

PAIN AND CONSCIOUSNESS THOUGHTS FROM THE DECADE OF THE BRAIN

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ABSTRACT

Pain is a subjective phenomenon with those characteristics that typify the mind: experience of the self representation, time integration, intentionality. Without consciousness there is no pain. Although pain is usually felt at the site of injury, the anatomical substrate of pain experience is the brain. Representational and psychic states are attributed to cortical activity as evidenced by novel functional brain imaging techniques. The sensory discriminative component of pain is assigned to bilateral activity in secondary somatosensory cortex areas (SII) with somatotopy and stimulus-response functions. Under narcosis, the cortex cannot explore the kind, size or site of the hurting event as SII activity is blocked. Consequently, pain is not felt. The nociceptive impact induced during surgery, however, may still reach pain-relevant structures in the brain, eliciting nocifensive responses, motor withdrawal reflexes and changes in blood pressure and circulation, and heart action. The emotional-aversive component, is very important for the perception of pain. It describes its negative quality, and is attributed to the posterior cingulate cortex. Intimate fibre connections link the relevant neuronal assemblies with the parietal lobe and other structures which evaluate the aversity of the stimulus. Opiates drastically reduce activity in precisely these areas.

Keywords: Pain - Consciousness - Cortical representation - Secondary cortices - Limbic system

INTRODUCTION

Pain is essentially linked with consciousness, with all the characteristics of mind: mental representation, i.e. the immediate knowledge about one's own mental states with self-relation and time integration as well as intentionality, the decision to act or to react by free will. Without consciousness there is no pain. Pain research therefore essentially touches the mind-body-problem, the greatest challenge in living memory of thinking, from time immemorial addressed by representatives of science, religion, philosophy and society.

For the physician, however, the mind-body problem becomes of immediate practical meaning in the fundamental ethical task to relieve pain, in particular to prevent pain from becoming chronic. Manipulation of pain manipulates consciousness: under opiates you should not drive a car because your vigilance is reduced. Or, during surgery operation the patient's consciousness is suppressed by general anaesthesia; the enormous nociceptive impact elicited by the surgeon still reaches pain relevant structures in the brain, but the patient does not feel pain, the brain is not able to unravel the neuronal assemblies towards consciousness. The third example meets the often discussed problem of the development of consciousness, name-

ly the question at which stage in ontogeny does pain arise: the answer is of highest importance in infant surgery, since general anaesthesia destroys neurons, which has to be avoided at all costs in the developing brain of newborns.

There is no doubt that the anatomical substrate of pain experience is the brain, though pain is usually felt at the site of injury. The decapitated animal - sorry, I am a physiologist -, for example the spinal frog in laboratory experiments or the beheaded cock, may still exhibit all those nociceptive behavioural reactions used in the laboratory animal to indicate the effects of "pain"-relieving drugs, in particular motor responses to noxious stimuli. But, despite of the emotional arguments of animal right activists, these dead animals do not feel any pain at all. Otherwise, we have to alter the definition of brain death, and the organ donor needs pain therapy before, during and after transplantation.

These examples insistently demonstrate that nociceptive reactions do not necessarily indicate pain. Noxious stimuli, such as injury, tissue damage, or alterations in tissue metabolism clearly induce nociceptive activity, but this neuronal activity is only the initiator for the pain felt by the subject. In other words, the nociceptive impulse pattern only opens the door to conscious pain experience, whether the subject really feels pain is a different matter. There are interactions

between nociceptive projection into the brain and its conscious experience. Conscious information processing depends on the state of arousal of the brain. In other words, both, attenuation of nociceptive activity or manipulation of arousal, can relieve pain.

Meanwhile novel functional brain techniques are available to non-invasively investigate neuronal assemblies which are active during cortical processing of pain. In this way circumscribed cortical areas which are active during various psychic states concomitant with pain can be attributed to different aspects of subjective pain perception. As already shown in the first PET study with volunteers, pain is processed, simultaneously and successively, in multiple brain areas. Direct tracing of pain pathways activated by brief phasic pain by means of brain electrical source analysis based on multihead electroencephalography revealed a considerable overlap of pain related structures in space and time (Bromm and Chen, 1995). Involved are the primary and secondary cortices SI, SII, the cingulate gyrus, and the frontal cortex. Subsequent PET, fMRI, and other BOLD studies extended these findings to subcortical structures, the medial mid-brain, thalamus, lentiform nucleus, cerebellum (for the latest review see Sandkühler *et al.*, 2000). Before addressing these findings in detail it seems reasonable - considering respect to the multidisciplinary character of this symposium - to focus upon some basic physiological knowledge about the pain mediating, nociceptive nervous system, and about the main nuclei and projection neurons involved in the control of arousal.

PHYSIOLOGY OF NOCICEPTION AND AROUSAL

Pain is widely agreed to be the result of an altered neuronal activity somewhere within the nociceptive nervous system. Enhanced nociceptive activity causes pain, pain relevant behaviour, and nocifensive reactions. The nociceptive system like all the other afferent sensory channels has been thoroughly well investigated, (for reviews see Willis, 1995, Kenshalo and Douglass, 1995). In brief, body surface and viscera are covered by slowly conducting nociceptive afferents - the thinnest myelinated Adelta- fibres (group III; conduction velocity around 15 m/s) and unmyelinated C-fibres (group IV, conduction velocity around 1 m/s). As soon as the pain information reaches the spinal cord, an incredible number of synaptic contacts modulate the input, balancing the pain message with other peripheral or central information, enhancing or diminishing the afferent impulse volley, and initiating nocifensive reactions to avoid persistent damage. In this way withdrawal reflexes, changes in local circulation, multiple receptive fields, Head zones, transferred pain and gate control mechanisms become plausi-

ble, pointing toward dramatic processes of neuroplasticity. In the dorsal horn of the spinal chord all those processes take place, which induce mechanisms of chronification of pain, as has been elaborated at all levels of measurement, from molecular subcellular mechanisms up to neuroplastic changes in projection pathways onto the brain.

Spinal information reaches the brain, mostly through the spinothalamic tract, but also through postsynaptic dorsal column neurons. The "door" to conscious perception are nuclei in the diencephalon, the thalamus (specific, unspecific, motor and associative nuclei), in which again the message is processed by settlement, modulation, balancing with other external and internal information, tuned by reciprocal fibres to and from the cortex. As has been estimated mainly by methods of information theory, only a minuscule fraction of all nociceptive information reaches the cortex, in particular those structures that are activated in the course of conscious pain experience (for introductory texts, see Popper and Eccles, 1977; Creutzfeld, 1983). As illustrated below there is some evidence that the parasyllian area particularly plays a decisive role in the conscious processing of pain experience.

Enhanced nociceptive activity is neither a necessary nor a sufficient condition for pain. The intense nociceptive impulse pattern, which is elicited, for example, by an injury during a sports competition, will not necessarily induce pain, at least not at the time of the accident. Many examples are known of injuries that do not hurt during battle; even severe bodily damage is not always accompanied by pain. In order to feel the pain, the brain needs to be alert and focus on the event. In fact, most cortical structures involved in pain processing are tonically pre-primed by projections controlling the arousal level of the brain.

An illustration of close relation between pain and attention is given in Figure 1. The infrared radiant heat pulse, elicited by a laser stimulator selectively activates nociceptive Adelta- and C-fibres, a fact which has been used extensively to study normal and pathological pain perception in volunteers and patients (for a review, see Treede *et al.*, 1995). Because of the considerably different conduction velocities a single laser stimulus induces a double pain sensation: first, pain appears with a mean latency of 240 ms and is described as a sharp and stinging, well localizable pinprick pain, induced by Adelta-fibre activity (mean velocity 14 m/s). It is followed by a second, more diffuse burning component with a mean latency of 1200 ms, which can be ascribed to C-fibre conduction (approximately 1 m/s). Similarly, late and ultra-late brain potentials are found with comparable waveforms and scalp distributions, consisting of a negativity at 240

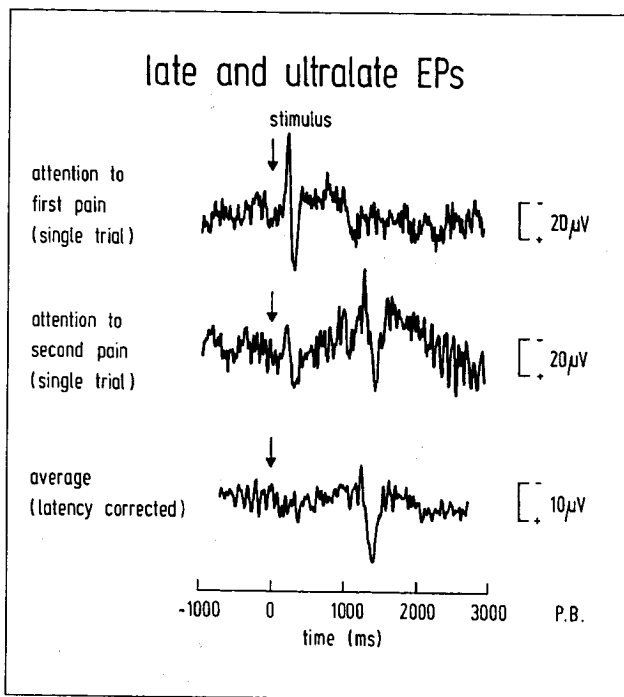


Figure 1: First and second pain and their electrical brain correlates modulated by shift in attention.

Late and ultralate cerebral potentials are given in response to CO₂ laser stimuli of 20ms duration and 18 W/20 mm², applied to the upper surface of the left foot. The stimulus activates both myelinated A-delta and unmyelinated C-nociceptors and, accordingly, induces two pain sensations with a delay of approx. 1000 ms. If the experienced subject shifts attention from first to second pain, the ultralate potential as correlate of C-fibre mediated second pain is increased (from Bromm, 1995).

ms (N240) and 1180 ms (N1180), and of a positivity at 370 ms (P370) and 1300 ms (P1300), respectively.

However, our brain is constructed such that, within certain limits of course, all attention is focussed on the event that appears first. Later information reaching the cortex within these time limits will be pre-dated to the first appearing event. Consequently, an inexperienced subject reports laser induced pain as pricking and burning, while A-delta-fiber mediated brain potentials are seen simultaneously (upper line). But with increasing experience the volunteer is able to differentiate between both kinds of pain such that the different components, and the time lag between them, are felt distinctly. As shown in the figure, if the attention of the trained subject focussed on the second pain, ultralate cerebral potentials are elicited as well (second and third line). The more the subject concentrates on the appearance of the second pain, the more distinct are the ultra-late cerebral potentials.

Both pain sensations elicited by one stimulus, as well as their neurophysiological correlates, depend on many factors and can emerge very differently in patients with a special loss in nerve conduction, for example due to syphilis (Treede *et al.*, 1995). Furthermore, the sensitivity of the ultra-late potentials sensi-

ve to analgesic drugs seems to differ. Such experiments provide some evidence that the late (or ultralate) cerebral potentials depend on attention and cognition, and reflect conscious pain experience.

Control of arousal is attributed to functions of the brainstem, thalamus and cerebral cortex. There is indisputably an activating system in the brainstem and midbrain. Electrical stimulation in the medial bulbar reticular formation, in the pontile and midbrain tegmentum, and in the locus coeruleus lead to an arousal reaction with desynchronization of EEG activity (for a review, see Kandel *et al.*, 1992). In other words, in the brainstem are neurons which modulate the momentary arousal level, the state of consciousness, the rhythm of wakefulness and sleep, other circadian rhythms, as well as autonomic functions governing cardiovascular and respiratory regulation (for a review, see Bromm, 1995). Stimulation of the brainstem reticular formation affects both arousal and sleep, depending on the specific neuronal populations (rostral or caudal) activated. Clinically, lesions in these areas usually result in permanent sleep and coma.

Power spectra analysis of the spontaneous EEG is often used as a tool for estimating arousal states. As already stated in the classical paper of Moruzzi and Magoun (1949), transitions from drowsiness to alertness are characterised by a "breaking up of the synchronisation of discharges of elements of the cerebral cortex", marked in the EEG by the "replacement of high-voltage slow waves with low-voltage fast activity". Vice versa, a decrease in the arousal level of the brain typically is reflected by a shift of EEG activity towards lower frequencies (Gray *et al.*, 1989; Steriade, 1995). The changes in EEG activity accompanying different sleep states are well-known (for a review, see Creutzfeldt, 1993). The spontaneous EEG is commonly used to monitor psychotropic effects of drugs as well (pharmac-EEG; see e.g., Herrmann, 1995).

Essential neurotransmitters for in the control of arousal are serotonin and noradrenaline (norepinephrine). Serotonin is found in the Raphé nucleus, and noradrenaline in the locus coeruleus. Both nuclei belong to the rostral brainstem. Release of serotonin decreases the state of arousal and induces sleep, presumably controlling specific "sleep substances". On the other hand, noradrenaline release is associated with an alert, attentive state, probably due to modulation of the threshold of activation centres in the brainstem and midbrain (for details, see e.g., Ganten and Pfaff, 1982). Under stress we surely are not drowsy. In any case, transmitter release of serotonin and noradrenaline in the brainstem is the mechanism mentioned most often in modern discussions about the mode of anaesthetic action.

cial play (Bekoff and Byers, 1998). Surely it does not follow that if social play has a biological function, thus it is not good. Quite a bit of play is harmless fun, and that surely counts as something good. Similarly, there may be evolutionary explanations for rape and aggressive behavior, but the fact that there are such explanations in no way implies that these behaviors are not bad and should be avoided or minimized. This argument against the truism founders because it conflates (supposed) facts with values. Pain may have evolved to function as a messenger, but it still may be bad.

DENY THAT NON-HUMANS SUFFER PAIN

A fourth strategy is to deny that non-humans suffer pain. The truism applies to all creatures who suffer pain, but it happens that humans are the only such creatures. On the face of it this strategy, reminiscent of Descartes's denial of animal minds, may seem singularly unpromising. But it is not as absurd as it may seem.

It is becoming increasingly clear that our everyday concept of pain is at least troubled and perhaps incoherent. We think of pain as essentially a sensation, yet I may enjoy a respite from my headache without supposing that I have suffered from two distinct headaches. My headache was there all along but for a while I didn't feel the pain. Indeed, our very language suggests that pains are there to be felt, and so presumably not to be felt. Just as I may perceive or not perceive a tree, so I may feel or not feel a pain. This way of speaking suggests that the pain is an object of perception rather than an object whose essence is in being perceived. We often think of pain as being essentially bad, yet people sometimes report various drug experiences as not extinguishing the pain, but of making the sufferer care about it less or not at all. Drugs sometimes extinguish pains; other times they allow us to better tolerate them.

In the face of such conflicting intuitions philosophers have moved in different directions. Some have insisted that pain is essentially subjective, and tried to

explain away the conflicting intuitions. Others have insisted that pains are essentially objective and tried to bury subjectivist intuitions. Other philosophers have argued for complex relational views, and still others have insisted that there really is nothing that corresponds to our everyday notion of pain (see Hardcastle, 1999, p. 95 for discussion).

At this stage it is hard to be confident about what will turn out to be the best account of our pain intuitions, especially in light of the growing evidence that they are also quite culturally relative. But this dispute should not shake our confidence in the truism, nor lead us to question its widespread application. The feature of pain that undergirds the truism is the fact that pain hurts. Perhaps there are pains that do not hurt, in which case the truism may not apply to them. But many pains do hurt and these are bad and should be avoided or minimized. And as Broom (2000) has shown, there is every reason to believe that pains that hurt are widely distributed among various animals.

CONCLUSIONS

In this paper I have defended a widely accepted truism that appears to be inconsistent with many of our everyday attitudes and practices regarding animals. There is quite a lot more to say on this subject. However, I hope enough has been said to make plausible the view that a simple, widely accepted truism about pain, may have sweeping implications regarding our treatment of non-human animals.

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