

# Developing concepts in allodynic pain

NG Shenker, HC Cohen and DR Blake

Allodynia is the perception of pain in response to stimuli that are not normally painful. The management of patients with chronic pain and allodynia is suboptimal, partly because of social stigmatisation. Patients are made to feel that they are malingering or looking for secondary gain. Unfortunately, the legal profession often propagates this myth and the adversarial nature of the courts contributes negatively to the patient's situation. Remarkable recent understandings of profound brain changes occurring in chronic pain patients will challenge the way that such medicolegal cases are decided. This ground-breaking conference related expertise and experiences from patients, clinicians and leading scientists in this field and was the fourth conference in an interdisciplinary series centred around pain and suffering organised by Professor David Blake.

## The brainy mind

The Watson Smith lecture underpinned the day and was delivered by Professor Richard Gregory CBE. Gregory argued that pain is perceived by the mind. The undisputed scientific view is that the brain generates the mind. There are many aspects of mind, from emotions to reasoning, but this fascinating exposition focused on perceptions.

Visual illusions demonstrated a speculative working model of perceptions as predictive hypotheses of the external world (Fig 1).<sup>1</sup> Different neural influences, such as 'bottom-up' sensory data or 'top-down' processing using past experiences (both conceptual and perceptual), were dominant in different illusions. The external world is therefore perceived (hypothesised) using Bayesian rules to generate qualia, for example the colour 'grey'. In Figure 2a the colour 'grey' is influenced by both 'bottom-up' sensory modifications and 'top-down' past experiences. Squares A and B are actually the same shade of grey but this is only appreciated when they are dislocated and placed side by side (Fig 2b). The brain is constantly seeking the best meaningful fit of reality rather than an accurate portrayal of the external world.

In understanding perception it is helpful to consider the brain's evolution. Three levels of brain response can be identified: reception, perception and conception. Reflexes and tropisms are examples of receptions. Perceptions are predictive hypotheses of the external world. Conception is explicit understanding.

Phenomena (eg pain) instruct explanatory theories. These theories change the observed expression of the original phenomena. Pain can be classified in a similar manner to visual experiences and this will permit a new understanding of its expression.

What immediate implication does this framework have? Acute pain drives the subject to respond immediately to an external object. Chronic pain is associated with cognitive deficits such as short-term memory loss and poor concentration. Chronic pain also affects behaviour without the patient's awareness. The pain matrix intimately involves structures in the brain related to emotions and these are intrinsic to the experience. All of these examples are of brain reception and perception rather than conception (explicit understanding).

## Neuropathic pain and altered perceptions

Ms Cath Taylor and Dr Candy McCabe described the under-recognised symptoms and signs that affect patients with complex regional pain syndrome (CRPS) from a bravely personal and objective view.

Allodynic pain has a superficial and a deep pain, usually described thermally, that is ill-defined and rated 'severe to extreme' by most patients.

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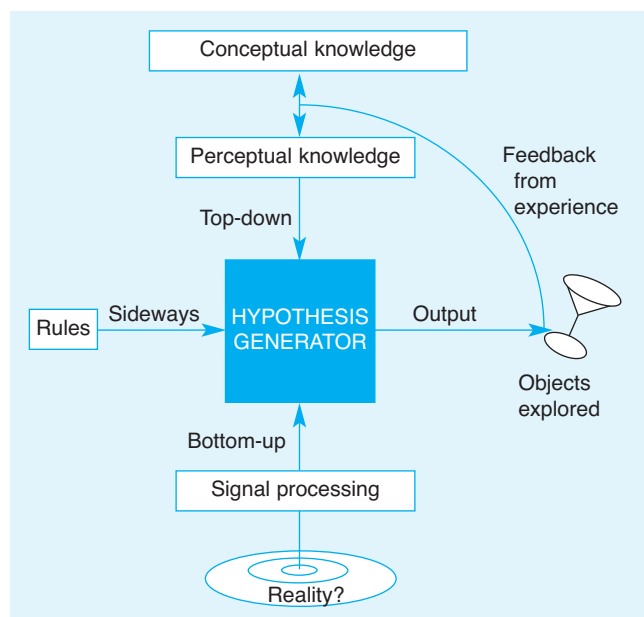
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**Fig 1. Speculative schema of how perceptions are generated.** Reproduced with kind permission of the Royal Society.<sup>1</sup>



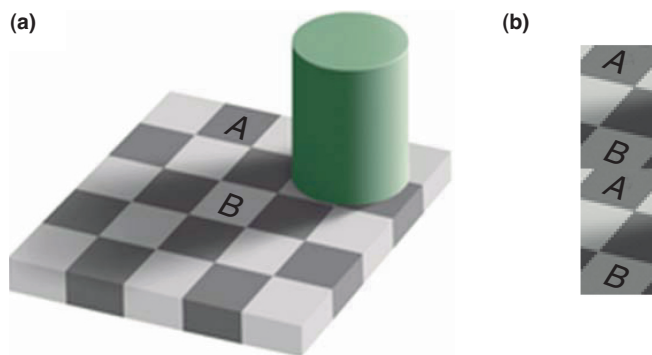


Fig 2. (a) Square 'b' looks lighter than square 'a' because of the surrounding colours and the concept that it is in a shadow. (b) Squares 'a' and 'b' are in fact the same shade of grey.

Table 1. Symptoms and signs suggestive of allodynic pain.

Symptoms

- Expressing negative feelings towards the affected area
- Depersonalising the affected area
- Alienation of the affected area
- Desire for autotomy

Signs

- Confrontational pain
- Referred sensations
- Feeling of altered size when visual input is deprived
- Alteration of normal body schema
- Neglecting the affected area
- Over-attending the affected area
- Misperceiving digits (especially fingers) when visual input is deprived
- Difficulty engaging the area for movement
- Right parietal syndrome

Confrontational pain is pain behaviour triggered by approach without touch. Patients with confrontational pain have terms applied to them including somatisation states and, especially in the medicolegal setting, 'abnormal pain behaviours'. This can not be appropriate as nearly all patients with allodynic pain exhibit this behaviour.

Certain groups of symptoms indicate allodynic pain states, especially CRPS. Negative feelings directed toward the affected body part, for example, may spill over into the consultation. Patients declare that they hate their affected part and that 'it' has ruined their life. Feelings of depersonalisation and alienation emerge by patients describing their affected area as 'it' rather than 'my arm' or 'my leg'. They describe their limb as being 'stuck on' or 'like an attached alien'. Finally patients express a wish to remove (autotomise) the affected area.

The 'neglect'-like phenomena reported by CRPS patients parallels features displayed by patients with organic right parietal lobe pathology. On formal parietal lobe testing clear abnormalities are seen despite no evidence of pathology (Fig 3).

Several groups have described objective signs reflecting

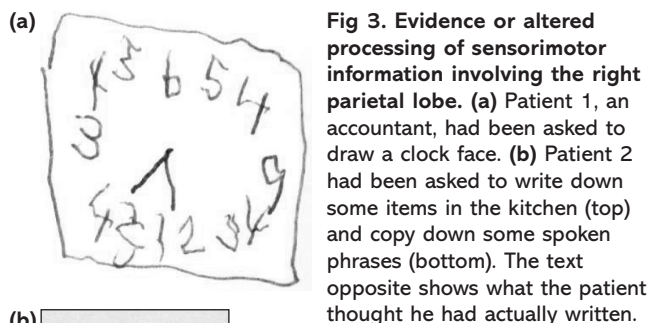
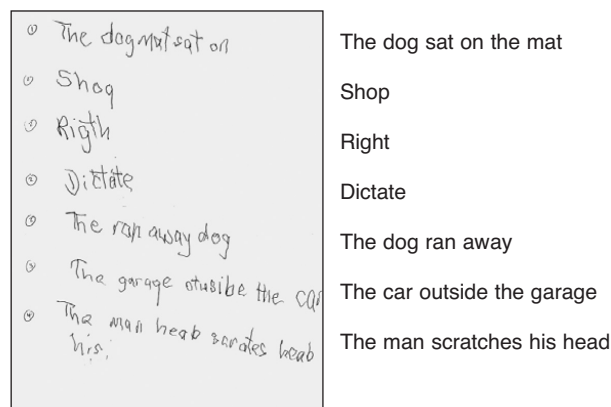
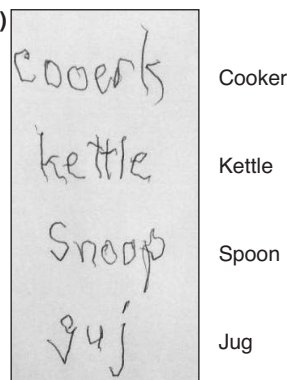


Fig 3. Evidence of altered processing of sensorimotor information involving the right parietal lobe. (a) Patient 1, an accountant, had been asked to draw a clock face. (b) Patient 2 had been asked to write down some items in the kitchen (top) and copy down some spoken phrases (bottom). The text opposite shows what the patient thought he had actually written.



altered perceptions in patients with CRPS. These findings are robust and their presence correlated with changes in functional brain imaging that resolve when the clinical state ameliorates. These signs include referred sensations, digit misperception, phantom swelling, and neglect of the affected area.<sup>2-6</sup> Furthermore, motor deficits have been documented in these patients. These include gait, posture, dystonias, tremor and difficulty engaging ('finding') the affected part in order to move. All of these signs share their aetiology in the plasticity of the brain to the external environment, most clearly seen as a reorganisation of Penfield's somatotopic maps. The same changes are seen in amputees with phantom limb pain, explaining the large overlap between the two conditions.

The psychiatric perspective

Patients with chronic pain states including CRPS are often classified using psychiatric definitions. These include F45.0 somatisation disorder, F45.2 hypochondriacal disorder, F45.3 somatoform autonomic dysfunction disorder, and F45.4 persistent

somatoform pain disorder. For example, somatisation disorder accounts for less than 0.2% of liaison psychiatric consultations and is defined by a two-year history, multiple and variable physical symptoms, refusal to accept reassurance, and impairment of family and social functioning.

There is growing dissatisfaction with this classification system because it does not reflect aetiology, is not accepted by patients and leads to stigmatisation and disengagement from medical services (sometimes encouraged by treatment protocols). The system underrecognises and undertreats depression and anxiety, and falsely reassures physicians who then miss organic disease. Patients with pain and depression delay seeking help when they should be encouraged as a significant proportion will benefit from treatments.

### Perceiving pain

Aberrant processing of painful stimuli occurs in rat models of neuropathic and inflammatory pain. New insights derive from differential gene expression seen in people with decreased pain sensitivity (eg GTP cyclohydrolase allele (GCP1)), adapter proteins involved in the assembly and expression of excitatory glutamate receptors (eg GRIP, PICK1, NSE, PSD-93 and PSD-95), and anion shift following inhibitory glycine and GABA release.

Professor Irene Tracey showed how the influence of genetics, cognitive set, mood, context and state of the nervous system (eg sensitised) changes the perception of pain. Functional magnetic resonance imaging visualises changes in blood flow and reflects neural activation. The spinal cord, thalamus, somatosensory areas 1 and 2, insula, anterior cingulate and prefrontal cortex are always active in relaying pain's somatotopic and affective components. Experimental protocols determine the effects of each of these influences on brain processing and pain reporting. Depending upon the individual and protocol there is also activation of the amygdala, hippocampus, posterior parietal lobe, basal ganglia and brainstem.<sup>7</sup> Distraction, for example, reduces anterior cingulate activation and increases brainstem periaqueductal gray activity, a descending inhibitory pathway. Anxiety increases the signal in the entorhinal cortex, an area associated strongly with emotions, and the posterior insula. Interestingly, the pain matrix can be switched on through hypnosis and, more importantly, through empathy.

Professor Salvatore Aglioti elaborated further on the role of empathy. Hutchison *et al* recorded activity from a single neuron in a conscious patient's anterior cingulate during open brain surgery. Each time the patient was in pain, the neuron fired. When a surgeon pricked the patient's finger the same neuron reacted demonstrating the power of a 'mirror' neuron.<sup>8</sup> Empathy teleologically allows the sharing of understanding to aid the continued survival of a community. This is dependent upon mirror neurons responding in the onlooker's brain in exactly the same way as in the subject's brain. This mechanism underpins much in human relationships, including those between a doctor and patient. Empathic doctors activate the same pathways that are active in their patients and this can affect them personally and influence their decisions.

### Conference programme

#### ■ The pain network and perceptual distortions

Professor David Blake, Royal National Hospital for Rheumatic Diseases, Bath (*conference organiser*)

#### ■ Attention, distraction and pain

Professor Irene Tracey, University of Oxford

#### ■ Pain and somatisation

Dr Ben Green, Cheadle Royal Hospital and the University of Liverpool

#### WATSON SMITH LECTURE

#### ■ The brainy mind

Professor Richard L Gregory, University of Bristol

#### ■ Pain empathy and survival

Professor Salvatore M Aglioti, University of Rome, Italy

#### ■ Neuropathic pain and altered perceptions

Dr Candy McCabe, Professor David Blake, Catherine Taylor, Reflex Sympathetic Dystrophy UK

#### ■ Neuropathic pain molecules

Dr Carole Torsney, University of Edinburgh

#### ■ Pain, ethics and palliative care

Professor the Baroness Finlay of Llandaff, Cardiff University; President, Royal Society of Medicine

#### ■ Summary

Professor David Blake

### New treatments in light of new understanding

The treatments for patients with chronic pain are poor. Most people are not affected by their therapies in the medium term. Effective treatments for patients with CRPS include desensitisation, physiotherapy, hydrotherapy, behavioural approaches and pharmacotherapies, including nerve blocks and bisphosphonates. Newer therapies include mirror visual feedback, motor imagery and hand laterality tasks.<sup>9,10</sup> Magnetic resonance images of the patient's pain matrix have been used as biofeedback. The patient is asked to focus on the anterior cingulate and learns how to reduce its activity. There was a change in the pain ratings of patients who mastered this technique. The emergence of genetics, biomolecular medicine and functional imaging techniques combined with a network-based approach will lead to newer, more effective treatments.

### The medicolegal perspective

Current practice invariably involves orthopaedic surgeons, usually because of initial physical trauma, who unfortunately have not received training in allodynic pain states. Reports often include terms like 'exaggeration', 'inappropriate signs', 'supratentorial' or 'functional' pain. Courts often expect a percentage quantification of how much of the pain is either physical or mental and a statement of whether the client is malingering. Malingering is a separate issue and can usually be detected with covert surveillance and

appropriate psychological profiling. The terms 'physical' and 'mental' do not fit into the current understanding of patients with chronic pain. If the question is rephrased to ask whether the client's problems are conscious or unconscious, controllable or uncontrollable then the scientific answer is that the patient's pain and the associated symptoms, signs and behaviours occurs at the unconscious and uncontrollable level.

### The ethical aspects: lessons from palliative care

Baroness Finlay of Llandaff relayed her experiences in palliative care and the House of Lords. In caring for patients with intractable pain small things count and attention to detail shows that they are being cared for. Families are secondary patients and need to be treated with respect and dignity. We have to be proactive and self-confident in propagating and defending our viewpoints, otherwise poor decisions will be made in both the NHS and society. The 'double effect' of morphine is an example of misinformation informing the wider debate on euthanasia, as there are serious doubts that morphine shortens life when given to ameliorate symptoms.

### Conclusion

By listening to patients with chronic pain and understanding the advances in the science of pain mechanisms, new symptoms and signs become obvious and meaningful, but only if the patient is examined appropriately. This is a major shift in the management of those with allodynic pain and services need to align accordingly. Understanding that patients with CRPS are no more in control of their symptoms than patients with, for example,

rheumatoid arthritis requires the medicolegal aspects to be addressed.

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