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Chapter 11

Inhibition and Facilitation of Nociception

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The intensity of pain felt by a patient may not always match the level of nociceptor activation. For example, immediately after an accident a severely wounded patient may feel no pain at all for some time, whereas a minor trauma might have evoked intense pain in the same person. In a healthy human subject, the intensity of pain induced by identical, repetitive noxious stimuli may vary with a circadian rhythm. In situations of emotional stress, during prolonged body exercise (e.g., among long distance runners), and during sexual intercourse the pain threshold may be elevated considerably. On the other hand during infection and other forms of disease, pain thresholds may be generally lowered as part of the sickness syndrome. This mismatch between the level of nociceptive input and the perceived intensity of pain can now be explained by neuronal circuits in the central nervous system that modulate the transmission of nociceptive information. Neurons in spinal dorsal horn or in its trigeminal correlate, the trigeminal subnucleus caudalis (medullary dorsal horn), are relay stations that receive nociceptive information from peripheral nociceptors and transmit this information to the brain, which ultimately leads to the sensation of pain. These relay stations are important sites for clinically relevant inhibition or facilitation of nociception. All vertebrates investigated so far, including humans, possess powerful endogenous antinociceptive systems that may reduce or even abolish transmission of nociceptive information at spinal or trigeminal relays. Some of the most effective forms of pain therapy known today activate these endogenous mechanisms of antinociception. The progress in the treatment of pain over the last decades witnesses some outstanding examples for rapid and successful transfers of discoveries made in basic sciences to clinical applications. On the other hand, effective clinical treatments of pain syndromes have guided basic researchers to identify new antinociceptive principles in the nervous system. The neuronal mechanisms of endogenous inhibition and facilitation of nociception and their clinical implications are summarized herein.

Various forms of endogenous antinociception have been identified that can be classified into two major categories: (a) descending inhibition of nociception in spinal or medullary dorsal horn by systems that originate from brainstem sites and (b) afferent-induced inhibition in spinal or medullary dorsal horn, which is evoked by stimulation of sensory nerve fibers. In any case, the final inhibition takes place at or near the first synapse of the nociceptive pathways. Even though most of the previous work has been dealing with spinal dorsal horn mechanisms of antinociception, numerous studies show that similar or identical mechanisms also apply to the trigeminal subnucleus caudalis (5,40). Recent evidence suggests that an imbalance in activity between brainstem nuclei mediating antinociception and vascular control may be relevant to the pathogenesis of migraine (28,47).

DESCENDING INHIBITION OF NOCICEPTION

Powerful supraspinal descending systems have been identified that are mainly inhibitory, but facilitatory effects have also been observed. These systems are tonically active and depress spinal nociception under physiologic conditions. In addition, descending inhibition can be activated by environmental stimuli, pharmacologically, or by deep brain stimulation.

Tonic Descending Inhibition

The existence of tonic descending inhibition of spinal nociception is now well established. Complete spinalization or circumscribed lesions in the lateral funiculi of the spinal cord invariably and immediately lead to a disinhibition of nociceptive neurons in spinal dorsal horn caudal to the lesion. Both background activity and stimulus-evoked responses of nociceptive spinal dorsal horn neurons are strongly enhanced and thresholds for nociceptive behavior are lowered in spinalized animals. This indicates