A lateral gaze at pain: the science of attention

Nicholas GN Shenker, Candy McCabe and David R Blake

Nicholas GN Shenker MRCP, Research Fellow

Candy McCabe PhD, Lecturer in Rheumatology

David R Blake FRCP, Professor of Joint and Bone Medicine

Royal National Hospital for Rheumatic Diseases, Bath

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Our current framework for understanding pain is the 'gate control' theory. Stimuli are processed peripherally and their transmission determined by a gate set both in the spinal cord and the subcortical regions. Higher centres then determine motor, and other motivational, responses as well as interpreting psychological aspects. The gate is set according to competing spatially similar and adjacent stimuli as well as the brain's arousal and attentive states.

This fascinating conference enriched this view with a series of bold and original observations and theories. Topics covered symptom science, central nervous system plasticity, cross-cultural studies of pain, and experiences from fields as diverse as cybernetics, economics, ecology and computer science. Drawing on this platform, intriguing therapies such as hypnosis, mirror-boxes and stinging nettles were discussed. This 'lateral gaze' at pain was the third in a series of multidisciplinary cross-specialty seminars dealing with various aspects of pain and suffering organised by Professor David Blake.

Conference programme

- **Pain in context**
  Professor Michael Sharpe, University of Edinburgh
- **Hypnotic imagery and pain**
  Dr David Oakley, University College London
- **Pain, cognition and symptom exaggeration**
  Dr Paul Green, Private Practise, Edmonton, Canada
- **Neglect; the science of inattention**
  Dr Masud Husain, Imperial College and Institute of Cognitive Neuroscience, University College London

Oliver-Sharpey Lecture

- **What phantom limbs can tell us about the neurology of body image and the meaning of pain**
  Professor VS Ramachandran, University of California, USA
- **Pain, attention and distress**
  Professor David Blake, Royal National Hospital for Rheumatic Diseases, Bath
- **The theory of pain**
  Dr Ben Seymour, Wellcome Department of Imaging Neuroscience, University College London
- **Perception, expression and social function of pain – and cross-cultural aspects**
  Professor Wulf Schiefenhovel, Research Institute for Human Ethology, Germany

Lessons from phantom limbs

Studies into patients with phantom limbs suggest that the central nervous system is not 'hard-wired' and provide insight into treatments that use this knowledge to alleviate pain.[1] A phantom is experienced following amputation and is the cortical representation of the peripheral body part. Several years ago, Professor Ramachandran studied a man with a phantom arm who felt his phantom fingers when different regions of the lower part of his face were touched. Similarly, he could also feel his fingers when his stump was touched. These sensations were topographically precise, modality-specific and these findings have since been replicated in other amputees. This odd phenomenon can be explained by cortical plasticity. The cortical area connected to the fingers is deprived of a peripheral stimulus following the amputation and becomes activated when adjacent cortical areas are activated. Penfield's homunculus predicts that the fingers are adjacent to both the face and the stump. The differential geographical distribution of electrical activity in the sensory cortex of the left and right hemispheres in unilateral amputees during face and arm stimulation supports this hypothesis.

Patients with phantom limbs often experience pain in their phantom and they also describe it to be in various positions. Functional brain studies of hypnotised patients with phantom limbs confirm that the motor cortex is active when the phantom is moved and that the anterior cingulate (a 'pain' centre) becomes active when the phantom is 'moved' to an uncomfortable position.[2] Some patients, especially in those whose pre-amputated limb was immobilised, describe their phantom as being painfully stuck.

In these immobilised patients the visual and proprioceptive feedback from the limb conditioned that no movement was possible following a motor command before amputation. This learned response persisted following amputation and the patient's perception was that the phantom was 'stuck'. To recondition the brain, it would be necessary to reintroduce visual feedback so that the limb was perceived as moving following a motor command. This could be made possible by using a mirror. A patient with a painful phantom was instructed to move both his phantom and normal hand while looking at the reflection of his normal hand superimposed onto the position of his amputated hand. His brain issued two separate motor commands and visual cues fed back that two normal hands were moving. His pain was much reduced as he felt he could move his phantom for the first time. Repeated congruent matching of motor commands with visual feedback (congruent movements) were associated with pain reduction and over time the phantom slowly vanished. This observation needs confirmation in clinical trials but other groups have had similar success. Interestingly, hypnotic imagery using this system can also help alleviate pain from phantom limbs.

Pain without injury

Professor Blake expanded on this theme by illustrating that this mirror system can produce pain using incongruent movements so that the visual feedback does not match with the motor command. When a group of normal individuals performed incongruent movements with one arm behind the mirror for just 20 seconds, the majority of them experienced unpleasant sensations that ranged from pain to weightlessness.

The concept of incongruent sensory inputs generating an unpleasant sensation is supported by nausea and vomiting following a sensory mismatch between the visual and vestibular systems. Centrally generated unpleasant sensations may also be responsible for some of the pain and stiffness seen in rheumatoid arthritis. Change in the joint's neural tone following inflammation alters proprioceptive input to create a mismatch. Chronic inflammation denervates the joint and creates a permanent mismatch.[3]

Mirror therapy also appears to work in another intractable condition, complex regional pain syndrome. In one cohort of nine patients treated with bilateral congruent movements when the affected limb was behind a mirror, three patients with early disease duration of less than six months demonstrated a good response; three with intermediate disease duration of about one year demonstrated a partial response; and three patients with chronic disease of more than three years did not respond.[4]

Pain as a symptom

Professor Sharpe noted that when 198 women were given a symptom diary, each recorded a significant symptom every three days. Pain, fatigue, common cold and headache were the most common symptoms and yet none of these women had a disease. Most symptoms are not related to organic disease. Across specialties one-third of patients will have symptoms not explained by a medically defined disease.

Pain is a symptom. When confronted with a medically unexplained symptom, health professionals respond in one of three ways: dismiss the symptom; hypothesise a rare diagnosis; or diagnose a psychiatric illness. All of these approaches are inappropriate for patients with 'dis-ease', the feeling of not being at ease with oneself. Functional brain imaging studies suggest that they do have disturbances in sensory processing and perhaps should be diagnosed as having a functional nervous disturbance.

Key Points

Pain is a common symptom and not indicative of organic pathology

Phantom limbs are cortically represented and demonstrate signs of brain plasticity that are amenable to therapy with a mirror box

Pain can be generated using a mirror with movements that generate incongruence between proprioception, visual feedback and motor commands

Pain is important as an evolutionary mechanism and different cultures tolerate pain in different ways

Professor Sharpe went on to advocate that positively diagnosing functional nervous disturbances has several advantages. By giving a clear diagnosis the implication that patients are 'putting it on'; or 'imagining' their symptoms, or that they are simply mad is very much reduced. It has been demonstrated that the number needed to offend (NNO) increases from two to 10 when this functional diagnosis is used, compared to the other strategies.[5] The patient can move on to focussing on therapies because 'if you have to prove you're ill, you can't get well'. Further investigation, time, effort and cost are saved. Symptoms are not merely 'signposts to disease', and developing symptoms science makes us reconsider our practice.

Chronic pain, cognition and symptom exaggeration

Another common complaint difficult to objectively measure is that of memory loss. Patients with chronic pain, fatigue and depression complain of impaired memory and this subjective claim has been documented on tests such as the Memory Complaint Inventory. Dr Paul Green provided a powerful argument that the complaint of memory loss does not always translate into an objective memory deficit. It does, however, correlate strongly with a lack of effort as measured by tailored effort tests. He suggested that cognitive tests should be viewed as invalid if they do not include an assessment of the degree of effort applied by the subject undergoing the test.

Dr Green has developed a combination effort and cognitive test using word pairs – the Word Memory Test. Using this test, about 30% of patients seeking compensation produced low effort scores. Poor effort produced a greater effect than severe brain injury on the cognitive deficit in patients making compensation claims in Canada.[6] Seeking financial compensation was an important factor in determining the failure rates for effort testing in patients with chronic pain. In a fibromyalgia population of 100 patients (50 claiming compensation and 50 not), two patients failed effort testing in the group not seeking financial compensation compared with 17 patients in the group who were.[7]

Changes in body schema and visual neglect

In a fascinating example given by Professor Ramachandaran, it may be possible to alter an individual's body schema so that an inanimate object is perceived as being part of that individual. The individual places his hand beneath a table. The experimenter starts to tap the part of the table over where the hand is hidden. A second experimenter then taps the hand beneath the table in synchrony with the first experimenter. Some individuals experience the strange sensation that the table is being tapped and is part of them. This illusion is so powerful that the individual displays an exaggerated galvanic skin response when a third experimenter threatens the table.

Patients with complex regional pain syndrome alter their body schema in relation to their affected area. This manifests itself in terms of feelings of denial or hate towards their limb. The right parietal cortex is recognised as important in body schema. A stimulating insight was given by Dr Husain into the neglect syndrome, a common disorder following right hemisphere damage, which is associated with lack of attention to items on the left. Neglect is associated with cortical lesions involving the right inferior parietal or inferior frontal lobe. It appears to be a heterogeneous syndrome, with different patients suffering different combinations of underlying cognitive deficit, depending upon the extent of their brain lesion.

Further evidence to support this can be seen from studies into visual neglect. Distinct abnormalities occur in patients with left neglect, including a salience of 'more-right' over 'less-right' objects *(*non-spatial deficit*)* and a lack of tracking ability (spatial deficit*)*. Either of these conceptual abnormalities can lead to a failure to explore the left side. Visual neglect does not consist of a uniform cognitive defect.[8]

Attention can be further categorised into many components including sustained and selective attention. The neglect syndrome appears to be influenced also by cognitive deficits that may not be primarily attentive, such as deficits in the ability to keep track of items that have already been inspected when viewing a visual scene.

Evidence to support this can be seen from studies on visual neglect. Dr Husain beautifully demonstrated distinct abnormalities in patients with left neglect, including a salience deficit (where objects on the right 'win' in the competition for attention) and impairment in keeping track of spatial locations when viewing visual scenes. When combined, such deficits can lead to recursive search of rightward items and failure to explore left space. How these concepts may apply to hyper-attentive behaviours and alterations of the body schema seen in some chronically painful conditions is intriguing.

Hypnotic imagery as therapy

Insights into a potentially useful tool for altering pain experiences came from Dr Oakley's seminar on hypnosis. Three forms of imagery are used in hypnosis to alleviate suffering: 'special-place', distraction and transformation. Dr Oakley's talk dealt with transformations. 'Dial transformation' changes a specific experience, such as pain, into a dial that the patient can control. Interestingly, the patient is first asked to turn the dial 'up' before then turning it 'down' (paradoxical injunction). Self-generated (ipsative) transformation imagery can also be used to manipulate experiences. For example, the painful pressure of a chronic neck injury can be transformed into that of a volcano that then explodes through the patient's head to allow relief. It is important that the patient leads both the self-generated image and the subsequent resolution strategy.

Functional brain studies illustrate the power of hypnosis over 'imagined' pain. The thalamus, anterior cingulate, insula, prefrontal and parietal cortices were activated following a painful stimulus generated by a heat lamp. Subjects were then asked to imagine this pain. Only the insula and secondary sensory cortex were activated. However, when the painful experience was suggested through hypnosis, the full pain matrix was reactivated.[9]

Human ethological view of the perception, expression and social function of pain

Professor Shiefenhövel's talk on cross-cultural studies in pain gave a valuable insight into the human condition. The threshold whereby a stimulus becomes painful is reasonably constant across sexes, ages and cultures. There is, however, a wide variation in when this stimulus becomes intolerable and the limb is withdrawn. This difference is almost entirely sociocultural. Charles Darwin commented in *The expression of emotions in man and animals* that we learn to interpret emotional behaviours and become 'habituated' to them. For example, among the Eipo in the Highland of West-New Guinea, infants are exposed daily to cold rain, insect bites and scratches and develop an approach to pain that is very different from Western societies. Affective processes, such as depression, are activated only following pain associated with 'internal' disease such as tropical ulcers and bacterial infections.

We are, however, not entirely free in our expression of pain and sadness. There are culturally independent facial expressions, gestures and body postures that convey pain and sadness. Indeed, children born deaf and blind demonstrate these same facial expressions regardless of culture. These expressions resemble infantile behaviour patterns that release parenting skills such as assisting, comforting and consoling. Furthermore, archaic methods of pain relief, discouraged in Western medicine, such as the use of bodies and hands to convey a feeling of support are widespread in other cultures. In general, pain is most closely related to the emotion of sadness but emotional manipulation for personal gain is the exception rather than the rule.

A theoretical approach to pain

The neuroscientist, David Marr (1945-1980), sought to gain an understanding of the brain as an information-processing unit through mathematical and neurobiological models underpinned by the basic evolutionary principle of optimality. This approach distinguishes between computation (understanding the problems that the brain has in processing information); algorithm (what solution has the brain used to overcome these problems); and implementation (what system does it use for this). Dr Seymour explained these concepts in terms of pain motivation, pain perception and social evolution.

The motivational aspects of pain may be illuminated using appetitive and aversive behavioural systems. Opponent motivational processes may underlie tonic pain and pain relief. As an example, the opposing post-labour semi-orgasmic pain-free state is consequent upon the pre-existing painful labour state. Related to this, fighting pain with pain is a useful therapeutic tool used by many cultures. Papuans and Austronesians with painful legs following a long walk rub stinging nettles into their skin.

Pain perception, as an inference of motivationally important aspects of a somatosensory event, can be viewed using a Bayesian framework. This approach has three important components that combine to provide a perceptual decision. These components are a prior distribution incorporating existing information concerning nociception; a likelihood function between nociception and its external cause; and a cost function that considers the inherent value of potential causes of pain.

Pain has a powerful role in empathy and altruistic punishment, both theories central to modern evolutionary theory. It also plays an important role in injury avoidance when there is competition within species. Pain is ubiquitous during childbirth and this suggests a conserved evolutionary role. It may, for example, encourage maternal bonding and societies seeking to abolish pain during childbirth may be affecting this process. As one of the speakers commented, perhaps modern medicine is too preoccupied with fighting pain to be able to marvel at the functionalism of this inborn protective device.

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