Convergent Referred Pain Mechanisms:
The research and implications for clinical practice

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Introduction

This paper will outline some of the research findings that shape our knowledge of convergent referred pain and relate these findings to current clinical practice of musculoskeletal pain medicine. Research has been performed using saline injections or intramuscular electrical stimulation (IMES) to look at patterns of referred pain and hyperalgesia. Various types of anesthetic blocks have been used to test patterns of referred pain and hyperalgesia. The definition of convergent referred pain adopted for this paper is pain perceived as arising from a location remote to the source of the pain.

The pain patterns are important to consider when treating chronic pain patients. Chronic pain patients may have a change in pattern or intensity of their pain with time that may be due to convergent referred pain pathways opening over that time. Convergent referred pain can remain after the original source of nociception has subsided, with the patient suffering from pain indefinitely. This residual pain may be a source of chronic pain and is amenable to treatment.

Mapping of deep pain

Referred pain is a phenomenon present in deep structures such as muscles due to poorly somatotopically mapped pain pathways.[1] The brain is unable to detect an exact focus for pain perceived from deep structures such as muscle or viscera. The neospinothalamic pathways that mediate cutaneous pain are highly organized somatotopically. Nociceptors, touch receptors, and pressure receptors are also stimulated when skin pain is present. The touch and pressure signals are delivered by the posterior columns which are better somatopically organized than the neospinothalamic pathways. The brain via the thalamus receives more than one set of information which allows an exact mapping of skin pain. The palaeospinothalamic pathways provide information to the thalamus for internal noxious stimuli. The somatotopic mapping is relatively poor and provides localization to within one segment of the spinal cord. The deeper the structure the less distinct its localization. There is no accompanying information from other receptors in deep tissues that helps the brain map deep pain precisely. In joints there are proprioceptors that travel in the posterior columns that are well mapped somatotopically and help localize joint pain.

The referred pain pattern of individual muscles does not depend on the dermatomes supplying the overlying skin but the underlying segmental supply of the muscle. For example, the top of the shoulder is supplied by the C3/4 dermatome. The underlying trapezius and the levator scapulae are supplied by C3/4 also. The referred pain by structures with a C5/6 segmental supply into the shoulder area is due to the shoulder muscles being supplied by C5/6 and not due to the overlying skin being supplied by these dermatomes. Shoulder and neck muscles can refer pain into the arm if they have similar segmental innervation. Referred pain due to irritation of the diaphragm by blood is referred to the shoulder tip because the diaphragm and the underlying shoulder structures having a similar segmental supply. The referral pattern is not due to the dermatomal distribution of the skin.

Studies on referred pain

Exogenous stimulation of muscle by injecting hypertonic saline or IMES to produce referred pain are the two most common methods used in the literature to stimulate muscle pain and referred pain. Excitation of afferents by hypertonic saline may be due to osmotic changes.[2] IMES has the advantage that it may be applied exactly with respect to time and localization. It can also elicit local and referred pain in an on-and-off manner, allowing temporal and spatial summation to be examined. It is also an easy method to use and produces high local (94%) and referred (78%) pain responses in healthy individuals.[3] Drawbacks are the stimulation of both efferent and afferent nerve fibres in an unnatural way and that it bypasses the sensory nerve endings thus giving no information on receptor transduction.

1. Referred pain patterns

IMES and saline injections can produce local pain and referred pain. Local pain after saline injections appears a few seconds after the infusion and lasts for several minutes depending on the concentration and volume of infusion. There is a delay of 30-40 seconds for referred pain to occur once the index pain has started.[4]

2. Positive correlation between stimulus, local, and referred pain

The greater the intensity of the stimulus the greater the intensity of local and referred pain. The greater the intensity of stimulus the more widespread referred pain is perceived. A significantly higher stimulus is required to produce referred pain compared to local pain.[3] For the diagnosis of convergent referred pain there would need to be symptoms at the primary site of nociception. If pain in the shoulder area is diagnosed as somatic referred pain from the cervical spine then pain in the region of the cervical spine should be present. However, the shoulder muscles to where the pain was previously referred may now be a primary pain generator and act independently of the initial noxious stimuli. Clinically, it is more likely to elicit referred pain by injection therapies (dry or wet needling) than deep tissue massage.[5]

3. Hyperalgesia

IMES has been used to determine pain thresholds in the referred pain areas. The lowest intensity to stimulate pain was taken as the pain threshold. Lowered pain thresholds have been found in referred pain areas, suggest-

ing a state of hyperalgesia exists in areas of referred pain. This correlates to clinical practice where the surrounding muscles around an injured area are tender.

4. Spatial summation

Stimulating an increased number of sites with IMES increases the pain experienced.[4] The mechanism responsible for this is likely to be an increased recruitment of nociceptor units giving increased input to the dorsal horn neurons. Clinically, a larger lesion is more likely to lead to greater pain than a smaller lesion of a similar nature.

5. Temporal summation

Temporal summation[4] produces an increase in the size of the referred pain. This may be due to increased nociceptive input to the dorsal horn generating an expansion of the receptive fields. Clinically, pain may increase in intensity and spread further the longer the pain persists. In patients with cervical spine pain referred into the arm, the greater the pain the further down the arm the referred pain spreads.

6. Nerve blocks and anesthesia

Studies that have anesthetized areas of referred pain have had contrasting results that may reflect anesthetic technique, duration and level of noxious stimuli, and site of primary pain.[4] Referred pain that was superficially anesthetized resulted in 23% reduction in referred pain intensity and complete anesthesia of the referred area resulted in 40% reduction in referred pain. The inability to abolish referred pain by anesthetizing it indicates that peripheral and central mechanisms play a role in the elicitation and maintenance of referred pain.[6]

Initial central sensitization and ongoing central sensitization has been proposed to explain referred pain patterns.[7] The stages proposed are initial central sensitization and ongoing sensitization which is influenced by peripheral sensitization. Initial central sensitization exists with the initial stimulus. Ongoing central sensitization occurs only if the focus of nociception is ongoing. With minor injuries the ongoing central sensitization is minimal.

With more extensive tissue damage, there is significant ongoing central sensitization. In studies of muscle stimulation where there is minimal tissue damage, the results will differ from studies where tissue damage is present after stimulation of muscles.

Anesthetizing the referred pain when minor tissue injury is present may eliminate the referred pain completely as the minor tissue damage may heal. Anesthetizing the referred pain when significant tissue damage is present may eliminate the referred pain until the anesthetic wears off. The referred pain returns as the injury causing the index pain has not healed (the ongoing central sensitization continues to be present and produce referred pain).

Central and peripheral mechanisms seem to be responsible for the generation of referred pain as it can be partly blocked by performing peripheral nerve blocks and anesthetizing the area of referred pain. Pain can spread to areas that do not share the same segment. Cardiac pain has been known to spread to the ear or may spread to the site of old injuries (angina has been described as being referred to an old vertebral fracture). Pain and hyperalgesia spreading to areas far removed from the injured area suggest central changes and facilitation are involved in the spread of hyperalgesia.

Theories of referred pain

Convergent-projection theory

Different afferents converge onto common spinal neurons[8] and are unable to be discriminated by higher centres. This theory explains the segmental nature of pain and also the increased referred pain intensity when stimulus is increased. This theory does not explain the delay in development of referred pain or the hyperalgesia or that referred pain has not been described as being a bi-directional phenomena. The threshold for local and referred pain is also different.

The axon reflex theory

Axons from two different structures converge prior to entering the dorsal horn and cause confusion regarding the site of nociception. These neurons are rare.

The thalamic-convergence theory

Convergence is occurring in the brain rather than the spinal cord.

The central-hyperexcitability theory

In animal studies noxious stimuli in muscles have been shown to open receptive fields at a distance from the original receptive field in the dorsal horn.[9] Latent convergent afferents in the dorsal horn are opened within minutes by noxious stimuli within muscle. Substance P is released in the dorsal horn from the primary afferents and is thought to play a role in the connectivity of the dorsal horn. Central hyperexcitability has also been shown in patients with chronic pain after whiplash and in fibromyalgia. When muscles were injected with saline the referred pain patterns was more widespread than for control subjects.[10]

Implications for management of pain

The treatment of acute pain needs to be optimal to prevent temporal and spatial summation. Optimal use of analgesia in the initial phase of acute injury should be able to reduce the pain input into the dorsal horn and reduce the chronicity and spread of pain. Optimal use includes regular reviews of pain medication in the initial phases. Somatic pain and neuropathic pain need to be recognized as treatment may vary. Ongoing monitoring of medication to increase and decrease doses or replace ineffective medication is imperative.

Referred pain patterns may outlast the original source of the pain. The muscles into which the referred pain has spread may become pain generators and need to be treated if symptomatic. The pain pattern may change with treatment of pain with the same segmental supply as the original source of pain. Referred pain may spread into all the muscles that are supplied by the segment that supplied the original injured structure. If the original injured structure heals, the referred pain muscles may become primary pain generators. In a shoulder injury that causes prolonged pain, referred pain may occur in all the muscles supplied by C5 and C6 (+/- one segment). Once the original shoulder structure heals the

muscles with the same segmental supply may remain painful.

Painful structures have a hierarchy of pain intensity with the most painful structure reaching the attention of the brain and suppressing other painful structures. The most common example is bilateral knee arthritis. Elderly patients often complain of one knee being severe and the other not bothering them. Once the painful knee is replaced then the other knee becomes painful after pain from the replaced knee settles. The other knee then often also requires knee replacement to alleviate the pain. The muscles in the segments where referred pain has spread are placed into a similar hierarchy. The most painful pain generator will produce pain that is consistent with its referred pain pattern that will be the most severe symptom. If this muscle is treated, then the next most painful muscle will surface with its pain pattern. This will often create a shift from one area to another often adjacent area. Sometimes a certain muscle can improve or become aggravated spontaneously due to certain postures while sleeping or awake. This can cause pain to shift within a region, a phenomena that is commonly described by patients.

Summary

Convergent referred pain can be responsible for chronic pain continuing despite the initiating noxious stimuli/ tissue damage healing. Patterns of referred pain need to be examined to find any sources of nociception. The segmental innervation of muscles will give a logical approach to treatment but the referred pain pattern is not restricted to only the segmental innervation. Deep muscles may be easier to reach using more invasive techniques such as injecting with marcain and saline. The multifidi in particular may require injections to reach them effectively. If there is a major structural lesion underlying the referred pain, then treatment will fail to give permanent relief of symptoms. The referred pain pattern may decrease with treatment but is likely to recur if the initial injured structure is still a source of nociception.

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