

## Pain-free animals: An acceptable refinement?

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### Abstract

Recent advances in the area of neuroscience have led to an increased understanding of nociception in mammals, including a recently discovered single gene mutation in humans that leads to complete pain insensitivity. Work on knock-out mice is already underway. This presents the biomedical sciences with the questions of if and how pain insensitive animals should be used in research. Utilitarian ethics, commonly cited as the framework for current lab animal protection standards based on the reduction of pain and distress, would clearly argue that pain-free animals would be a superior choice in the lab setting. However, a historical examination of other animal uses suggests that there may be substantial public outcry to the development and use of such animals. In order to examine attitudes towards the development and use of genetically engineered pain-free animals, we designed a survey that queried populations, including lab scientists and animal welfare advocates, on their moral opinions on the development and use of pain-free animals. Results from this survey are reported, examining the attitudes from a spectrum of people, from those who are intimately involved in the conduct of animal research to those who are most opposed.

**Keywords:** refinement alternative, ethics, genetic engineering, pain, intrinsic value

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### Introduction

Within the United States, the Animal Welfare Act regulates experimental procedures on animals based on the severity of pain and distress involved (1970). In practice, this regulation is based solely on the severity of pain in the experimental animals. The level of justification required to gain approval from an Institutional Animal Care and Use Committee (IACUC) for an experiment correlates most directly with the amount of pain caused to experimental animals and whether this pain is relieved. Distress is assumed to correlate with the level of pain, as researchers are never asked to rank the amount of distress that will be caused to animals, but are required to rank the amount of pain that will be inflicted.

Not surprisingly, similar logic is echoed in surveys of public opinion on animal use in biomedical research (Pifer et al. 1994). Generally, a majority of people support conducting animal research when advances in knowledge can be made from the research. However, this support decreases dramatically as the level of pain that will be inflicted on the experimental animals increases. The general

public uses utilitarian ethics to make decisions about the acceptability of animal research, which highly resembles the decision making process dictated to animal care and use committees (IACUCs) by the Animal Welfare Act.

Utilitarian ethics is commonly understood to be a set of ethical principles that dictates 'the greatest good for the greatest number'. Utilitarians initially extended moral consideration to animals in 1789 when Jeremy Bentham wrote, "The question is not, 'Can they reason?' nor, 'Can they talk?' but rather, 'Can they suffer?'.... The time will come when humanity will extend its mantle over everything which breathes." (Bentham et al. 1970) Bentham's work is often cited by animal welfare organizations, and is often used as the basis for arguments against animal experimentation that claim that animal research cannot be conducted without the suffering of animals, and should therefore not be conducted at all.

Recent advances in the areas of neuroscience and genetic engineering have opened several paths to the generation of animals, specifically mice, that do not feel pain. Recently, Cox et al. characterized several families living in Pakistan whose members carried

one of three possible single amino acid nonsense mutations in the gene *SCN9A*, which codes for a subunit of a voltage-gated sodium channel,  $Na_v1.7$  (Cox et al. 2006). People who carried a mutation in this gene lacked the ability to perceive any form of pain, but were otherwise physiologically normal. Work on knock-out mice that lack this gene is already underway, and several mice strains have already been generated using knockout techniques that delete entire sections of the gene (Nassar et al. 2004). It is only a matter of time before a mouse is generated that carries one of the same nonsense mutations in *SCN9A*, and is tested for its pain-sensing abilities. In addition, the Allen Brain Atlas project has made public their database which gives genome-wide expression analysis on a cell by cell basis in the mouse brain (Lein et al. 2007). This could give researchers the underlying information they need to manipulate gene expression in a highly controlled fashion in the mouse brain. It is possible that genes related to nociceptive pathways will be targeted, and that "pain-free" animals could be generated.

The use of pain-free animals could potentially solve many of the issues currently cited for the restriction and prohibition of animal experimentation, especially those based on utilitarian ethics. The pain involved in the experiment would be minimized to the point of non-existent. Given that the current regulations give very little consideration to distress, or the emotional experience of the experimental animal, this would theoretically grant investigators, at least in the U.S., a considerably greater range for experimentation under the current regulations. The use of pain-free animals would even be considered to be a refinement, as it would reduce the level of pain involved in an experiment.

Given that pain-free animals are a distinct technological possibility, the ethical acceptability of using these animals in research must be considered. We designed a survey that allowed us to analyze the

acceptability of the generation and use of pain-free animals in biomedical research, especially amongst key stakeholders in the debate on animal research. We explicitly targeted laboratory scientists (including those who use animals in their research), as well as members of the animal protection community (people who classify themselves as belonging to one or more animal advocacy organizations, such as the Humane Society, People for the Ethical Treatment of Animals, or the Society for the Prevention of Cruelty to Animals). Here we present the initial findings of this survey.

### Materials and methods

A brief internet-based survey was designed to gauge opinions on the development and use of pain-free animals. Participants were asked for their opinions on a variety of animal uses, including training and research in the life sciences. Participants were allowed to respond on a scale ranging from strongly disagreeing with the practices in question to strongly agreeing with the practices in question. The list of questions asked about animal use is shown in Table 1. The survey was evaluated and tested by faculty members in the Department of Environmental Health Sciences at the Bloomberg School of Public Health.

The target population for this survey included the animal welfare community and laboratory research scientists. Permission was obtained to contact members of several organizations, from academic communities and businesses to non-profit groups. Emails were sent out notifying members of email listserves, including the CAAT listserve, that the survey was available online. Also, a link to the survey was posted on the AltWeb site ([altweb.jhsph.edu](http://altweb.jhsph.edu)).

All survey activities were overseen and approved by the Committee on Human Research at the Bloomberg School of Public Health.

Table 1. Questions from the CAAT Internet-based Survey

1	Is it acceptable to use animals to make or develop goods for human use?
2	Is it acceptable to use animals in surgeries or dissections to train doctors learning to conduct medical procedures?
3	Is it acceptable to use animals in surgeries or dissections to teach science students about anatomy and physiology?
4	Is it acceptable to use animals in science fairs or exhibitions, such as using animals in live demonstrations of current technologies or protocols?
5	Is animal experimentation acceptable if medical advances can be made with the knowledge gained from the experiments?
6	Is animal experimentation acceptable if medical advances can be made even if the experimental animals would experience pain during the experiment?
7	The technology now exists to create mice that are genetically engineered to feel no pain. Should these animals be created for the purposes of biological research?
8	Is it acceptable to use animals that are engineered to feel no pain in biological experiments that would otherwise involve painful experiences for the experimental animals?
9	If animals that could not feel pain were to be created, would scientists be morally obligated to use these animals instead of pain-sensing animals in experiments that cause pain?
10	If animals that could not feel pain were to be created, should scientists be free to conduct any experiment with those animals?
11	If animals that could not feel pain were to be created, would it be acceptable to use that animal in an experiment if the animal was scared or distressed during the experiment?

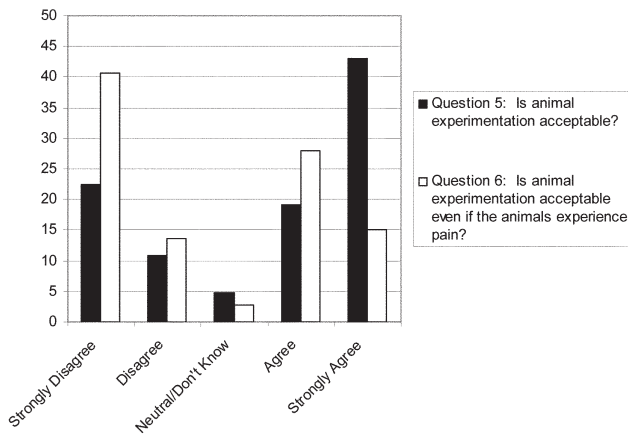


Fig. 1. Participants follow historical trends on the acceptability of animal research. Overall participants' responses to the questions, "Is animal experimentation acceptable if medical advances can be made with the knowledge gained from the experiments?" (shown in black) and "Is animal experimentation acceptable if medical advances can be made even if the experimental animals would experience pain during the experiment?" (shown in white). Participants were less likely to approve of animal research if the experimental animals were to experience pain.

## Results

At the time of analysis, 221 people had provided answers to the online survey. Of the participants, 60.5% were female and 39.5% were male. 20.5% of the participants were under 30, 35.7% were between the ages of 30-50, and 43.8% were over 50.

45.5% of the participants work as laboratory scientists and 62.8% of those scientists use animals in their work. 77% of the participants have companion animals, 29% are vegetarians, and 22% are members of animal advocacy organization. The pool of participants is clearly enriched for laboratory scientists, with nearly half of the total respondents classifying themselves as a laboratory scientist. Vegetarians and members of animal advocacy organizations (which we will refer to as the animal protection community) have also been enriched for, with nearly a third of the population reporting to be vegetarians and confirming that they do not eat poultry, red meat, or fish.

Overall, the respondents followed historical trends that have been observed in other surveys on animal use in life sciences. These surveys showed that animal experimentation is considered to be acceptable to a majority of people, but that the level of approval fell when it was explicitly mentioned that the animals would feel pain during the experiment. Participants in the current survey also agreed by majority that animal testing was acceptable if medical advances could be made with the knowledge gained, as seen in Fig. 1. This level of agreement decreased when participants were asked if animal research was acceptable when the animals were in pain during the experiment. Far fewer participants strongly agreed and far more

strongly disagreed with animal experimentation if it caused pain. Very few people classified themselves as not knowing or being neutral in either case.

When participants were asked if pain-free animals ought to be created for the purposes of biological research (Question 7), overall participants were divided more or less evenly amongst response categories, with the largest number of people disagreeing that pain-free animals should be engineered, as seen in Fig. 2. Of the overall participants 31.6% strongly disagreed and 16.5% somewhat disagreed that pain-free animals ought to be created. Scientists were somewhat more likely to agree that pain-free animals ought to be created with

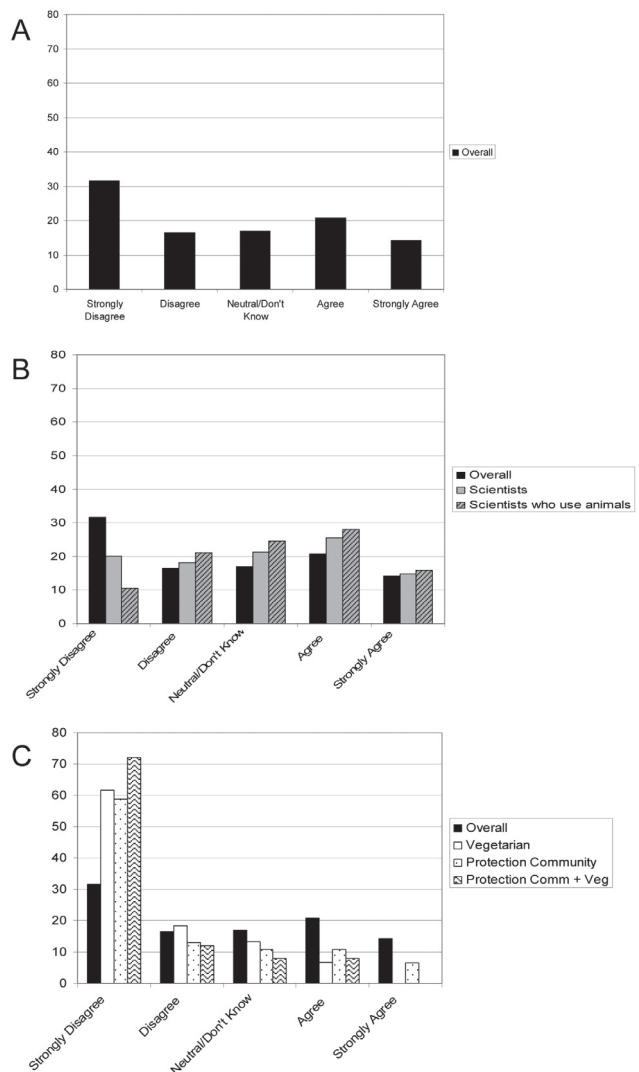


Fig. 2. The acceptability of the generation of pain-free animals differs by demographic group. Participants were asked (Question 7), "The technology now exists to create mice that are genetically engineered to feel no pain. Should these animals be created for the purposes of biological research?" Overall (A) participants were evenly divided between agreeing and disagreeing with the practice, and scientists (B) followed this trend. Participants who classified themselves as a member of an animal advocacy group or as a vegetarian were much more likely to disagree with the practice (C).

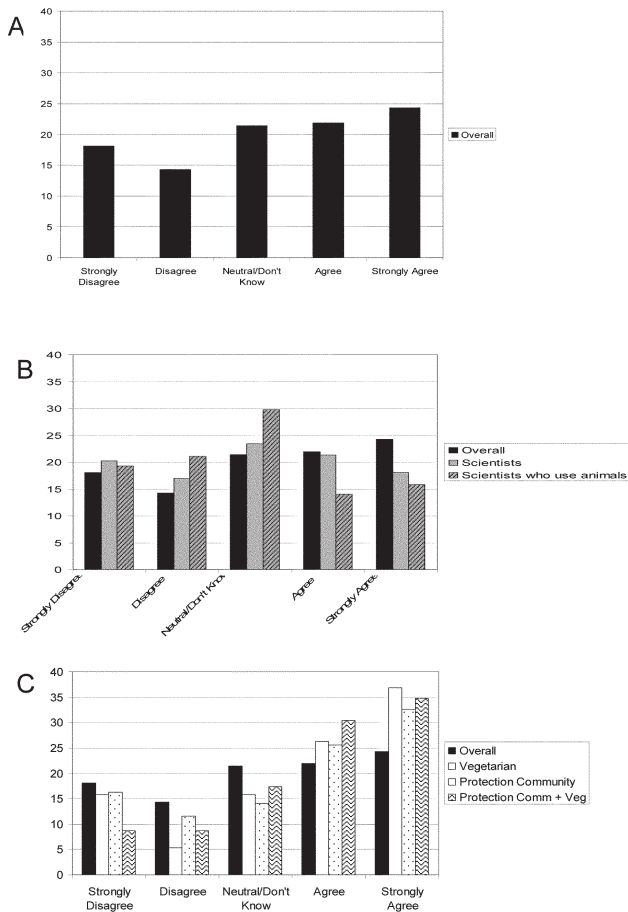


Fig. 3. The acceptability of using pain-free animals does not correlate with the acceptability of generating pain free animals in all demographic groups. Participants were asked (Question 9), "If animals that could not feel pain were to be created, would scientists be morally obligated to use these animals instead of pain-sensing animals in experiments that cause pain?" Overall (A) participants remained largely divided between agreeing and disagreeing with the practice, and scientists (B) followed this trend. Participants who classified themselves as a member of an animal advocacy group or as a vegetarian (C) were more likely to agree or strongly agree that pain-free animals ought to be used instead of pain-sensing animals in painful experiments.

14.9% strongly agreeing that pain-free animals should be created, and 25.5% somewhat agreeing. However, 38.3% of the scientists either strongly disagreed or somewhat disagreed that pain-free animals should be created. Vegetarians and members of the animal protection community were much more likely to strongly disagree that pain-free animals should be created. 58.7% of the protection community strongly disagreed that pain-free animals should be created, and 72% of the protection community that is also vegetarian strongly disagreed.

This strong disagreement with the acceptability of pain-free animals is shifted within the vegetarian and animal protection community groups when the participants are asked if a scientist would be morally obliged to use a pain-free animal in an otherwise painful experiment if the pain-free animals were to be

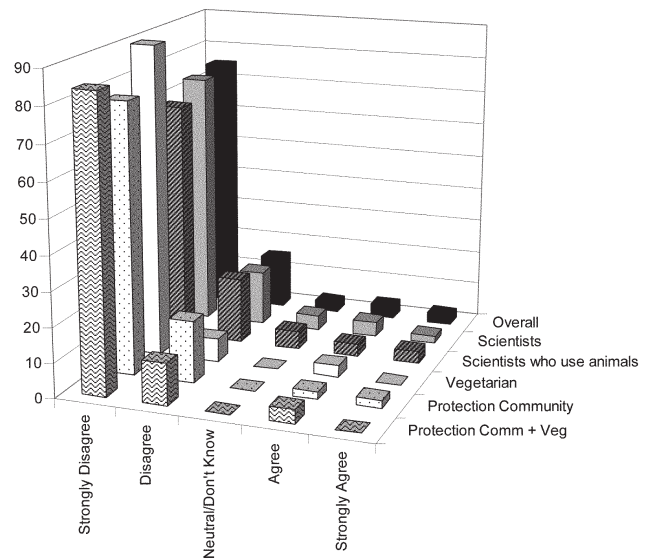


Fig. 4. Participants uniformly reject the notion that scientists would have the freedom to conduct experiments without constraint on pain-free animals. Participants were asked (Question 10), "If animals that could not feel pain were to be created, should scientists be free to conduct any experiment with those animals?" The majority of participants in all demographic groups disagreed or strongly disagreed that scientists would be granted this freedom by using pain-free animals.

created (Question 9). 58.2% of the animal protection community members and 63.1% of the vegetarians agreed or strongly agreed that a scientist would be morally obliged to use the pain-free animal instead of a pain-sensing animal, as shown in Fig. 3. In fact, of the 48.1% of all people overall who strongly disagreed or disagreed that pain-free animals ought to be created for biological purposes, 39.8% strongly agreed or somewhat agreed that scientists would be morally obliged to use pain-free animals instead of pain-sensing animals.

By vast majority, participants from all demographic groups strongly disagreed that scientists would have the freedom to conduct any experiment with pain-free animals (Question 10), as shown in Fig. 4.

### Discussion

Utilitarianism is the most commonly relied upon ethical framework when decisions are being made about the conduct of experiments on animals. Our debates and our regulations are built around maximizing the benefits in terms of knowledge gained from an experiment while minimizing the pain and distress inflicted upon the experimental animal. However, we have shown that utilitarian ethics cannot adequately explain the guiding ethical principles that participants used to determine appropriate uses of animals. Using the principles of utilitarianism, a pain-free animal would be a preferable animal in the lab setting. Participants, however, were clearly mixed on whether pain-free animals ought to be created,

with most shying away from a purely utilitarian response. These responses, in addition to comments we received, indicate that participants recognize an intrinsic value in animals (and that this value extends to mice).

However, participants seemed to be relying more on utilitarianism when they were confronted with the choice of using a pain-sensing or a pain-free animal in an experiment that would otherwise cause pain. Participants are clearly relying on several different ethical systems in order to answer difficult questions about animal research. This use of different ethical frameworks was most obvious among the participants that were members of the animal protection community or were vegetarians.

Despite differences in the acceptability of the generation of pain-free animals across different demographic groups, respondents uniformly recognize that engineering of pain-free animals might lead to cruelty or abuse, which is unacceptable. A large majority of the participants stated that scientists would not have the freedom to conduct any experiment using the animals. Once again, this indicates an underlying belief in the intrinsic value of animals amongst participants in all categories.

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