COLLEGE LECTURES

Don't look now! Pain and attention

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This article is based on a lecture given at a conference on Chronic Pain and the Science of Attention at the Royal College of Physicians on 15 September 2004 by **David Blake** FRCP, Professor of Rheumatology/ Locomotor Medicine, Royal National Hospital for Rheumatic Diseases, Bath

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Clin Med 2005;**5**:482–6

ABSTRACT – Attention and pain are linked inexorably. The manipulation of attention, via either distraction or focused attention, has been used as a therapeutic initiative for generations. Imaging evidence and clinical observations demonstrate that attention can be altered with associated changes at the cortical level and this may have positive or negative effects on the individual. New theories suggest that cortical remapping and visual attention may play key roles in a cortical model of pain specifically involving the motor control system. Within this system, the relationship between allocentric (external) and egocentric (internal) stimuli are managed; where conflict occurs, somaesthetic disturbances may be generated. If an individual pays too much attention to such sensory disturbances, then they may report the disturbances as abnormal symptoms, which may explain the diverse symptomatology of fibromyalgia. The use of a therapeutic optokinetic device to correct existing imbalances in the motor control system is also discussed.

KEY WORDS: allocentric, attention, egocentric, human pain models, motor control system, optokinetic, pain

A child sits on his mother's knee, waiting for an inoculation. As the nurse moves the needle towards the child's arm, both mother and nurse distract the child through speech or activity in order to avert his gaze from the injection site and apparently reduce the pain of the needle. Distraction, or modification of attention, is one of the most commonly used non-pharmacological methods for controlling pain in children during invasive medical procedures.[1] On a more dramatic scale, reports of soldiers describing the extensive injuries of war as being minimally painful because of the benefit and distraction of an early discharge home are further examples of how attention and pain are linked inexorably.[2,3]

Attention is the direction of mental faculties to specific aspects of the internal or external environment, in order to accomplish goal-directed activities or for protection.[4] In this article, we describe how the interaction between attention and pain may be displayed and manipulated in the clinical setting and the possible mechanisms involved at the cortical level.

Attention and pain

Objective evidence of the link between attention and pain at the cortical level has been demonstrated using neuroimaging techniques. When subjects are asked to either focus or distract themselves from a painful stimuli, activation changes within the cortex. Specifically, during the distraction phase, there is an increase in activity in the periaqueductal grey region and the affective division of the anterior cingulate cortex, which coincides with subjects' reports of less pain.[5,6] Concurrently, areas that are usually associated with pain (eg thalamus, insula, cognitive division of anterior cingulate) show reduced activity. This activity can be modulated by the subject's expectation of pain. If pain is anticipated in an experimental setting, and a delay is built in before a painful or innocuous stimulus is delivered, then an enhanced attentional state is created during the anticipation period. This has been observed as an increase in heart rate. Cortical changes on functional magnetic resonance imaging (fMRI) demonstrate heightened expectation and a pain-related response, despite no painful stimuli being received.[7]

Increased attention and pain-related anxiety in people already experiencing pain have been shown to have negative effects, with patients displaying a greater tendency to overpredict new pain and be more fearful of movement.[8] Counterintuitively, if a limb is neglected following a stroke, ie dramatically reduced attention, the limb does not become pain-free. Patients commonly report ongoing burning, cold pain in paralysed limbs.[9] In the same manner, both motor and cognitive neglect have been described in complex regional pain syndrome type 1 (CRPS1), in which the limb is intensely painful.[10–12] In both conditions, central origins are attributed to the generation of these symptoms.

Immobility of a limb

Disuse of a limb in the absence of comorbidity can generate pain. This has been demonstrated in human and animal models using casting to immobilise an otherwise healthy limb.[13,14] Guo and colleagues described an animal model in which the hind limbs of rats were immobilised in plaster casts for a period of four weeks; only half of the rats had sustained a fracture of the tibia.[14] When the plaster casts were removed, both groups had evidence of raised temperature, mechanical allodynia, periarticular osteoporosis and oedema in the casted limbs. However, the allodynia and increased temperature resolved more quickly in the rats that had not sustained a fracture (resolution of allodynia: 6 weeks (non-fracture) versus 10 weeks (fracture); resolution of increased temperature: 2 weeks (non-fracture) versus 20 weeks (fracture)). Human subjects have reported symptoms of neglect after limb fracture, whereby they became less consciously aware of the existence of the fractured limb and felt that they lost control of the limb unless they looked at it.[15]

In stroke and CRPS1, increased attention towards the affected limb becomes the primary therapeutic goal. This may be achieved via desensitisation techniques, intensive physiotherapy or, in the case of stroke, constraint-induced movement therapy. The rationale behind this latter treatment is to force the patient to engage actively with the neglected limb by immobilising the unaffected limb with a splinting device. Over time, this treatment has been shown to influence changes at the cortical level, with the cortical area representing the affected hand muscle significantly increasing in size to match the contralateral side.[16,17]

Imagined movement and vision

Even when a limb is absent, attention and pain play a significant role, as demonstrated by the experience of amputees. Phantom limb pain (PLP) occurs in approximately 70% of patients after amputation, and phantom sensations occur in 90–100% of amputees.[18,19] When upper-limb amputees are instructed under hypnosis to 'move' the phantom limb into a painful position, they report higher levels of pain than when it is 'moved' to a more comfortable position.[20] Positron-emission tomography (PET) imaging has demonstrated that these reports of pain from a missing limb coincide with increased activity in the thalamus, anterior cingulate and lateral prefrontal cortex,[20] confirming that the same central processes are involved in PLP as when the body is intact.

Imagined movement has also been shown to evoke changes in the experience of pain and other sensations in patients with CRPS1. When requested to imagine moving the painful limb, patients reported increased levels of pain and the perception that their affected limb had swollen.[21] Other altered perceptions of body image have been reported in this group of patients: when their eyes are closed, some perceive the apparent absence of digits and other discrete sections of the affected limb. However, when visual attention is directed to the limb, these perceptions are lost.[22]

The influence of visual attention on 'phantom' sensations has been described in people with rheumatoid arthritis and fibromyalgia. With their eyes closed, these patients describe

Key Points

Attention can be manipulated in order to modify the perception and generation of pain

Immobility and/or neglect of a limb can generate pain

Conflict between the allocentric and egocentric interface, as monitored by the motor control system, can generate somaesthetic disturbances in the absence of nociceptive injury

Corrective visual attention can be used to alleviate pain

excessively swollen distal limb regions; when they view the area, however, this sensation is lost.[23] Equally, in some clinical conditions such as somatosensory loss after stroke, visual feedback of the affected limb during testing can significantly improve reported perception.[24]

Vision is our primary sense, and there is increasing evidence that it may play a key role in the manipulation of the experience of pain and other sensations. Visual data are used to inform the motor control centre of the position in space of our limbs, to assess any imminent threat, and to help inform the direction of future movements. It has been proposed that errors within the motor control system may generate pain and other sensations.

Role of the motor control system in the generation of pain

One of the roles of the motor control system is to manage the relationship between motor commands and sensory feedback. This is to optimise the precision and efficacy of a movement, because every movement results in an immediate sensory response. Frith and colleagues have suggested a possible, widely recognised model of how this relationship between motor commands and sensory response is managed.[25] The model proposes that because it is impossible to predict a sensory response purely from the motor commands, the motor control system relies on information known as 'state variables'. These include allocentric (external) and egocentric (internal) variables such as joint angles, the current state of the system, and the state of the external environment before implementation of the motor command. Following assimilation of this information, the motor control system 'predicts' a certain response from the sensory system. Controllers within the system compare this desired state with the motor command required to achieve that state. The controllers then produce the appropriate motor commands in order to achieve the desired outcome (Fig 1).

The prediction, or 'efference' copy, is often only a rough approximation of the actual consequences of a motor command, but it is needed to prepare the system for the consequences of that movement, to assess performance if there is a delay in response, to differentiate between egocentric and allocentric influences on the system, and to maintain a constant update on the interplay between sensory and motor systems.

This prediction is then compared with that of actual sensory feedback, and the current state of the system is modified accordingly.[26] The consequence of this chain of actions is that sensory events are analysed in terms of the appropriate motor response. In everyday life, one is made aware of such a system if we misjudge the height of a step or fail to anticipate the drop from a pavement edge. The difference in actual sensation from that which was anticipated takes us by surprise.

If large or continuous errors occur between motor and sensory systems (such as disruption in egocentric information via cortical reorganisation or allocentric information from altered sensory input with an immobilised limb), then the system is alerted to the conflict, and pain and other sensory changes may be experienced. Aspects of this have been reproduced experimentally in asymptomatic volunteers by using an optokinetic system to distort sensory feedback.[27] Forty-one subjects conducted a series of bilateral upper- and lower-limb movements for a timed period of 20 s while paying attention to a mirror or whiteboard that created varying degrees of sensory/motor conflict during congruent/incongruent limb movements. Twenty-seven (66%) subjects reported somaesthetic changes at some stage in the protocol, despite the absence of nociceptive damage. The most frequent report occurred when the subject performed incongruent movement while viewing the reflected limb in the mirror, the time of maximum sensory/motor conflict (24 subjects, 59%). Sensations ranged from perceived changes in temperature and weight to altered body image, disorientation, numbness, 'pins and needles', moderate aching and/or a definite pain. Once normal visual input was restored, the anomalous sensations resolved rapidly – just like viewing the approaching pavement edge or that final step removes the element of surprise.

Subjects varied in their responses, with some being particularly sensitive and others reporting no sensory changes. This suggests that there may be variance in an individual's susceptibility to generate or perceive these somaesthetic disturbances. Age may play a part, as proprioceptive accuracy is thought to diminish with age. This may explain the increasing aches and pains of old age, but further studies are required to validate this theory.

Central monitoring mechanisms

The motor control system appears to act as a central monitoring mechanism, possibly one of many such systems in the body. We have proposed the term 'ominory system', from the Latin *ominor* (to prophesy, predict, foreboding).[23] Our studies have focused on the mechanism that monitors motor/sensory conflict, but a separate ominory mechanism could generate motion sickness when there is discordance between body position, balance and equilibrium. The key feature of these mechanisms is that when they are triggered, they generate sensory disturbances such as nausea with motion sickness, pain in a phantom limb and a multitude of unpleasant sensations in CRPS. We have termed these resultant states 'dissensory', from the Latin *dissensio* (conflict, disagreement). These are feedback-dependent states that will continue to trigger the ominory mechanism; ultimately, either via duration or intensity of this state, the subject will suffer pain. In this model, the motor control system is constantly scanning for irregularities in information-processing. Inevitably, discrepancies will occur throughout the normal day, such as described above. Sensory disturbances will be generated constantly, albeit perhaps at an unconscious level. However, some people are far more aware of changes in their bodies and report recurrent multiple medical symptoms that have no organic cause. This somatisation, or overattention to oneself, may result from a reduced threshold to these normal sensory changes, and consequently subjects start to report them as abnormal symptoms. This may explain the constant flitting of symptoms in people with fibromyalgia, who, like the healthy volunteers discussed above, describe changes in body schema, mild generalised pain and changes in body temperature.[28,29] We have also found that if sensorimotor feedback is generated artificially in people with FMS using the optokinetic technique, as described above, then far greater sensory anomalies are reported than those at baseline.[30]

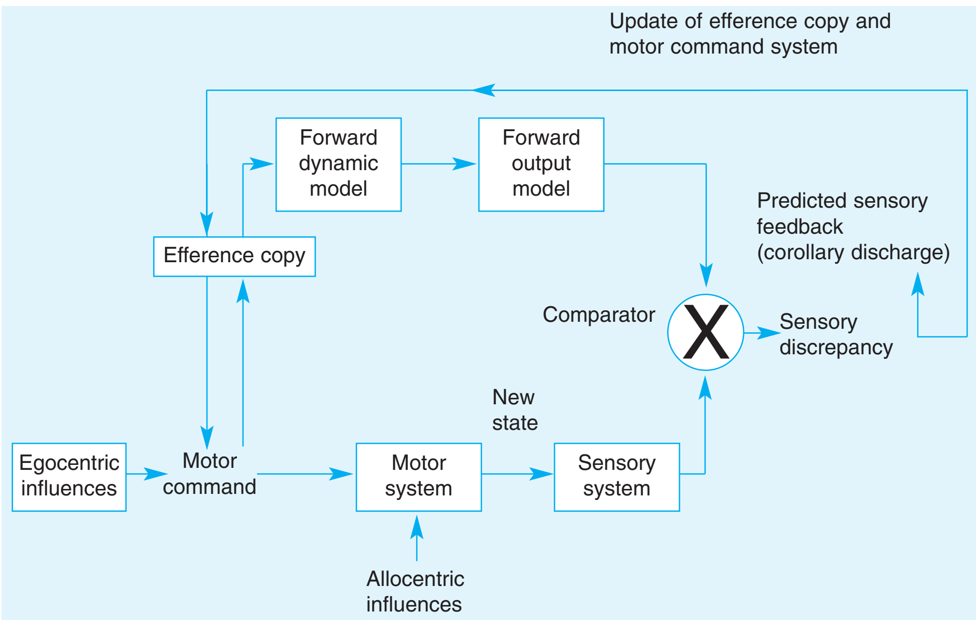

Fig 1. Schematic diagram depicting the role of the motor control system in the detection of conflict between motor output and sensory input.

Attention and the autoimmune system

We have seen that when conflict occurs in the sensorimotor system, whether through immobilisation of a limb following injury or casting or induced artificially, as in asymptomatic volunteers, not only are sensory changes generated but vasomotor changes (unilateral temperature changes) and emotional/behavioural responses are altered (neglect of a limb, perceived disorientation). This suggests that perceived conflict in the motor control system has a direct effect on the autonomic nervous system, which may have significant implications on how apparently unconnected central and peripheral changes are linked in chronic pain conditions such as CRPS1.

Therapeutic implications

This new theory on the generation of pain without nociceptive input may have important implications for the therapeutic management of people with chronic pain. Neglect and lack of use of a limb will perpetuate the sensorimotor mismatch, but active mobilisation and enhanced sensory input should promote normalisation of the system and thereby relieve symptoms. This may explain the efficacy of intensive physiotherapy and constraint-induced movement therapy, as discussed above.

In studies on PLP and CRPS1, vision has been found to have an analgesic benefit.[31,32] In these studies, the mirror image of the remaining (PLP) or unaffected (CRPS1) limb was used to give the subject the illusion of a normal contralateral limb. The underlying hypothesis for both studies was that by providing corrective sensory input via the mirror, an existing mismatch between motor output and sensory input would be corrected. Pain was relieved in six of 12 patients with PLP and five of eight patients with CRPS1. Further work in this area has shown that even greater improvements can be achieved if premotor tasks are rehearsed (hand-laterality identification and imagined movements) before the use of mirror visual feedback.[33]

Conclusion

Attention plays a significant role in how pain is perceived and perhaps even generated. The manipulation of attention has been utilised in healthcare settings for decades, either via distraction from an invasive procedure or as focused attention to re-engage an individual with a neglected limb. However, only now are we starting to understand the mechanisms behind such therapeutic approaches.

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