THE EVOLUTION OF PAIN

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ABSTRACT

Pain is an aversive sensation and feeling associated with actual or potential tissue damage. A pain system involving receptors, neural pathways and analytical centres in the brain exists in many kinds of animals. Feelings of pain in many species are indicated by physiological responses, direct behavioural responses and ability to learn from such experiences so that they are minimised or avoided in future. Species differ in their responses to painful stimuli because different responses are adaptive in different species but the feeling of pain is probably much less variable. In early evolution, pain must have involved cell sensitivity and localised responses but efficacy would have improved with efficient communication within the individual and sophisticated brain analysis. Pain systems have probably changed rather little during vertebrate evolution. Pain may be a greater problem for animals with less cognitive ability. The distinction between pain and nociception does not seem to be useful.

Keywords: Pain – Animal – Evolution

INTRODUCTION

The pain system and responses to pain are part of the repertoire used by animals, including man, to help them to cope with adversity during life. Where the welfare of an individual is its state as regards its attempts to cope with its environment (Broom, 1986, 1996) pain is clearly an important part of welfare. Pain can be an indicator that the environment outside the control systems in the brain is having an impact such that, the individual is having difficulty in coping. Pain may also indicate that there is likely to be a failure to cope in the long term.

Pain is defined here as an aversive sensation and feeling associated with actual or potential tissue damage. This is an improvement on a previous definition used by the author and is similar to that of the International Association for the Study of Pain "Pain is an unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Iggo, 1984). One difference from Iggo's definition is that "aversive" is used instead of "unpleasant" because aversion is more readily recognised and assessed than unpleasantness, particularly in non-human species. Aversive behaviour is not always shown and sometimes the feeling of aversion is overcome in the individuals concerned, for example in those who choose to inflict pain on themselves, but the aversion and hence the pain are still present. A second difference is the reference to feelings rather than emotion because feeling implies some degree of awareness. A feeling, as described at greater length by Broom (1998) is a brain construct involving at least perceptual awareness which is associated with a life regulating system, is recognisable by the individual when it recurs and may change behaviour or act as a reinforcer in learning. An emotion is a physiologically describable electrical and neurochemical state of particular regions of the brain which may result in other changes in the brain, hormone release or other peripheral changes but which need not involve awareness (Broom, 1998; Sommerville and Broom, 1998). Hence as emotion may involve feelings but need not do so, it is better to refer to feelings when defining pain. The third difference from Iggo's definition is that pain is a "sensation *and* a feeling" rather than a "sensory *or* emotional experience" because a sensory experience could be as little as a sensory input which reaches a low level in the brain and can be remembered very briefly. Most authors (Blood and Studdert, 1988) consider that a feeling is involved in pain and that input which does not involve some awareness is not pain. The fourth difference is that Iggo (1984) refers to the possibility of pain being described in terms of damage. Since damage can do no more than indicate the likelihood of pain, this is not included in the definition.

Part I of this Symposium was published in *Vlaams Diergeneeskundig Tijdschrift*, 69, 2000, p. 385-411.

CHARACTERISTICS OF PAIN SYSTEMS

In order to feel pain, animals need to have receptor cells in appropriate places in the body, peripheral and central neural pathways with neuro-transmitters and adequate brain analysers. The pain system would be expected to have links between these brain analysers and an output system which can initiate a behavioural or other response. Acute pain could result in behavioural avoidance, repeated risk of acute pain could result in learning so that potential damage could be avoided and chronic pain could result in suppression of activity and behaviour which ameliorates adverse effects. A mechanism for switching off the feeling of pain would also be expected because if pain has a great effect on behaviour, such an effect would sometimes be dangerous.

Pain receptors in man and other mammals, when compared with other sensory receptors, have high thresholds and continue to fire during repeated stimulation (Scheme 1). Sensitisation of nociceptors may occur at wound sites when bradykinin, histamines or neurokinin are released but may also be caused centrally.

Scheme 1

Characteristics of pain systems

1. Long-lasting output from specialised nociceptors with high thresholds and with little adaptation to repeated or continuing stimulation.
2. Output from other highly stimulated receptors.
3. Sensitisation of nociceptors (threshold lowered) possible.
4. Neurotransmitters such as substance P and glutamate.
5. Possibility for rapid response, e.g. by reflex.
6. Behaviour change in response to pain.
7. Learning to minimise future pain.
8. Involvement of some phylogenetically old parts of brain.

The advantages of feeling pain are that action can be taken to stop or ameliorate damage and future risk of damage can be reduced because pain acts as a reinforcer in learning to avoid potential damage (Scheme 2). Even chronic pain may be advantageous because it induces reduction in activity level or other changes in behaviour which improve the chances that normal, functional behaviour can be shown and body damage minimised (Wall, 1979). However some pain is likely to be an accidental consequence of the system and unadaptive, for example that resulting from a kidney stone stuck in the ureter (Bateson, 1991). Even writhing in agony could have a function such as the dislodging of gas in the gut, but would not be useful in this way if the cause was different.

Scheme 2

Possible functions facilitated by feeling pain

1. Distinguish at the peripheral level between potentially harmful stimulation and that which is intense but, nevertheless, is harmless and carries further information that might be useful.
2. Promote actions which stop or ameliorate damage.
3. Learn to avoid conditions or stimuli previously found to be associated with potentially harmful stimulation.
4. Inhibit other competing activities to promote escape from or removal of potentially dangerous stimulation and avoidance of the likelihood of damage.
5. Inhibit activities that might delay recovery from disease or injury.
6. Localise inhibition of activities where this might increase the risk of exposure, starvation or predation.

(modified after Bateson, 1991)

WHICH ANIMALS FEEL PAIN?

Although some people have thought of pain as limited to humans or mammals, many of those involved in pain research have found such ideas improbable. Melzack and Dennis (1980) made these statements:

"The nervous systems of all vertebrates are organized in fundamentally the same way."

"The experience of pain is often inferred from the behaviors of mammals, and it is not unreasonable to attribute pain experience to birds, amphibia and fish" (and presumably, reptiles).

The problem which is often expressed in relation to pain in species other than man is that the animals cannot tell you when they are in pain or how bad it is. The major method used in human pain studies is self-reporting, for example on a scale from no pain to very severe pain, but how reliable is this? People can lie or deceive themselves in relation to pain. Perhaps measures of observed behaviour or physiological change, like those used in non-human studies, are more accurate in at least some situations.

Some methods for recognising and assessing non-human pain have been used for a long time. For example the tail flick response of rats since 1941, the jaw opening response since 1964, limb withdrawal since 1975 and self-mutilation for much longer (Dubner, 1994). Sophisticated behavioural measures are being used more and more in studies of pain. However, there are problems in pain recognition which make comparisons between species difficult. Severe pain can exist without any detectable sign. Individu-

als within a species vary in the thresholds for the elicitation of pain responses. Most difficult for the general public, as well as for those studying the subject, is that species vary in the kinds of behavioural responses which are elicited by pain (Morton and Griffiths, 1985). Hence it is important to consider which behavioural pain responses are likely to be adaptive for any species which is being considered. Humans, like other large primates, dogs and pigs, live socially and can help one another when attacked by a predator. Parents may help offspring and other group members may help individuals who are attacked or otherwise in pain. Hence distress signals such as loud vocalisations are adaptive when pain resulting from an injury is felt. In species which can very seldom collaborate in defence, for example African antelopes which are subject to attack by lions, leopards, hyaenas or hunting dogs, or sheep which are subject to attack by wolves, lynx, leopards or mountain lions, the biological situation is quite different. The predators select apparently weak individuals for attack and vocalisations when injured might well attract predators rather than conferring any benefit. As a result, these animals do not vocalise when injured. A sheep which is caught by humans, put upside down in a holding frame, has a 15 cm diameter area of skin around the anogenital apertures cut off with a pair of scissors in the Mulesing operation, and is then turned over and released, makes no sound and walks away. Farm staff who do this often believe that sheep do not feel pain. However, sheep have all of the normal mammalian pain system and they produce high levels of cortisol and ß-endorphin after the mutilation (Shutt *et al.*,1987). Another example concerns monkeys which, although normally very noisy, are very quiet when giving birth, a time when they are at increased risk from predators. Their silence does not mean that parturition involves no pain. A knowledge of the selective pressures affecting the species is needed before behavioural responses to pain can be properly interpreted. Peripheral anatomical and most physiological aspects of the pain system, on the other hand, vary little amongst species.

Most vertebrate animals which have been investigated seem to have very similar pain receptors and associated central nervous pathways. Even some invertebrates have such systems, for example Kavaliers (1989) reports that gastropod molluscs have nociceptors with an output following tissue damage which indicates that such damage causes sensitisation. The most primitive vertebrates are the lampreys and hagfish which are considerably more different from modern teleost fish than are humans. When Martin and Wickelgren (1971) and Mathews and Wickelgren (1978) made intracellular recordings from sensory neurones in the skin and mouth of a lamprey (*Petromyzon*) during heavy pressure, puncture, pinching or burning, the output was like that which would be recorded in a mammalian pain receptor. The conduction velocity was slow relative to other sensory neurones, so they are probably of small diameter. There was no fatigue with repeated stimulation and the receptors were sensitised following local tissue damage. The neurotransmitter substance P occurs in small fibres in the dorsal horn of the spinal cord in both mammals and fish. In studies of elasmobranch fish, Cameron *et al.*(1990) found substance P, serotonin, calcitonin, gene-related peptide, neuropeptide Y and bombesin in the outer part of the substantia gelatinosa of the dorsal horn and met-enkephalin in the lateral part. Ritchie and Leonard (1983) found substance P in the afferent neurones of the elasmobranch substantia gelatinosa. These distributions are similar to those in mammals (Gregory, 1999) and substance P occurs more in the regions of the trout brain receiving input from pain receptors, the hypothalamus and fore brain, than in other parts of the brain (Kelly, 1979).

Within the Mammalia, there is considerable uniformity in the areas of the brain which have particular functions. However, different vertebrate groups vary considerably in the locations of function. Some analysis which occurs in the neocortex in mammals, takes place in the striatum in birds and within the different groups of fish there is diversity in the localisation of complex analysis. It is necessary to look for the site of any particular function rather than assuming that it will be in the same area as in man and it is not logical to assume that, because an area which has a certain function in man is small or absent in another group of vertebrates, the function itself is missing.

Behavioural responses to stimuli which would be expected to be painful occur in those vertebrates which have been studied. For example, Verheijen and Buwalda (1988) stimulated the mouth of a carp electrically and whilst a mild stimulation led to some fin movements and bradycardia, a current three times as strong resulted in freezing, or in erratic darting movements in which the glass tank was bumped. When carp were hooked in the mouth using a certain kind of bait, both Beukema (1970) and Verheijen and Buwalda (1988) reported avoidance of such bait afterwards for many weeks or a year in one case. This shows that the carp showed learned avoidance as a result of the hooking experience. Avoidance learning is reported for fish by several authors, for example Brookshire and Hoegnander (1968) administered a shock to paradise fish when they entered a black compartment and

found that they avoided the black compartment subsequently and learned to activate an escape hatch to avoid further shocks. In a study of pain thresholds to pressure and thermal stimuli, Chambers (1992) found these to be the same for various species of animal.

Opioids have many functions, one of which is natural analgesia. Met-enkephalin and leu-enkephalin are present in all vertebrates which have been tested and there are at least six opioid receptors described for teleost fish (Dores and Joss 1988, Dores et al 1989, Dores and Gorbman 1990, McDonald and Dores, 1991). When goldfish are subjected to difficult conditions, there is an elevation of pro-opiomelanocortin just as there would be in man (Denzer and Laudien, 1987). Goldfish which are given electric shock show agitated swimming but the threshold for this response is increased if morphine is injected and naloxone blocks the morphine effect (Jansen and Greene, 1970). Work by Ehrensing *et al.* (1982) showed that the endogenous opioid antagonist MIFI down-regulates sensitivity to opioids in both goldfish and rats. In general it is clear that there are very many similarities amongst all vertebrates in their pain systems.

NOCICEPTION

Pain receptors are often called nociceptors and a specific term for them, which distinguishes their input to the pain pathways from that from other kinds of receptor seems useful. However, the use of the term nociception to refer to the simpler parts of the pain system is questionable. It would seem that the distinction between nociception and pain is a relic of attempts to emphasise differences between humans and other animals or between "higher" and "lower" animals. The visual and auditory systems involve receptors, pathways and high level analysis in the brain but the simpler and more complex aspects are not given different names. A perception of pain can exist without the involvement of pain receptors, but so can visual or auditory perceptions exist without their receptors being involved. Wall (1992) said that the problem of pain in man and animals was "confused by the pseudoscience surrounding the word nociception." The use of the term nociception, which separates one part of the pain system from other parts when the system should be considered as a whole, should be discontinued.

HOW PAIN MIGHT HAVE EVOLVED

The likely functions of feelings, including pain, and the ways in which they might have evolved are discussed by Broom (1998). Possible stages in the evolution of pain are summarised in Scheme 3.

Scheme 3

Stages in the evolution of pain

1. Cell sensitivity develops and cells respond to potentially damaging effects.
2. Localised body responses occur when damage occurring or likely.
3. As above but system with brain analysis; could involve whole body responses.
4. Special features: specialised receptors and neural transmitters, sensitisation possible, behaviour responses, learning.

5A. Functioning of this system involves activation of non-essential parts of or pathways in the brain.

or

5B. Pathways in the brain system which were initially necessary become redundant but do not cease to be activated.

6. As a consequence of 5A or 5B, epiphenomena exist which result in the feeling.

7A Feeling has harmful effects - likely to disappear rapidly.

or

7B Feeling has no benefit - likely to disappear eventually.

or

7C Feeling has beneficial effect - likely to develop further.

Once the special features had evolved and the feeling had become part of the system, changes might have been slight. Provided that the system functioned adequately, would there have been any great selection pressure leading to further change? It would appear that the pain system is an old one. However, improvements in cognitive ability have occurred during vertebrate evolution so these could have an effect on the feeling of pain. It has sometimes been assumed that greater cognitive ability would mean that pain is a greater problem. However, there appears to be no logical foundation for this. Indeed, greater cognitive ability is likely to result in a greater ability to deal with problems. Some methods for coping with adversity require sophisticated rationalising ability. Hence it may well be that pain is a greater problem in animals with less good cognitive ability (Sommerville and Broom, 1998).

CONCLUSIONS

1.Pain is an aversive sensation and feeling associated with actual or potential tissue damage.
2.The pain system has evolved and is probably old in evolutionary terms.
3.Most aspects of the pain system, including the feeling of pain, are functional and adaptive.

4.There is evidence for the pain system in all vertebrates which have been studied and there is evidence for some aspects of it in invertebrates.
5.The similarities in the pain system across vertebrates are considerably greater than the differences, except in respect of behavioural responses to pain.
6.The term nociception may not be of much use.
7.Pain might be a greater problem in animals with less cognitive ability.

ACKNOWLEDGEMENTS

I thank Murray Corke, Neville Gregory and Steve Kestin for information.

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