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[Gifford L 2004 Re-writing 'Colonel Bogey' – can chronic pain be forgotten? PPA News 17, July. 3-6]

Re-writing 'Colonel Bogey' – can chronic pain be forgotten?

In the early 1990's I became fascinated by the known biology of pain, in particular the central mechanisms involved. A paper by Pat Wall on 'central mechanisms' (Wall 1991) hugely stimulated my interest, for the simple reason that it helped make sense of chronic pain – obliterating in one simple hit all the traditional mechanical and tissue based reasoning that I had been taught.

In the paper Pat described how 2nd order neurones in the dorsal horn of the spinal cord were of two basic types – NS or 'nociceptive specific' cells and WDR or 'wide dynamic range cells'. NS cells in normal physiological conditions only fired when a noxious stimulus was given to the tissues whereas WDR cells would respond to stimuli over a wide spectrum of inputs – from very light to noxious. The exciting bit was that when an injury occurs in peripheral tissues – the afferent barrage that arises causes CNS changes – the NS cells now 'convert' to the characteristics of WDR neurones. The key clinical revelations were that these second order cells, given the 'right' circumstances, could become so sensitive that they would respond massively to minor peripheral inputs, respond to inputs from primary afferents innervating non-damaged tissues, or even more incredible, were capable of producing massive outputs themselves with no peripheral stimulus.

At last a better explanation for ongoing pain, for the mad hyper-reactivity and hypersensitivity of chronic pain that was out of all proportion to the damage done or the physical 'inputs' given. An immediate effect of this message was that this type of pain was totally and utterly useless – it was something biologically 'maladaptive' and importantly, something that need not be feared. This simple insight shifted my attention, reasoning and clinical explanations from the tissue focused disorder to the disorder of processing.

Initially I realised that it was **MY FEAR** of pain that had been overcome, and this helped me enormously to move on in my reasoning. I went on to teach a great many patients that their pain was of little value and that it was okay and safe to start moving. It often resulted in the start of a far more productive process of improving physical function and fitness – my fear was gone and as a result the patient's fear gradually subsided too. Hurt does not mean harm and many pains are way out of proportion to what might be actually 'needed' by injured tissues. Since then I have come to realise that this is often the case in a great many acute and sub-acute pains too. Think about the extraordinary severity of the pain of some acute sciaticas in relation to the actual physical damage that has occurred in the nerve – relatively tiny compared to the pain! Maladaptive from the word go!

I wanted to understand these central mechanisms and the known physiology and was helped by a very complex but now classic paper:

Coderre R J, Katz J, Vaccarino A L et al 1993 Contribution of central neuroplasticity to pathological pain: review of clinical and experimental evidence. Pain 52: 259-285

It was not easy reading and assumed a great deal of background knowledge in neural science. I read more widely and then by accident came across an article on memory in a Scientific American publication:

Kandel E R, Hawkins D H 1993 The biological basis of learning and individuality. Mind and Brain W H Freeman and Company, New York 40-53

Eric Kandel, recently awarded a Nobel prize, has devoted his life's work to the study of memory.

The biology of memory and in particular, Long Term Potentiation (LTP), that Kandel and Hawkins explained was so similar to the biology of pain described by Coderre and others. Was pain being learned by the nervous system? Could it be that chronic pain was an established and 'imprinted pathway' in the nervous system? Was it like an ongoing memory – or an annoying tune, I always think of 'Colonel Bogey' the nauseating brass band marching tune, constantly playing into consciousness in those who suffer?
The consequence of thinking like this is that once a strong memory has been established, it is very difficult to get rid of. The logic runs: Chronic pain, like the memories of a life-time, may be a permanent feature and therefore patients have to learn to live with it, accept it and get on. This immediately shifts the focus of therapy from pain relief to pain management. Easy to say, but very hard to do! And, is it fair?

In my dealings with chronic pain patients at the time I found that the few who were happy to grasp the idea that their pain was merely a meaningless annoying tune found that they could focus more on getting their lives back together, getting fitter and feeling generally better in themselves. A great many reported that by having less concern about their pain, hence less focus – it actually got a great deal less.
This later transmitted into management of more acute and sub-acute patients – especially those with 'peripheral neurogenic' pain presentations like sciatica, but even the day to day annoying aches and pains associated with common joint degeneration that causes so many people to pack up and stop the things they often enjoy. Shut the pain up as soon as possible – and stop it from becoming a malignant imprint - seems a rational and useful stance to adopt and teach our patients.

The thing that lingered in my mind was that we all remember things but that most of those things don't constantly remain in consciousness – old memories just don't continually bother us unless we deem them as really important and dwell on them all the time.

Students of memory biology will be aware of Donald Hebb, a widely lauded Canadian psychologist who studied 'associative' memory and learning and is now famous for his beautifully simple rule, in its simplified version:

'Cells that fire together, wire together'.

The rule in fact was this:
'When an axon of cell A … excites a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased.'

Basically, the more two neurones fire together the more their synaptic connectivity increases and the more efficiently they fire together. It takes less and less of cell A firing to make cell B fire… It's as if they fall in love and permanently unite! Hebb wrote this back in 1949!
The 'cells that fire together, wire together' rule may well help in the neurological translation of simple Pavlovian conditioning: – Remember the dog experiment - meat plus food =salivate… Do bell plus food = salivate a few times and you then get bell alone = salivate. Cells that fire for the bell wire with the cells that fire when food arrives which in turn wire to the salivation cells – so that after a few repetitions the bell 'circuit' wires itself directly to the salivation 'circuit' – and a new association forms. But, keep ringing the bell while leaving out the presentation of the food – and the circuit gets wise – the bell ceases to produce the salivation.
Now we have another great rule: 'Cells that fire apart – Depart'

(see: Robertson I 1999 Mind sculpture. Your brain's untapped potential. Bantam Press, London)

I will come back to fitting these rules in, in a moment. For the time being though, for pain we can have on the one hand - the biology of 'sensitisation' (remembering/learning) and on the other, the biology of habituation or extinction (forgetting).

I am very excited by some recent work which gives great hope for the idea that pain circuits, may, in some cases, be able to be 'unwired'. There are two important works. The first has been reproduced here with kind permission of the publishers, Oxford University Press, and is the article by Candy McCabe and colleagues later on in this journal (note that Pat Wall was one of the authors here,and according to Candy this may well be his last published work before he died. I'd like to think that this is of some considerable importance!).

The pilot study uses mirrors for the treatment of Chronic regional pain syndrome(CRPS) (to read more about the use of mirrors in the treatment and understanding of phantom limb pain, see Ramachandran & Hirstein 1998, Ramachandran & Blakeslee 1998). With CRPS the patients perform movements of their good limb while peering into a mirror and watching an image of it, – in other words what they are watching is normal movement of an *image* of their affected limb. While doing this the 'bad' limb is out of view on the other side of the mirror. What their study shows is that those patients, with severe limb pain and highly restricted movement of up to about 1 year duration, find that by watching the 'normal movement' image and at the same time moving their (hidden) bad hand/arm synchronously with the 'good movement' – their pain very rapidly goes and they can move it with greater and greater ease. Regular daily practice over a few weeks clears the problem. This is astonishing for a pain syndrome that is renowned for being incredibly hard to treat and incredibly easily provoked by even the gentlest attempts by physiotherapists to induce movement.

The second paper is by Lorimer Moseley, an Australian physiotherapist working and researching out of the University of Queensland:

Moseley G L 2004 Graded motor imagery is effective for long-standing complex regional pain syndrome: a randomised controlled trial. Pain 108(1-2): 192-198

Before describing a little of this study I would like to come back to the 'fire- together wire-together' and 'wires-apart-depart' ideas in relation to pain treatments…

I've been thinking like this: If pain comes on when a patient moves then the cells that 'fire' for pain may well 'wire' with the cells that 'fire' for movement. Pain is also powerfully linked to the emotions of anger and fear/anxiety – the pain fires with the emotion and the two wire together – hence stress and anxiety linking more and more easily to pain. Think of environmental cues too, like office pain…, armchair pain, in the presence of spouse pain, tired pain, food intolerance pain and so on.
How to stop it? – simple, cells that fire apart, DEPART… for movement linked to pain: Get movements going without pain – graded exposure... start with nice easy big confident movements (low on fear too…) – better then if chosen by the patient (give them several options to choose from…) … and *progress* on from there – movements without pain (as in Candy McCabe's patients with their mirrors) – start to unwire themselves from the pain circuitry so that normal movements – without the mirrors, become pain-free. Teach your patients the two rules so they understand what they are doing.

In this second paper, Lorimer made the point that in his experience the CRPS patients who were really chronic (having it for over one year) –found that performing movements using mirrors severely aggravated the pain. Even *imagining* doing the movement aggravated the pain in some patients!
How far back in a graded hierarchy is it possible to go?
In the article Lorimer describes movement as involving a sequence of first of all the activation of the 'pre-motor' cortex followed then by the 'primary' motor cortex. His reviews of the brain scanning literature showed that 'recognising a pictured hand to be a left or right hand activates the so-called pre-motor cortices, whereas explicitly imagined movements also activate the primary motor cortex.'
Apparently, CRPS patients have been shown to take longer at recognising the hand that corresponds to their affected hand – due to a possible disruption of the internal 'body schema' (think Melzack's neuromatix – see introductory chapter in Topical Issues in Pain 3). Fascinating too is that the recognition time gets more when the hand posture is perceived by the patient as likely to be painful – the more painful the slower the recognition! As Lorimer puts it – there appears to be high level guarding mechanisms that even impacts motor intent and motor planning. 'Forget trying that bud…'

In his study using a 'Motor imagery programme' for *chronic* CRPS (over one year in duration), the patients went through three, two week phases. These phases are clearly hierarchical/graded:

Phase 1:
The patients were given a computer that ran a programme which randomly brought up on the screen 56 pictures of hands in various positions –and the hands were either right or left. Patients simply had to recognise whether the hand presented was left or right as quickly and accurately as they could by pressing a left or right designated key on the key-board. Times were recorded. Patients were asked to do this for the 56 hand pictures 3 times in every waking hour! (takes approximately 10 minutes every hour).

Phase 2:
In this phase patients still used the computer programme which now randomly generated 28 pictures of the *affected hand* in different postures and positions. This time the patients were instructed to…. 'deliberately imagine moving their own hand to adopt the posture shown in the picture, three times'. They were asked to repeat the process three times every waking hour. The emphasis was on accuracy, not speed.

Phase 3:
This phase was similar to that of McCabe and colleagues, in that patients now used a mirror. They were presented with 20 different paper copies of hand positions of the *unaffected* hand. These positions involved 'less complex' hand positions. Patients were asked to 'slowly and smoothly adopt the posture shown in each picture with both hands, 10 times. The affected hand was concealed in a mirror box and the emphasis was made on watching the reflection of the unaffected hand in the mirror. They were asked to do this every hour.

The results in this incredibly hard to help patient group were astonishing – and long lasting. For example, 6 weeks after the completing the programme approximately 50% of the patients no longer fulfilled the diagnostic criteria for CRPS-1 and the numbers needed to treat a greater than 50% reduction in pain was 3. Not only did pain diminish but also the 'physical' measure of finger circumference did too – this being quite significant *even during the initial phases where no movements were involved. Changes in central processing were apparently having significant effects in the periphery.*

For me, what this work gives us is a beautiful potential to extend a graded exposure hierarchy of difficulty even further back for patients with severe pain that is powerfully linked (wired!) to movement. Get back far enough and we can still find that cells that fire apart –do indeed, depart. One thing is clear though, that just like many kinds of learning, this unlearning, or perhaps more accurately 'new learning' to over-ride the old, requires a great deal of practice.
Remember too that learning/unlearning/new learning becomes far more efficient when the event or experience is strongly attached to a powerful emotion. High anger and fear therefore enhance memory acquisition of the experience that caused the anger/fear, just as the positive emotions like love, do too. Our most vivid memories are very likely to contain strong underlying emotional content. They are also the ones that are hardest to forget. No wonder that a high level of distress at the onset of pain is a significant yellow flag predictor of a poor outcome.
Emotions are powerful because they are strongly linked to the value that we might give to an event (good/bad) – and here, clearly, we are all quite different in how we appraise a given event.

It seems logical now that a process of 'new learning' of pains 'detachment' from movement will be enhanced when patients enter the process with a positive attitude (desire), belief and emotion toward the process? In this way it may be our duty when instigating any graded hierarchy programme to inform the patients of these links and hence muster a productive atmosphere of enthusiasm. To learn anything quickly and well you have to want to learn it, you have to be keen and motivated. In this sense we must 'sell' what we do – hence - 'BO' – Belief and Optimism (a la placebo) are likely to be important ingredients. I believe that we need to be more explicit with our patients here – especially since the biological evidence, given a few rather lateral, but quite comfortable steps of logic, is thoroughly supportive! I always like to underline with the patient that what they are doing and the way they are doing it must make sense to them, and if it doesn't I need to know that it doesn't and so try again until it does. Clearly my belief is a hugely important factor too (see the article 'Magnets and medicine are poles apart' for a good example of the difficulty some therapies can cause us.)

Earlier I mentioned habituation / extinction and would like to come back to it here. All of us are well aware that a novel experience usually produces quite a marked response, yet the more often we do it, the more the novelty, and hence our response to it, wears off – we basically get bored with it and eventually come to take no or very little notice of it. 'The thrill is gone' to quote from on of BB King's famous blues….! Clearly the same can occur with pain – hence 'de-sensitisation' programmes (or more amusingly how about: pain-boredom-acquisition-processing!). Here, patients do an activity – which creates a pain response that wears off – then they repeat the activity later on – the response occurs again but a little less, and so on, repeating the activity until the response habituates and extinguishes. Repetition trains it out – think mechanisms that may underlie progressively declining pain responses to exercises, or manual therapy…. This simple and well established response is quite the reverse of the 'cells that fire together wire together' approach discussed.
Here, we are actually doing two things together (pain and movement) yet they're wiring apart? – Quite the opposite of what has been discussed, - what's the deal? The answer appears to be that it's simply lack of interest, lack of value, lack of threat – take away the fear, the emotion, take away the threat, and the response habituates. This occurs in all of the animal kingdom that has a nervous systems – why bother wasting energy on an unnecessary response to a recurring stimulus when it has no value! When its novel – don't trust it, withdraw/be careful, hide in your shell, but when its proven not to be a threat - ignore it. But you cannot ignore something if you are frightened of it or it's attached to a threat.. Again it has to be done, as per good old graded exposure, a little at a time and in an atmosphere of confidence and understanding and it often takes time. No worries. Everyone's different. Some people can just never overcome the fear, others find it a cinch!
As in all interactions and treatment or management processes I think – 'top down before bottom up' needs a great deal of emphasising - set the brain up to run in harmony with the physical rehabilitation process that is proposed. TALK then DO.

There we are, two ways to go, we've been doing it for years, but here's a 'central nervous system/neurobiological' spin on it perhaps – one that goes away from pain (backward before forward) – to get the wires to depart and the other that goes into the pain until it dulls out via habituation, both with the same ultimate effect of 'unlearning'. Some conditions may like to go one way more than the other – and

CRPS, since it is at the far end of the 'hypersensitivity spectrum', is one we can all learn from. It's thanks to McCabe and colleagues and to Moseley for some great insights as to which way to go with CRPS if we are considering helping with the pain. Readers might like to contrast and marry these approaches with the CRPS case history described by Suzanne Brook in Topical Issues in Pain 3 (Brook 2002).

I think we are in very exciting times – look at the work presented in this PPA News, celebrating our 10 year lifespan – and all so relevant to this discussion -

- Herta Flor who is coming to present our annual 'The Patrick Wall Annual lecture at congress – her article on 'Painful memories – can we train chronic pain patients to 'forget' their pain?'
- Bud Craig on 'mapping pain in the brain'
- Check out : 'My painful feet – a case history' in relation to forgetting and reducing concern as discussed here.
- Check out too, Clare Dunlop's excellent review of PAIN IN EUROPE IV - "Europe Against Pain, Don't Suffer in Silence". Most of the topics reviewed are strongly associated with the issues discussed….
- Robert Coghill and colleagues work on brain mapping and individual differences – see 'On the web' section.

Successful therapist – how do you work ? –
By re-mapping and re-wiring the brain – get excited!
And maybe plan to get more interested in bio-feedback too (see the Helen Phillips reference on the web).

Many thanks to all the amazing contributors to this edition of the PPA News - that is really celebrating 10 years of the PPA. Thanks therefore to those who started this whole thing up in the first place – in particular Heather Muncey, Sue Mickleburgh, Jan Williams, Vicki Harding and Carol Sweet.

Special thanks to Ian Stevens who's tireless trawling of the net has uncovered many of the topics and papers in this issue.

Enjoy it, talk about it, pass it round and get new members!
Have a good summer
With best wishes to you all.

Louis Gifford.
Editor PPA

Some further reading and references:

Brook S 2002 Improving fitness and function in complex regional pain syndrome. In: Gifford L S (ed) Topical Issues in Pain 3 Sympathetic Nervous System and Pain. Pain management. Clinical effectiveness. CNS Press, Falmouth 161-171

Gifford L S 1998 Central mechanisms. In: Gifford L S (ed) Topical Issues in Pain 1 Whiplash - science and management Fear-avoidance beliefs and behaviour CNS

Press, Falmouth 67-80 – *see the section on pain memories and the patient examples – page 71-75*

Herta Flor's work…. See her article her and…. go to congress!!

Katz J, Melzack R 1990 Pain `memories' in phantom limbs: review and clinical observations. Pain 43: 319-336

Le Doux J 2002 Synaptic self. How our brains become who we are. Vicking Penguin, New York

LeDoux J 1998 The Emotional Brain. The mysterious underpinnings of emotional life. Weidenfeld & Nicolson, London

Helen Phillips, San Francisco… 'Brain-watching helps suppress pain' - go to -

http://www.newscientist.com/news/news.jsp?id=ns99994931

Ramachandran V S, Blakeslee S 1998 Phantoms in the Brain. Probing the mysteries of the human mind. Quill, New York

Ramachandran V, Hirstein W 1998 The perception of phantom limbs. The D O Hebb lecture. Brain 121: 1603-1630

Rose S 1992 The making of memory: From molecules to mind. Bantam Press, London

Do a search and check out works written by Jurgen Sandkuhler if you want more on Long Term Potentiation and pain- especially in relation to TENS and acupuncture. E.g. Sandkuhler J 2000 Learning and Memory in pain pathways. Pain 88(2): 113-118

Wall P 1991 Neuropathic pain and injured nerve: Central mechanisms. In: Wells J, Woolf C (eds) Pain mechanisms and management British Medical Bulletin Churchill Livingstone, Edinburgh 631-643

Zusman, M. (2004). "Mechanisms of musculoskeletal physiotherapy." Physical Therapy Reviews **9**(1): 39-49.