Sensory neural processing in work-related upper limb disorders

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Pain in the upper limb is a common complaint in adults, and is often attributed to or exacerbated by occupational activities. In many patients there is no demonstrable pathology in the neck or arm to account for the symptom, and this has prompted the hypothesis that such cases might arise through abnormal neural processing of sensory information with a lowering of pain thresholds. In this paper we review the evidence in support of this theory and suggest directions for future research.

Key words: pain; perception; upper limb

INTRODUCTION

Pain in the upper limb is a common complaint, and surveys of adults in the general population have generally indicated a 1-year period prevalence in excess of 20%.1 In some people the symptom arises from a specific disorder of the neck or arm, such as cervical spondylosis, capsulitis of the shoulder, epicondylitis or De Quervain's disease. Often, however, there is no demonstrable pathology to account for the pain, even though it may be severely disabling.

Many cases of upper limb pain, both specific and non-specific in origin, are thought to be caused or exacerbated by occupational activities. However, occupational causation cannot necessarily be inferred simply because the patient's work involves forceful or repetitive movements of the upper limb, or because the illness makes tasks at work more difficult. Unless there are distinctive features of the individual case (e.g. visible inflammation that resolves when the patient is away from work and returns when occupational activities are resumed), the link with work can only be made on the basis of epidemiological evidence.

Epidemiological investigation is difficult when the pathogenesis is uncertain and there are no objective diagnostic criteria. Studies are then forced to fall back on subjective reporting of symptoms as a measure of disease, with all the scope for bias that this entails. Our understanding of non-specific upper limb disorders and their causes would be advanced considerably if we could firmly establish the mechanisms underlying symptoms.

Knowing the pathogenesis of non-specific upper limb pain could also lead to improvements in patient care. New lines of treatment might be suggested, and providing patients with a clearer explanation for their symptoms might in itself be therapeutic.

The occurrence of pain, in the absence of any detectable inflammation or injury to the tissues of the neck or arm, has prompted the hypothesis that in these circumstances the symptom arises from abnormal processing of sensory information from the upper limb.2,3 In this paper, we review the evidence in support of this idea and discuss ways in which it could be further developed and tested.

THE PHYSIOLOGY OF PAIN

The International Association for the Study of Pain has defined pain as 'An unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage'.4,5 Most tissues of the body can give rise to pain when stimulated appropriately, notable exceptions being the lung, liver, spleen and parts of the brain itself. However, nociception (the detection and signalling of a noxious stimulus) and the experience of pain do not always go together. Pain is 'physiological' when it results from the activity of healthy nociceptive afferents excited by intense stimuli that exceed an appropriate threshold.

Nociception is mediated principally through small myelinated A-delta fibres and non-myelinated C fibres. C fibres are normally activated by strong mechanical stimulation, pinprick, heat or cold, or by noxious chemicals such as histamine, and the brain interprets...
the input as painful. A-delta fibres are activated by pressure, high temperature or chemical irritation, and when stimulated electrically they produce a stinging sensation.

Both the A-delta and the C fibres synapse in the dorsal horn of the spinal cord with neurons of the contralateral ascending spino-thalamic tract, other ascending tracts, and with interneurons connecting to other parts of the spinal cord grey matter. Among other things, the latter are important in mediating reflex withdrawal from painful stimuli. The ascending tracts carrying pain signals synapse in the thalamus, lateral reticular formation, periaqueductal grey matter, raphe nuclei, and other parts of the brainstem and midbrain, with complex onward connections to other parts of the brain including the frontal cortex, anterior cingulate gyrus and somatosensory cortex. There is thus scope for modification of nociceptive input at many points.

FACTORS INFLUENCING THE PERCEPTION OF PAIN

The normal physiological perception of pain can be altered by several mechanisms. 'Peripheral sensitization' occurs when tissue damage from whatever cause leads to the release of inflammatory mediators such as prostaglandins, bradykinin, substance P and calcitonin gene-related peptide (CGRP), which cause nociceptive nerve endings to become hyperexcitable. As a consequence, stimuli that would not normally be interpreted as noxious become capable of activating the nociceptors and causing pain. Thus, in acute gout, even gentle pressure on an inflamed joint is extremely painful.

Pain may also develop if injury to sensory neurons causes them to become hyperexcitable at ectopic locations along their course. It has been postulated that this is one of the mechanisms underlying the back pain that occurs when a herniated inter-vertebral disc presses on a nerve root. It may also contribute to the pain that sometimes occurs in a limb stump following amputation, the excitation occurring in neuramata which form at the end of severed nerves.

More centrally, nociceptive signalling can be altered in the spinal cord through a process of 'gate control' that was originally postulated by Melzack and Wall. This involves the action of neurotransmitters such as glutamate and aspartate, and of neuromodulators such as substance P. The latter are released by neurons, but tend to be slower acting than neurotransmitters, and to have more prolonged and varied effects. In the cord, neurotransmitters and neuromodulators are produced both by local interneurons and by fibres descending from the brain to the dorsal horn. Most dorsal horn neurons with nociceptive input also receive input from innocuous mechanical stimuli, and are organized on the basis of surround inhibition. Thus, pain from a noxious thermal stimulus can be reduced by simultaneous vibratory stimulation of the adjacent or contralateral dermatome, whereas no such effect is observed when the vibration is applied at a distance of two or more dermatomes. This type of inhibition underlies the use of transcutaneous nerve stimulation in the treatment of patients with chronic intractable pain.

Evidence for descending influences on nociceptive signalling in the cord comes, for example, from the observation that while the nociceptive reflex induced by electrical skin stimulation can be altered in normal subjects by the drug ketoprofen, no such modification occurs in paraplegic patients. In experimental animals, electrical stimulation of selected brain sites can inhibit reflex responses to noxious stimuli, although the animal remains alert and active. Additionally, further modification of nociceptive information occurs in the brain itself. For example, direct injury to the thalamus from a stroke can cause 'central' pain.

Changes in the neural processing of nociceptive information in the cord and brain are thought to explain why soldiers do not always experience pain from their wounds during the heat of battle, why patients with anxiety or depression are more likely to develop back pain than people with a normal mental state, and why pain can be reduced by placebos, hypnosis and distraction. It is possible that central sensitization through altered neural processing could also underlie the complaints of pain in the upper limb that occur without obvious associated pathology.

PAIN PERCEPTION IN PATIENTS WITH UPPER LIMB DISORDERS

If this hypothesis is correct, patients with non-specific upper limb pain should have unusually low thresholds for pain perception in the affected arm and perhaps elsewhere. Few studies have investigated the pain perception in patients with non-specific upper limb pain, but those that have do indicate lower thresholds than in controls.

Arroyo and Cohen tested 15 patients with refractory cervicobrachial pain and 10 normal volunteers by transcutaneous electrical nerve stimulation. They found that the thresholds for sensory perception and pain tolerance in the patients' unaffected limbs did not differ from those in controls, but that in symptomatic limbs pain tolerance was significantly reduced. Moreover, this was accompanied by a tendency of the unpleasant sensation to spread and by the persistence of dysaesthesiae.

Greening and Lynn explored tolerance to vibratory stimulation of the soft tissues of the forearm in 17 patients with 'repetitive strain injury', 29 asymptomatic office workers who used computer keyboards and 27 other controls. All of the asymptomatic subjects were tolerant up to a maximum amplitude of 400 μm, whereas 14 of the 17 patients experienced an allodynic response to vibration below this level. The response was observed in one or both arms, and was more marked on the side that had the worse symptoms. It is unclear how far the patients had been investigated to exclude specific pathologies in the neck or arm, but it is likely that most had non-specific upper limb pain.
Together, these two studies give strong encouragement to further research in this area.

DIRECTIONS FOR FUTURE RESEARCH

The findings of Arroyo and Cohen and of Greening and Lynn support the theory that upper limb complaints commonly arise from abnormal sensory processing, but they need to be confirmed in larger numbers of subjects. Furthermore, the anatomical distribution of abnormal pain perception needs to be more clearly defined. The study by Arroyo and Cohen suggests that, in contrast to fibromyalgia, where reductions in pain tolerance tend to be more generalized, the effect is confined to the symptomatic arm. However, the report by Greening and Lynn is less clear on this point. Demonstration that the effect is confined to the symptomatic arm, and not only by modulatory influences of the brain. It would also be helpful to explore tolerance for other types of sensory stimulation such as pressure and temperature.

Another technique that has been used to test for central sensitization to pain, and which could usefully be applied in patients with painful upper limb disorders, is the measurement of capsaicin-induced hyperalgesia. The test involves retaining a small volume of a dilute solution of capsaicin on the skin for 30 min and then measuring the surrounding area of mechanical hyperalgesia. This test potentially could usefully be applied in patients with painful upper limb disorders, is the measurement of capsaicin-induced hyperalgesia. The test involves retaining a small volume of a dilute solution of capsaicin on the skin for 30 min and then measuring the surrounding area of mechanical hyperalgesia. The area of hyperalgesia is increased in a number of disorders, and the observation that such effects can be reduced by drugs such as ketamine and alfentanil, which are believed to act mainly at central sites, suggests that, at least in part, it reflects central sensitization.

In applying these various neurophysiological techniques, comparisons should be made not only between patients with non-specific upper limb pain and asymptomatic controls, but also with patients who have pain from specific pathology in the neck and arm. If abnormalities can be confirmed in cross-sectional studies, a next step might then be to follow them longitudinally, both in established cases, some of whom would be expected to improve over time, and also in occupational populations, initially asymptomatic but with a high risk of developing upper limb disorders during follow-up.

CONCLUSIONS

In summary, the frequent absence of detectable pathology in the neck or arm of patients complaining of pain in an upper limb suggests that the symptom may be attributable to a reduced threshold for pain perception. Two published studies support this theory, but their findings require confirmation and amplification. If the hypothesis proves correct, it will open up important new avenues for epidemiological research, as well as scope for improving treatment.

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