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# Output mechanisms

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## Introduction

Output mechanisms can be divided into: somatic motor, autonomic, neuroendocrine, neuroimmune, and descending pain control systems. There may well be others to consider.

Output activity is governed by multiple level CNS/brain processing of inputs from the environment, inputs sampled from the body, inputs derived from previous experiences (memory), and current conscious appraisal of the situation (see Ch. 2). Thus all physiological levels, including the physiological processing that goes on concerned with activities of the mind, are involved in governing CNS/brain output. It is well established that the way we think and feel alters our behaviour and our muscle tone, changes autonomic and neuroendocrine activity, and alters the immune system's responsivity. Activity in all these systems may influence the level of pain perceived and the degree of function obtained directly or indirectly.

## Somatic motor

Our response to threat is to change our behaviour. Pain is frequently a component of physical threat and by its very nature demands a change in behaviour. Behaviour is a motor response; what we do when we are in pain, the way we move, the way we talk, the postures we adopt, the quality and range of movements we display when examined, the grunts and groans made, are all motor responses that convey protection to the part concerned and convey information to others. Humans as social animals have evolved behavioural patterns that convey powerful messages to others to help us (or to avoid us!). Fundamentally, help means talking and touching—input via mind and input via body; but how much talking and touching and the way in which it is done are hugely variable. In this respect, every individual's requirements are different and are ultimately an expression of

the culture and beliefs and knowledge of a given individual.

At a more 'physiological' level, adaptive motor responses are governed by reflex activities—hence protective reflexes, increased or decreased tone (Mense 1997) of muscles that surround or are capable of influencing the hurting part, and alterations in patterns of movement. But, again, tonal changes and alterations in reflex postures and movement patterns can be overcome or altered once the mind intervenes. 'If we pick up a hot cup of tea in an expensive cup we are not likely simply to drop the cup, but jerkily put it back on the table, and then shake our hand (Melzack & Casey 1968).'

Patients with chronic whiplash related pain not uncommonly have markedly restricted and jerky movement patterns when performing active movements in examination and focusing on them. In some situations where it is possible to alleviate patients' fear of damage and instruct regarding the positive nature of normal smooth movement, it is often the case that given simple help and guidance better range and better quality of movement can quickly be achieved (see Chs 7, 8, 9, 13 & 14).

Prolonged maladaptive or inappropriate muscle activity should be considered as a mechanism that can add to the discomfort of the tissues via increased nociceptive drive (Ohrbach & McCall 1996). The following is an interesting example of the indirect influences that there can be on the behaviour of pain. Herta Flor and colleagues (Flor et al 1991, Flor et al 1992, Birbaumer et al 1995), using electromyographic (EMG) measures, have shown that subgroups of chronic pain patients show markedly increased muscular activity and tension when they are in pain and when they are exposed to personally relevant stressful situations. The increase in muscular response was found to be localised to the site of pain and maintained for a prolonged period when compared to healthy controls. They also noted that patients with pain exhibit a reduced capacity to consciously perceive and voluntarily regulate their levels of muscular tension.

In any pain state there may be an increased muscle response which may well add to the barrage of afferent impulses that help maintain the pain state, the often multiple pain mechanisms responsible, and the levels of perceived pain (see Ohrbach & McCall 1996, Flor & Turk 1996 for an excellent critical overview of current theories).

Clinicians are advised to review a recent report by Mense (Mense 1997) who challenges the age old 'vicious circle' notion that pain leads to muscle spasm and hence more pain. If the primary source of nociception and pain is from a muscle the evidence suggests that its EMG activity is actually decreased, not increased. Thus…

> The pain-spasm-pain concept is not substantiated by critical analysis. Strong arguments against this concept are that very commonly the painful muscle (even though it may feel tense) shows no EMG activity and that in animal experiments inhibition of the motor neurons supplying the painful muscle is a much more common finding than excitation (Mense 1997).

This makes blatant adaptive sense—if you injure a muscle, going into spasm is likely to make matters much worse; far better to turn the muscle off, not on. Mense (1997) goes on to argue that increased tone will occur only if there is a strong descending fascilitatory command.

 It is important not to take from this the message that increased tone does

not occur; the discussion only relates to primary injury to muscle. Clearly in chronic pain states, or in acute nocicepiton that has its origins in joint injury, the response mustered may be quite different. This has already been noted in chronic pain patients from the discussion of the work by Flor and colleagues above.

According to Mense (1997) joint injury may well be accompanied by increased muscle tone and/or heightened reflex sensitivity. Preventing joint movement, slowing it down or even abruptly stopping it as soon as it occurs may be a very protective reaction for freshly injured joint tissues. Problems arise when this process out-lasts its biological usefulness. The role of cognitively derived descending fascilitatory/inhibitory commands links the acute well ingrained 'reflex' responses that prevents movement of the injured part to the much longer termed maladaptive maintenance of the reflex. For example if an individual is under the impression that rest is vital and that any pain is a signal to stop moving then a degree of consciously derived facilitation of reflexes concerned with the protective maintenance of 'no movement' will be kept up. Perhaps the long term result is that the tonal changes and inhibitory reactions to movement become subconsciously ingrained as a form of 'habit' or 'learned reflex'. Recall that Flor et al (1991, 1992) noted that some patients with chronic pain exhibit a reduced capacity to consciously perceive and voluntarily regulate their levels of muscular tension. From a chronic pain management perspective this is all strongly persuasive for the inclusion of relaxation techniques and the gradual and progressive relearning of relaxed and comfortable movement patterns and posturing. New 'good' habits need to be laid down on top of biologically well ingrained 'bad' ones. In the language of conditioning, the unhelpful reflex response needs to be 'extinguished'.

From the acute perspective rehabilitation requires progressive restoration of function in parallel with relevant information related to the best conditions for adequate healing.

# Autonomic

In terms of pain and the broad topic of stress biology, the major focus of attention and investigation as far as the autonomic nervous system is concerned, has been on the sympathetic system. Little attention has been given to the role of the parasympathetic system in injury, pain states, and repair and healing mechanisms. When science starts to turn its attention towards understanding the mechanisms of natural healing, the parasympathetic system should receive more attention.

The activity of the sympathetic nervous system has been singled out as a primary factor in many severe and intractable pain states for quite some time (for a good current overview see Janig & Stanton-Hicks 1996).

There are two major points of discussion:

First, that the sympathetic nervous system is likely to be activated/influenced more intensely than would be normal in all pain states. This does not mean that it necessarily has a direct role to play in producing or enhancing the immediate perception of pain.

Second, that the sympathetic nervous system's efferent (secretory) activity,

in a small but significant patient group, can be a significant mechanism that is responsible for enhancing and maintaining pain (for an overview of this mechanism see Campbell 1996, Gifford 1997).

1 It is the opinion here that the sympathetic system has a role to play in all pain states that result in suffering, simply because pain is unpleasant, is biologically interpreted as a threat to the organism, and hence will always activate this system to a greater or lesser degree. Activation of the sympathetic nervous system is strongly linked to threatening events that precipitate a feeling of anxiety and stress and that alter mood states (Chrousos & Gold 1992, Sapolsky 1994, Chrousos et al 1995). The most notable role of the SNS is in physiologically preparing the organism for the more or less instinctive reactions of freeze, fight or flight that are so important to survival. If you really think about it this is a very potent example of a psychosomatic reaction—the largely cognitive assessment by the CNS/brain (psycho) of the danger, followed by the appropriate physiological (somatic) adjustments in preparation for survival action/inaction (Weiner 1991).
Spare a thought for the sympathetic nervous system activity of the whiplash patient with ongoing pain who is frequently in low mood and is often subjected to unpleasant experiences—including physiotherapy, physical examinations and techniques! Pressing thumbs into hypersensitive tissues, performing techniques that produce further pain, putting patients in odd and often threatening postures and positions during techniques and testing, especially when novel and done with little explanation or care and skill, are surely powerful sympathetic nervous system activators. Therapists are urged to consider frequently that the CNS/brain may well be processing a very potent 'threat' message resulting in powerful physiological (and behavioural) 'threat' blunting responses, that includes sympathetic activation. A good example is a whiplash patient positioned for the first time in long-sit slump position, with their head in flexion, and their trunk in flexion plus side flexion plus rotation with the therapist eagerly digging their thumbs into a sore and stiff 5th or 6th rib angle. It might be fine for a patient who has come expecting to be tied in knots and who has been given an adequate explanation of the procedure, but for many people the position and technique are uncomfortable and unpleasant, potentially worrying and of great cause for alarm—even with a reasonable explanation. Patients often look as if they understand and believe in what you are doing, but underneath they may be very uncertain. It is important that as therapists we should always consider ourselves as representing a potential biological threat to any given patient. It is not uncommon for patients to demonstrate abnormal sweating, skin flushing and to report nausea when undergoing tests in examination. Therapists are urged to consider far more than the mechanical features of the sympathetic system and to avoid unreasonable labeling of a 'sympathetic' component to a problem based on responses such as those mentioned. A male physiotherapist performing a SLR or upper limb tension test on a semi-undressed, young, shy, female patient suffering from unexplained and unrelenting post whiplash symptoms, regardless of the discomfort produced,

may be a very unpleasant experience that adds to the sympathetic activity already generated by the pain and the anxiety of the first consultation.
Ongoing SNS overactivity (or altered activity—it may become dulled/dysregulated in its response), as the result of the ongoing negative consequences of pain, may well have further unhelpful consequences for the immune and neuroendocrine systems and hence may have far reaching effects on such things as general health, healing responses and the metabolism and circulation of the tissues of the body. The speculative assumption is that ongoing altered sympathetic activity may have far-reaching detrimental and accumulative consequences on the health of the individual and hence have some influence, all be it relatively indirect, on the level of pain and the resultant impairment/dysfunction.

2 Although the SNS may be considered to be involved in all pain states, it is only in a few where symptoms are distinctly linked to its direct activity.
The concepts of sympathetically maintained pain (SMP) and reflex sympathetic dystrophy (RSD) have come under much scrutiny and criticism of late (see Stanton-Hicks et al 1995, Campbell 1996, Haddox 1996, Janig & Stanton-Hicks 1996). The overwhelming message is that presentations that appear to have much in common and which are lumped together for the sake of clinical utility, often have multiple and quite different underlying mechanisms.
As far as the role of the SNS is concerned in any pain state, the determining factor as to its relevance is the relief of pain (or a single aspect of the pain) by a local anaesthetic block of the sympathetic ganglia that serve the painful area. Since there is no definitive way to diagnose SMP on the basis of signs and symptoms or clinical history, diagnostic blocking of relevant sympathetic nerves, or the blocking of receptors on nociceptors that are responsive to noradrenaline secreted by sympathetic nerve terminals in the painful area, are the only tools available (see Campbell 1996). The fact that many pain states, that are commonly labeled as being SMP or RSD in the clinic, show no response to sympathetic blocking/receptor blocking, has lead to the introduction of the term 'sympathetically independent pain' or SIP (Campbell et al 1993).
Just because a patient's affected limb may be either warmer or substantially cooler, show more profound sweating response, or show atrophic changes does not denote that a patient has a direct sympathetic mechanism to the pain state.
One finding of significance to the non-invasive testing and diagnosis of the sympathetic mechanism is that all patients with SMP, proven by analgesic block, demonstrate cooling hyperalgesia, whereas only 50% of patients with SIP demonstrate this phenomena. In the laboratory, sensitivity to cooling is tested by placing a drop of acetone on the painful area (see Campbell et al 1993). The only clear clinical assumption that can be made is that if patients indicates that cooling the painful area has little impact on their pain they are unlikely to have a sympathetic mechanism to their pain! However, Campbell (1996) suggests that the following two factors are the only strong indicators

of suspicion of a sympathetic mechanism: the painful area has to be in the extremity or face, and there must be cooling hyperalgesia. He specifically emphasises that the more classic features: oedema, atrophic changes, temperature changes, abnormal sweating, or other dystrophic changes, are not included.

A fundamental aspect believed to be at the heart of understanding the role of the SNS in pain is that there is no evidence of anything being actually wrong with the sympathetic system. The crux of the matter is that SNS normal secretions of noradrenaline/adrenaline can activate sensitised nociceptors or sensitised damaged neurones and cell bodies of peripheral nerves and hence cause pain. The latest research findings suggest that the abnormality lies in the cell walls of nociceptors and damaged neurones which have been shown to be capable of acquiring enhanced noradrenaline sensitivity in animal models (e.g. see Janig & Stanton-Hicks 1996). The key issue is that in order for a neurone to be sensitive to noradrenaline/adrenaline there have to be specific receptors for these chemicals in the cell wall. These receptors are called adrenoreceptors.

A wise stance to adopt is to accept the fundamental role of the SNS in all pain states and that, to a greater or lesser degree, its secretions may be involved in the production and maintenance of nociception/pain from within the tissues where the pain is felt and which are mechanically hypersensitive. No two pain syndromes are the same, have the same mechanism participation and the same participation from one moment to the next. What needs to be accepted, especially in difficult syndromes like the ongoing pain states following whiplash, is that sympathetic activity is most easily modified by the thoughts and feelings an individual is having regarding their current situation and that the more novel and threatening an environment or thing is perceived to be, the more potent is the ensuing SNS response.

## Neuroendocrine

The sympathetic nervous system can be seen as a strong effector system that is subservient to the whims and needs of higher mental processing (this ultimately means bodily and genetic survival). If the needs of survival are to run away, the appropriate sympathetic activity ensures that the appropriate tissues have the capacity to perform. The neuroendocrine system has a similar close relationship with the mind/consciousness, yet unlike the very rapidly acting SNS, its responses, since it acts on its target organs via the circulation, are naturally far slower and less focused.

The relationship between mental and physical stress and alterations in the activity of the hypothalamus-pituitary-adrenal (HPA) 'axis' has been the focus of a great deal of research since Hans Selye pioneered the scientific scrutiny of the 'stress response' in the 1930s (Selye 1978, Sapolsky 1994). When something stressful happens, or you think a stressful thought, the hypothalamus secretes corticotrophin releasing factor which in turn causes the release of adrenocorticotrophic hormone (ACTH) from the pituitary into the blood. Within a few minutes ACTH arrives at the adrenal cortex and triggers the release of the

steroid hormone glucocorticoid.

A major role of glucocorticoid is to work in parallel with the sympathetic system to provide the best conditions for an adequate response to threat. It thus helps provide suitable levels of energy for the activities desired and required as well as substantially inhibiting any processes that may be unnecessarily utilising vital energy stores. Hence such things as the inhibition of glucose uptake from the blood, the suppression of growth and repair processes, and the inhibition of inflammation and of the immune system's activities. Efficient energy mobilisation and provision 'at all costs' is its strong characteristic, hence mobilisation of glucose from fat stores and the catabolic break down of muscle commonly associated with prolonged exposure to glucocorticoids.

The adaptive nature of this classic stress response is apparent when considering conditions, cultures and environments where the major stressors or threats are physical in nature and are quickly dealt with. However, the stresses of modern cultures and societies are far removed from those of our ancestral environment in that most are ongoing, are not physically life threatening and are far harder to adequately deal with. Ongoing pain and the ongoing mental and physical 'stress' which can accompany it is an example of a situation that has the potential to cause an ongoing stress response. Ongoing stress may ultimately precipitate maladaptive changes in neuroendocrine responsiveness. For example, some whiplash patients are classified as demonstrating post-traumatic-stress disorder (see Ch. 10) and this condition is being shown to demonstrate subtle but persistent alterations in HPA axis responsiveness (Yehuda 1997).

The important point is that maladaptive neuroendocrine responsivity may well have detrimental effects on tissue health and its recovery mechanisms, and hence may have an indirect influence on nociceptor activity and pain perception.

## Neuroimmune

The close links of the immune system to the brain, the SNS and neuroendocrine system have already been discussed. Traditionally immune system activities are tied to identifying antigens, making antibodies and fighting pathogens. However, a close look at the processes of inflammation and repair, the sensitisation of nociceptors, and the relaying of information from damaged areas to response centres like the liver and brain, reveal a much more complicated system than has previously been thought. Not only is the immune system known to act at the tissue physiological level but it is also now known to have quite powerful influences on our mood states, on our behaviour patterns and even our sensitivity to pain (Watkins 1994, Watkins et al 1995, Pennisi 1997). In turn, our mood states, our mental well-being, or simply our 'stress' levels, can influence the immune system's responsiveness and reactivity (see Ader et al 1991, Stein & Miller 1993, Sternberg & Licinio 1995, Stratakis & Chrousis 1995, Martin 1997). The interplay between the brain, the mind and the immune system is, not surprisingly, very complex. The main mediators of control are via the neuroendocrine HPA system and the sympathetic nervous system

which innervates immune organs and plays a part in regulating inflammatory reactions throughout the body (Sternberg & Gold 1997). Links between the immune system and the CNS/brain are mediated via the cytokine messenger system (see Ch. 3).

Many patients with ongoing pain states have high levels of distress, depressed mood and depressive symptoms (e.g. see Banks & Kerns 1996). The recognition that whiplash/road traffic accident victims can go on to suffer post-traumatic stress disorder (PTSD) is strengthening (see Ch. 10), and the sciences of psychoneuroimmunology and psychoneuroendocrinology are firmly linking the influences of the mind and body to each other. Statements like: 'The popular belief that stress exacerbates inflammatory illness and that relaxation or removal of stress ameliorates it may indeed have a basis in fact' (Sternberg & Gold 1997), are helping the merger and better balancing of physical and psychological approaches to the complex problems that surround ongoing illnesses and pain complaints like those following whiplash trauma. The neuroimmune system is yet another example of an output mechanism that ultimately feeds back to the tissues and hence influences their health status, and the potential for ongoing nociceptor activity.

## Descending pain control systems

In the psychology and stress literature the term 'stress induced analgesia' is commonly used (e.g. Gray 1987). It recognises that injury in the presence of acute threat may not produce any feeling of pain at the time, as pain would merely hinder any physical activity needed to escape the threat (McCubbin 1993, Blank 1994, Fields & Basbaum 1994).

The important point is that the CNS/brain has a system that permits a 'choice'—between allowing nociceptor messages to produce the sensation of pain, or preventing them from doing so (Fields & Basbaum 1989, 1994). In the standard linear way of thinking about nociceptive messages ascending to the higher centres this is merely seen as a system that can prevent or promote the stream of nociceptive information and hence prevent or promote the perception of pain. However, taken from the viewpoint of the Mature Organism Model the CNS/brain can be seen to be acting in the first instance as a receiver of information—via nociceptor flow from the tissues, but also from inputs whose origins stem from the environment; and secondly, as a processor that says 'OK nociceptive message = damage, but big life threat here—dampen flow of nociceptor traffic, ignore pain, activate behavioural strategies that are likely to result in survival…' While the gating out of pain can be scientifically reduced to subconscious processing involving hypothalamus and brain stem inhibitory circuitry, the bigger picture involves conscious scrutinising, the influence of emotions and subsequent output to these centres too. One message is that the reflex activity of the pain control systems are strongly influenced by more rostral processing. A problem for those who are in pain is that access to it is not at our beck and call.

A further point is that how much we perceive our body is extremely variable.

It is well known that focusing on some activities or tasks cuts out awareness of many bodily sensations. For example when under pressure at work we may well continue with a particular task for quite a long time being unaware that our bladder is full, yet as soon as the work pressure is removed the feeling of urgency becomes all to apparent! To a large extent what we perceive is influenced by the value we put on an experience or sensation. Consider the difference between the way in which we perceive or focus on a pain in the back of the head following a drinking binge compared to one which suddenly appears for no apparent reason and gets worse and worse. Or following a whiplash accident, when several weeks later pain starts to appear in the arm, head and thorax for no apparent reason. Pain that is not diagnosed convincingly or is not properly validated by medicine is often the source of much concern and anxiety; sometimes it precipitates anger. Thus, our focus of attention and the value we give to a sensation or experience may help to enhance its significance and hence its neurobiological imprint within our nervous system. As already discussed, therapists must be alert to the dangers of continually focusing on pain and its behaviour in the clinical setting—we could well be inadvertently promoting its retention (Byl & Melnick 1997).

# Conclusions

The aim of Chapters 2–5 has been to introduce the reader to the science of pain mechanisms and the broader biological and clinical repercussions in terms of the whole organism. The striking feature of the phenomenon of pain is that, on the one hand, it is remarkably complex yet, on the other, it is only a small part of the full picture relative to bodily insult like whiplash.

It can be argued that ongoing whiplash pain has to be more than a tissue lesion like a sore or arthritic zygapophysial joint or an annular tear in a disc (see Ch. 1). An acceptance of the complex biology of pain, and the poor healing potential of nearly all the tissues injured requires a modest shift in therapeutic emphasis from 'fix' and 'relieve' to best possible physical and mental functional recovery. This incorporates carefully graded return of physical health within a realistic time-frame of recovery, the recognition of cognitive and affective influences on pain and behaviour, and their powerful physiological influence on the many output pathways of the brain. Changing the way individuals see their problem, what they believe, what they feel and how they move does more than alter their perception of the pain and their illness behaviour. If current literature is to be believed, positive or 'helpful' psychological states look as if they have healthy biological effects at many physiological levels too.

The incorporation of pain mechanism analysis into physiotherapy diagnostic protocols and clinical reasoning is becoming ever more important (Gifford & Butler 1997, see also Introductory Essay). Hopefully these chapters have presented material that will encourage a broader and more helpful analysis of the pain our patients are suffering.

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