PART 1 BASIC SCIENCE

OVERVIEW OF PAIN PATHWAYS 1

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A major barrier to appropriate pain management is a general misperception that pain and nociception are interchangeable terms. This encourages the belief that every individual will experience the same sensation given the same stimulus. This is analogous to suggesting that all individuals will grow to the same height given the same nourishment – a situation that all would agree is unlikely!

Nociception is the neural mechanism by which an individual detects the presence of a potentially tissue-harming stimulus. There is no implication of (or requirement for) awareness of this stimulus.

Pain is 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage'. Thus, perception of sensory events is a requirement, but actual tissue damage is not.

The nociceptive mechanism (prior to the perceptive event) consists of a multitude of events as follows:

- *Transduction*:
  This is the conversion of one form of energy to another. It occurs at a variety of stages along the nociceptive pathway from:
  – Stimulus events to chemical tissue events.
  – Chemical tissue and synaptic cleft events to electrical events in neurones.
  – Electrical events in neurones to chemical events at synapses.
- *Transmission*:
  Electrical events are transmitted along neuronal pathways, while molecules in the synaptic cleft transmit information from one cell surface to another.
- *Modulation*:
  The adjustment of events, by up- or downregulation. This can occur at all levels of the nociceptive pathway, from tissue, through primary (1°) afferent neurone and dorsal horn, to higher brain centres.

Thus, the pain pathway as described by Descartes has had to be adapted with time (see Figure 1.1).

The chapters that follow address the pathophysiological events occurring along the 'pain pathway'. It is important to recognise that all the anatomical structures and chemical compounds described are genetically coded. Therefore, to suggest that all individuals

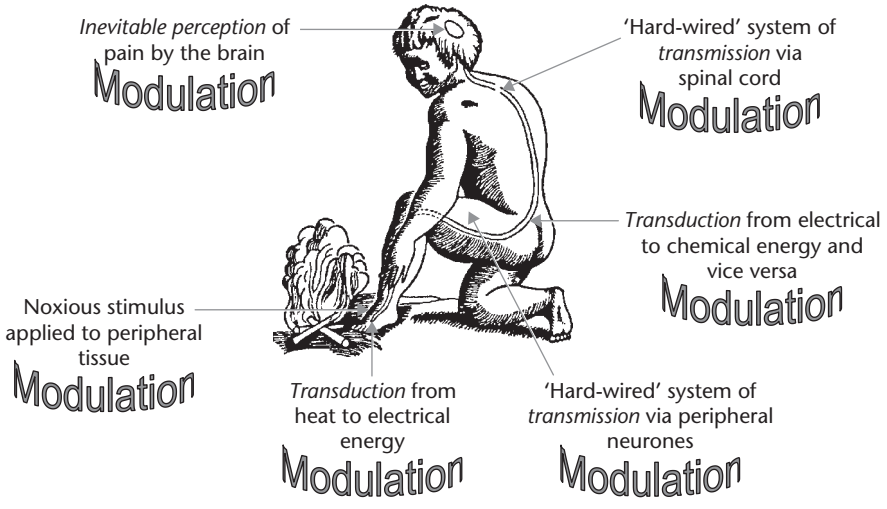

Figure 1.1 Development of the original 'hard-wired' pain pathway first described by Descartes in 1664 showing sites where modulation occurs.

will perceive pain in the same way (and if they do not they are at fault) is unsustainable.

For example, we would not suggest that eye colour is something over which people have total control – we accept that this is genetically determined. Yet, we suggest that an individual who is unfortunate enough to suffer severe pain (perhaps consequent upon the expression of particular populations of receptors responding to nociceptive chemicals) is somehow 'over-reacting' to a stimulus. Moreover, we understand that the presence of male pattern baldness requires not only the presence of a gene, but also a particular hormonal environment (high testosterone levels). Why should we be surprised, therefore, that a particular stimulus may be perceived differently in individuals with varying hormonal make-up?

This is not to suggest that all pain is entirely genetically determined, but rather it is not 'all in the mind' – a phrase often used with negative connotations in regard to pain patients. Previous experience of pain can undoubtedly alter perceptions, but this should not suggest any 'unreality'. The presence of lung cancer is frequently consequent upon prior experience – in this case, of smoking. Similarly, prior experience of pain may facilitate activity, in particular neuronal pathways, leading to a reduction in pain threshold at a later date.

A variety of tissue-damaging stimuli leads to the production of a 'chemical or inflammatory soup'. This consists of a wide variety of substances, knowledge of which is continually being expanded. Whatever the composition of this soup, pain events are generated by chemical binding with receptors on 1° afferent neurones. Such receptors consists of three major groupings: excitatory, sensitising and inhibitory. It is the balance of outcomes of these events that determines whether an action potential is generated in the neurone (Figure 1.2).

Once electrical activity is generated within the 1° afferent neurone, information is transmitted to the dorsal horn of the spinal cord. Activity is induced in the second-order neurone in a similar fashion. Quantal release of neurotransmitters from the 1° afferent neurone is dependent upon: (a) activity within the neurone, (b) external events affecting alterations in neuronal activity, for example, inhibitory and excitatory inputs upon pre-synaptic terminal. Activity in the second-order neurone is again dependent upon the balance of inputs upon it (Figure 1.3). These may arise from the 1° afferent neurone, inter-neurones or descending neurones from the brain stem and cortex.

The majority of second-order nociceptive neurones within the spinal cord cross to the contralateral side, where they synapse upon neurones in the antero-lateral aspect of the cord. Again modulation of transduction events will occur, prior to transmission in spino-thalamic pathways towards the cortical sensory centres.

While we have long considered neurological pathways to be hard wired, it is becoming increasingly clear that this is not the case. Indeed, the brain and spinal cord are able to learn and facilitate activity in commonly utilised pathways. This occurs not merely as regards useful details (e.g. how to drive a car), but also in relation to innocuous (e.g. what the blue colour looks like) and unpleasant (e.g. presence of ongoing pain in a now amputated limb) information. Thus, we should not be surprised that previous experiences can and do alter later pain perceptions. Plasticity of neuronal activity is the norm.

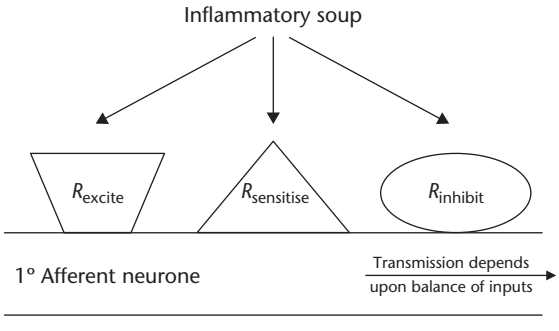

Figure 1.2 Tissue-damaging stimuli produce an 'inflammatory soup' which acts upon a variety of receptors. Onward transmission depends upon the balance of inputs affecting the 1° afferent neurone.

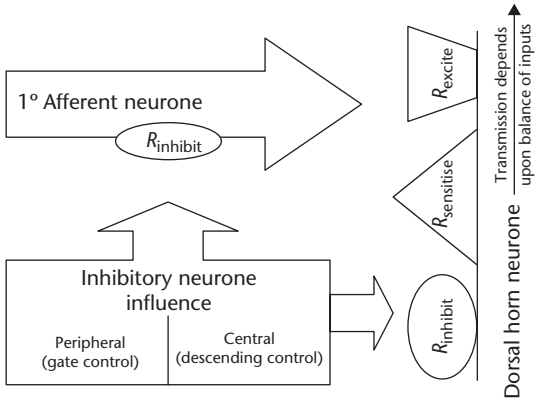

Figure 1.3 Onward transmission of information to higher centres, from the spinal cord, depends upon the balance of inputs effecting activity in the dorsal horn neurone.

The genetic basis of pain (using human and animal data to demonstrate the concepts) will be considered specifically in Chapter 4. However, when reading Chapters 2 and 3 on the peripheral and central mechanisms of pain, you should remember that the chemicals and structures described are genetically encoded, as are the receptors discussed in Chapter 8. Chapters 5–7 will deal in detail with the ways in which previous activity within the nociceptive pathways may alter current activity (and thus pain perception).

The psychological processing and consequences are central to all our human experience. Specific focus is placed on these in Chapters 13 and 47. The challenge now is to unite psychological and chemical (and thus genetic) events in an appropriate fashion when considering the problems faced by patients in pain.