

Ethical Guidelines for Investigations of Experimental Pain in Conscious Animals¹

(See Ethical Guidelines for Pain Research in Humans)

The Committee for Research and Ethical Issues of the International Association for the Study of Pain (IASP®) is concerned with the ethical aspects of studies producing experimental pain and any suffering it may cause in animals. Such studies are essential if new and clinically relevant knowledge about the mechanisms of pain is to be acquired. Investigations in conscious animals intended to stimulate chronic pain in man are being performed. Such experiments require careful planning to avoid or at least minimize pain in the animals.

Investigators of animals models for chronic pain, as well as those applying acute painful stimuli to animals, should be aware of the problems pertinent to such studies and should make every effort to minimize pain. They should accept a general attitude in which the animal is regarded not as an object for exploitation, but as a living individual.

In practice, investigators engaged in research on pain in animals should consider the following guidelines aimed at minimizing pain in animals and, when submitting a manuscript, state explicitly that they have been followed. The guidelines are concerned with the importance of the investigation, the severity and the duration of the pain.

1. It is essential that the intended experiments on pain in conscious animals be reviewed beforehand by scientists and lay-persons. The potential benefit of such experiments to our understanding of pain mechanisms and pain therapy needs to

¹ International Association for the Study of Pain [homepage on the Internet]. Ethical guidelines for investigations of experimental pain in conscious animals. Available from: <http://www.iasp-pain.org/AM/Template.cfm?Section=Home>

be shown. The investigator should be aware of the ethical need for a continuing justification of his investigations.

2. If possible, the investigator should try the pain stimulus on himself; this principle applies for most non-invasive stimuli causing acute pain.

3. To make possible the evaluation of the levels of pain, the investigator should give a careful assessment of the animal's deviation from normal behavior. To this end, physiological and behavioral parameters should be measured. The outcome of this assessment should be included in the manuscript.

4. In studies of acute or chronic pain in animals measures should be taken to provide a reasonable assurance that the animal is exposed to the minimal pain necessary for the purposes of the experiment.

5. An animal presumably experiencing chronic pain should be treated for relief of pain, or should be allowed to self-administer analgesic agents or procedures, as long as this will not interfere with the aim of the investigation.

6. Studies of pain in animals paralyzed with a neuromuscular blocking agent should not be performed without a general anesthetic or an appropriate surgical procedure that eliminates sensory awareness.

7. The duration of the experiment must be as short as possible and the number of animals involved kept to a minimum.

The investigators should cooperate with the Committee for Research and Ethical Issues or seek its advice. It is expected that responses from readers will help to improve these guidelines. The Committee intends to edit a comprehensive set of guidelines aimed at giving advice to investigators, local ethical committees and editors of journals who may be concerned with animal experiments on pain, or with general animal experimentation involving pain

The above Guidelines have been approved by the Council of IASP in December 1982. They replace a previously published version and account for comments and suggestions of scientists as solicited in a Newsletter of IASP (Pain, 13/2; 1982).

The Committee suggests that all those concerned should read the following publications:

Bowd, A.D., Ethics and animal experimentation, *Amer. Psychol.*, 35 (1980) 224-225.

Covino, B.G., Dubner, R., Gybels, J., Kosterlitz, H.W., Liebeskind, J.C., Sternbach, R.A., Vyklicky, L., Yamamura, H. and Zimmermann, M., Ethical Standards for Investigations of Experimental Pain in Animals, *Pain*, 9 (1980) 141-143.

Halsbury, The Earl of, Ethics and the exploitation of animals, *Conquest*, 164 (1973) 2-11.

Hoff, C., Immoral and moral uses of animals, *New Engl. J. Med.*, 302 (1980) 115-118.

Iggo, A., Experimental study of pain in animals: ethical aspects. In: Bonica, J.J., Liebeskind, J.C. and Albe-Fessard, D.G. (Eds), *Advances in Pain Research and Therapy*, Vol. 3, Raven Press, New York, 1979, pp. 773-778.

Smyth, D.HY., *Alternatives to Animal Experiments*, Scolar-RDS, London, 1978.

Sternbach, R.A., The need for an animal model of chronic pain, *Pain*, 2 (1976) 2-4.

Wall, P.D., Editorial, *Pain*, 1 (1975) 1-2.

Wall, P.D., Editorial, *Pain*, 2 (1976) 1.

For the Committee: Manfred Zimmermann, Chairman 1978-1990, Heidelberg (Germany)

Ethical Guidelines for Pain Research in Humans

The following Ethical Guidelines are the product of a lengthy period of deliberation by the Committee on Ethical Issues of the International Association for the Study of Pain (IASP®). The guidelines published here have been approved, after modification, by the Council of IASP.

These guidelines may not be perfect and are intended to stimulate debate among members. Council of IASP encourages suggestions for improvement which can be made through the correspondence columns of this journal or directly to the current chairman of the Committee on Ethical Issues: Dr. George Mendelson, Suite 18, 33 Queens Road, Melbourne, VIC 3004, Australia.

Membership of the Committee on Ethical Issues has undergone much change during the preparation of these guidelines and names of members who contributed are printed at the end of this article.

E. Charlton
Secretary IASP

Ethical Guidelines for Pain Research in Humans

The International Association for the Study of Pain (IASP) endorses the ethical principles for research involving human subjects given in the following documents: the World Medical Association's Declaration of Helsinki, Recommendations Guiding Doctors in Clinical Research (1964, revised 1975), the Ethic Principles of the American Psychological Association (1973), the Declaration of Lisbon, the Rights of the Patient (1981), the proposed International Guidelines for Biomedical Research Involving Human Subjects, and Council for International Organizations of Medical Sciences (1982).

IASP believes further guidelines are necessary to supplement the ethical principles contained in these documents.

The goal of pain research is to acquire new knowledge on the mechanisms, pathogenesis, diagnosis, and treatment of pain. This requires research on humans and animals. Human research may be undertaken on both healthy persons and patients. This research may involve painful stimuli or delaying pain

relief in patients. The primary intention is to advance knowledge so that patients in general may benefit; the individual patient may or may not benefit directly.

Guidelines

The health, safety and dignity of human subjects have the highest priority in pain research. The investigator is personally responsible for the conduct of research and its effects on the experimental subject at all times, even though the patients have given their consent to participate.

1. Before starting any study of human subjects, the proposed experimental protocol must be reviewed and approved by an independent committee on human research. The functions of the committee are as follows:

2. a) to ensure that participants are not coerced or harmed,
- b) to evaluate the potential for undesirable physical or psychological effects occurring during the research,
- c) to decide whether the proposed research should be the subject of regular review.

The committee should be appropriately constituted and normally should include scientists, health care practitioners and lay members.

The scientific merit of the proposal and the research methods proposed normally should be the subject of independent evaluation by an appropriately constituted peer review committee. The scientific review process normally should take place before the consideration of ethical matters.

1. Potential participants should be informed fully about the goals, procedures and risks of the study before giving their consent.

2. Healthy subjects and patients must be able to decline, or to terminate, participation at any stage without risk or penalty whatsoever.

3. Written consent must be obtained to indicate that the subject understands the nature and purpose of the proposed study, has had the opportunity to ask questions and agrees to participate on a voluntary basis. Where possible, informed consent should be endorsed by an independent signatory.

4. There is a duty to protect those who may be incapable of giving fully informed and voluntary consent. These include children, the elderly, the mentally handicapped, prisoners and those very ill with other disease. Such persons should not be used for medical research unless they are essential for the goals of the proposed research. In such cases, consent must be obtained also from those who have legal responsibility for their welfare.

5. In any pain research, stimuli should never exceed a subject's tolerance limit and subjects should be able to escape or terminate a painful stimulus at will. The minimal intensity of noxious stimulus necessary to achieve goals of the study should be established and not exceeded.

6. In all circumstances, including studies that employ placebo and sham treatment methods, an effective, accepted method of pain relief must be provided on request of the patient or subject. The availability of alternative pain relief should be made clear in the consent form and the instruction before the study begins.

References

American Psychological Association, Ethical Principles in the Conduct of Research with Human Participants, 1973, pp. 58-69.

Council for International Organizations of Medical Sciences, Proposed International Guidelines for Biomedical Research Involving Human Subjects, 1982.

World Medical Association, Declaration of Helsinki: Recommendations Guiding Doctors in Clinical Research, 1964, revised edition, Tokyo, 1975.

World Medical Association, Declaration of Lisbon: The Rights of a Patient, 1981.

Further Reading

McNeill, P.M., *The Ethics and Politics of Human Experimentation*, Cambridge University Press, Cambridge, 1993.

Membership of the Committee on Ethical Issues

C. Benedetti, Columbus, Ohio (USA)

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