of spinal pain. However, the data did not alter the thrust of the conclusion of previous studies. In the lumbar spine, referred pain from the zygapophysial joints could occur in the buttock or lower limbs but not in a reliably distinctive segmental pattern. In the cervical spine, the patterns were more consistent and distinctive, as shown by Dwyer et al[13] (Figure 4).

Work not yet published, but under peer review, will show that the pain patterns reported for the cervical zygapophysial joints (Figure 4) is not specific for zygapophysial joints, for the cervical intervertebral discs exhibit essentially identical pain patterns. Referred pain maps, therefore, are not indicative of the structure that is the actual source of pain, but they do indicate the likely segmental location of the structure. The common factor is neurology. Referred pain maps indicate the segmental innervation of the source of pain but not the responsible structure. Thus, for example, all structures innervated by C5,6 refer pain to the C5-6 area (Figure 4), be they a disc or zygapophysial joint.

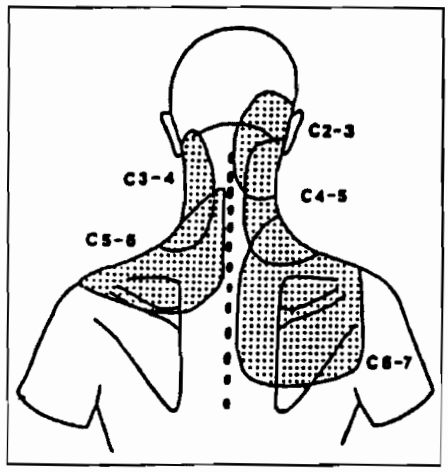

Figure 4. The distribution of referred pain following the stimulation of cervical zygapophysial joints in normal volunteers, at the segmental levels indicated. Based on Dwyer et al.[13]

Summary

Clinical experimental studies in normal volunteers have shown that:

- deep somatic structures are nociceptive;
- in rank order, the sensitivity of structures is periosteum > ligament > joint capsule > tendon > fascia > muscle;
- pain from deep, somatic structures is referred to remote sites;
- pain from muscle tends to be referred to the joint on which the muscle acts;
- pain from spinal structures is referred in a quasi-segmental fashion, at thoracic levels to regions of

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thoracic and abdominal walls, at cervical and lumbar levels into the respective limb girdles and limbs.

- Of specific structures of the spine, those that are nociceptive and capable of producing referred pain are:
  the interspinous ligaments
  the paraspinal muscles
  the zygapophysial joints
  the sacroiliac joint.

Comment

The concept of "sclerotomes" was invented to provide an explanation of the patterns of deep, somatic referred pain. It implies that deep tissues are innervated in a segmental fashion analogous to dermatomes and myotomes, and therefore, referred pain is perceived in deep tissues with the same segmental innervation as the source of pain.

Although this concept is attractive as a helpful explanation of referred pain, there is no explicit evidence for it. Dermatomes and myotomes are valid anatomical entities. Their segmental innervation can be demonstrated by anatomical and physiological means. Dermatomes were mapped by studying the zones of eruption of the vesicles of herpes zoster, which constitute a physical tracer of segmental nerves; and by studying the zones of numbness after dorsal rhizotomies. Myotomes were established by mapping zones of weakness after segmental nerve injury, and by mapping EMG activity evoked by electrical stimulation of segmental nerves. Were the experiments ethically feasible, dermatomes and myotomes could be determined by introducing tracer substances into segmental nerves.

There is no equivalent evidence about sclerotomes. No-one has traced segmental nerves to deep tissues using anatomical or physiological means. Sclerotomes lack a physical substrate. Maps of sclerotomes have been based exclusively on the subjective descriptions of patterns of referred pain in individuals undergoing experimental noxious stimulation of deep, somatic tissue.

Although sclerotomes may, indeed, reflect deep segmental innervation that has yet to be demonstrated, another interpretation is that they simply represent perceptual patterns, in which case they are determined more by connections with the central nervous system than by peripheral patterns of innervation. This contrasting interpretation does not invalidate the concept or utility of pain maps but it does challenge the propriety of regarding a sclerotome as an anatomical substrate for deep somatic pain. Rather than a physical entity it may be a psychophysical entity.

Anatomical Studies

Towards the end of the 19th century and in the early 20th century, anatomists had studied the innervation of various tissues: the epithelia of skin and cornea, teeth, mucous and serous membranes, and blood vessels. The pursuit of the anatomical substrate of deep, somatic pain in humans began in 1940.

Weddell and Harpman[18] studied the sensations evoked from deep fascia, tendons and periosteum, and correlated these with the structure of nerve endings found in these tissues. Some 20 years later these studies were complemented by those of Stillwell,[19] on tendons and aponeuroses, and by Ralston et al[20] who studied human fasciae, tendons, ligaments, periosteum, joint capsules and synovium.

Deep tissues were found to be innervated by three types of nerve endings: free nerve endings, complex, unencapsulated receptors, and encapsulated receptors. Fasciae, joint capsules and ligaments typically exhibited all three types of endings. Tendons contained mainly free nerve endings and relatively simple unencapsulated endings and small encapsulated endings. Periosteum exhibited all three types of endings, which were particularly abundant near the sites of attachment of muscles, tendons or ligaments. In synovial membrane, only free nerve endings were detected. The anatomists ascribed a nociceptive function to the free nerve endings. To the unencapsulated endings they ascribed a proprioceptive function. The encapsulated endings they considered to be pressure transducers.

Receptors in spinal tissues were first systematically studied by Jackson et al[21] in 1966, who established that the ligaments and joints of the spine were innervated in a manner like those of the appendicular skeleton. More recent studies, using immunohistochemical and other advanced staining techniques, have confirmed and elaborated these findings.[22-25]

Whereas it was accepted that the spinal ligaments, muscle and synovial joints received a nociceptive innervation, the innervation of intervertebral discs remained controversial until 1980. The earliest studies found nerve endings in the outer most fibres of the anulus fibrosus but subsequent studies failed to confirm this. Malinsky's study[26] in 1959 was definitive and was later corroborated by others.[27-29] The outer third of the anulus fibrosus is consistently innervated from birth. Accordingly the intervertebral discs join the other deep, somatic tissues as having an innervation.

Animal Experiments

Animal experiments on deep, somatic pain lagged substantially behind clinical experiments. Consequently more was known sooner about the phenomenology of somatic pain and somatic referred pain than about its physiological mechanisms. The reasons for this lag are multiple. Foremost is probably fashion. For many reasons neurophysiologists focused their attention on the operation of nerves, synapses, muscle spindles and neu-

romuscular effectors. Leadership and expertise developed in these domains; and young scientists were more likely to pursue a career in one of these established disciplines than to enter a field that lacked leadership. Pain research became possible and attractive when individuals trained in other domains of neurophysiology turned their attention to pain. As a result, the concerted study of pain physiology did not commence until the 1970s. A second factor was technology. Pain is mediated by small diameter peripheral affected fibres and by small neurons in the spinal cord. These could not be studied until devices were developed that provided access to small neurons. Thirdly, once the incentive arose to study pain and once the necessary technology to do so became available, it was convenient and pragmatic to study cutaneous pain first. The study of deep, somatic pain followed.

Articular Nociception

The earliest electrophysiological studies of the cat knee joint, by Gardner[30] in 1950, and by Skoglund[31] in 1960, described the effect of stimulating articular nerves on reflexes evoked from the joint. The first concerted efforts to study joint nociception electrophysiologically were undertaken by Schaible and Schmidt, who performed preliminary work in the late 1970s, and published their first comprehensive study in 1983.[32,33] They showed that group III and group IV afferents could be activated by mechanical and by noxious stimuli.

Work undertaken since that time has conveniently been reviewed by Schaible and Grubb.[34] The following summarises the cardinal features of contemporary knowledge of articular nociception:

- The fibrous tissues of joints – periosteum, capsules, menisci and ligaments are well endowed with nerve endings.
- Earlier studies provided conflicting results concerning the innervation of synovium, but immunohistochemical studies have confirmed the presence of nerve fibres in this tissue.
- The articular nerves of joints consist of myelinated and unmyelinated fibres, the proportion differs in different nerves but the majority of fibres (ca 80%) are unmyelinated.
- A minority of myelinated fibres are group III fibres with free nerve endings.
- Half of the unmyelinated fibres are group IV fibres with free nerve endings.
- Fibres with free nerve endings exhibit a beaded structure suggestive of multiple transducer sites.
- Group III and group IV fibres exhibit a variety of response characteristics.
- Some are low threshold mechanoreceptors with respect to innocuous movements but also in a graded fashion to increasingly noxious strains of the joint.
- Some are weak low threshold mechanoreceptors that respond to innocuous movements but exhibit a graded response only to noxious stimuli.
- Some are high threshold mechanoreceptors that respond to extremes of movement and also in a graded fashion to noxious strains.
- Some fibres respond only to noxious pressures applied to the joint capsule.
- Some fibres respond only to chemical stimuli.
- Other fibres are silent under normal conditions but become sensitive in inflamed joints.
- Glutamate and substance P are the cardinal neurotransmitters of primary afferents from joints.
- Joint afferents project to lamina I, laminae V and VI, and the dorsal part of lamina VII of the dorsal horn.
- Spinal cord neurones responding to articular stimulation are located in laminae I, and IV-VIII of the dorsal horn.
- Joint afferents activate interneurones, motor neurones, and cells of the spinocerebellar and spinothalamic tracts.
- Second order neurones in the dorsal horn, responsive to joint afferents consist of nociceptive-specific and wide-dynamic-range neurones.
- The receptive fields of second order neurones innervated by joint afferents are under tonic descending inhibitory control.

Inflammation

Articular nerves not only mediate nociception from inflamed joints, they also contribute to the inflammation. In regard to the latter, the role of articular nerves can be regarded as nocifensive in that the nerves act to promote repair of an ostensibly damaged joint.

Inflammation affects articular afferents in different ways. Group II afferents are minimally affected, if at all.[34] In contrast, many but not all Group III and Group IV afferents are either activated or sensitised.[34] Low threshold mechanoreceptors respond more strongly; high threshold mechanoreceptors respond at lower thresholds; and silent nociceptors become active.

Articular afferents are sensitised by serotonin, PGE_2, PGI_2 and bradykinin.[34] Bradykinin is the most potent mediator and acts initially on B_2 receptors but subsequently on B_1 receptors which become upregulated in inflamed joints. The prostaglandins facilitate the effect of bradykinin. All these mediators are released from damaged tissue cells or inflammatory cells.

The inflammatory process is promoted by substance P, neurokinin A and CGRP, which are released from the peripheral terminals of articular nociceptors.[34] Substance P increases vascular permeability, and CGRP causes vasodilatation. These effects

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are compounded and reinforced by noradrenaline and neuropeptide Y, that are released from sympathetic nerve terminals.[34] Collectively these processes constitute neurogenic inflammation, that is, sensory and sympathetic nerves contribute to mechanisms of inflammation.

Afferent input from inflamed joints also affects second-order neurones that subtend those joints.[34] The threshold for activation of nociceptive-specific neurones is lowered. The response of wide-dynamics-range neurones is increased. Receptive fields enlarge. More cells exhibit ongoing discharge; and descending inhibition is increased. This probably reflects a continued input from the inflamed areas.

Muscle Nociception

The first neurophysiological study of nociception from muscle was that of Paintal,[35] in 1960, who demonstrated that muscle nociception was mediated, at least in part, by group III afferents. He showed that these afferents could be activated by pressing or squeezing muscle fibres, and that they were activated by injections of hypertonic saline, like those used by Kellgren[2] to elicit pain from muscle in humans.

However, the study of muscle nociception remained relatively dormant for some 20 years. It was resurrected by Mense and Schmidt,[36] and sustained by Mense,[37,38] in the mid 1970s. These investigators showed that Group IV afferents from muscle could be activated by bradykinin, potassium, serotonin, and histamine. Progress since that time has been summarised in a review by Mense.[39]

The cardinal features of muscle nociception are:

- Muscles are innervated by nerves which differ in their composition, from muscle to muscle, but a typical profile would be 40% myelinated and 60% unmyelinated fibres.
- Of the myelinated fibres, 60% are motor.
- Of the unmyelinated fibres, about half are sympathetic efferents.
- Of the myelinated sensory fibres, 50% are Ia, Ib and Group II afferents; 20% are Group III afferents.
- About half of the unmyelinated fibres are Group IV afferents.
- Of the Group III and Group IV afferents, at least 40% are nociceptive.
- Most of the nociceptive afferents are activated by squeezing the muscle or by chemical stimulation with bradykinin, serotonin or potassium ions.
- Some nociceptive afferents are silent under normal conditions and become active only in damaged or inflamed muscles.
- Some nociceptive afferents exhibit ongoing activity in undistributed resting muscles.
- Muscle nociceptive afferents project to second-order neurones in lamina I and lamina V of the dorsal horn which project to the thalamus and hence to the cortex. (These pathways are not necessarily exclusive to muscle afferents, for they may involve convergence with cutaneous and other deep afferents.)
- Second-order neurones are subject to tonic descending inhibition.
- The peripheral terminals of muscle nociceptive afferents release substance P and CGRP.
- Muscle nociceptive afferents are sensitised by bradykinin, prostaglandins and serotonin; they are desensitised by LTD_4.
- Muscle pain is induced by trauma, inflammation or ischaemia of a muscle; each of these processes seems to involve the activation of muscle nociceptors by bradykinin, prostaglandins or potassium.
- There are no experimentally validated explanations of chronic muscle pain in the absence of inflammation.

Referred Pain

A mechanism for somatic referred pain has been demonstrated in multiple animal experiments. Both articular and muscle afferents exhibit convergence.[34,39] They synapse on second-order neurones that also receive an input from other deep somatic tissues and from skin. With respect to spinal referred pain, animal studies have revealed hyperconvergent neurones – ones that respond to stimulation of muscles, joints and intervertebral discs of the lumbar spine as well as the lower limbs.[40]

Accordingly, referred pain can be explained on the basis of perceptual ambiguity. When a dorsal horn neurone is stimulated by one of its convergent afferents, pain is evoked but the neurone does not convey information to the brain as to which of its afferents was the source of pain. At best, the cortex deduces that the source lies in one or other or all of the structures subtended by the activated neurone. The experience becomes one of pain throughout all of the structures rather than from a single, specific source.

Intriguing are recent studies of spinal pain mechanisms.[41] Noxious stimulation of intervertebral discs evokes reflex muscle activity in the paraspinal muscles. Distension of the zygapophysial joints inhibits this activity. These observations indicate that therapeutic interventions directed at one element in a vertebral motion segment can influence the effects of nociception arising from other elements in the same segment.

Muscle Spasm

Deep somatic referred pain can be associated with involuntary activity in muscles. How consistent this phenomenon is has not been determined, nor has the distribution of such activity been mapped for particular sites of noxious stimulation. Nevertheless, it

seems that muscle activity can occur in muscles adjacent to and remote from a site of noxious stimulation. In the case of lumbar spinal pain, activity can occur in paraspinal muscles, and in muscles of the lower limb girdle and lower limb. Such phenomena have been observed in human experiments[5,7,10,12] and reproduced in animal experiments.[39,42]

The teleological purpose of such activity has not been explained. It cannot be ascribed to guarding, for that does not explain activity in remote sites. Activity in gluteal and hamstring muscles does not serve to guard the lumbar spine in the same way as spasm of the abdominal muscles might be perceived to protect underlying viscera. There is no evidence to suggest that it is more than an epiphenomenon of local and referred pain.

Vexatious is the issue of whether this muscle activity is a secondary source of pain. There is no evidence that it is. More particularly, there is no evidence in support of a pain-muscle spasm-pain cycle, and some evidence against this concept. Although a popular concept in some clinical circles, it has not been substantiated experimentally, and recent reviews have dismissed it as invalid.[39,42]

Incomplete Explanations

Clinical experiments have shown that the joints and muscles can be sources of local and referred pain. Complementary animal studies have shown that joints and muscles have a nociceptive innervation that under normal conditions can be activated by excessive strains or pressure, or by chemical insults. Comprehensive models are available for pain produced by inflamed joints or muscles. What remain unexplained are the mechanisms of chronic pain from joints or muscles that are not inflamed.

Whereas injury and inflammation are adequate explanations for acute muscle pain, there is no satisfying or compelling model for chronic pain stemming from muscle, and no evidence, clinical or experimental, that it occurs. Even ischaemia in tonically active muscle has been challenged as an explanation of acute, let alone chronic, pain from muscle.[39]

With respect to joints, inflammation is clearly an acceptable explanation for the mechanism of pain in rheumatoid arthritis, in which features of inflammation are clinically obvious. However, the same does not pertain to osteoarthrosis. In that condition, inflammation is not consistently present. It is manifest in sudden "flares" or effusions,[43] but at other times the degree of inflammation varies between patients at different phases of the disease.[44,45] Although prominent in some cases of osteoarthrosis, inflammation is low grade or absent in others.[44,45]

Among the proffered, alternative explanations are capsular contracture and intraosseous venous hypertension.[45] Capsular contracture is a valid explanation for joint stiffness, and even of pain at the limits of available movement, but it does not explain pain at rest. On the other hand, intraosseous venous hypertension could.

The model proposed that as subchondral sclerosis occurs in osteoarthrosis, venous channels become obstructed, causing distension of veins proximal to the obstruction.[46] Stretch of the adventitia of these veins becomes the mechanism of nociception.

Testing this theory is difficult for it requires puncture of the putatively painful bone and manometric study of its intraosseous veins. Such studies of this nature that have been conducted reveal trends in favour of the model but insufficient differences to discriminate consistently between normal and painful joints.[46]

Another emerging but unexplored concept is that of subchondral bone pain. Histological studies have demonstrated nerves in the subchondral bone of synovial joints[47-49] and in the end plates of intervertebral discs.[50] This invites the proposition that if, as a result of age, injury or disease, the subchondral bone is weakened, it might undergo excessive strain under compression loading, which activates the subchondral nerves. Such a process would explain pain in weight-bearing joints that is relieved by rest, and may gain favour as an explanation of lumbar discogenic pain.[50]

These various concepts have one thing in common. They place the nociception of joint pain not in the fibrous tissues or synovium of the joint but within its bones. Proof or refutation of either the concept of intraosseous venous hypertension or of subchondral bone pain awaits the next technological advance in the study of deep, somatic pain: the ability to study the neurophysiology of nerves inside, or innervating, bones.

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Discussion Topics

What criteria would have to be satisfied for you to credit that a patient's pain is arising from:

a muscle?
a ligament?
a joint?
a bone?

What clinical evidence (a) is available, (b) might be pursued, that is consistent with the proposition that the pain of osteoarthrosis is due to intraosseous venous hypertension? Does any of this evidence prove the mechanism? What would you consider to be the most definitive data that should be obtained?

Explain why resurfacing an osteoarthritic knee so promptly relieves pain.