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Neurobiology of the myofascial trigger point

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The varied manifestations of chronic myofascial pain syndrome (MPS) have been difficult to understand and difficult to explain in neurophysiological terms until recently, when investigators began to unravel the mechanisms of cutaneous, visceral, somatic and articular pain perception. Myofascial pain is pain of muscle origin, although the central feature, a painful trigger point, can also be found in skin, tendon, periosteum and ligament. The properties of MPS that define it clinically and differentiate it from other painful muscle conditions are: (a) the exquisitely tender trigger point in a taut band of muscle; (b) the restriction of range of motion related to the taut band; (c) a local twitch of the taut band within muscle when physically stimulated; (d) the appearance of zones of referred pain; and (e) the development of satellite trigger points within the zones of referred pain (Table 1) (Travell

Table 1. Clinical characteristics of myofascial trigger points.

Localized tenderness in a taut band of muscle
Local twitch response to the contracted, taut band
Referred pain felt in a distant region
Restricted movement
Weakness
Autonomic dysfunction

and Simons, 1983). Central to the concept of the trigger point is its extraordinary tenderness and its ability to produce pain in a distant site. In neurophysiological terms, the trigger point is hypersensitive and has an expanded receptive field that includes distant areas that are usually distal to the primary trigger area of pain. Persistent and hypersensitive trigger areas with patterns of referred pain that do not follow easily understood dermatomal, myotomal, neural or vascular pathways have been well described since the 1940s (Travell et al, 1942, 1944; Travell and Rinzler, 1952), but have not been well explained. Questions that still need to be addressed have to do with the nature of the trigger point itself, and with how a painful area in muscle can be associated with pain referred to other areas.

Baillière's Clinical Rheumatology—
Vol. 8, No. 4, November 1994
ISBN 0-7020-1867-8

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NEUROPHYSIOLOGY OF MYOFASCIAL TRIGGER POINTS

Attempts to characterize the myofascial trigger point (MTrP) pathologically have been disappointing. Biopsies of tender areas in both fibromyalgia and MPS have shown amorphous ground substance (Awad, 1973, 1990), ragged-red fibres (Bengtsson et al, 1986a; Larsson et al, 1988), and 'rubber band structures' (Bartels and Danneskiold-Samsøe, 1986), but no consistent anatomical change has been identified using light microscopy, electron microscopy or histochemistry. A recent re-examination of the problem showed no characteristic light microscopic changes or immunoenzymatic abnormalities, and only non-specific degenerative changes on electron microscopy (empty basement membrane sleeves and lipofuscin inclusions) (Drewes et al, 1993).

Similarly, attempts to delineate physiological changes have not been much more successful. The finding of reduced high-energy phosphates in tender points in the trapezius muscles of fibromyalgia patients indicates a metabolically stressed area in the muscle (Bengtsson et al, 1986b). These studies were extended to a group of patients that very likely had MTrPs (Larsson et al, 1988), in a study of histopathological and histochemical changes in trapezius muscle biopsies of ten subjects with work-related myalgia. Ragged-red fibres consistent with mitochondrial dysfunction were seen in the subjects, but not in the controls, and suggest that the changes in the tender areas of muscle could be due to a local, temporary hypoxia. Low oxygen tension has been postulated to occur as a result of a zone of ischaemia in trigger points, but if so there is no broad body of evidence that would implicate such a finding as a cause of muscle pain emanating from a trigger point. None of these or similar findings has led to a clear concept of the nature of the MTrP.

A recent magnetic resonance imaging (MRI) study of tender points in the trapezius muscle of 18 subjects with fibromyalgia failed to identify any morphological changes (Kravis et al, 1993). The study was not intended to evaluate MPS, but the trapezius muscle is one of the most commonly affected muscles in MPS. My own personal experience is that most persons with fibromyalgia have at least some trigger points in the trapezius muscle as well as tender points. The assumption, therefore, though unverifiable, is that some of the subjects in the study had MTrPs.*

The failure to find an inflammatory response in the MTrP and lack of any firm evidence that prostaglandins play a role in the development of trigger point pain mean that non-steroidal anti-inflammatory drugs have only a general analgesic role in the treatment of MPS. There would seem to be no specific role for the inhibition of cyclo-oxygenase and the interruption of the conversion of arachidonic acid to prostaglandins in the inactivation of the MTrP.

Calcium binding to troponin, a protein complex on the thin, actin-

* Editor's footnote: The Editor's view is that most FMS patients seen in primary or rheumatic practice do not have trigger points in the trapezius muscles, but the majority do have tender points.

containing filaments of muscle, regulates vertebrate striated muscle contraction (Ebashi and Endo, 1968; Hannon et al, 1993). Travell and Simons (1983) postulated that the taut band associated with the trigger point could be the result of activation of the actin-myosin complex by calcium. Calcium could be released either by rupture of the sarcoplasmic reticulum due to stress overload, or through a failure to restore the adenosine triphosphate (ATP) that is essential for the calcium pump. Failure to restore ATP could be the result of a local energy crisis; e.g. that produced by local ischaemia. This could cause the ATP-dependent calcium pump to fail, resulting in an inability to recapture ionized calcium. It could also result in failure of the ATP-dependent release of the actin–myosin complex, thereby perpetuating local muscle contraction. Reduced high-energy phosphate levels have been found in the painful muscle of fibromyalgia (Bengtsson et al, 1986b), supporting the concept that ATP-dependent events could be impeded, although whether MTrPs were included in the fibromyalgia muscle studied is not known. In either case, the contracted taut band could persist in the absence of electrical activity through the failure to replenish ATP stores (Simons, 1988).

ELECTROMYOGRAPHY OF MTrPs

Hubbard and Berkoff (1993) found that persistent low amplitude (about 50–700 μV) spontaneous activity was present in the MTrP when the adjacent muscle tissue 1 cm away was electrically silent. Two types of spontaneous activity were described: a low amplitude constant background activity of about 50 μV, and an intermittent higher amplitude activity of 100–700 μV. They showed that curare abolishes all voluntary activity, but does not diminish the spontaneous MTrP activity. However, phentolamine (a selective sympathetic blocking agent that blocks the action of noradrenaline) administered either intramuscularly or intravenously does abolish the MTrP activity, but not the voluntary muscle activity (D. Hubbard personal communication), suggesting that the MTrP is driven by the sympathetic nervous system. The structure which Hubbard and Berkoff (1993) think meets these criteria is the muscle spindle, since the intrafusal fibres of the spindle are sympathetically innervated and are not under the control of the alpha motor neurone. It is possible that the spindle is altered when the muscle is injured, and that the distortion or possibly distension is responsible for the pain, but this hypothesis is unproven.

End-plate electromyographic activity has been studied using a histological method for localizing the needle tip or point of recording (Jones et al, 1955). In these studies a low amplitude discharge of 50–700 μV was also found, similar to the observation of Hubbard and Berkoff (1993), and localized to an area of small intramuscular nerves. Denervation abolished the activity after 24 h, indicating that an intact motor nerve was necessary. Insertion of the needle was associated with acute pain. Brief muscle twitches were sometimes observed as the needle entered the active zone. These phenomena suggest that Jones and colleagues (1955) were putting the needle

into a trigger point, and that the needle tip was close to small intramuscular fibres. Moreover, they were unable to identify muscle spindles near the needle tip. Their work raises the question of whether the low amplitude activity that Hubbard and Berkoff describe is really end-plate activity rather than spindle activity. However, Hubbard and Berkoff were able to abolish this activity with phentolamine and not with curare, indicating that the activity could not be associated with normal alpha motor neurone fibres. Localization of the structures at the needle tip in the studies of Hubbard and his colleagues using a marker such as the iron deposition technique described by Jones et al (1955) will answer the question about the nature of the structures from which this electromyographic activity originates.

The issue that these studies raise is the fundamental one of the nature of the MTrP. There is no proven anatomical correlate of the MTrP at this time. It is clearly an electrophysiological phenomenon, however, as Hubbard and Berkoff (1993) have shown, and as the studies of the local twitch response discussed later in this chapter demonstrate. The origin of the low amplitude, persistent electrical activity described by Hubbard and Berkoff as characteristic of the MTrP has not yet been identified. However, it may represent end-plate activity, as described by Wiederholt (1970) in his investigation of end-plate noise, rather than muscle spindle activity. Wiederholt (1970) found a low amplitude (under 100 μV) activity that was confined to a small area, with spread less than approximately 0.3 μm, and a second, more sporadic activity of higher amplitude. The low amplitude activity had an initial negative polarity characteristic of miniature end-plate potentials. The location of the electrode needle tip was determined to be at the end-plate region using iron deposition techniques. Tubocurarine injected intra-arterially obliterated the end-plate noise activity. Wiederholt suggested that this end-plate noise is the same as that sometimes encountered when studying normal subjects in whom a low amplitude irregular baseline activity occurs when an 'active' area is encountered by the electromyography electrode, and that this is sometimes accompanied by a brief twitch of a strip of muscle and by a complaint of deep, boring pain. This is, in fact, a description of the clinical response to needling a MTrP. A significant distinction between the findings of Hubbard and Berkoff and Wiederholt is in the response to pharmacological manipulation. Curare abolished the end-plate noise activity in Wiederholt's study, but did not in Hubbard and Berkoff's study, while phentolamine abolished the spontaneous trigger point activity in Hubbard and Berkoff's study. (Wiederholt did not study the effects of phentolamine in his experiments.)

The response to phentolamine indicates an element of sympathetic influence underlying the spontaneous electrical activity of the MTrP found by Hubbard and Berkoff (1993). Gillette and his colleagues (1994) showed that sympathetic stimulation directly activates primary afferent fibres of non-nociceptive receptors, which may then secondarily activate dorsal horn neurones. This is evidence of sympathetic control of sensory input in certain circumstances. To reconcile the seemingly contradictory findings of Hubbard and Berkoff (1993) and Wiederholt (1970), one would have to postulate that there is similar sympathetic innervation of muscle end-plates,

at least at a MTrP, corresponding to the activity described by Gillette et al (1994) for the sensory afferent receptors. Such sympathetic innervation would explain the persistence of MTrP electrical activity during exposure to curare that is abolished by exposure to phentolamine. If such a role for the sympathetic system were to be proven, then the persistent spontaneous MTrP activity identified by Hubbard and Berkoff (1993) would not necessarily come from the muscle spindle, but could arise in the motor end-plate. This dilemma will finally be resolved if and when data are obtained demonstrating sympathetic control of motor end-plate activity and the anatomical localization of the electrode tip in electromyographic studies of the MTrP.

That there is a motor afferent-efferent loop between the trigger point and the spinal cord has been well shown by studies of the local twitch response elicited by physical stimulation of the tender point in the taut band (Dexter and Simons, 1981; Fricton et al, 1985; Hong et al, 1986; Hong, 1994). The characteristic electromyographic signature of the local twitch response in a specific muscle is greatly reduced or abolished when the corresponding peripheral nerve is cut or rendered ischaemic. However, though this finding has implications for the motor activity of the taut band, it does not tell us about the nature of the trigger point as a source of pain.

NEUROPHYSIOLOGY OF TRIGGER POINT PAIN

If the MTrP is considered to be a peripheral pain generator, essential questions can be asked about how such a peripheral pain source induces a reaction in which there is increased sensitivity causing either hyperalgesia or allodynia, wherein a normally non-noxious stimulus produces pain. A second question to be answered is how pain in one muscle site produces pain felt in a distant area. A third question relates to the development of MTrPs in the zone of referred pain. How is the painful active trigger point maintained for prolonged periods of days, months or even years? How is it that this chronic pain can be rapidly abolished once the trigger point is inactivated? Other questions to be considered have to do with the changes of skin or limb temperature associated with trigger points, and how myofascial pain causes weakness (Table 2). The answers to some of these questions can be inferred from experimental studies conducted in animal models as well as the results of careful clinical studies.

Table 2. Unanswered questions in MPS.

What is the physical representation of the myofascial trigger point?
How can a painful trigger point in one area in one muscle cause pain in a different site, even in a different muscle?
How does a painful muscle trigger point cause a non-noxious stimulus to feel painful?
How does a trigger point develop in the distant zone of referred pain?
What are the mechanisms leading to persistence of the trigger point over months or years?
How is it that chronic pain can be rapidly abolished once the trigger point is inactivated?
How is it that limb temperatures can be altered in the presence of a trigger point?
What causes muscle weakness in the absence of atrophy in MPS?

In considering muscular pain, the clinician is struck by its dull, aching, poorly localized nature, like visceral pain. In contrast, cutaneous pain has an initial 'first' pain that is sharply localized, and results in a rapid reflex withdrawal. This 'first' type of pain is associated with activation of A-delta fibres, the thinly myelinated group III fibres found in cutaneous tissues, which conduct at a rate of about 20 m/s. A-delta nociceptors respond either to heat or thermal stimulation or are responsive to high-threshold mechanical stimulus (mechanoreceptors) (Cross, 1994). 'Second' pain is the dull, aching pain associated with muscle or the pain which lingers after the initial sharp cutaneous pain associated with the protective withdrawal reflex has subsided. 'Second' pain is mediated by thin, unmyelinated group IV C fibres. These are slowly conducting fibres, conducting at 2–5 m/s. C fibres respond to mechanical, thermal and chemical stimulation; hence, they are called polymodal (see Table 3 and Figure 1). They are the nociceptive fibres

Table 3. Characteristics of peripheral nerve fibres.

Nerve type	Myelin	Conduction velocity	Stimulus
A-delta (group III)	Thin	20 m/s	Thermal, mechanical
'C' fibres (group IV)	None	2–5 m/s	Polymodal (thermal, mechanical and chemical)

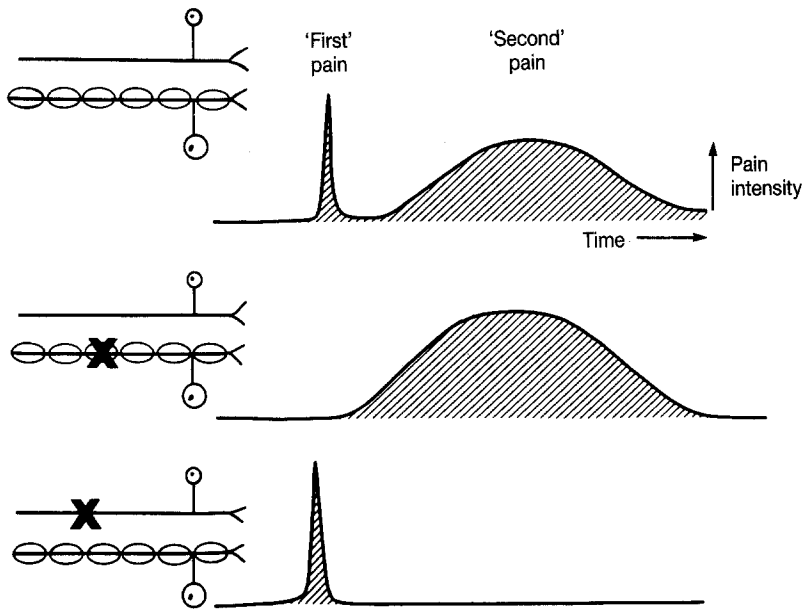

Figure 1. Diagram illustrating 'first' and 'second' pain mediated by two different fibre types. 'First' pain is transmitted by small, thinly myelinated A-delta fibres. 'Second' pain is transmitted by small, unmyelinated C fibres. Blocking selected fibres eliminates the associated 'first' or 'second' pain associated with that fibre. From Fields (1987) *Pain*. New York: McGraw-Hill, with permission.

present in skin and in muscle, situated in close relationship to blood vessels in muscle.

Peripheral mechanisms

Free nociceptive nerve endings are not found within muscle fibrils. Group III and IV free nerve endings are located in tight spatial connection to muscular arterioles and capillaries, and so are related to the vascular supply of the muscle. The free nerve endings of group IV C afferent units (unmyelinated, slow-conducting fibres) are sensitive to the naturally occurring pain-producing substances bradykinin, 5-hydroxytryptamine (5-HT) and histamine (Mense and Schmidt, 1974). Chemically induced pain, as opposed to mechanically induced pain, is mediated by both unmyelinated group IV C fibres and thinly myelinated group III A-delta fibres (Mense, 1977). Much of the work studying the response and modulation of these peripheral nociceptive receptors and also of the central pain mechanisms has been based on a model which uses a pain-inducing chemical stimulus injected into muscle. The reasonable assumption is made that mechanical injury to muscle, such as from trauma or even repetitive stress syndromes, releases naturally occurring painful substances that behave similarly in the intact animal. There are no studies, however, which demonstrate the release of noxious substances like bradykinin or histamine from injured muscle in the development of the clinical MTrP in humans. Nevertheless, this model has been fruitful in the study of pain of muscle origin because it produces a defined and limited peripheral injury allowing study of peripheral and central components of pain transmission and modulation. One further drawback is that the experimental design only permits the study of relatively short duration events, and does not necessarily address the problems of chronic myofascial pain. Hence, these studies must be interpreted cautiously.

A noxious or inflammatory lesion in muscle can sensitize the peripheral receptors, possibly leading to allodynia (Mense and Meyer, 1988). Bradykinin, injected into skeletal muscle, activates both nociceptive and low-threshold mechanosensitive receptors. Most such sensitized receptors have increased responses to mechanical rather than to thermal stimuli. Thin myelinated group III fibre nociceptive receptors are sensitized more than non-myelinated group IV fibre nociceptive receptors. The mechanical threshold of nociceptors is lowered into the innocuous range, leading to activation of the pain transmission pathway by normally non-pain-producing stimuli. This phenomenon is also well described for cutaneous hyperalgesia (Dubner, 1991; Willis, 1992). The responsiveness of peripheral nociceptor free nerve endings can be modulated by a large number of factors. For example, opioids have been shown to have an analgesic effect when infiltrated locally at a site of peripheral inflammation in muscle (Stein et al, 1988). Furthermore, adrenaline (epinephrine *USP*) sensitizes peripheral nociceptors in damaged muscle but not in normal muscle, suggesting a possible mechanism for peripheral sensitization to sympathetic activity in muscle injury that may occur in sympathetically maintained pain syndromes (Kieschke et al, 1988). These observations are of interest for several

reasons. First, they suggest that agents may act locally to alter (heighten or lessen) peripheral nerve nociceptive responses. Consequently, drugs that do not cross the blood-brain barrier may still have an effect on peripheral pain receptors. Second, mechanical or electromechanical manipulations such as acupuncture, which may alter local opioid levels, could modulate the sensitivity of peripheral nociceptor receptors. Detailed reviews of this subject have recently been published (Mense, 1993a,b). These mechanisms are not unique to muscle, but represent more general properties of pain receptors, and are seen in other tissues as well (Schaible and Grubb, 1993).

The central connections of muscle peripheral afferents have been mapped in the experimental animal (Mense and Craig, 1988). The small diameter group III and IV (A-delta and C) fibres terminate in the superficial dorsal horn (lamina I) and lamina V of the spinal cord, and are probably monosynaptic in their projection to the thalamus via the spinothalamic tract. Cutaneous afferents project to dorsal horn laminae II, III and IV primarily, so that there is a difference in the somatopic distribution of primary nociceptive afferent fibre projection between skin and deep somatic tissues. Modulation of the afferent pain signal in response to inhibitory and facilitory influences both from peripheral receptors and from spinal and supraspinal centres occurs in the dorsal horn laminae where the small diameter fibres terminate.

Central mechanisms

Modulation of the incoming pain signal occurs in response to physical and pharmacological manipulation at both the peripheral receptor site and the central pathway, from the dorsal horn neurone to the cerebral cortex. These changes have important implications clinically, as they alter threshold sensitivity to different stimuli and the size and distribution of receptive fields. Translated to the clinical situation, modulation of the pain signal may explain hyperalgesia and analgesia, and expand our understanding of the phenomenon of referred pain.

Referred pain

The first published reports of referred pain patterns arising as a result of muscle injury were by Edeiken and Wolferth (1936) and by Kellgren (1938a). The latter studied the distribution of referred pain in patients presenting with muscular tenderness, and then studied volunteers whose muscles or ligaments were injected with hypertonic saline. He described eight patients who had tender areas in muscle which when stimulated with firm palpation produced a sensation of pain and tenderness in other muscles. He infiltrated the tender sites in the muscle with procaine and diminished both the local and the referred pain and tenderness, and restored the previously restricted range of motion of the affected limb. Kellgren then induced pain by injecting hypertonic saline into muscle and mapped the resulting patterns of referred pain, thereby establishing the concept of referred pain from muscle (and from other deep structures such as perios-

teum, tendons and ligaments) both clinically and experimentally (Kellgren, 1938b, 1939; Lewis and Kellgren, 1939).

Mechanisms underlying the phenomenon of referred pain were not elucidated for many years following these early studies. Ruch (1979) elaborated the convergence-projection theory that Selzer and Spencer (1969) included in a discussion of possible mechanisms of referred pain. The theory of convergence of afferent pathways has become the most well established, though it is not the only mechanism that has been experimentally substantiated. The mechanisms for the development of referred pain are similar in different tissues such as skin, muscle, viscera and nerve. Patterns of referred pain may involve only one organ (e.g. skin only or muscle only) or mixed organs (e.g. skin and viscera or skin and muscle). Branching of unmyelinated peripheral sensory afferent nerves, with branches distal to the dorsal root ganglion arising in different sites or organs, provides one mechanism for nociceptive input arising from two separate sites converging on one afferent nerve, and therefore on one dorsal horn neurone (McMahon and Wall, 1987).

Electrical stimulation of afferent inputs to the nociceptive neurones of the trigeminal subnucleus caudalis from facial skin, oral mucosa, tooth pulp, laryngeal mucosa, cervical skin and muscle, and jaw and tongue muscle produces activity of single neurones (Sessle et al, 1986). Neuronal activation is produced by stimulation of afferents outside of the natural receptive field of these neurones, indicating enlargement of their normal receptive fields. Stimulation of muscle fascicles in the median nerve produces referred pain in proximal muscles outside of the innervation territory of the median nerve (Torebjork et al, 1984). Enlargement of cutaneous receptive fields and the appearance of dissociated distant receptive fields as well as hyperalgesia occurred following the injection of complete Freund's adjuvant into the rat forepaw (Hylden et al, 1989). A similar phenomenon occurs in muscle when a noxious stimulus is applied. Injection of bradykinin into an area in muscle outside of the receptive field of specific dorsal horn neurones produces new receptive fields in 42% of these neurones. The new receptive fields were all in muscle, and had the properties associated with high-threshold mechanosensitive neurones (Figure 2) (Hoheisel et al, 1993). This study shows that a painful stimulus in muscle can induce widespread changes in receptive fields without requiring a noxious stimulus of the specific dorsal horn neurone whose field is altered. Hence, as pointed out by the authors, there appear to be latent connections between dorsal horn nociceptive neurones and peripheral receptors that can be activated or made effective in the face of appropriate noxious or inflammatory stimulation. Activation of these potential connections could explain the presence of the zones of referred pain described in MPS (Travell and Simons, 1983). A similar phenomenon occurs when mustard oil is used to create an inflammatory lesion in the masseter muscle (Hu et al, 1992). Facilitation of the response of brainstem neurones in trigeminal nerve subnuclei to cutaneous electrical stimulation results, presenting as increased spontaneous activity of the neurone. The cutaneous mechanoreceptive field also expands. Thus, both sensitization of the dorsal horn cell and enlargement of the cutaneous field

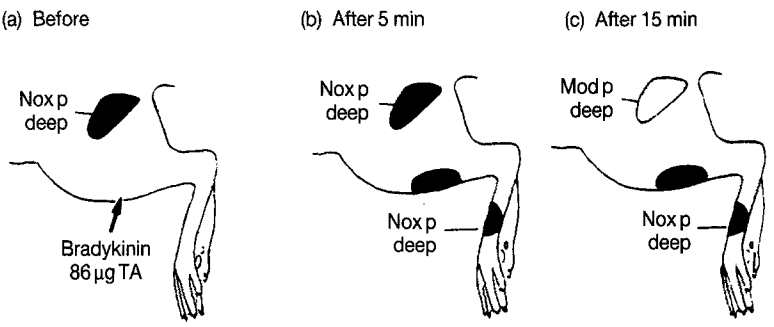

Figure 2. Appearance of new receptive fields in muscle following noxious stimulation of skeletal muscle. Bradykinin is injected into the tibialis anterior (TA) muscle of a rat and changes in the receptive field of a dorsal horn neurone are mapped. A. The location of the original receptive field to noxious deep pressure stimulation (nox p deep). B. Five minutes after injection two new receptive fields are present in deep tissue which have a high mechanical threshold. C. Fifteen minutes after injection the original receptive field had a lowered mechanical threshold and responded to moderate deep pressure (mod p deep), whereas the two new receptive fields still required noxious deep pressure stimulation, indicating a high mechanical threshold. From Hoheisel et al (1993), *Neuroscience Letters* **153:** 9–12, with permission.

Table 4. Consequences of neuronal plasticity.

Sensitization
Enlargement of receptive field size
Increase in receptive field number

results from a deep muscle inflammatory lesion. The changes in the receptive fields in muscle and skin are representative of the general property of neuronal plasticity (Table 4), which leads to hyperexcitability, and to expansion and movement of receptive fields in response to noxious stimuli in different tissues (Dubner, 1990).

Central modulation of dorsal horn cell activation

The dorsal horn neurones to which primary muscle afferents project are mainly of two types, similar to the dorsal horn cells that mediate cutaneous pain: low-threshold mechanoreceptors and high-threshold mechanoreceptors, the latter being nociceptive specific, responding only to noxious stimulation. A third cell type responds to both noxious and non-painful stimuli, including non-nociceptive mechanical stimulation. These cells are termed wide dynamic range neurones and are found in laminae I and V of the dorsal horn. Dorsal horn neurones can be further classified by the source of their input. Some receive input only from deep tissues, and some receive input from both cutaneous and deep tissues (Hoheisel and Mense, 1990). Neurones receiving input from skeletal muscle always receive input from either skin or other deep tissues as well. Thus, no neurones receive input

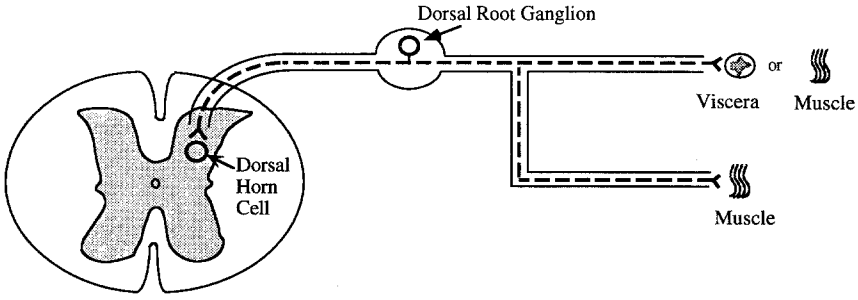

Figure 3. A peripheral sensory afferent nerve can branch distal to the dorsal root ganglion, one branch going to a deep muscle and another going to a viscera or to another site in the same or in a different muscle. Afferent impulses from the two (or more) different sites converge on a single dorsal horn neurone. Nociceptive impulses from one site may then be interpreted as coming from either or both sites, with the effect that pain may be poorly localized or that pain is felt to arise from two distinct areas.

exclusively from skeletal muscle. The dorsal horn neurones receiving skeletal muscle input have two receptive fields: a deep (muscle) field and a cutaneous field, usually distal to the muscle. Input from two separate receptive fields therefore converge on the same neurone, forming the basis for a cutaneous representation for deep muscular pain (Figure 3). Moreover, when a cold block is applied to the spinal cord (Wall, 1967), thereby blocking descending impulses affecting dorsal horn neurone function, the neurones become more responsive to stimulation (sensitized) and the receptive fields of the neurones increase. This important study not only demonstrates the presence of a mechanism that can account for at least one type of referred pain phenomenon with separate receptive fields in skeletal muscle or in muscle and skin, but it also shows that inhibiting descending spinal impulses can result in heightened neuronal activity, including expansion of the receptive fields of specific neurones.

The clinical counterpart is that a condition that blocks descending inhibitory impulses or that activates descending facilitory impulses can lead to hyperalgesia and the appearance of new or enlarged areas which respond to mechanical stimulation such as touch or innocuous pressure as if they were noxious stimuli. In a further study, reversible cold block of the spinal cord affected neurones with input from deep tissues (muscle, tendon, joint) more than cells receiving cutaneous input only (Xian-Min and Mense, 1990). These studies demonstrate that dorsal horn neurones receiving group III and IV afferent nociceptive input from muscle have innate connections with other neurones, or that the primary afferents have potential connections with other neurones that are not normally operative, but that in either case can become active and can result in multiple or enlarged receptive fields. This has important implications for the concept of referred pain and hyperalgesia in persons with MPS, since MTrPs can be associated with one or more areas of referred pain or a local zone of pain much larger than the trigger point itself.

Modulation of descending inhibitory influences

Changes in the descending modulation of dorsal horn neurones can be produced in a number of different ways, such as stimulation of the nucleus raphe magnus in the brainstem or the systemic infusion of the 5-HT antagonist methysergide, and in other models studying nociception in different tissues. The results are similar in each system in that there is a changeable descending control from rostral spinal cord to distal spinal cord (Chiang et al, 1989; Saito et al, 1990). Mense and coworkers looked at the response of nociceptive-specific dorsal cell neurones that receive both cutaneous and deep input to alterations in the descending control mechanism (Yu et al, 1991). Opioidergic, adrenergic and serotonergic antagonists (naloxone, phentolamine and methysergide, respectively) were used in order to determine if any of these substances play a definable major role in descending inhibition. The antagonists were injected into the cerebral ventricle and the response to noxious stimulation was assessed. Naloxone alone resulted in the strong enhancement of deep receptive fields indicating that tonic descending inhibition of nociceptive input from muscle and other deep tissues is partly mediated by opioid receptor-related synapses. This expands the concept of supraspinal influences on dorsal horn neurone function and illustrates the effect pharmacological manipulation may have on pain of muscle origin.

Sympathetic nervous system influences

Mense and colleagues (Yu et al, 1991) found a reduction in the response to stimulation of deep receptive fields when phentolamine, an adrenergic inhibitor, was injected into the cerebral ventricle. This result is in keeping with the finding that clonidine, an alpha-2 agonist which suppresses the peripheral action of noradrenaline, administered intrathecally produces analgesia rather than sensitization in the rat tail flick and hot plate tests (cutaneous thermal stimulation) (Tjolson et al, 1990). Alpha-2 receptors are thought to occur on the postsynaptic sympathetic terminals. These results, in both cutaneous and deep tissue systems, suggest that the descending inhibitory system affecting nociception is not mediated by noradrenergic systems in the spinal cord or brain. The interplay of the sympathetic system and the MTrP in what can be termed sympathetically maintained myofascial pain must occur at either the peripheral receptor or the dorsal horn neurone. The clinical presentation that we have frequently seen is a MTrP associated with a cool, dusky limb, or rarely locally increased skin temperature or piloerection. Some patients complain of a burning sensation near the trigger point or at a distance from it. Activation of the trigger point may accentuate these physical findings and subjective sensations. Inactivation of the trigger point by needling (either dry needling or by injection with local anaesthetic) produces a rapid change that occurs in seconds, so that the limb temperature normalizes, piloerection disappears or the burning hyperalgesia stops. Campbell et al (1992) at Johns Hopkins University hypothesized that sympathetically maintained pain occurs when peripheral tissue injury results in

the expression of alpha-1 receptors. Alpha-1 receptors are activated by noradrenaline release from sympathetic terminals and in turn activate nociceptive receptors that cause pain. The maintenance of sympathetically enhanced pain occurs because the pain that results from activation of the peripheral nociceptors increases synthesis of alpha-1 receptors in the nociceptors which respond to the release of noradrenaline from the sympathetic nerve endings, creating a vicious circle. Roberts and Kramis (1992) argue that non-nociceptive afferents from deep tissues are known to produce longer duration central sensitization than cutaneous nociceptors and may be involved as well as the cutaneous nociceptors, and that the 'deep aching' component of this kind of pain suggests an involvement of the deep tissue nociceptors. Hence, they would broaden the concept of peripheral components to include both deep nociceptor and non-nociceptor afferents rather than just the cutaneous nociceptor afferents implicated by Campbell et al (1992).

Studies by Mense (1994) have led him to propose that the mechanism of referred pain from muscle involves the central convergence of afferent input at the level of the dorsal horn neurone. Moreover, he thinks that unmasking previously ineffective dorsal horn connections by substance P release from nociceptive afferent fibres and stimulation of synaptic changes in the spinal cord by noxious afferent input are important factors in the development of new receptive fields.

MUSCLE WEAKNESS IN MPS

Mild weakness without atrophy occurs in persons with myofascial pain. This phenomenon may occur because of restricted motion and effort secondary to pain (Travell and Simons, 1983) or because shortening of the muscle causes weakness compared with the fully stretched muscle, according to Starling's law that 'length makes strength'. However, weakness could result from reflex inhibition of anterior horn cell function as a result of painful sensory input. This unproven assertion is suggested by the clinical phenomenon of the buckling knee: the sudden weakness of the vastus medialis muscle that contains MTrPs.

A study designed to test the hypothesis that a painful lesion of skeletal muscle causes an increase in the neuromuscular component of muscle tone by activating gamma motoneurones (Mense and Skeppar, 1991) instead found that gamma motoneurone activity was inhibited. To the extent that such activity facilitates alpha motoneurone activity, inhibition of muscle spindle input might produce muscle weakness.

SUMMARY

The clinical phenomenon of the MTrP is accessible to any clinician who takes the time to learn to palpate skeletal muscle gently and carefully, and who is willing to learn the functional anatomy necessary to understand the

regional spread of MTrPs through functional muscle units (Travell and Simons, 1992). Yet despite the years of clinical study of MPS, the pathophysiology of the central feature, the trigger point, has remained elusive. Many investigators have contributed to the general understanding of the mechanisms of pain perception, but we owe a particular debt of gratitude to Dr Seigfried Mense of Heidelberg for his pursuit of the study of pain originating in muscle lesions. However, Dr Mense would be the first to caution us against the direct transference of the results obtained with an inflammatory lesion produced in the experimental animal to the pain of MTrPs in the clinic patient. Notwithstanding that, researchers in the field of pain have given us an understanding of the basis for the hyperalgesia, allodynia and the previously difficult-to-understand finding of referred pain zones that we see daily in our patients. Finally, the interesting initial observations of Hubbard and Berkoff (1993), suggesting that the muscle spindle may be associated with the trigger point, open yet another door in our understanding of the nature of MPS.

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