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The 3Rs Principle – Mind the Ethical Gap!

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Summary

Over the 50 years since they were first proposed, the 3Rs (Replacement, Reduction, Refinement) have made a tremendous impact. These principles seem to unify concerns for better science with causing less harm to animals. The ideas behind the 3Rs are so intuitively compelling that it is tempting to believe that full implementation is merely a matter of time, and once the 3Rs are widely implemented, the public will fully support any continued laboratory animal use that is deemed necessary. In this paper, we argue that these conclusions are unlikely to be correct, in part because the 3Rs are rich in ambiguities, and any implementation requires resolving the dilemma that promoting one R will sometimes directly or indirectly conflict with promoting another. For example, should Reduction be conceived in absolute or in relative numbers? Is it really possible (or desirable) to use relative Replacement (i.e., switching from a "higher" to a "lower" species)? Which of the 3Rs should receive priority? Until now, some scholars have focused on identifying Replacements for the use of live animal experiments in research, while others have focused on Reduction in the number of animals used and Refinements in procedures such that animals experience less harm. Meaningful contact between these camps may be limited, however. In some cases, the goals of Reduction and Refinement actually conflict, as, for example, in the choice to re-use animals (and hence reduce total animal usage) or to avoid re-use (and hence avoid the negative effects of repeated exposure to harmful procedures). We conclude that there is now a need for a more thorough ethical discussion on how to resolve these issues.

Keywords: 3Rs, value conflicts

1 Introduction

The goals of the 3Rs (replacing animals with non-animals (or animals of lower sentience), reduction in the number of animals used, and refining procedures so less harm is caused to the animals that are used) have gained wide acceptance over the 50 years since they were first proposed. These goals are now widely known and generally well accepted, both among institutions using animals in research and testing and among those working to protect animals from the harm caused by this use. These goals are explicitly referenced in many legislative texts and guidelines and are 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.

These principles seem so clear and comprehensive that it is tempting to believe that the only remaining challenge is to see that these 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, there are important ethical issues that the 3Rs do not address, e.g., to what extent it is acceptable to genetically modify animals, or does the purpose of the experiment justify animal use. These issues are discussed elsewhere (Schuppli et al., 2004; Ibrahim, 2006) and will not be addressed in this paper. Instead, we focus on controversial ethical issues hidden within the 3Rs principle. We will highlight five such hidden value conflicts and argue that these conflicts will challenge the idea that the 3Rs principle is bound to generate a wide public consensus. We argue, rather, that underlying value differences will lead to conflicting interpretations on how to apply the 3Rs principle.

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. Reduction also should proceed in lock step with Replacement, as every animal test replaced by a non-animal alternative represents a reduction in the number of animals used. Unfortunately, the data available (Taylor et al., 2008; Ormandy et al., 2009) indicate there is no longer any real progress in reducing the total number of animals used. Indeed, animal use has been stable or on the rise since the 1990s.

This evidence is taken by some critics of animal use (BUAV, 2011) as an indicator that we have failed to meet the goal of Reduction. Policymakers seem to have abandoned the idea of setting numerical targets for Reduction (see EBRA, 1996), and some scientists have argued that reducing the total numbers used

is not even desirable, as it might limit the expansion of animal research into new areas (Hagelin et al., 1999). Major institutions that promote the 3Rs now describe Reduction in relative rather than absolute terms as "methods that minimize animal use and enable researchers to obtain comparable levels of information from fewer animals or to obtain more information from the same number of animals"[1].

Overall, this issue illustrates how different groups of people differ in how they interpret goals such as Reduction. These differences likely reflect underlying disagreement on values. For those who think that using animals in research is in itself wrong, the goal should be to reduce all use, and thus only absolute reductions in the numbers of animals used can be considered progress. For those who consider the scientific goals as paramount, the issue of animal use is simply a question of efficiency. The use of fewer animals to achieve the same scientific goal is better, but the total number of animals used can increase if this results in more knowledge.

3 Reduce or Refine?

Some procedures can be performed such 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 using 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.

The goal of Reduction follows from the "badness of killing" argument (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 a good life while they are alive." By extending this line of thinking, one could argue that killing more animals is acceptable if it allows each animal used to live a better life, and perhaps especially if this would avoid that animals live in conditions where the animal was considered unfortunate to be alive (FAWC, 2009). Weighing animal numbers versus the burden placed on the individual animals this way could 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 individuals trade-off the harm of killing versus the harm of suffering will vary with 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 to be the ethically preferable alternative, while 60% found it preferable to use more animals but to reduce the harm done to each individual (Franco et al., 2010).

4 Are Replacement and Reduction always relevant?

In 2006, science communicators and animal welfare researchers initiated the Rodentia project in three Portuguese primary schools. The aim was that through the study of and interaction with laboratory rats 4th-grade children would learn about scientific methodology and animal behavior (see 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 learned about basic aspects of the scientific method. This project was perceived as stimulating, engaging, and educational 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 euthanized. Despite this success, the project has given rise to some intense debate 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, perhaps especially in the case of teaching, where it is typically assumed that the educational objectives could have been met in other ways. But should these ideals really apply in cases like this when animals are not subjected 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. We suggest 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 their 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 has received widespread support, in part because it is the only goal that is fully compatible with the animal rights perspective that animal use solely for human benefit should not be permitted. In this sense, Replacement is probably the easiest of the 3Rs to communicate; "not tested on animals" is a more powerful message than, "tested on fewer

[1] NC3Rs. What are the 3Rs? http://www.nc3rs.org.uk/page.asp?id=7 (accessed 26.09.2011).

animals" or, "tested on animals that experienced less distress." Replacement models also often 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, BUAV 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" (http://www.buav.org/humane-science/key-criticisms/). If Replacement is within reach, and especially if it will happen soon, the goals of Reduction and Refinement become of little 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 Replacement is the only R given specific funding.

In contrast, laboratory animal scientists often contend that animals are still being used in large numbers and that this use is likely to continue. A leading 3Rs expert recently declared that "entire animals are indispensable as we chart unknown and new scientific waters ... there is no replacement for these animals – we do not yet know what can be replaced" (Fosse, 2010). For those who take this view, continued work on Reduction and Refinement remain as important today as they were for Russell and Burch in 1959.

These differences in outlook probably stem from the divergent interests of the activists versus the scientists using animals. Routine activities such as testing have captured the interests of activists, perhaps because this use is seen as being more trivial, and 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 (2010) 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, whereas a focus on Reduction and Refinement is more in line with the view that it is OK to use animals, as long as we do it for a good reason and look after the animals' welfare as far as possible.

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). It is made explicit in legislation such as the European Directive, which requires scientists, when selecting between procedures, to choose those that "involve animals with the lowest capacity to experience pain, suffering, distress or lasting harm" (article 13.2) (European Union, 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 that there is no clear-cut way of defining capacity to experience pain, suffering, or distress. To implement 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). More cognitively 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 put periods of suffering into balance 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 how they are perceived by humans, with those highly valued at the top of the scale and those considered harmful or repulsive at the bottom. 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 not to say that the socio-zoological scale lacks moral relevance; for those taking a contractarian or a relational outlook 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 how to interpret and apply the 3Rs principle.

7 Concluding remarks

The wide acceptance of the 3Rs has provided a roadmap for addressing issues in laboratory animal welfare, 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 sensible policies that address these issues. Since closing it is bound to be an impossible task, minding the ethical gap may be the best we can do to avoid falling into it.

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