Mechanisms of Pain

This review is an examination of the current conventional physiological literature, relating to both the mechanisms of pain and to the principles and practice of electrical pain relief, in order that the following experimental stages of this thesis are based on the most up to date evidence available at the time of writing.

Pain is one of the common symptoms in medicine and is said to be the prime cause of one third of all first consultations. While curing the causative condition usually relieves the pain, it may on the other hand continue beyond its diagnostic usefulness, either because the disease is itself incurable, or because irreversible anatomical changes lead to continuing noxious stimulation (Bowsher 1987). Acute and chronic pain control is now a major concern especially with population aging and associated pain of the chronic degenerative conditions of the elderly such as osteoarthritis, post-herpetic neuralgias, trigeminal neuralgia, reflex sympathetic dystrophy, 'thalamic pain syndrome' and malignant diseases. Thus in an aging population the medical, social, and economic consequences of chronic pain may be expected to increase (Bowsher 1987).

Mechanisms of pain

The purpose of this brief review of the mechanisms of pain is to provide a certain amount of current insight into its complexities, and to serve as a basis for the discussion of the various physiological mechanisms surrounding the three main techniques of electro-analgesia discussed later in this section.

Pain and thresholds

Pain is not a simple, straightforward sensory experience, in the manner of, for example, seeing or hearing, as it has both emotional and physical components (Baldry 1993). The definition of pain recommended by the International Association for the Study of Pain is that it is an unpleasant sensory and emotional experience associated with actual or potential tissue damage (Merskey 1979). For a given noxious stimulus the intensity with which pain is felt varies from person to person, and with regard to this a distinction has to be made between an individual's pain threshold and pain tolerance (Baldry 1993). The pain threshold, like other sensory thresholds, is fairly constant, but pain tolerance level defined as the amount of pain a subject is prepared to put up with, varies enormously and clinically patients do not usually seek medical advice until they are beyond pain tolerance level, that is the degree of pain within which an individual can usefully be measured by using a visual analogue pain scale (Bowsher 1987). There are, however, several methods used to measure pain including the McGill Pain Questionnaire - a verbal selection method; the Submaximal Effort Tourniquet Test - a comparative physical test method; the Visual Analogue Scale - a progressive method using a 10cm line anchored by 2 extremes of pain; the 101-point Numerical Rating Scale (NRS-101) - a progressive numerical scaling method from 1-100; and several behavioral and verbal rating scales. A recent comparison of methods of measuring clinical pain intensity favored the NRS-101 numerical rating scale as the most practical index, to the degree that a standard measure of pain intensity is needed to facilitate comparisons of treatment outcome, and to index chronic patient's pain intensity levels at different times in their lives (Jensen 1986).

Types of pain

Pain is occasionally purely psychogenic, though this is somewhat rare, but more often (when seen from a western neurophysiologic viewpoint) it is an organic physio-emotional experience occurring either as a result of the primary activation of visceral or somatic nociceptors, by disease or trauma or from potentially damaging stimuli, (nocigenic or nociceptive pain), or as a result of actual damage to the peripheral or central nervous system (neurogenic or neuropathic pain) (Baldry 1993). Referred pain is pain felt in a site or zone some distance from the primary site. There is much evidence to support several explanatory mechanisms for this phenomenon, and there are variations by case too, but it remains unclear which of these mechanisms are significant at this time. The structures identified, so far, in the complex processes of pain and pain relief include the sensory receptors, their associated afferent nerve fibers, the dorsal horns, ascending and descending pathways, the reticular formation in the midbrain and medulla, the thalamus, the limbic system and the cerebral cortex (see figure III).

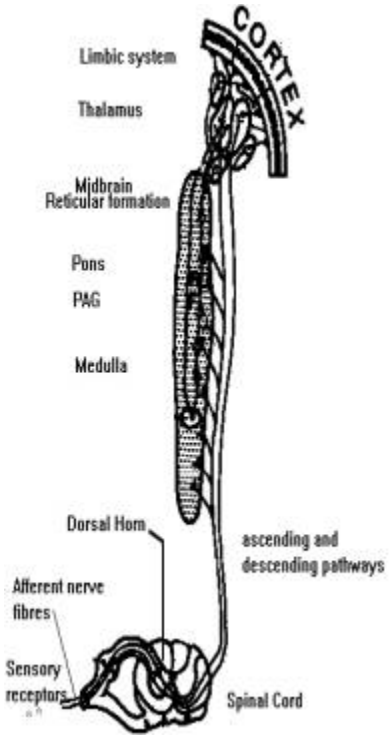

Figure III: The structures involved in pain and pain relief

Nocigenic pain, pain receptors, and their afferent nerve fibers

Although the experience of nocigenic pain ultimately depends on interpretative processes in the neurons of the cerebral cortex, it occurs primarily as a result of a noxious stimulus activating myelinated and unmyelinated nociceptors (Baldry 1993). Two distinct types of receptor and peripheral nerve fibers subserve two distinct sensory experiences; A-d nociceptors, with a multipunctate receptive field, transduce pricking or stabbing sensations (fast or first pain) which cause organisms to withdraw, whilst C-polymodal nociceptors, usually in a single receptive area, convey messages generated by tissue damage, (slow or second pain), which cause the organism to immobilize. The latter is morphine-sensitive; the former to all intents and purposes is not (Bowsher 1987).

A-d nociceptors: are connected to the spinal cord's dorsal horns via medium diameter myelinated A-d nerve fibers, and are found mainly in and just under the skin. They are activated by noxious stimuli such as pressure, surgery, ischemia, and sharps and are known as high-threshold mechanoreceptors. Some also respond to heat and are known as mechanothermal nociceptors. There are also a certain number of A-d (Groups II and III) nerve fibers in muscle. (Nerve fibers are classified by size and according to whether they originate in skin or muscle: large diameter myelinated nerves A b [skin] or type I [muscle] carry 'touch' and proprioception, respectively. Small diameter myelinated A d [skin] or types II and III [muscle] carry 'pain'; the smallest unmyelinated C [skin] and type IV [muscle] also carry 'pain'. Types II, III, IV, and C also carry non-painful messages (Stux and Pomeranz 1991).

C-polymodal nociceptors: are connected to the spinal cord's dorsal horns via small diameter unmyelinated C afferent nerve fibers. They are called polymodal because of their ability to respond to a mechanical, thermal or chemical stimulus. However, such activation is invariably only produced by chemicals released as a result of the ensuing tissue damage. The C nerve fibers connected to those present in muscle are called Group IV fibers. It is the stimulation of C-polymodal nociceptors in any deeply situated tissue such as muscle that leads to the development of slow onset pain, characterized by a widespread, ill-defined, deep seated and dull aching sensation. This activation is due to the effects of substances released and triggered by the damaged cells, which include bradykinin, histamine, leukotrienes, prostaglandins, platelet-activating factor and subsequently platelet serotonin, and substance P released from sensitized C-sensory afferents (Davis 1993).

The pain impulses, as afferent information, pass along the A-d fibers and C fibers to the central nervous system. A-b mechanoreceptors are also present in the skin, muscles, tendons and joints and are not responsive to noxious stimuli but are activated by innocuous ones such as light touch and hair movement. A-b proprioceptors in muscle are present in the form of Type I muscle spindles, and in tendons as tendon organs. They are connected to the spinal cord's dorsal horn via large diameter A-b myelinated nerve fibers.

The Dorsal Horn and segmental mechanisms

The cells of the spinal cord are arranged in layers or laminae, six in the dorsal horn (I-VI), three in the ventral horn (VII-IX) and an additional column of cells clustered around the central canal as Lamina X (Baldry 1993 - Figures IV-V). The thin unmyelinated C nociceptive afferents terminate mainly in Laminae I and II where their axons secrete Substance P (SP) or (VIP) Vasoactive Intestinal Polypeptide, according to whether they arise from somatic structures or visceral ones respectively (Figure V). The medium size myelinated A-d afferents terminate chiefly in Laminae I. II and V. The A-b afferents on entering the spinal cord, give off branches which make contact with gamma-aminobutyric acid (GABA) mediated interneurons but most pass directly up the dorsal column to the medulla oblongata's gracile and cuneate nuclei. Axons from these nuclei form the medial leminiscus which terminates in the thalamus. The medial leminiscus is connected, via the anterior pretectal nucleus, to the periaqueductal grey area in the midbrain at the upper end of the opioid peptide mediated serotinergic descending inhibitory system (Baldry 1993). As a result of these connections, A-beta afferent activity is enabled to block the C afferent input to the spinal cord by promoting activity in this descending system (Bowsher 1991).

It therefore follows that the high-frequency TENS, which exerts its pain modulating effect by recruiting A-b nerve fibers, could be seen to achieve this effect partly by these fibers when stimulated evoking activity in the opioid peptide mediated descending inhibitory system and partly by them evoking activity in dorsal horn GABA-ergic interneurons (Baldry 1993).

There are three main types of dorsal horn transmission neurons - low-threshold mechanoreceptor cells, nociceptive-specific cells, and wide dynamic range cells which are responsible for transmitting sensory afferent information to the brain. The dorsal horn excitatory and inhibitory neurons modify the C afferent nociceptive information before reception and projection by the dorsal horn transmission cells.

The Gate Control Theory

Melzack and Wall (1965), developed their now-famous theory on pain mechanisms, which postulated that in each dorsal horn of the spinal cord there is a gate-like mechanism which inhibits or facilitates the flow of afferent impulses into the spinal cord before it evokes pain perception and response. Their theory was proposed as an alternative to the specificity theory of pain, which holds that pain is a specific modality with its own specialized sensors, neuronal pathways and centers and the pattern theory which maintains that stimulus intensity of non-specific receptors and central summation were the critical determinants of pain. The theory, as originally propounded, stated that the opening or closing of the 'gate' is dependent on the relative activity in the large diameter (A-b) and small diameter fibers (A-d and C), with activity in the large diameter fibers tending to close the 'gate', and activity in the small diameter fibers tending to open it (Baldry 1993). Recent research by Garrison and Foreman (1994) supports this theory insofar as their study shows that dorsal horn neurons which can potentially transmit noxious information to supraspinal levels, can have their cell activity decreased during TENS application to somatic receptive fields. These findings are consistent with the concept of the 'gate control theory of pain' in that less noxious information would be involved in the pain perception process (Garrison and Foreman 1994). They also showed that there is a differential effect in that more cells respond to conventional high frequency, low intensity (TENS) variables than they do to low frequency, high intensity (ALTENS) variables. These results will also be considered again later.

The gate control theory proposes that the substantia gelatinosa, which caps the grey matter of the spinal horn in the spinal cord, is the essential site of control. The control mechanism is referred to as a 'gate' and is operated by external and internal influences. Pain impulses can only pass through when the gate is open, and not when it is closed (Davis 1993). So if nociceptive input exceeds a-b fiber input, then the gate is open and the pain impulse ascends the spinal cord to the brain. If A-b fiber input exceeds nociceptive input then the gate is closed and the pain impulse is stopped or diminished due to the action of the inhibitory neurotransmitters and, therefore, does not pass up the spinal cord (Davis 1993). An essential part of the theory ever since the time it was first put forward is that the position of the 'gate' is in addition influenced by the brain's descending inhibitory system (Baldry 1993 - Figure VI).

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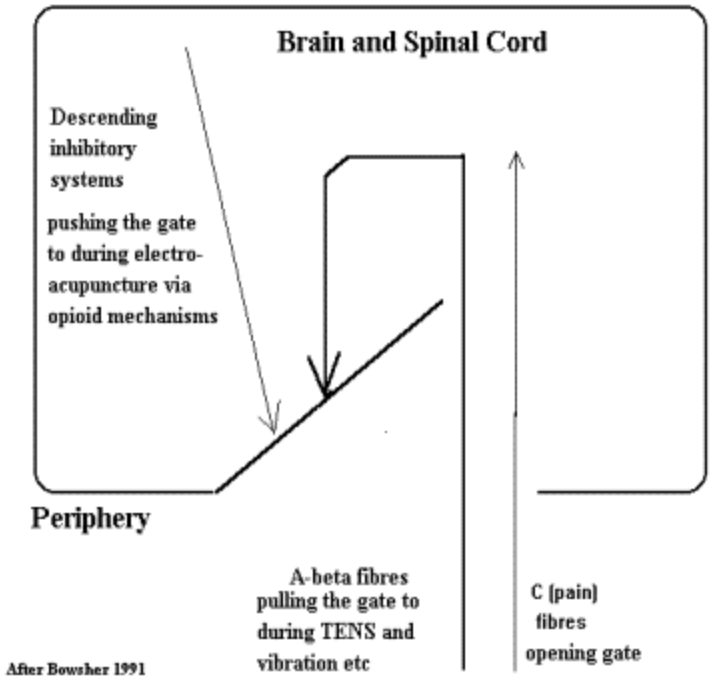

Figure VI: The Gate Control Theory of Melzack and Wall in relation to electroanalgesia as TENS and electro-acupuncture

So entry into the central nervous system can be visualized as a gate, which is opened by pain-generated impulses and closed by low-intensity stimuli such as rubbing or mild electric stimulation (TENS), furthermore, it can also be closed by endogenous opioid mechanisms which can be activated from the brain or peripherally by acupuncture (Bowsher 1987) or by gentle rubbing, massage, electrical stimulation and hot or cold therapies. Comments and criticisms of the gate control theory are examined more fully in the discussion section (3.4.13).

Non-opioid peptide mediated descending systems

It is now accepted that there are several descending control systems, and that, whereas one of these is opioid peptide mediated, others must be mediated by various other transmitters. Most of these have yet to be discovered and their transmitters identified. However, Melzack and Wall in 1988, describe one such system that is known to have its origin in the dorsolateral pons where noradrenalin-containing cells project into the spinal cord (Baldry 1993). It is also possible that there is more than one system active at any given time.

Neurogenic pain

Burning and/or stabbing neurogenic pain is caused by lesions of the nervous system, resulting in structural damage to the peripheral or central nervous units, rather than by receptor stimulation as described above. Neurogenic pain is much less responsive than nocigenic pain to the electroanalgesia techniques of evoking activity in endogenous opioid peptide and non-opioid peptide mediated pain modulating mechanisms. It is also mostly resistant to narcotic analgesics, as well as the endogenous opioid peptides, but can sometimes be relieved by sympathetic blockade, tricyclics (which facilitate noradrenergic inhibition) and anticonvulsants (Bowsher 1987). However, some elderly patients with neurogenic pain respond very well clinically to electrical stimulation.