A Good Life for Laboratory Animals – How Far Must Refinement Go?

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Summary

Refinement typically is viewed as a means of reducing harms to animals used in laboratory research. Examples of recent research on refinement include improved methods of handling and euthanasia. Focus in the animal welfare literature is now shifting from simply reducing harms that we cause to animals to promoting positive experiences; the question has become "do the animals under our care experience a good life?" Achieving a good life may require that we provide environments that allow animals to express natural behaviors that they are motivated to perform and provide opportunities for positive emotional experiences, such that positive experiences far outweigh negative ones. Recent research in animal welfare science has begun to develop methods for identifying and assessing positive emotional states and assessing how animals view their own condition. Judgments regarding a good life for laboratory animals ultimately require public input, and researchers must seek out effective methods for informed engagement with the public on the quality of living conditions we provide for the animals under our care.

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1 Introduction

A few years ago I was invited to lead a discussion on the welfare of laboratory animals for a *Café Scientifique* session. The aim of these sessions is to bring discussion about science into the community. The venue was Vancouver's Railway Club, an old bar located just a little on the wrong side of our downtown core. I found the poorly lit room at the back of the bar, introduced myself and started speaking with the audience (most of whom I guessed had simply stumbled in looking for a quiet table or the way to the washroom). But what at first seemed like another failed attempt at knowledge translation turned into one of the best conversations I have had about the welfare challenges involved in the use of animals in research. The audience (all involved in some capacity with the use of laboratory animals) was so engaged in the topic that they too had braved a rainy Vancouver night to come out for the discussion.

Why did this dark room in the Railway Club succeed better than most attempts at engaging lab animal users in more convenient and comfortable settings on campus? Were participants hungry for a discussion that could only happen in a dark room over a glass or two of beer? Audience members mentioned that they were reluctant to discuss these issues with their colleagues, family, and friends. In social situations they would describe themselves as "cancer researchers" or "immunologists" but avoid any mention of the animals they worked with.

Perhaps this reticence is a product of a culture of fear and embarrassment around the use of lab animals. Let me contrast two facilities that I use for my research animals. For my research on laboratory rodents I use a facility that is identified by an acronym hiding a euphemism (CDM; the Centre for Disease Modelling). The facility is housed in an unmarked basement behind two sets of unmarked doors, all accessible only with security codes and key cards reminiscent of an old James Bond film. My work on dairy cattle happens at the UBC dairy farm. The farm proudly advertises its presence on the main highway (and a slick web site) for all to see. The farm encourages visits by the public, is always open for tours, and hosts a regular open house receiving hundreds of visitors, including the local Girl Guide troop. It makes sense that UBC takes pride in their cows; almost all dairy farmers are proud of their animals. Even though they struggle with welfare problems, no dairy farmer has the goal of reduction or replacement; these goals only make sense if we believe what we are doing is somehow harmful to the animals.

What would it take to similarly empower animal researchers? Can we refine our methods of care of laboratory animals to the same point where we too are proud of our association with these animals?

2 Mouse dystopia

We should start with an honest assessment of how far it is we need to go. In preparation for this talk, I spoke with one of the leaders in refinement research for lab animals, Joe Garner from Stanford University. When I asked for his vision of a utopian environment for laboratory mice, he said that I should instead consider the reverse. This mouse dystopia might consist of a physical space hundreds of times smaller than their natural home range; the space would be open, lack cover, and be high above the ground in ways known to induce fear; the space would be barren, kept much colder than is comfortable and would not contain material that the mice could use to build suitable protection from the cold. The animals would be kept at light levels much brighter than

they prefer and without the natural dawn and dusk periods when they prefer to be active. Now add a high-pitched whine (from lighting and other equipment), and wind and vibration (from the ventilation). The mice would be handled by creatures they likely perceive as predators, and these creatures would disrupt their furnishings and social landmarks during routine cleaning[1].

Yes, we have a long way to go.

3 Examples of refinement research

The situation is not hopeless. There are many examples of refinements that improve the lives of laboratory animals. I will take you through a few of these to give you a better sense of the science in this area and what it can accomplish. These methods and ideas will, I hope, show you some of the ways we can solve some of the immediate problems in our current methods of housing and caring for lab animals.

Mice typically are housed in rooms kept just over 20°C, but their thermo-neutral zone is in the high 20s. Work for the Garner lab shows that when mice are provided the choice, they spend the majority of their time in warmer enclosures (Gaskill et al., 2009). Cool rooms can still be comfortable if mice are provided appropriate nest building materials that allow them to use their natural skills as nest builders to create microenvironments that provide excellent protection from the cold.

A second example relates to routine handling. One common method of picking up lab mice is by the tail, but new work suggests that this method may be aversive to the animals. Hurst and West (2010) trained mice with three different handling methods: restraint by the tail, restraint in a glass tube that animals could enter freely, or cupped in the researcher's hands. After the training, mice were much more likely to approach the handler if they had experienced either the tube or cupped hands handling method, and these animals showed less evidence of fear when tested in an elevated plus maze.

A final example of refinement research comes from our group's work on gas euthanasia. Mice and rats are most often euthanized using carbon dioxide gas, but high concentrations (>40%) cause pain. A series of studies has shown that both species find concentrations of more than 15% sufficiently aversive that they are willing to abandon a valued food reward to escape from the gas. These animals never choose to stay in a chamber being filled with carbon dioxide to the point of ataxia, let alone recumbency (e.g., Makowska et al., 2009). An alternative method of euthanasia is to first render animals unconscious using an anaesthetic gas such as isoflurane. In a study presented at this conference, Wong et al. (2011) provided rats the choice between staying in a dark chamber filling with either carbon dioxide or isoflurane, or escaping to a brightly lit chamber. Rats find brightly lit areas aversive, so this experiment asks animals to choose which condition they find less aversive. Rats always left the dark chamber when it was filling with carbon dioxide, typically at a concentration of about 8%. In contrast, most rats chose to stay in the dark chamber filling with isoflurane until they were unconscious. These results indicate that rendering animals unconscious with isoflurane is a humane alternative to carbon dioxide.

These examples are encouraging as they illustrate the ways in which simple changes in housing and management can improve the lives of laboratory animals.

4 Benchmarking performance

Developing refinements is a good start, but ultimately we need to find methods of having these implemented in laboratories. How can we do a better job of encouraging research labs to take on these ideas? This problem has received considerable attention in the farm animal welfare literature. The emerging consensus is that documenting animal-based outcome measures, and showing farmers how their performance compares with their peers, motivates farmers to adopt practices that improve performance. Our work with dairy farmers has shown that documenting rates of lameness and leg injuries on farms (an important welfare problem on many dairy farms) has increased farmer awareness of these issues and motivated many farmers to change practices in ways that address the problems (von Keyserlingk et al., 2011). The bad news is that, to date, there has been little or no uptake of this approach to the assessment of research labs, perhaps due to a culture of fear that makes it difficult to gain access to many labs.

5 A good life

Refinements are often thought of as a series of concrete changes that help to mitigate known harms such as rooms that are too cold, handling that induces fear, and exposure to aversive gases. But can a series of small steps aimed at mitigating harms ever take us to a system of care that we can brag about to friends and family and encourage visits by the local Girl Guide troop?

The Farm Animal Welfare Council (2009) encourages us to judge the lives we provide the animals under our care in one of three ways: a life not worth living, a life worth living, and a good life. The types of refinements we have discussed thus far may help take us from "a life not worth living" to "a life worth living," but can standard living conditions for laboratory rodents ever provide the conditions of "a good life?" Fraser (2008) outlines some of the criteria he feels are important in providing a good life for animals. These include 1) that animals should be healthy and thriving, such that one aspect of functioning is not enhanced at the detriment of others, and behavior and physiology systems should not be pushed to where health may break down, 2) that animals have the ability to do things they are strongly motivated to do, including the freedom of selecting among different environmental conditions, and 3) that animals can enjoy life, i.e., that they can experience positive states and that negative states are minimized.

[1] Unfortunately, this pretty much describes the care and housing of laboratory mice housed in ventilated cages used in laboratories around the world.

This way of thinking about animal welfare is now inspiring work on the crucial question of how the animal perceives its overall condition. The affective state of humans can result in consistent perceptual biases, such as perceiving ambiguous stimuli as fearful or upsetting. A series of recent experiments also has shown evidence of such "cognitive bias" in animals (Mendl et al., 2009). In one experiment, researchers trained rats to distinguish between positive and negative training tones. Some rats were kept in standard housing and others were kept in unpredictable housing conditions known to induce a mild state of depression. Rats from the unpredictable housing were more likely to show negative responses to ambiguous test tones (at frequencies intermediate to the two training tones).

Despite the development of promising new techniques, the scientific assessment of animal affect is still in its infancy. The simple truth is that understanding the quality of life of another individual, especially animals that are very unlike us, remains a challenge. One obvious approach to this problem is to preferentially use animals with whom we have a closer bond and for which it is likely easier to interpret mental states. Hanno Würbel at the University of Bern takes this stance when he provocatively argues that we should switch from using laboratory rodents to using dogs because we can more easily establish good relationships with dogs, because they can be easily trained to participate in research, and because this "work" can itself be a source of enrichment for the dogs. We also have a strong, shared societal view of what it means to provide a good life for dogs, which would set clear bounds on the type of care that researchers and the public would consider acceptable.

6 Public values

Just as appraisals of quality of life in human health care settings revolve around the patient, the caregivers, and societal perspectives on a good life and a life worth living, our appraisals of the lives of laboratory animals must also require input from caregivers and society at large. But caretakers have little opportunity to discuss these issues, and the culture of secrecy makes it difficult for the public at large to participate in an informed debate on questions regarding the care and treatment of lab animals. In a series of studies our research group has used a web-based platform to facilitate discussion on animal use (e.g., Schuppli and Weary, 2010). Our aim is to provide easy access to information on lab animal use, along with the opportunity for informed debate on issues of concern. We invite your input at: www.yourviews.ubc.ca/labviews

Hiding lab animals in unmarked bunkers reflects a culture of fear and embarrassment around the quality of life we provide for these animals. We may avoid some controversy in the short term by keeping the public unaware of common practices, but without engaging the public we provide no path for methods of care to come into harmony with public expectations. The use of battery cages for laying hens has been the subject of much public scrutiny and criticism, but this public debate has allowed the industry to move forward. For example, the United Egg Producers (an association of egg producers in the United States) has recently pledged that it will work together to discontinue the use of the conventional battery cages to better align poultry housing methods with public values. More effort will be required on the part of lab animal users to engage with the public in a way that facilitates similar changes in animal laboratories.

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