Peripheral nociceptor terminals

Nociceptors are essential for the appreciation of pain. These primary sensory neurones have cell bodies in the dorsal root or trigeminal ganglia, and possess naked peripheral endings that terminate in the skin, mostly in the epidermis (juxta-). Intra-central neurones have a key role in the integration of stimuli such as heat or pain-producing chemicals, as illustrated in F. The innervation of skin (ultrastructural view) is shown in C. Inflammation will result in the production of a large number of mediators of pain and inflammation, such as prostaglandins, histamine, and nerve growth factor (NGF). These neurones lead to G-protein-coupled receptors or, in the case of NGF, tyrosine kinase receptors on the nociceptor terminal, resulting in the activation of multiple second messenger pathways that have an important role in sensitization.

Sensitization is achieved by receptor- and channel-modulation and, over a longer period of time, by alternative gene expression. One example of such sensitization is shown in D, where the activation of protein-kinase C facilitates the response of sensory neurones to capsaicin.

Peripheral nerves and the DRG

In peripheral nerves, sensory neurones have unmyelinated or thinly myelinated axons. In peripheral nerves, nociceptors have unmyelinated or thinly myelinated axons (as defined by the International Association for the Study of Pain). These neurones are the first line of defence against tissue damage and are involved in the transmission of pain information to the spinal cord and higher brain centres. The primary afferent neurones have a lower threshold for sodium channels than lower-order neurones (as defined by the International Association for the Study of Pain). These neurones are involved in the transmission of pain information to the spinal cord and higher brain centres. The primary afferent neurones have a lower threshold for sodium channels than lower-order neurones (as defined by the International Association for the Study of Pain).

Pain mechanisms

Stephan McMahon and David Bennett

Pain is an unpleasant sensation resulting from the intricate interplay between sensory and cognitive mechanisms. Chronic pain, resulting from disease or injury, affects nearly every fifth person in the Western world, constituting an enormous burden for the individual and society. Sensitization of pain signalling systems is a key feature of chronic pain and results in normally non-painful stimuli eliciting pain. Such sensory changes can occur not just at the sites of injury, but in surrounding normal tissues. This and other observations suggest that sensitization occurs within the CNS as well as within nociceptor terminals. Here we consider the consequences of a noxious stimulus applied to our unfortunate builder’s hand, from sensory transduction to pain perception. We describe the structural and functional elements present at different levels of the nociceptive system, as well as some of the changes occurring in chronic pain states. Although our posterior heightens a flow of information from the periphery to the CNS, it should be noted that higher brain centres exert both inhibitory and facilitatory controls on lower ones. The challenge for the next decade will be to fully understand the development of novel analgesic agents for better pain relief.

Defining nociceptors

Nociceptors: The detection of stimuli that are capable of producing tissue injury. Pain: An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage (as defined by the International Association for the Study of Pain). Nociception: The detection of stimuli that are capable of producing tissue injury.