In addition to the initial question of the right that humans have to impose constraints on animals for the sake of furthering knowledge (Monamy, 1996), experimenters are duty bound to question their methods for assessing the suffering of experimental animals (Veissier, 1999). This questioning is essential on two accounts. On the one hand, as regards ethics, we are straight away aware of the fact that suffering must be controlled. In addition, if it cannot be reduced (for example to assess the properties of analgesic substances), then it is essential to assess the profit/cost ratio or, in other words, the scientific relevance of the experiment vis-à-vis the treatment of a human pathology (Bateson, 1992). This assessment is generally the task of an ethics committee, regardless of the form it may take due to the national regulations in force. On the other hand, suffering through physiological consequences leads to an experimental artefact that means that results obtained in such conditions are inappropriate for scientific use. In fact, acute (like chronic) suffering particularly leads to activation of the corticotrophic axis and opioidergic systems (Yasui et al., 1991).

It is impossible to talk of animal pain in the broad sense of the term, as it is necessary to distinguish between acute versus chronic pain and somatic versus visceral pain. Although the first division is now standard, the second is more recent. It mainly stems from progress in neuroimaging and electrophysiology of sensory receptors (Aziz et al., 2000). However, given current knowledge, it is probable that this division will only be able to be applied to primates and developed mammals.

**Acute versus chronic pain**

Acute pain is a physiological function of the nervous system, which therefore acts like an alarm to protect animals from injury or disease. Acute pain most often comes from an injury or inflammation. All these phenomena lead to the activation of afferent neurons and/or the sensitisation of afferent neurons. Afferent neurons may be specialised in pain perception and consequently referred to as nociceptors (Siddall and Cousins, 1995) (mainly present in skin) or they may be non-specialised (Cervero and Laird, 1999). In the latter case, the nociceptive message is coded by receptors that are sensitive to mechanical or chemical stimuli that can...
arise in relational life without necessarily causing pain. A specific case is represented by sensory receptors sensitive to mechanical stimuli whose intensity is never reached except in the case of painful episodes — case of silent oesophageal receptors which code pain felt during oesophageal reflux (Gebhart, 2000). Information from peripheral receptors is conveyed by the spinal cord (and in some cases by the vagus nerve for visceral pain) and is then processed by the central nervous system. At all these stages, the nociceptive signal undergoes a modulation enabling pain intensity to be adjusted. This peripheral and central modulation also changes the perception of the areas where the pain is felt. In fact, it is likely that secondary hyperalgesia observed at a distance from the primary pain area stems from the recruitment of spinal neurons in functional contact with some skin nociceptors (Ringkamp et al., 2001).

The well-known text from Melzack and Wall (1965) revolutionised our understanding of the mechanisms involved in modulating sensory signals from the periphery. In this notion, pain is seen as a central activation from convergent somatosensory activity. This activity is conveyed by neurons — which have broad dynamic response and are present in the spinal cord — to a detector located in the thalamus and somatosensory cortex. This notion is currently being disproved (Craig, 2003; Craig, 2003). In fact, this pain theory is incapable of explaining why neither stimulation nor destruction of the cortex or somatosensory thalamus affect pain. Recent data suggests a new view of pain as a homeostatic emotion like temperature, itching, hunger or thirst. From this viewpoint, pain emerges as a physical sensation generated by specific sensory pathways with direct thalamocortical projection (Craig, 2003). Pain therefore becomes an aspect of interoception and a reason for specific behaviour.

The modern conception of pain leads us to reassess the perception of pain whether we consider primates (or even certain developed mammals) or other species. Spinal cord activity (linked to pain perception) mainly comes into play in several bulbar nuclei in non-primates whereas in primates there is a direct thalamocortical pathway to the posterodorsal insular cortex (Beckstead et al., 1980), (Blomqvist et al., 2000). At this level, we can demonstrate a topographical and selective representation of all related activity from the spinal cord (and the vagus via the tract of the solitary nucleus) through imaging and electrophysiology. This pathway is primitive in non-human primates but highly developed in humans for whom, at insula level, there is a metarepresentation of the state in which the body finds itself in association with the acknowledgment of the physical entity (Adolphs, 2002; Adolphs, 2002). The discovery of a thalamocortical pathway towards the insular cortex (that is found in
primates but not in other mammals) has direct repercussions as far as ethics is concerned. On the one hand, it is not possible for us as humans to assess animal pain according to our own conception of pain. In fact, the absence of direct activation of a cerebral area associated with the metarepresentation of the physical entity in non-primates necessarily leads to a concept of pain that is different from our own. On the other hand, this difference in the ultimate perception of pain cannot be interpreted in quantitative terms. In fact, it would be a major mistake to consider the pain felt by non-primates as lesser (with identical nociceptive stimuli). On the contrary, the precautionary principle tells us to maximise the potential perception of nociceptive stimuli in non-primates.

Chronic pain, unlike acute pain, can be compared to a badly functioning alarm. It cannot be associated with an intercurrent pathology which, when corrected, suppresses pain. Chronic pain mechanisms are still poorly understood, especially as in humans and probably in certain animals chronic pain can cause anxiety and depression. In addition, depression itself intensifies pain through a mechanism that introduces intracerebral serotonin (Briley, 2003; Trivedi, 2004). Finally, chronic pain is often accompanied by allodynia i.e. perception of pain from stimuli that are not usually painful (Brooks and Tracey, 2005). In this case, the area affected by allodynia is located at a distance from the initial pain site. The mechanisms behind allodynia currently remain putative.

**Somatic versus visceral pain**

The vast majority of research concerning pain has focused on somatic pain, as it can be triggered by thermal stimulation on the skin so much so that for many years it was not thought that viscera were able to code a pain signal. This belief was mainly based on the absence of pain responses when certain viscera were cut or thermocoagulated in a clinical context (Sarkar et al., 2001). Recently, neuroimaging has enabled detailed studies of cortical representation of visceral pain (Aziz et al., 2000; Hobson et al., 2000; Hobson and Aziz, 2004; Hobson and Aziz, 2004). Visceral pain differs from somatic pain in many ways: imprecision of location, tonic increase in muscular activity, evocation of intense responses from the autonomous nervous system (change in heartbeat and blood pressure).

Unlike somatic pain, whose projection on the primary somatosensory cortex shows a homuncular organisation, visceral pain is mainly projected on the secondary somatosensory cortex where spatial representation is diffuse. This difference explains why the location of
visceral pain is diffuse. Activation of the secondary somatosensory cortex during episodes of chronic pain also gives rise to involvement of the limbic structures, thus explaining the intensity of neurovegetative episodes observed during this type of pain and the significance of affect on the perception of visceral pain (Hobson and Aziz, 2003; Phillips et al., 2003).

Conclusions

A better understanding of the origin and interpretation of pain phenomena is essential for the experimenter. Assuming that it suffices to block pain using opiate analgesics to meet the ethical criteria of animal experimentation is a mistake. In fact, visceral pain is practically resistant to opiates. Similarly, there are currently no pharmacological substances able to suppress neuropathic pain. This is why it is important that experimenters also comply, as closely as possible, with the 3Rs (Replacement, Reduction and Refinement) and that they follow the conditions for ending experiments set by themselves beforehand. Independently of these safeguards, they should above all call on their clinical sense to judge, with all the shortcomings this entails, when to end the experiment to prevent pain that cannot be controlled by pharmacological devices.

Glossary

- **Thalamus**: a part of the brain located under the cerebral hemispheres, close to the third ventricle. It acts as a relay, forwarding information to the cortex. The loops made in this way have a role to play in consciousness.

- **Limbic areas**: the limbic areas comprise different structures (tonsils, hippocampus, cingular gyrus, etc.) and are involved in processing emotional responses to given situations.

- **Afferents**: carry information from the periphery to the central nervous system.

- **Somatic**: relating to the skin and muscle.

Bibliography


