4

The 'central' mechanisms

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This chapter addresses the central mechanisms that follow on from tissue damage, nociception and peripheral nerve injury (peripheral neurogenic mechanism). Its major purpose is a clinical perspective and the reader should refer to the cited references for more details of the sometimes complex biology.

There are several areas of focus: Alterations in processing deals with the known dynamic changes that occur in central nervous system pathways following tissue damage, nociception and peripheral nerve injury. Pain memory, focuses on the potential for ongoing barrages of impulses, that may be derived from tissue or peripheral nerve damage, to actually form an imprint or memory trace in the CNS/brain. Hence the potential for a 'pure' central mechanism whereby pain is actually a result of central nervous system neuronal activity that has become independent of the target tissue origins. Last, the affective and cognitive mechanisms/dimensions integrates the more conscious aspects of 'processing' into the clinical picture.

Alterations in processing

The central nervous system is capable of altering its sensitivity state very quickly and very easily. Following tissue injury or peripheral nerve injury, there is an increased impulse discharge of all sensory afferents which results in increased input into the dorsal horn of the spinal cord (see Dubner & Basbaum 1994, Woolf 1994). This barrage of afferent impulses impinges on second order neurones in the dorsal horn and electrochemically alters their sensitivity state too. Thus, dorsal horn cells (second order cells), many of which transmit onwards to higher centres, become increasingly excitable in the first few hours following tissue injury. This central sensitisation has several repercussions:

1 Dorsal horn second order cells alter their responsivity

Dorsal horn neurones that formerly only responded to inputs from nociceptors may start to respond to inputs from other fibre types too. Thus an Aβ fibre, which normally transmits impulses in response to non-noxious inputs like light touch and joint movement, now becomes capable of driving or stimulating neurones in the central nervous system that ascend to areas of the brain to produce pain sensations (Dubner & Basbaum 1994, Woolf & Doubell 1994). These Aβ fibres innervation fields may be in quite normal and undamaged tissues. This means that mechanical stimuli like light touch, gentle joint movement, palpatory pressures, performing neurodynamic tests like the upper-limb tension test or slump test, can produce pain from tissues that may be perfectly normal. This phenomenon is known as secondary hyperalgesia and amounts to a false positive for the tissues under scrutiny when tenderness is detected or standard physical 'differentiating' tests reproduce pain (Gifford 1997). The fact that it is a false positive for the tissues under scrutiny does not mean that the pain is not real, or is non-organic or psychosomatic in any way.

Clinically it is often the case that acute sprains and strains produce marked and widespread tenderness and most tissues under test easily provoke pain. Think of the acute back strain where tests of the SI joint, the lumbar spine, the SLR and Slump and PKB may be acutely positive, or a sprained and swollen knee joint where the whole area has become tender to palpate and all movements and tests hurt. Identifying a culpable specific faulty structure is often extremely difficult. However, several days later, when the acute inflammatory phase has settled it is common to find that this widespread hypersensitivity, or hyperalgesia, diminishes to become far more focused on the actual tissues that were originally injured or that need to maintain protective sensitivity. Sensitivity that actually relates to the damaged tissues is termed primary hyperalgesia and is thus a true positive—the tissues under test that hurt are abnormal (for a full discussion of hyperalgesia and allodynia see Gifford 1997).

In more devastating injuries, especially where peripheral nerves have been injured to some degree, ongoing enhanced tissue sensitivity may continue for a long time in a great many tissues. Clinically the problem of tissue labelling based on reproduction of pain and the discovery of hypersensitivity has to be interpreted very carefully. Knowledge of secondary hyperalgesia helps us understand the potential for widespread enhanced sensitivity, but it leaves us with a clinical dilemma—is the sensitivity adaptive and therefore protective, or is it maladaptive and preventing adequate functional rehabilitation? We can only confidently address this if we have better knowledge of issues like tissue healing time, tissue strength while healing and the physical needs of injured tissues in general. Widespread mechanical hypersensitivity may well be highly adaptive in the first days after a whiplash, it certainly is not after a few weeks/months or one or two years.

2 Dorsal horn cells enhance their responsivity to nociceptors

Not only do dorsal horn cells come to fire far more volleys of impulses following an injury, they also fire for a long time after the peripheral stimulus stops. Further, if the peripheral stimulus is repeated over and over these cells fire more and more every time—a phenomenon known as wind-up (Dubner & Ruda 1992, Dubner & Basbaum 1994).

In clinical terms if I were to extend my neck back until it hurt, one nociceptor in the tissues stretched might hypothetically fire 5 impulses into the dorsal horn and be relayed on as 7 or 8 impulses by second order neurones—enough to make me feel discomfort and enough to stop me pushing further perhaps. If I actually sprained the neck tissue, in the next few hours the relevant dorsal horn cells would receive a building afferent barrage in parallel with building tissue inflammation, and hence become sensitised. Now, extending the neck back very gently initiates say 15 impulses from the sensitised nociceptor, the dorsal horn cells respond by producing 60 impulses in the first few milliseconds and the volley continues thereafter for seconds if not minutes. Hence, a nasty pain far earlier in range that goes on for some time after. Keep repeating the movement and the volleys build and build with a proportionate exacerbation of the pain.

3 Dorsal horn cells increase their receptive fields

A receptive field is the area of tissue that an individual neurone will respond to when an appropriate stimulus is given. It could also be said to be the area of tissue that a given neurone 'looks after' (Thacker, pers comm). Thus, an individual C fibre, whose terminal branches may be in the skin overlying the neck, may have a receptive field with a diameter of, say 15 mm. Perhaps the best way to understand a receptive field is to imagine looking down the neurone in question and 'viewing' the tissues it supplies. In order to view a single second order dorsal horn cell's receptive field it is necessary to 'look down' many individual afferent neurones, since many afferent neurones terminate on a single dorsal horn cell. There is thus a marked convergence of input onto the one cell. In this way a single dorsal horn cell's receptive field may be quite large, perhaps as much as the skin over the whole of one side of the lower neck. Dorsal horn cells are actually physically connected to many thousands of arriving neurones but many of the connections may be inactive or silent under normal conditions. When conditions change, as in injury, many of the sub-threshold or 'sleeping' connections wake up and become active. Hence, the receptive field increases in size. It is as if we are looking down a viewfinder that in normal conditions reveals a relatively limited view, but in injury conditions the viewfinder is capable of marked expansion to incorporate a great number of tissues not otherwise 'seen'.

The following are examples from the literature that show how vast a single dorsal horn cell's receptive field can be:

- Gillette et al (1993) showed that individual second order cells in the dorsal

horn of spinal segments L4-5 of the cat have receptive fields in the back/hip/leg that included both skin and deep somatic tissues innervated through both the dorsal (back/hip) and ventral (leg/ventral spine) rami (Gillette et al 1993). Dramatically, many of the cells were found responsive to stimulation of many different somatic tissues including skin, muscles, facet joint capsules, ligaments, dura, intervertebral discs and periosteum. It is important to realise that the CNS is largely incapable of making an accurate map of many of the body's tissues, especially the deeper ones, and that what we perceive in terms of sensation as a result of a noxious stimulus to an individual deep tissue may well be very different to what we would logically expect.

- In association with chronic experimental arthritis in rats, Grubb et al (1992) have demonstrated receptive field expansion of second order neurones normally only associated with the ankle joint, to increase in size to include the thigh, the tail, abdomen and the contralateral leg.
- While the potential size of an individual dorsal horn neurone's receptive field is striking, it is important to realise that this expansion is controlled by powerful ongoing, or 'tonic', descending inhibitory currents from higher brain centres (Schaible & Grubb 1993). These workers have shown massive increases in single neurone receptive field sizes in cats where descending inhibitory currents were prevented by using cold blocks on the spinal cord. The fact that descending inhibitory currents may be influenced via conscious mechanisms adds weight to the potential maladaptive influence that emotional and cognitive states may have on neuronal intracellular relationships.

The messages from all this for whiplash are useful in that they help to explain the often widespread sensitivity and pain that are beyond the traditional dermatome/myotome boundaries set down in textbooks and rather dogmatically adhered to by much of medicine (including physiotherapy.) The reality of the standard textbook is perhaps light-years away from the reality of the patient, and the patient suffers because of this. A reasoned understanding of pain mechanisms validates the reality of ongoing unrelenting and often untreatable chronic post-whiplash pain. It also enables a reasonable speculative leap that links the complexities of reductionist biology with an individual's psychological state. Thus, worsening pain and an often massive spread of tenderness into multiple tissues can be tied in with an interaction of early low level biological 'tissue input' related neural plasticity, as well as with unhelpful emotional and cognitive responses that so often accompany these types of injury. Both 'inputs' ultimately interact to bring about the plasticity changes. The danger of making links like this is that it can easily be translated into a focus on the fault lying with the patient and issues of personal weakness, blame and inability to cope that are so disparaging. Perhaps the skill of the therapist is to provide the correct level of input to enhance the ability to cope—physically and mentally (see Ch.7).

Finally, it would also seem reasonable to presume that every individual, being genetically unique, and having had a unique life experience, will at any given time, have an established sensitivity variability capacity. Thus, as a result of the combined biological effects of inheritance and past and current experi-

ence, some individuals may be more predisposed to entering a highly sensitised pain states than others.

4 Dorsal horn cells may become spontaneously active

This concept relates to the pain memory issues discussed in detail below. Importantly, spontaneous activity of a cell, that as far as the brain perception networks are concerned represents huge tissue receptive fields, means that we can perceive pain when nothing untoward is wrong or happening in the tissues. The concept of a pain memory expands this to move beyond the dorsal horn population of cells to incorporate integrated networks of cells that represent the pain but that need no, or very little, peripheral input to activate them.

Pain memory

The proposal is that many, probably all, ongoing pains have a major component of their pain source within the central nervous system in the form of a somatosensory memory or imprint (see Katz & Melzack 1990, Melzack 1991a, Melzack 1991b, Flor et al 1995, Melzack 1995, Basbaum 1996, Hill et al 1996, Melzack 1996). This is **not** the same as suggesting that the pain is non-organic or 'functional'. What it is doing is suggesting a firm physiological basis to ongoing pain, whose roots are in the biology of memory and synaptic efficacy (e.g. Dudai 1989, Rose 1992, Kandel & Hawkins 1993, Meller & Gebhart 1993, Kandel et al 1995, Pockett 1995).

The concept of a somatosensory memory is not new, especially in relationship to the understanding of post amputation phantom limb pain (Katz & Melzack 1990, Hill et al 1996). All that is required is a shift in view to see that any powerful or ongoing nociceptive input into the central nervous system (CNS) may leave an imprint, or central representation of the pain. Three examples follow, the first two from the work of Lenz et al (1994, 1995, 1997):

1 The first example involves a 69-year-old woman who was undergoing an operation to implant a deep brain-stimulating electrode for treatment of chronic leg and perineal pain secondary to arachnoiditis. Her previous history involved nine years of exertional angina that had been treated via angioplasty and had been stabilised. At the time of the operation she reported having not had an angina episode for two months. During the operation specific sites in the thalamus were identified and stimulated using microstimulation techniques and the awake patient reported feeling angina of exactly the same location and quality as normally experienced during an attack. Further, the researchers were able to turn the angina pain on and off using the stimulator. The angina could even be reproduced in the presence of nitroglycerin, a vasodilatory drug normally self administered by the patient to relieve angina. The authors pointed out that performing the exact same stimulation techniques in the same areas of other patients, but who did not have a history of angina, failed to reproduce any symptoms.

2 In another patient, thalamic electrical stimulation evoked intense pain in the peroneal region. On stimulation at one thalamic site the patient responded that she 'thought she was having a baby'. At a second site the stimulation reproduced pain experienced during sexual intercourse. As in the first example, intense pain experiences had left their mark.
The current general view, only recently challenged, is that electrical stimulation of the brain does not produce pain. All that is reported are perceptions like music, pictures, tingling and odours, but rarely the elicitation of pain (Basbaum 1996). It is notable that until recently, all the electrical stimulation studies of the brain had only been done on asymptomatic healthy people. What is now apparent is that previous pains can be reproduced in stimulation studies of subjects who have a significant past pain history. They appear to have a 'pain memory', albeit a subconscious one.
3 This example relates to a female patient (from Hill et al 1996) who had had a below knee amputation because of recurrent infection of a leg wound over a two year period. During this time she had suffered much pain following infection, multiple surgeries and damage to her popliteal nerve. The most distressing pain experienced was evoked by the treatment procedure carried out on the open drainage site on the calf, which had to be cleaned and repacked twice daily. During this time the patient was very distressed, not only by the pain, but also by the prospect of having to have the wounds dressed regularly. In order to manage the procedure as comfortably as possible she was administered both diazepam and morphine prior to the treatment. For additional pain relief, a mixture of nitrous oxide and oxygen was also self administered during the procedure. When even this did not alleviate her pain the decision was made to amputate.
Subsequent to the amputation she experienced phantom limb pain of two kinds: that which was ongoing, experienced only in the distal parts of the limb, and infrequent episodes which remarkably resembled some of the pre-amputation pains associated with the open drainage site. Triggers to this second pain were recorded by the researchers (Hill et al 1996) and varied from more physical antecedents, like a stump abscess problem, after receiving a new prosthesis, and during a flu virus; to more cognitive/emotional ones, such as following a discussion of her pre-amputation experience with a friend and while watching a television drama which showed an individual with a leg injury being given nitrous oxide and oxygen to relieve pain.

If this analogy with memory holds some truth, then there are several important clinical messages:

- Memories are hard to get rid of (Connolly & Tully 1996) and if ongoing pain has a large memory component it may be beyond any tool/therapy we presently have. Certainly even the most dramatic brain surgeries for ongoing pain states appear to fail repeatedly (Gybels & Sweet 1989) and have been strongly criticised (Wall 1995, Wall 1996). Adequate management in the acute stage that recognises the biopsychosocial, and hence neurobiological impact of injuries like whiplash is probably the best hope at this time (Ch.

7).

- Treatments and approaches which tend to focus the patient on pain and on the alleviation of their pain need serious inspection. There has been a helpful shift in focus in the literature to restoration of physical function in parallel with strategies that positively address the patients' negative or unhelpful thoughts and feelings (Caudill 1995, Harding & Williams 1995, Cohen & Campbell 1996, Gatchel & Turk 1996, Harding 1997) (see also Chs 8, 9, 13, & 14 in this text). The emphasis is to address the dimensions of suffering and the physical dysfunction, and the focus is far less on pain ablation or relief, especially in the ongoing pain situation. It seems likely that the long held focus on the concept of an 'irritable' pain state, and hence on damaged or inflamed tissues (e. g.Brown 1828, Buckwalter 1995, Maitland 1986), has held back the functional restoration of many patients with ongoing pathologically benign pain states (see Ch. 15 and Zusman 1997).
- One very useful message is that hurt does not necessarily equal harm. A far better message for the patient is to view the tissues as being 'deconditioned' rather than damaged.
- Another aspect is the need to integrate diagnosis of pain mechanisms rather than over-focusing on tissue based diagnosis (Gifford 1997, Gifford & Butler 1997, Gifford 1998, and Introductory Essay to this volume). If a tissue is thought to be at 'fault' by the patient (and the therapist) then it is hardly surprising that the patient and therapist are going to fear doing anything that causes more pain—it adds to the problem of hurt equals harm (see also Chs 12 & 15, and Zusman 1997).
- Memories can be put into subconsciousness but dragged back up if given the right cues. Some memories and experiences may, if given great significance, stay continuously in our consciousness, rather like an annoying tune or nagging worry tends to. If this goes on for long enough it becomes very distressing and in some ways could be seen as a mental 'habit' that may be extremely hard to overcome.
- Many clinicians may be inadvertently helping to keep pain in consciousness by over-focusing on the relief of pain, on pain response during treatments and afterwards by actively getting the patient to pay great attention to post-treatment pain behaviour. From a patient's perspective, over focusing on pain, expecting pain, being vigilant for the pain, giving great value to pain, worrying about it, being frustrated by it, or being in fear or anxious about it…may all help to maintain its presence in consciousness and its neurobiological underpinnings.
- A nice example from a recent article in the journal Pain provides splendid evidence that if patients can be helped to accept their pain better, then they are likely to report 'lower pain intensity, less pain-related anxiety and avoidance, less depression, less physical and psychosocial disability, more daily uptime, and better work status' (McCracken 1998).
- Successful cognitive behavioural approaches to pain management steer patients away from a focus on pain and pain related behaviour and towards

positive functional achievements (see Harding & Williams 1995, Klaber-Moffett & Richardson 1995, Harding 1997, Klaber-Moffett & Richardson 1997).

For ongoing pain states, the simple statement 'close the pain gate to consciousness by focusing less on the desire for pain changes and pain relief and more on functional achievements and helpful thinking', may be a useful way for clinicians to understand the shift in emphasis by pain management and cognitive behavioural approaches. Perhaps defocusing on pain is a new skill that needs to be taken on—by us primarily and as a consequence by the patient. A wise action approach might be initially to seek to understand the pain, the nature of the disorder, the tissue status, the spread of tenderness/hyperalgesia, and the level of suffering and disability (requiring a degree of focus on pain during assessment)—but subsequently to defocus on it for management purposes (see Chs 8 & 9). A warning is that merely telling the patient not to focus on their pain is likely to be very unhelpful since it is an incredibly difficult thing to do when pain has firmly established itself or when pain is very severe.

Arguments about giving less emphasis to pain, like this, need to be made with caution. We need to recognise that significant pain in the acute stages of a disorder is a major predictor of chronicity (Dworkin 1997). For example, Reid et al (1997) found that workers who report intense pain (greater than 7 on a 0–10 scale) during the first two weeks of their problem were more likely to be on sick leave two months after injury. The clear message is for early and effective pain control—which may be a combination of pharmacological and non-pharmacological interventions. Relaxation techniques, loan of TENS machines and graded exercises may be more worthwhile than passive therapies alone, since they encourage independence and control by the patient rather than total reliance on visits to a therapist. Fordyce (1992) warns us that adequate pain control must take place in a therapeutic setting that does not overlook many other key issues that affect performance. We should not get carried away by overfocusing on just one thing—the alleviation of pain and single modality treatments. Pain has multifactorial components which requires a multifactorial approach (see Preface).

Patients in pain are often disparaged or accused of malingering if they are seen to be capable of normal movements one moment, yet when asked to perform a test movement another moment demonstrate quite remarkable pain behaviour and verbalise a strong pain complaint. A biological perspective of this apparently 'inconsistent' phenomenon tends to view it as consistent with mechanisms that work in favour of survival. Thus, pain inhibiting systems (pain gates to consciousness closed) operate quite powerfully when the organism is occupied and focused on some important task. At times of little threat/safety these inhibitory systems are relaxed, pain returns and consciousness is reflexly 'requested' to spend some time attending to the area containing pain—a very adaptive mechanism for acute injury. Having continuous pain and continuously being forced to adopt tissue protective movement patterns and behaviours is just not consistent with survival. We are designed to heal while we move and

function, but alongside this there are powerful tissue-friendly pain mechanisms that dictate the need for rest/altered behaviour whenever it can be achieved safely. If you think about it, modern humans are far safer for far longer than our ancestors ever were. We may have too much time that allows too much focus, and too much conflicting evidence that may promote too much concern.

By focusing patients on their pain or by repeating movements that have been associated with the onset of pain many times before we simply trigger the opening of 'pain gates' to consciousness. It would be far better if the inconsistent behaviours and complaints frequently associated with chronic pain, and usually viewed as evidence of malingering, are wisely viewed as maladaptive since they have gone on for far too long.

The affective and cognitive mechanisms/dimensions

How our thoughts and feelings not only influence the way in which we perceive pain but also influence the outputs of the brain that powerfully govern recovery control systems and our behaviour has already been discussed (Ch. 2).

There are many problems with misguided day to day clinical application of psychological and psychiatric theory to pain states, in particular when a patient's thoughts and feelings are over-focused on as the reason for their pain problems (see Chs 8, 9, 10, 13 & 14). An appropriate stance is that:

1 Low or depressed mood, and other maladaptive alterations in psychological function that are commonly found in ongoing pain states are largely the result of the pain state rather than the cause of pain (For a review of psychological factors in chronic pain see Gamsa 1994a & b, Banks & Kerns 1996, Gatchel 1996.) Patients can happily accept this; what they cannot accept, and what most rational investigative science cannot accept either, is that their emotions or their 'mind' are wholly causative or blameworthy for their pain state, or maintaining it for reasons of gain (for a good overview see Mendelson 1995, Banks & Kerns 1996; see also Ch. 10).
On the other hand, it would be wrong to dismiss this notion entirely. It is recognised that ongoing low mood, depression, or psychologically stressed states cause alterations in sympathetic, neuroendocrine and neuroimmune function, and, that people who are in low spirits adopt unhealthy behaviours that lead to deconditioned tissues (Martin 1997). Thus, unhealthy behaviours, like doing little exercise, increased use of mood enhancing drugs, poor diets, or insufficient sleep, all contribute to a weakened physical and mental capacity to cope. It may well be that an individual's capacity to cope is severely 'physiologically' strained by ongoing psychological and associated behavioural factors, and that stresses that normally would have little impact actually do precipitate problems that are otherwise adequately dealt with. Again, the adverse psychology is not the sole prime cause, but it may well add to the plethora of potential predisposing factors that weakens the

natural stability and strength of the tissues and our homeostatic 'coping' mechanisms (e.g. see Gatchel, 1996). Hence,

2 Low or depressed mood and other maladaptive alterations in psychological function powerfully influence the health of the body and hence the perception of pain (see Figures 4.1 and 4.2). In terms of the Mature Organism Model, the CNS/brain senses that its 'body' is weak/vulnerable and that its capacity for recovery may be compromised. It thus allows minor or modest injuries and the subsequent nociceptive/input events, that would otherwise be dealt with quite adequately utilising subconscious physiological processing, or only modest awareness, to be given a highly significant status and hence give rise to a pain state of great significance.

Figures 4.1 and 4.2 emphasise the circular, and forward and back interactions between psychology, behaviour and tissue health that have important implications for management. The starting point can be anywhere on the circle (Fig. 4.2) since one state feeds off the other, and the best approaches are likely to be those that address them all together.

The 'affective' pain mechanism still stands and is in use today to help clinicians in their evaluation of factors involved in their patients pain states (Gifford & Butler 1997). It is by no means perfect for two reasons:

1 The affective 'pain' mechanism, in isolation, implies that the emotions are a primary source of pain. This is obviously dangerous in the evaluation of pain that is 'physical' in character, in history and in nature. However, to most open-minded people, it is reasonable to link pain with emotions like sadness, grief, anger, disgust, extreme anxiety, and even love, for it can 'physically' and 'mentally' hurt when you are deeply emotional (e.g. see Cassell 1991, Morris 1991, Damasio 1995). Problems arise when a psychological component is used and viewed in terms that disparage and suggest hysteria

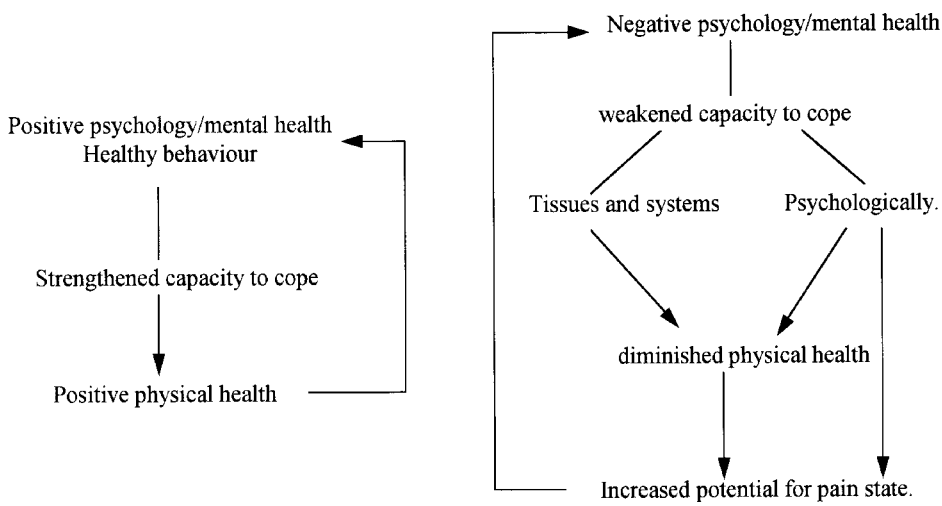

Fig. 4.1 The influence of 'psychological state' on tissue healing

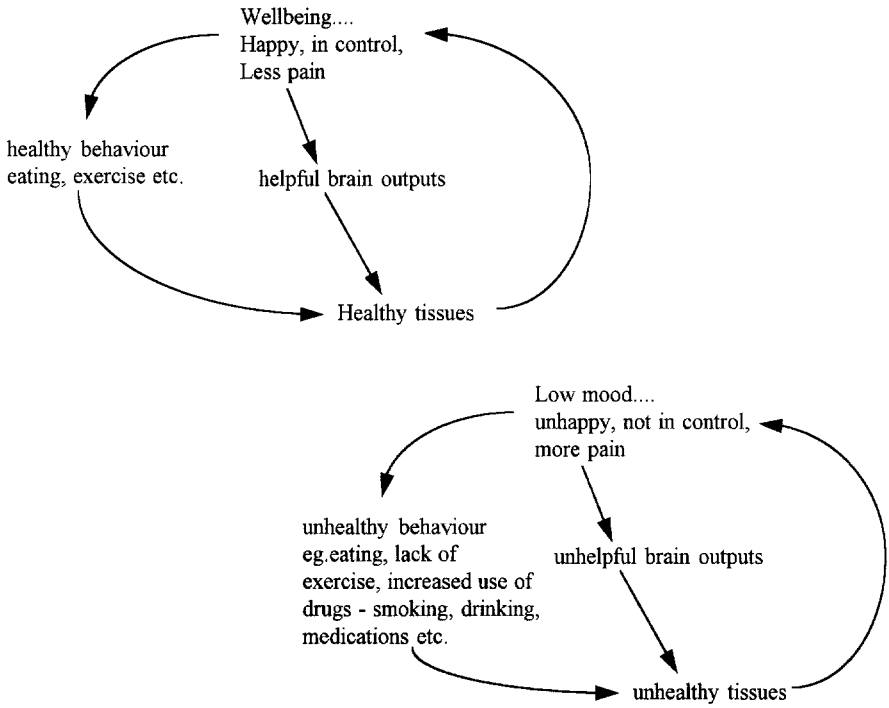

Fig. 4.2 Diagrams to show patients the interactions of positive and negative mood states with behaviour and tissue health.

or even dishonesty and malingering.

2 By only using the word 'affective' it unfortunately omits the 'cognitive' dimensions and factors discussed. Thoughts influence feelings and the interaction of thoughts and feelings influence the perception of pain, the health of the body as well as determining behaviour patterns.

It may be a wise and open-minded step to rename this category 'psychological/mental processing mechanisms' and leave it at that.

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