

## Editorial

Gifford LS 2005 Editorial: The sickness response and the vulnerable organism. When you're low you hurt more easily.... PPA News 19:3-5

### **The sickness response and the vulnerable organism. When you're low you hurt more easily...**

For years thoughtful writers on pain have gone out of their way to emphasise that pain precedes depression/low mood/emotional changes rather than the other way round. The pain starts with a physical cause and the psychosocial obstacles follow. Let me quote Gordon Waddell (2004 page 153).

'Psychosocial factors influence how patients respond to back pain and they are important in low back disability, but they do not cause the pain. Back pain is not a psychological problem. Back pain starts with a physical problem in the back.'

While I generally agree I would rather like to take this to task a little because for years I have been listening to patient's stories and more often than not found it hard to find a reasonable physical cause to explain the amount and ongoing nature of the problem they describe. What is evident, if you have time to really listen, is that there is a great deal going on in the patient's life. A great many of those with a complicated pain problem have a complicated 'life' story to accompany it. Many patients are simply 'low' and have been low, on and off for a long time before the problem started. Minor things, or nothing that is obvious at all, often surround major physical pain problems. These unfortunate individuals seem pre-sensitised in some way.

During the winter of 2002-2003 I was in training for the Paris Marathon on 6<sup>th</sup> April 2003 (My 50<sup>th</sup> birthday present from Philippa!!). During one training run about a mile from home, after being out for 2<sup>1</sup>/<sub>2</sub> hours, feeling weary and extremely tired, my left hand happened to knock onto my right hand and this gave me an instant cascade of pins and needles in both hands and lower arms. I was rather startled by this and didn't quite pass it off as just one-of-those-things, but thought, for a rather mischievous moment - positive 'Tinel's sign' !! Neuropathy! For the last few miles I had also become aware of a deep aching pain in my right shoulder – the old shoulder strain pain I'd had a year or so before that had taken 3 or 4 months to clear up but had never come back – it was there too!

It was simple – 'When you are low, weak, out of sorts, exhausted (mentally or physically or both) – you can hurt more easily'. From this grew the 'vulnerable organism' idea of mine....

From the stress literature we know that if you put an organism under prolonged stress (physical or mental or both) it not only gradually weakens and may get 'sick' (e.g. see Martin 1997), but also up-regulates the sensitivity state of its sensory systems. The CNS/brain perceives that 'its body/mind' is weak/not coping and hence, vulnerable, and responds by increasing sensitivity to the constant stream of sensory information arriving from the body. Inputs that normally do not reach conscious awareness may now get the opportunity for easier access. It makes evolutionary sense to go carefully if you are physically weak and/or lack confidence. Introducing a hypersensitivity state may be a significant way of achieving this.

Some of you may recall Bud Craig's 'homeostatic' model of the brain (in PPA News Issue 17 page 25, May 2004). Here he proposed that the brain contains an 'interoceptive' cortex (The Vmpo and its parieto-insular cortical target): – an area of the brain that specifically monitors the health/state of the body (via inputs from the nociceptive system). Recall also from the Mature Organism Model (Gifford 1998) that the nociceptive system, at least as I see it, equates to a 'sampling' system that continually provides the brain with information about the health status of the body for the brain to make what it will of in the context of day to day survival/activity. It seems likely to me that old injuries (now scar tissue), arthritic joints, wear and tear, age related changes in tissue compliability and strength, old nerve injuries and nerve impairments – will be continually bombarding the CNS with their own selfish nociceptive activity... their constant droning and pestering to the CNS monitoring systems runs ... 'I'm not so good you know, I'm this bad you know, I need you to be kind to me thank you...' The 'tissue sick/below par' representational neural circuitry, from the tissues and throughout the body neuromatrix in the CNS, quietly sings its little tune and mostly gets thoroughly ignored by consciousness until the individual enters a vulnerability state – as I did from running and felt my old shoulder pain (It has never come back since by the way).

Have you, like me, noted how pain sensitive you become when you have flu, or even when you are a bit stressed or pressured? – Small knocks and movements often seem to really hurt and only the gentlest of foods seem to sooth... a small glass of wine gives you a thumping headache...

The notion that when you are sick you hurt more easily hasn't received a great deal of attention until relatively recently: 'Hyperalgesia' has now been added to the plethora of effects induced by infection and sickness (see Watkins & Maier 2000).

The classic 'sickness response' is an evolutionary masterpiece: When you are under threat from an invading microorganism the body mounts a local response via the immune system. At the same time the immune and nervous systems send messages to inform the brain – which runs something like – 'conserve energy at all costs and do anything you can to help overcome this thing'. To this end cytokine messengers emitted into the circulation by damaged tissues and the immune system reach and enter the brain. Then, via complex secondary and tertiary systems, they bring about cognitive, behavioural and physiological changes appropriate to the situation. Hence, we go quiet, we rest, we don't feel like moving, we get moody and grumpy, we find a place of safety and sleep a lot. We lose interest in pleasure activities, we feel uncomfortable and we hurt more easily. The sickness response causes hyperalgesic and sensitisation systems to enhance their efficiency while dulling the efficiency of analgesic systems.

Important points and thoughts:

- Inflammatory agents (mainly cytokines) are thought to be the primary mediators that initiate and stimulate a generalised centrally mediated hyperalgesic state. These agents could originate from simple tissue injury, inflammation in joints and musculoskeletal tissues that are arthritic/degenerate as well as from immune cells now known to be involved in nerve injury and nerve degeneration. Hence the sensitised state has an underlying physical cause.
- Feeling low, coping poorly or being under stress may be background mental states that also prime the central hypersensitivity circuitry. Hence

spontaneous onset of physical symptoms due to the unmasking of muted nociceptive activity or circuitry. Hence psychological factors may be an important factor in arousing pain states or making them more likely. That there may not have been an obvious physical incident can be irrelevant if we consider that as most of us age we harbour more and more abnormalities and imperfections that are silently signalling their status to the CNS.

- Does the ‘interoceptive cortex’ also receive inputs from areas of the brain that monitor our *mental* well-being and vulnerability states? If the vulnerable organism hypothesis is correct this would be expected.
- The notion of a pain ‘pre-sensitised’ or ‘pain vulnerable’ individual must include balanced thoughts relating to genetic as well as environmental/developmental factors.
- Minor injuries to peripheral nerves can often precipitate massive afferent nociceptive activity. Post injury neural activity may begin many days, possibly weeks after the event (See Devor & Seltzer 1999). Hence a purely peripheral cause to explain ‘pain out of all proportion to the injuring incident’.
- The notion of a ‘vulnerable organism’ should provide a management opportunity – with the underlying goal *for the patient* to feel strong, confident and fit and the goal for the therapist being to help get them there. A simple change in mood may be enough – it’s surely a common clinical observation!

In this edition of PPA News there are two articles that contain fascinating hypotheses linked to the sickness response.

Bruce Charlton explains his hypotheses that depression is a disorder of sickness behaviour and that antidepressants are helpful because they alleviate the discomforting physical feeling of malaise caused by the sickness response. Hence, the improved mood occurs secondary to the relief of the physical discomfort.

Dylan Evans looks at the placebo and notes that all the conditions reported to be influenced by placebo administrations are linked in that they all show to a greater or lesser degree some activation of the ‘acute-phase’ response. The acute-phase response is very much a part of inflammation, sickness behaviour and the sickness response. Evans proposes that the placebo works by suppressing or modulating the inflammatory process involved in the acute-phase response.

I hope my thoughts and all the articles presented bring about some healthy discussion – and even some letters and comments!

Thanks to all contributors as usual, plus a special thank you to Ian Stevens who brought a great deal of the articles and features to my attention.

Louis Gifford  
Editor.

#### References/reading:

Martin P 1997 *The Sickening Mind*. Brain, behaviour, immunity and disease. Harper Collins, London

Devor M, Seltzer Z 1999 Pathophysiology of damaged nerves in relation to chronic pain. In: Wall P D, Melzack R (eds) *The Textbook of Pain*, 4th edition. 4th edn Churchill Livingstone, Edinburgh 129-164

Watkins L R 2000 The pain of being sick: Implications of immune-to-brain communication for understanding pain. *Annual review of Psychology* 51: 29-57

Ursin H, Eriksen H R 2001 Sensitization, subjective health complaints and sustained arousal. *Ann N Y Acad Sci* 933: 119-129