

Understanding pain: the enigma of pain and suffering

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Three broad themes emerged from this multi-disciplinary conference. In understanding pain and suffering it was important to explore the basic psychophysiological mechanisms that underlie the development and maintain the chronicity of pain syndromes. The practice of improving pain was the focus of several talks. Finally, the role of complementary medicine was discussed.

In memoriam: Professor Patrick Wall

Imbuing the entire day was the memory of Professor Patrick Wall. His ideas and wisdom permeated many of the talks and Professor Halligan's introduction to the keynote lecture touched on the impact that the gate control theory had had on the field of pain. Prior to this paradigm shift, pain had been described essentially as nociception, a passive process in keeping with Descartes' original concept of pain acting as a 'signalling' system to reflect tissue injury. However, the 'specificity' and 'pattern' theories of the day did not explain phantom pains; the persistence of pains in the absence of injury; and the absence of pain in the presence of gross tissue injury. Melzack and Wall's psychoneurophysiological theory¹ was revolutionary at the time and not only reflected but also influenced the biopsychosocial synthesis of disease states, as published by Engel in *Science* 10 years later².

Mechanisms underlying the development of pain

Placebo and nocebo responses

Placebo and nocebo responses give insights not only into the basic mechanisms of pain and perception, but also into the efficacy of some therapies. Affective, cognitive and conditioning models to explain these responses have been developed but perhaps the most interesting insight was into the neurobiology of the placebo response. Levine *et al* were able to block a placebo response through the use of naloxone³.

Patrick Wall did not think of these responses as perceptual stimuli in the classic sense because they only work if the patient is aware of them. Placebos and nocebos are not active in their own right but are inextricably linked to awareness. Sensations can be interpreted not as simple stimuli but as an awareness

of possible appropriate action. For example, the sensation of pain is an awareness of a series of need states. The need state of pain is terminated by seeking and accepting an appropriate therapy. The sensation of the need state disappears once consummation is complete. The placebo is therefore an appropriate response rather than an appropriate stimulus.

The importance of fear in chronic pain

Understanding chronic pain as a 'phobia' allows the alleviation of suffering through appropriately targeted treatments. A phobia is described as an intense irrational fear. Lang described a bio-information theory of fear in phobias in which three levels of neural information were processed⁵: the semantic level gives meaning, the perceptual level gives attention and the response level gives action. In phobias, abnormal meaning can be seen in catastrophising, abnormal attention in hypervigilance, and abnormal action in escape or avoidance behaviour. Chronic pain can be interpreted as a phobia of movement: kinesiphobia.

Hypervigilance is demonstrable in fearful patients with painful conditions when compared to non-fearful patients and healthy controls. Reaction times were measured to both geometric figures and innocuous electrical stimuli placed on volunteers' arms and legs. No differences in reaction times between these two stimuli were seen in healthy controls. However, when volunteers with low back pain were divided into low- and high-fearful groups there were differences. Although the reaction times to geometric shapes were the same in both groups, the reaction times to electrical stimuli were less in the high-fearful group than the low-fearful group.

Fear urges escape behaviour. Patients with non-specific back pain were asked to watch a video on a range of lifting activities and asked to rate whether they would avoid them or not. They had been previously categorised into fearful and non-fearful groups. Those that were fearful were more likely to avoid lifting activities than those in the non-fearful group, and this was a better predictor than pain levels or personality questionnaires. This finding has been corroborated in chronic fatigue syndrome and osteoarthritis. Patients with high fear levels are also four times as likely to have disability from their back pain.

Treatments for patients based on this model must first activate the phobic network before new disconfirming information can be provided. The pyramid for achieving this is a four-step process with increasing time spent on each subsequent step. The steps are reassurance, education, exercises and then exposure *in vivo*. For patients with chronic back pain this has met with some success.

Basic science in understanding pain mechanisms

The human body can translate a response to a stimulus from one side of the body to the other (see Fig 1). This novel concept could explain the symmetry seen in chronic painful and inflammatory diseases such as rheumatoid arthritis and psoriasis. The mechanism and clinical features of this response was considered in relation to neurogenic inflammation.

Referred sensations are a sign of central cortical reorganisation and were described for the first time in Complex Regional Pain Syndrome (CRPS) type I by Sister Candy McCabe. Patients with phantom limb pain also describe referred sensations. Further neurophysiological evidence suggests that part of the reason that patients get pain in their phantom limb following an amputation is because of the discrepancy between the motor output to proprioceptive neurons and visual sensory feedback from that area. This has successfully been treated using a 'mirror-box technique' where the mirror is placed in front of the amputated limb and the reflection of the normal limb gives visual feedback that there are two limbs present again. This mirror-box technique has successfully been applied to three patients with CRPS who had only had the syndrome for a few months. Five patients who had had CRPS for a longer period demonstrated partial or no responses to this mirror-box therapy.

Understanding chronic pain through understanding chronic fatigue

The study of chronic fatigue parallels the study of chronic pain. Professor Wessley suggests that fatigue, like pain, is a universal condition. In a large population study, the amount of fatigue was distributed in a normal distribution and at one end of this normal curve were people who not only had fatigue as a symptom, but also had many other symptoms. Further community and hospital studies show that the patients who fulfil the criteria for chronic fatigue are more likely to have other symptoms. These can then be grouped together to form diagnostic categories, such as fibromyalgia, irritable bowel, non-cardiac chest pain or deep pelvic pain. These diagnostic labels relate to the primary presenting complaint and the specialist rather than the syndrome as a whole. These diagnostic labels should be abandoned. The number of symptoms are, however, a marker of distress.

The risk of depression for patients with chronic fatigue syndrome is three to four times greater than for those with similar conditions with similar amounts of fatigue. Unsurprisingly, similar treatments appear to work for chronic pain as well as chronic fatigue, such as cognitive behavioural therapy, using a step approach not dissimilar to that outlined above for pain. However, societal attitudes represent the principal difference between chronic pain and chronic fatigue, leading to the politicisation of fatigue. Societal unease about technology, lifestyles, and the environment is reflected by patients who themselves are fuelled by a press eager for sensational headlines. Underpinning this is a deep distrust of the psychiatric profession to whom patients with chronic fatigue feel they are consigned if no clear causal relationship can be found for their symptoms. There is, however, no published evidence that somatisation is a result of the 'denial' of a psychiatric disorder.

Psychosocial obstacles to recovery

Whilst recognising that there are structural and disease states in the aetiology of back pain, the psychological and social aspects of musculoskeletal pain are also important in its impact. Distress, beliefs about pain and disability, and behavioural patterns all interact. An example of this is 'enmeshment' where the concept of self is fundamental. For example, if a person's identity is derived mainly from his job but he loses his job due to chronic pain, the pain may become enmeshed in the loss of income, self-esteem and quality of life.

The locus of control may also be important in chronic pain. Interestingly, the role of complementary medicine in creating a more passive role for the patient in this setting gives a conflicting message. Fear-avoidance certainly is important.



Fig 1. Intradermal injection of capsaicin (left arm) mirrors both hyperalgesia (lines) and allodynia (crosses) to the right arm over one hour. Arrow indicates site of capsaicin injection. Different assessment times are represented by different colours.

A pain ladder can therefore be described. To start with, uncertainty and fear can lead to catastrophisation with both anger and blame involved. Failed treatment can then cause a feeling of helplessness and depression. Avoidance and sick leave result in invalidism.

As well as red flags identifying worrying pathological features of a patient's back pain, a yellow flag system predicts psychosocial predictors of chronicity. Blue flags describe the perceptions of work and working conditions in back pain. Orange flags identify those patients for whom a psychiatric opinion ought to be sought. Finally black flags are the grand social forces which are beyond immediate influence, such as government policies and work regulations.

Education is the most important factor in influencing the chronicity of back pain. Educational programmes, occupational

health services and aids such as the *The Back book*⁴ have all been shown to help.

The alleviation of pain and suffering

Preventing chronic back pain: a futile exercise?

If GPs were to identify those patients whose acute low back pain does not resolve rapidly, and refer them for treatment, the epidemic of chronic back pain could be reversed. This hypothesis underpins guidelines from the Clinical Standards Advisory Group, the Royal College of General Practitioners, and the National Institute for Clinical Excellence. It is based on three premises: namely that there is a back pain epidemic, that GPs see many patients with preventable chronic disability, and that there are effective treatments. There is, however, little evidence for any of these premises. Community studies do not reflect an increase in the prevalence of back pain, although there was an exponential increase in the days of benefit for spinal disorders. GPs need 680 consultations in order to have the opportunity to prevent one new, long-term benefit claim and this number is too large to make targeting these patients possible through primary care. Professor Underwood suggested that there are no evidence-based effective treatments that prevent long-term pain and disability.

Despite the paucity of conventional data, practitioners' experience is that some patients appear to benefit from treatment. New research methods to inform the management of back pain could include exploring the patient's and practitioner's models of pain and disability, as well as the tensions between physical, psychological and social models of pain and disability.

A holistic approach to pain management – practical in today's NHS?

Pain services are not a priority, nationally or locally, and long waiting lists for pain services and patchy quality is the reality in the NHS at the moment. Even if there were enough time and money, it is doubtful that infinite expansion of secondary care is the answer to the problems. What is needed is a fundamental change in working patterns so that consultants collaborate with patients to find solutions. An encouraging development that comes into effect next year requires clinic correspondence to be copied to the patient.

In defence of the weed

The plant cannabis has 65 unique compounds of which Δ -9-tetrahydrocannabinol (THC) is the main psychoactive component. Cannabidiol (CBD) may modulate the activity of THC. A specific receptor (CB-1) is found in the nervous system for which the endogenous ligand was found to be anandamide. The CB-1 receptor is ten times more prevalent than ν -opioid receptors. The CB-2 receptor is found on the immune tissue. Specific antagonists for CB-1 (SR141716A) and CB-2 (SR144528) receptors have been synthesised.

Conference programme

■ The placebo and nocebo response to pain

Professor David Blake, RNHRD, Bath, and Ms Gillian Myers, Bristol University Medical School

■ In memory of Patrick Wall

Professor Peter Halligan, University of Cardiff, Wales

■ Pain, fear and suffering

Professor Johan Vlaeyen, Maastricht University, The Netherlands

■ Pain – suffering the dangers of alternative medicine

Professor David Blake, RNHRD, Bath

■ Pain and fatigue

Professor Simon Wessley, Guy's, King's and St Thomas' School of Medicine, London

■ Pain and the future without drugs

Professor Edzard Ernst, University of Exeter

■ Psychosocial obstacles to recovery

Professor Chris Main, Hope Hospital, Salford

■ Pain: in defence of the weed

Dr Philip Robson, Warneford Hospital, Oxford

■ Treating acute back pain; a futile exercise?

Professor Martin Underwood, Barts and the London, Queen Mary's School of Medicine and Dentistry

■ Mirror-imaging to pain and inflammation

Dr Richard Haigh, Royal Devon & Exeter Hospital, Dr Nicholas Shenker and Dr Paul Mapp, RNHRD, Bath

■ A holistic approach to pain management – practical in today's NHS?

Dr Catherine Stannard, Frenchay Hospital, Bristol

■ Setting standards for complementary medicine

Professor Edzard Ernst, University of Exeter

■ Phantom responses in rheumatology – commonly ignored?

Sister Candy McCabe, RNHRD, Bath

Research has concentrated around THC, CBD and their interaction. THC has psychoactive, antiemetic, relaxant and antinociceptive properties. THC also causes a reduction in acetylcholine levels and NMDA receptors in the hippocampus leading to possible memory effects. THC causes a tachycardia that is reduced by high levels of CBD. The THC 'high' is also reduced by high levels of CBD. CBD appears to have anti-convulsant, anxiolytic, antipsychotic, antioxidative, relaxant as well as antinociceptive properties.

The effectiveness of cannabis is coloured by its social image, for better or for worse. There are no published clinical trials to show that it either works or does not work as an analgesic. Case reports and crossover trials, however, support larger studies into its analgesic effects. Potential worrying side-effects are cognitive distortion and dependence. Although no irreversible cognitive effects have been demonstrated, it is conceivable that subtle effects on information processing occur in long term users. Seven to eight percent of people presenting to drug dependency units are psychologically addicted to cannabis. Despite this, cannabis is a promising treatment for chronic intractable pain states.

The role of complementary medicine

The future without drugs and double standards

Professor Ernst reflected that patients think that complementary medicines help their pain. They think that heat, massage and exercise therapies are the most effective. However, there are problems in designing trials to assess the efficacy of complementary therapies, not least the concept of a placebo to acupuncture or massage, for example. However there have been great attempts overcome this.

Meta-analyses and good randomised controlled trials have demonstrated the benefit of massage therapy in low back pain and labour pains; acupuncture for chronic pain states; and exercise in chronic musculoskeletal pain. Further reviews have assessed the role of a chiropractor and the use of transcutaneous nerve stimulation in low back pain, without being able to demonstrate a positive effect by either. Despite conflicting views on some of these trials, these treatments are potentially useful and they should be evaluated by scientific methods.

Unfortunately western science does not provide a level playing field for the study of complementary medicine. Charities fund most medical research to the tune of £134 million per year; 2.3% of this is spent on clinical trials, of which 0.05% is spent on complementary medicines. Preliminary data are scarce because of a lack of funding. This means it is difficult to generate well-formed hypotheses which in turn makes it difficult to obtain funding in the first place.

There is also publication bias. When two identical trials were submitted for publication, the only difference being the substitution of a single phrase to make one an allopathic treatment and the other a complementary treatment, the complementary trial was three times more likely to be rejected for publication. Similarly, complementary medicine is not devoid of risks, but

these are simply not reported. For example, 300 serious side-effects have been documented from spinal manipulation including vascular accidents, disc herniation and cauda equina. For complementary medicine to contribute in the field of pain it must be given equality.

The dangers of complementary medicine

Complementary and allopathic schools of medicine share many of the same central values. This can be seen historically in figures such as Paracelsus who gave us the therapeutic index, is considered the father of medicinal chemistry, and yet also strongly influenced the development of homeopathy through his doctrine of signatures.

Aristotle philosophised that anything may be defined along four mutually exclusive criteria: composition, form, function and the interaction with the environment. Differences between complementary and allopathic medicine can be seen to arise from a failure to understand Aristotle. This is evident in the field of pain.

Fundamental differences also arise in the area of diagnosis. Although both schools use phrases such as 'common things are common' and 'think horses, not zebras' to summarise approaches to patient care, little emphasis is placed on diagnosis in complementary medicine. Although appropriate diagnosis is not essential for successful therapy, western medicine also adds in the crucial rider that 'it is important to diagnose the treatable and the important', such as cancer. Much of the damage that an unregulated complementary medicine industry can cause comes from its lack of expertise in dealing with this. Examples include a lady with dyspareunia and arthritis caused by chronic gonococcal septicaemia, and a gentleman with back pain caused by metastatic cancer. Western medicine is strictly regulated so that these uncommon causes of symptoms can be detected and treated early enough. Complementary medicine is not. The lack of diagnostic skills to exclude serious and treatable conditions is unacceptable.

References

- 1 Melzack R, Wall PD. Pain mechanisms: a new theory. *Science* 1965;150: 971–9.
- 2 Engel GL. The need for a new medical model: a challenge for biomedicine. *Science* 1977;196:129–36.
- 3 Levine JD, Gordon NC, Fields HL. The mechanism of placebo analgesia. *Lancet*, 1978; 2:654–7.
- 4 Royal College of General Practitioners. *The back book*. London: NHS Executive, 2002.