Pain, 30 (1987) 129–130
Elsevier

PAI 01094

Ann Arbor, MI, 2 February 1987

Dear Editor,

In rejecting unequivocally my major conclusion, Drs. Dubner and Bennett accept the position that there are good scientific and clinical reasons for causing an animal subject to experience chronic pain as I defined it [1]. I fear that such a position, widely held, may lead to the conduct of experiments that invite the imposition of severe, even prohibitive, restrictions on animal research in some countries. That is why I opened the argument.

An important justification for many animal models of human disease is that such models permit the study of the pathogenesis of a simulated disease by a known or suspected agent. Drs. Dubner and Bennett, however, acknowledge that chronic pain is not a causal agent, but the object of study. They assert that chronic pain models are necessary, even mandatory, to study the therapy and pathophysiology of persistent, intractably painful conditions such as those due to primary peripheral or central neurologic disease. Unfortunately, my colleagues do not provide evidence to support their position.

Lacking a widely accepted source when I composed my remarks, I defined chronic pain as '... present during most waking hours for at least 1 week and usually much longer' [1]. The IASP Subcommittee on Taxonomy has subsequently published its conclusion that 3 months is the point at which acute pain becomes chronic [2]. Is there clinical evidence that the use of any animal model of any chronic pain syndrome requires that the subject experience at least a week or more of chronic pain — intensity aside? Is there a potentially effective treatment for chronic pain that can be tested only under such conditions, or that requires such a prolonged observation of chronic pain before effectiveness can be judged? Is there a chronic pain syndrome that requires such a prolonged experience of chronic pain before the syndrome is established and recognized? In humans, the onset of neuropathic or central pain may be delayed or may develop slowly for weeks or months after the neurologic damage. But it does not take a week or more of obvious pain to establish the condition. And, once established, the syndrome can be recognized quickly. If an animal model of neurogenic pain is developed, there is, therefore, no reason to withhold treatment of the pain for a week or more after the syndrome is recognized. For some studies, euthanasia could be performed as soon as the clinical condition has been established. The use of chronic decerebrate preparations may be appropriate, as Wall [3] and Woolf [4] suggested. In long-term studies of the central nervous system of intact, awake subjects, local or systemic analgesic treatment could be periodically withheld for short periods to allow physiological, biochemical or pharmacologic observations as necessary. There is no need to restrict

scientific investigation to the periphery or to surgically or pharmacologically altered central nervous systems, nor was this suggested in my letter.

The IASP guidelines [5] are not at issue here. Specific issues are most appropriately handled *within* the guidelines, which urge peer and lay review and indicate generally, but do not specifically define, the boundaries of acceptability (e.g., '... minimal pain necessary ...' [5]). I support these guidelines and see no need to change them to address the details of specific issues.

No one using animals in pain research wants unnecessarily restrictive limits placed on experimentation. I agree fully with Drs. Dubner and Bennett and with Dr. Wall [3] that research on pain, especially on chronic intractable pain, must proceed apace at peripheral and central levels. It is possible that there are or will be sound, ethically acceptable reasons for requiring that, in an animal model, the subject experience chronic pain. If so, these reasons must be stated very clearly. Meanwhile, we must continue to examine in detail the clinical and scientific reasons for the animal models we develop and the limitations that those reasons should impose on the conduct of experiments. This will add strength to the case for facilitating the continued use of animals in research, especially research relevant to the problem of pain.

Univ. of Michigan Medical Center, Kenneth L. Casey
Chief, Neurology Service,
Veterans Administration Medical Center,
Ann Arbor, MI (U.S.A.)

References

1 Casey, K.L., Letter to the Editor, Pain, 26 (1986) 270–271.
2 Merskey, H. (Ed.), Classification of Chronic Pain, Pain, Suppl. 3 (1986) S5.
3 Wall, P.D., Reply from the Editor, Pain, 26 (1986) 272.
4 Woolf, C.J., Long term alterations in the excitability of the flexion reflex produced by peripheral tissue injury in the chronic decerebrate rat, Pain, 18 (1984) 325–343.
5 Zimmermann, M. et al., Ethical guidelines for investigations of experimental pain in conscious animals, Pain, 16 (1983) 109–110.