Harms to Animals – Can We Agree on How Best to Limit Them?

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Summary

The harm benefit framework seems to have wide public support as a basis for making decisions about the use of animals in biomedical research. The present paper, which is the first of two papers that deal with the conceptual underpinning of the harm-benefit analysis, focuses on the assessment of harms to animals. The goals of the 3Rs have gained wide acceptance over the 50 years since they were first proposed. However, there are controversial ethical issues hidden within the 3Rs principle. Five such hidden value conflicts are highlighted and it is argued that these conflicts challenge the idea that adherence to the 3Rs is bound to generate a wide public consensus. It is argued that underlying value differences will lead to conflicting interpretations of how to apply the 3Rs and thereby decide when and how to limit the harm imposed on animals.

Keywords: harm-benefit analysis; 3Rs principle; ethics

1 Introduction

People do not agree about the moral acceptability of using animals for biomedical research. Recent studies undertaken in Denmark (Lund et al., 2012, 2014) identify three kinds of stances among members of the Danish public: Disapprovers (16%) uphold the view that concern for protecting animals outweighs potential benefits to humans; reserved people (49%) hold an ambivalent position and typically shift between approval and disapproval of specific experiments depending on harm-benefit evaluations; approvers (35%) tend to put more weight on potential human benefits than on protecting animals against suffering. Another relevant result of the studies is that most people seem to accept the harm benefit framework as a basis for making decisions about the use of animals in biomedical research.

It is unclear what the outcomes of these studies might be if conducted in other countries. Our guess is that at least in other Western countries the framework will be the same even though there may be some variation in the distribution among the three groups. It is nonetheless likely that there will be a large middle group whose views will depend very much on how harms to animals are balanced against benefits for humans. Viewed in this light, the idea of making harm-benefit assessment a key element in reviews of animal experiments seems likely to find broad public support.

This is the first of two papers that deal with the conceptual underpinning of the harm-benefit analysis. The second paper deals with what is meant by benefit assessment and balancing harms against benefits, whereas the present paper focuses on the assessment of harms to animals. The starting point for our discussion, which is based on a paper published elsewhere (see Olsson et al., 2011), is what seems a near unanimous agreement about using compliance with the 3Rs as a practical way of measuring to what extent one has achieved a reduction in the harms imposed to animals through experimentation.

The goals of the 3Rs – replacing animals with methods not involving live animals [or involving animals of lower sentience], reducing the number of animals needed to get scientifically valid results and refining procedures so that less harm is caused to the animals that are used – have gained wide acceptance over the 50 years since they were first proposed (Russell and Burch, 1959). These goals are now widely known and generally well accepted, both among institutions using animals in research and testing and those working to protect animals against the harm caused by this use. These goals are explicitly referred to in many legislative texts and guidelines and often cited by animal users in their comments to the public. Thus, the 3Rs seem to be used as evidence of the research community's commitment to meet high ethical standards in the care and use of laboratory animals, thereby reducing the harms imposed on animals through experimentation to an absolute minimum.

These principles seem so clear and comprehensive that it is tempting to believe that the only remaining challenge is to make sure that they are fully implemented in laboratories around the world, and that this full implementation will pave the way for broad public support for any continued use of animals deemed necessary. However, we suggest that there are controversial ethical issues hidden within the 3Rs principle. We will highlight five such hidden value conflicts and argue

that these conflicts challenge the idea that adherence to the 3Rs is bound to generate a wide public consensus. We argue that underlying value differences will lead to conflicting interpretations of how to apply the 3Rs and thereby decide when and how to limit the harm imposed on animals.

2 Reduction: Fewer animals used or more efficient animal use?

At first glance, reduction should be a clear and easily measurable target – after all, it is simply a question of counting. However, when Russell and Burch (1959) coined the definition of reduction they contextualized it more in relative than in absolute terms. The *R* for reduction stands for optimizing the number of animals used to achieve a given scientific goal, interpreted as either reducing animal numbers without compromising results or getting more data without increasing sample sizes (Festing et al., 1998). Hence, even if fewer animals are used for each experiment over a given period, global numbers may nevertheless remain unchanged or even increase if more experiments are carried out.

The adoption of reduction measures – such as sophisticated experimental designs, more sensible and accurate tests, minimizing environmental and animal variability and adequate statistical analysis – may have had an impact on the overall decrease in the number of animals used in science in the 1970s-1990s (Hagelin et al., 1999), but progress in the development of replacement alternatives also contributed greatly to this downward trend (Rowan, 2007; Stephens et al., 2001). As the adoption of reduction strategies become widespread, their influence on animal use will tend to plateau, as scientific output continues to grow (as shown by Ware and Mabe, 2012). Therefore, achieving the goal of steady reduction in animal use (as described by the Humane Society of the U.S. (Stephens, 2012) and the European Commission (Louhimies, 2012)) will largely depend on whether non-animal methods can be developed and readily adopted to replace current procedures where animals are needed. Scientists have argued, however, that scientific criteria, rather than political agendas, should guide which methodological approaches should be sought (Hagelin et al., 1999). Scientists have also criticized what they perceive to be overemphasis by animal protection groups on numbers, without considering the increase in scientific activity (Fosse, 2012a).

This example illustrates how groups of people differ in the way they interpret goals such as reduction. These differences likely reflect underlying disagreement on values. According to those who think that using animals in research is wrong, the goal is to avoid all use, and only absolute reductions in animal use are considered progress. For those who consider scientific progress to be paramount, reducing animal use is more a question of efficiency. Reducing overall or relative numbers of animals used may imply a heavier burden on each individual animal or demand the use of more "ethically troublesome" species – such as primates – as we address below.

3 Reduce or refine?

Some procedures can be carried out in a way that they either inflict less harm on more animals or inflict more harm on fewer animals. Examples include the reuse of animals in different experiments versus naïve animals for each experiment, taking more blood from fewer animals versus a smaller amount from a greater number, or in toxicology, testing the use of a higher dose (which produces a greater effect and thus requires fewer animals, but can cause more serious harm to each animal used) versus using lower doses on more animals (De Boo et al., 2005). Reduction/refinement dilemmas may also appear when there is a choice between using one species or another, particularly between rodents or non-human primates or, more commonly, between rodents and fish.

According to some people, the goal of reduction seems to be based on the reverence for life (i.e., one should, as far as possible, avoid taking the lives of animals; Hansen et al., 1999). However, for other uses of animals including the use of animals in food production farming, this argument seems to garner little public support. Instead, the prevailing ethic is something like "it is OK to kill animals as long as they have good lives while they are alive". By extending this line of thinking, one could argue that killing more animals is acceptable if it allows each used animal to live a better life, and perhaps especially if focusing on keeping numbers down results in living conditions where the animal is considered unfortunate to be alive (FAWC, 2009). Weighing animal numbers against the burden on individual animals in this way could also be supported by a moral view that considers "fairness to the individual animal" (Tannenbaum, 1999), i.e., by spreading the load of distress.

The way in which individuals balance the harm of killing against the harm of suffering will vary according to how much value they place on each element. When participants in laboratory animal science training courses were presented with a hypothetical choice between submitting the same mouse to 20 procedures or submitting 20 mice to one procedure each, 40% considered the greater harm to fewer animals the ethically preferable alternative, while 60% found it preferable to use more animals, but to reduce the harm done to each individual (Franco and Olsson, 2014). However, answers shifted when scientists were asked to make the same assessment for non-human primates and companion species, suggesting that the value of life in itself may have a different bearing against the value of quality of life, depending on the species in question.

For a number of reasons (mostly logistic), larger species are usually used – and often re-used – in much lower numbers than small rodents. Hence, if from a sentience point of view all vertebrate (or at least mammalian) species can be considered equal (as some animal welfare scientists have argued; see Baumans et al., 2007), the use of species bearing more anatomical, physiopathological, environmental or phylogenetic similarities with humans (or companion species, for veterinary medicine) would favor reduction without compromising refinement.

4 Are replacement and reduction always relevant?

In 2006, science communicators and animal welfare researchers initiated the Rodentia project in three 4th grade classes in Portuguese primary schools, which aimed – through the study of and interaction with laboratory rats – to foster the development of scientific reasoning competencies and positive attitudes towards animals (Fonseca et al., 2011). The project involved housing laboratory rats in tailor-made habitats in the classrooms, where the children cared for the animals and studied their behavior, both in the home cage and in simple behavioral tests that were planned by the young pupils as they gradually learnt about basic aspects of the scientific method. This project was perceived as stimulating, engaging and educative by the humans involved. The rats remained calm and friendly and regular veterinary monitoring revealed that they were in good health until advanced age when they were euthanised. Despite this success, the project has given rise to some intense debates about this form of animal use.

Why was the Rodentia project controversial? Probably because it conflicted with the ideals of reduction and replacement that aim to avoid animal use when possible, especially in cases where the educational objectives could have been met in other ways. But should these ideals really apply when animals are not subject to any suffering? Indeed, one might argue that the high quality of care provided to these rats met or exceeded the level of care typically provided to companion animals. It may be suggested that applying the goals of reduction and replacement is nonsensical in cases in which animals are provided a good quality of life. Most people would not consider it appropriate to apply these goals to the keeping of companion animals or even farm animals, as long as the quality of life is good.

5 How realistic is replacement?

Replacement enjoys a particular standing among the 3Rs. It was the first of the Rs to be introduced by Russell and Burch (1959), reflecting the intended order in which the Rs were to be considered. Questions about reduction and refinement are only relevant if replacement has first been considered and excluded. The goal of replacement also found widespread support, in part because it is the only goal that is fully compatible with the animal rights perspective, stating that animal use solely for human benefit should not be permitted. In this sense, replacement is probably the easiest of the 3Rs to be communicated; "not tested on animals" is a more powerful message than "tested on fewer animals" or "tested on animals that experienced less distress." Replacement models often also illustrate technical and scientific innovations, typically the result of years of development, which probably adds to their allure. Recently, however, scientists have started to become aware of the potential risk of *overselling* replacement.

Policy and planning for biomedical research will vary depending on how realistic one perceives the option of full replacement. The anti-vivisection movement often argues that full replacement is imminent. For example, the British Union for the Abolition of Vivisection (BUAV, 2014) argues that "it's time to move on. In the 21st century we have technological options not available before – computer modelling, human cell and tissue cultures, microdosing, sophisticated imaging and analysis." If replacement is within reach and especially if it is going to happen soon, the goals of reduction and refinement lose their relevance and there is no need for long-term investment to develop approaches that use fewer animals and cause them less harm. The pre-eminence of replacement is clear even in the policies of research funding agencies. For example, the European Commission Framework Programs (the joint instrument for funding collaborative research in the European Union) directs applicants to take the 3Rs into account, but the only R that is given specific funding is replacement.

In contrast, laboratory animal scientists often highlight that animals are still being used in large numbers and that this use is likely to continue. A leading 3Rs expert recently declared: "As things stand today, it's hard to imagine a world where animal research has been replaced with alternative methods. To be frank, I don't foresee this happening any time soon" (Fosse, 2012b). This is also the stance of the Basel Declaration signatories (Basel Declaration Society, 2010). For those who hold this view, continued work on reduction and refinement remains as important today as it was for Russell and Burch in 1959.

These differences in the outlook probably stem from the divergent interests of activists and scientists using animals. Routine activities such as testing have captured the interests of activists, perhaps because this use is seen as more trivial and because it is for these routine tests that we have seen rapid and promising developments in replacement (Baker, 2011). In contrast, many scientists are most interested in discovery research addressing new ideas, often using newly developed methodologies. It is for this type of research that Fosse and others find it unlikely that non-animal alternatives will soon be available. But there is also a moral disagreement underlying the two points of view: the focus on replacement stems from a no-use view (in line with the disapprovers mentioned in the beginning of the text), whereas a focus on reduction and refinement is more in line with the view that it is acceptable to use animals as long as we do it for a good reason and look after the animals' welfare as far as possible (in line with the reserved people and the approvers).

6 Is relative replacement reasonable?

The idea that there is an ethical gain in moving from "higher" to "lower" organisms was originally referred to as "comparative replacement" (Russell and Burch, 1959) and is made explicit in legislation such as the European Directive 2010/63/

EU which requires scientists, when selecting between procedures, to choose the ones that "involve animals with the lowest capacity to experience pain, suffering, distress or lasting harm" (article 13.2) (EU, 2010). This seems intuitively correct: a procedure carried out on an animal with less capacity to experience pain would result in less harm than the same procedure carried out on an animal with more capacity to suffer. The problem is that there is no clear-cut way of defining the capacity to experience pain, suffering or distress. Implementing this approach in practice would require some type of sentience scale, a hierarchy of species based on their capacity to suffer. Attempts have been made to define criteria and to distinguish larger groups of species (Smith and Boyd, 1991), but even this is debatable (Hubrecht, 2011). Cognitively more complex animals may have a greater ability to anticipate, remember or otherwise relive unpleasant experiences and, hence, have greater potential for suffering. However, these abilities may also allow for a greater use of gating mechanisms that distract animals from pain or the ability to compensate for periods of suffering with positive life experiences.

Rather than reflecting the ability to suffer, existing rankings seem instead to relate to the socio-zoological scale (Arluke and Sanders, 1996). This ordering of animals is based on the way they are perceived by humans, with those highly valued at the top of the scale and those considered harmful or repulsive at the bottom (Driscoll, 1992). Among the vertebrate species used for research, the hierarchy starts with the great apes (at the top), followed by other non-human primates, dogs and cats, pigs, etc., with rodents and fish near the bottom. This is reflected in the way using different animal species is seen by both the general public (Eurobarometer, 2010) and scientists (Franco and Olsson, 2014).

This is not to say that the socio-zoological scale lacks moral relevance; for those holding a contractarian or relational view on ethics, this scale will be central (see Olsson et al., 2010), but for those who are more focused on animal welfare or respect for animals, this is not a relevant consideration. So again, moral principles are at stake when deciding on how to interpret and apply the 3Rs.

7 Concluding remarks

The wide acceptance of the 3Rs has provided a roadmap for addressing issues regarding harms caused to animals as part of animal experimentation, but important disagreements about the values that underline the Rs must be better understood and addressed. Some of these disagreements cannot be easily settled as they result from differences in underlying views on the human-animal relationship. These disagreements do not undermine the value of the 3Rs, but rather reinforce the need for deliberation, involving researchers and the public in developing widely accepted compromises concerning policies that address these issues.

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