

Avoiding and Alleviating Pain in Research Animals

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Abstract

Animal use for research purposes is conditionally supported by the community, in that any animal used must not suffer and pain is avoided. There are strong ethical and moral reasons why researchers need to consider pain as a major issue and the argument from a scientific standpoint is equally compelling.

The Australian Code of practice for the care and use of animals for scientific purposes (the Code), has provided the basis for guiding researchers to consider every mechanism available to avoid pain in their animals. If any pain might be inflicted, it and its consequences must be alleviated. Each State and Territory in Australia has incorporated the Code and these considerations into their legislative framework.

The ethical review process for animal use for scientific purposes, obliges researchers to attempt to predict the possibility of pain, to refine if possible their experimental design to minimise any pain and its impact and to use the best analgesic protocol available to treat any pain involved.

The NHMRC has also developed "Guidelines to promote the wellbeing of animals used for scientific purposes" to assist researchers. These Guidelines focus largely on pain and how to control pain.

Introduction

Any discussion of pain in animals should firstly examine what might be meant by "pain" in animals. People who work and spend their lives closely caring for animals will tell us that animals do have "feelings" and yes, they also feel pain. However, at the start of this 21st century there is still considerable debate by some about animals and pain (Wilson, 2002). Pain is obviously a subjective experience and we cannot know for certain if animals do feel pain or what that "feeling" entails. A commonly made suggestion is that only humans have the capacity to feel pain and that because animals differ from humans in various ways, notably in the anatomy of the brain and nervous system, that any reaction of an animal to an "apparently" painful situation is just that – a "reaction". As suggested by Church (2000) another approach by some people is to consider pain as a form of aversive sensation – to be avoided.

Like Schofield and Williams (2002), however, I take the somewhat anthropomorphic position and consider that animals do perceive negative physical and emotional sensations from conditions I would call painful. One of

the better analogies relating to animal pain is found in the Nuffield Council report (2005): “Since we would feel pain on being exposed to boiling water and would rapidly retract an exposed body part, it could seem reasonable to assume that an animal that shows a similar reaction on being exposed to boiling water would feel a similar kind of pain”. If on the other hand we use animals as a model to study the nature and methods of relief of pain for the human condition, does this not also support the position that animals feel pain? If they did not then the model is not useful (Tannenbaum, 1999 and Linderoth and Foreman 2006). An accepted position in Australia and elsewhere internationally, is that an animal with anatomical / physiological / biochemical capacities (as recognised in humans) will have the same capacity to perceive pain as humans know it.

If we accept that animals do feel pain, what does this mean for human-animal relationships? “Intentionally causing pain to another human is considered among the most socially abhorrent of actions. Likewise, painful procedures on animals are among the most emotive of public concerns about animal welfare (Weary et al 2006). Tannenbaum (1999) clearly indicated that many people in some societies believe they have a primary ethical obligation to animals to avoid unnecessary or unjustifiable pain. It is in this context that animals in research need particular scrutiny. Apart from some notable exceptions, the community and “thoughtful researchers” (Gautier and Griffin, 2005) have concerns about the welfare of animals used in research for human and animal conditions. Pain is the most important feature of this concern.

Of all forms of animal use, their use in research (and teaching) is of greatest interest to the general public. There is a range of opinions on whether animals should be used at all in research. The same or similar arguments involving scientific and ethical (philosophical) perspectives are used to argue both for and against the use of animals in research. The Nuffield Report (2005) states that the most important issue is that arises when humans inflict pain and suffering on animals, especially if those animals used will not benefit directly from the outcomes. As discussed in earlier papers, the broader community will accept animal use in research, but their concerns are that those animals should not experience pain or distress during the process.

As a consequence of human relationships with animals, there is a generally accepted moral and ethical responsibility for humans to have concerns for the welfare of those animals – especially those who suffer pain and more especially if that pain is linked to the relationship between those animals and the human activity with which the animals are involved. The ethical imperative for scientists seeking to use animals is to clearly identify that the scientific use of animals will lead to “valid, useful and relevant results” (Nuffield report, 2005). Pain and distress, must at best, be avoided or at least, minimised.

Where does pain in research animals come from?

Animals used in research can be subjected to a number of situations capable of causing some or a great deal of pain and distress. Diseases can be induced in animals to study the effect or process of the disease or to assist in

the development of cures or preventive mechanisms. Procedures such as surgery can cause immediate pain and can result in post surgical pain. Studies to understand the nature of certain toxins or to test for the safety of products destined to be used for human and animal treatments may also cause pain (Stokes, 2000). The understanding of pain itself and pain mechanisms for alleviating pain in animals and humans still requires the use of animals that can feel pain and respond in ways similar to that of humans experiencing pain (Tannenbaum, 1999; Karas, 2006).

Does science have other interests in pain in research animals?

Researchers have recognised for many years that any factors capable of influencing data from experimental animals are undesirable and need to be controlled. Pain and distress are factors that can alter the quality of research results (Bazin, 2004). However, some researchers will still argue that the use of analgesics to minimise the effects of pain could affect the goals of some studies (Karas, 2006). Nevertheless it is generally agreed that to achieve the best scientific practice, the identification and control of any conditions such as pain and distress, which could cause undesirable responses in the animal models and so influence research results, is essential.

The challenge for researchers

While the majority of researchers will strive to prevent pain or to attempt to reduce it on either ethical and / or for scientific imperatives, there appear to be a number of barriers to the process. Karas (2006) has listed 6 categories of barrier to the rapid adoption of good analgesic practice in research animals, notably rodents, even though in veterinary companion animal practices rapid advances have occurred in recent years. Karas' categories are as follows:

1. Lack of widespread knowledge of effective techniques to assess, monitor and treat pain
2. The extent of the Principal Investigator's knowledge about or personal attitude towards pain in animals
3. The amount of institutional support for veterinarians, technicians and Institutional Animal Ethics Committees (AEC)
4. Flawed AEC processes
5. Understaffing, lack of overnight care and oversight
6. Analgesics or other pain reducing strategies omitted because the Principal Investigator cited limitations in study design.

In addition she suggests that there could be a lack of useful available information on which to base good recommendations for many of the laboratory species. There seems also to be a view that anaesthetics will provide the necessary analgesia for surgically induced pain as well as the process of assisting with immobilisation of the animal (Bazin et al 2004 and Schofield and Williams 2002). The latter authors remind us that the most popular single drug anaesthetic regimes in use for research animals (e.g. pentobarbitone and ether) are very poor analgesics and any effect will not provide control of post operative pain. Their recommendations are for multimodal therapies to treat and minimise any pain induced. Therapies

should be assessed on the basis of the degree of trauma per unit body mass and be planned to be introduced prior to surgery and continuing well after the surgical event is concluded.

Specific Australian perspectives

The Australian community will generally give conditional support to animal use in research. For more than 30 years Australia has had a Code of Practice, which was originally developed with the strong support of researchers. The Code is regularly reviewed under the auspices of the NHMRC and endorsed by the major research bodies in Australia. The Australian Code of Practice for the Care and Use of Animals for Scientific Purposes 7th Edition, 2004 has provided strong guidance for the research community. In the context of pain the Code requires that animal use must first be justified on scientific grounds. This justification must be weighed against any potential effects on the animals involved. Researchers are obliged to design projects to avoid pain and distress. If pain is unavoidable an assumption must be made that animals will experience pain in a manner similar to humans (Code clauses 1.19 and 1.20). The Code indicates that alleviation of pain or distress as a result of the protocol must take precedence over completion of the project. If pain cannot be controlled, the animal must be euthanased without delay (Code clause 1.21).

A cornerstone of the Code which is now incorporated into Legislation in every State and Territory is the concept of regulated self-regulation of animal use by the research community. The Code established the practice of ethical review of proposals to use animals in scientific purposes by identifying the need for establishments to appoint Committees (AECs) with defined membership to examine proposals to use animals in research. As part of this review, the AEC will expect researchers to provide arguments that animal use is essential and the principals of Russell and Burch's 3 Rs have been satisfied, vis:

- That animal use has been **Replaced** with alternatives if possible
- That where animals are essential their numbers will be **Reduced** to the minimum required by good study design
- Where pain or distress can be expected, the study design has been **Refined** to minimise the effects of that pain or distress.

Potentially, it is easier to achieve the first two requirements. As Gauthier and Griffin (2005) indicate "refinement is the least 'exciting' of the 3 Rs since it produces the least obvious change in animal use if numbers are regarded as the most important measuring tool." They remind us though that Russell and Burch did place a greater emphasis on controlling pain in the individual animals than on reducing the numbers of animals in general. Apart from pain control through adequate use of analgesic techniques, researchers are able to utilise processes such as the development and use of humane endpoints to reduce the severity and duration of pain and distress, especially where there might be a restriction to the use of analgesics (Stokes, 2000). An interesting proposal by Sedcole (2006) is to consider designing experiments to vary group sizes so that the groups with animals expected to suffer pain or distress should have fewer animals, while groups such as controls would have more

animals. His concept is that by using appropriate statistical processes, results can still be analysed, but the number of animals suffering would be reduced.

In addition to the Code in Australia, the NHMRC is sponsoring the development of Guidelines to Promote the Well-being of Animals Used for Scientific Purposes. These guidelines are being produced to assist researchers and members of ethics committees to achieve the goals of the Code by promoting the well-being of animals in research where pain or distress might be involved. The guidelines recognise the need to maintain animals in stable and defined physiological states to reduce confounding effects on experimental results. The guidelines outline important issues to be considered at every phase in the study process from the planning stage to completion of the project. Included will be species specific recommended practices to assist to minimise pain and distress.

Conclusion

With the conditional acceptance of animal use for scientific purposes by the community, animals will continue to play an important role in science. As discussed, this poses significant challenges to researchers hoping to use animals in this way. The Australian Code and State and Territory Legislation through incorporation of the Code, place the research community 'on notice' with respect to their responsibilities to those animals. What is not acceptable is that "even when people acknowledge the potential for animals to experience pain, appropriate treatment does not always follow" (Weary et al 2006). It is clear (Karas, 2006) that while considerable efforts are being taken to treat pain in Companion Animals, the adoption of the same practices in laboratories is much slower.

If pain and distress are not managed better in experimental animals, the community will be less inclined to approve their use. We would potentially reach the situation as outlined by Weary et al (2006) where scientists would be required to dispense totally with procedures that cause pain or to dispense with injuries or diseases that would cause pain or distress. The community insists that all methods to minimise pain and distress must be adopted successfully.

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