The Ethics of Animal Research: A UK Perspective

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Abstract

The Nuffield Council on Bioethics, an independent body in the United Kingdom, has published a 2005 report titled *The Ethics of Research Involving Animals*. The Report, produced by a Working Party that represented a wide range of views, seeks to clarify the debate that surrounds this topic and aims to help people identify and analyze the relevant scientific and ethical issues. The Working Party considered the arguments surrounding whether animal research yields useful results, and recommends that its predictability and transferability should be evaluated more fully, particularly in controversial areas. Commonly encountered ethical questions and arguments were considered in order to understand what lies behind disagreement on the moral justification of animal research. Four possible ethical positions on animal research, which represent points on a continuum, are described. Despite the range of views that exist among members of the Working Party, the Report presents a "Consensus Statement" that identifies agreement on several important issues. Building on this statement, recommendations are made for improving the quality of the debate and promoting the 3Rs (refinement, reduction, and replacement).

Key Words: animal research; ethics; experimentation; moral; Nuffield

Introduction

Research involving animals has been the subject of intense debate in the United Kingdom, the rest of Europe and the United States. The tactics employed by organizations campaigning to end animal experimentation, peaceful or otherwise, regularly feature in the British media. More recently, scientists have become more active in their defense of animal research by organizing protest marches and petitions, which have received significant media attention. Similarly, while controversy about animal research has existed in the United States for several decades, a recent increase in violent and threatening behavior by animal rights activists has heightened attention on the issue. In both countries, too often the debate on animal research is portrayed in a polarized manner, differentiating only between those "for" and those "against" all animal research. However, a closer examination reveals a more complex picture: people have very different views on particular kinds of research depending on the aims, type, and location of research, the species of animal used, and the degree of suffering experienced in the different contexts.

The Nuffield Council on Bioethics is an independent body in the United Kingdom that examines ethical issues raised by new developments in biology and medicine.[1] The Council has published a Report, *The Ethics of Research Involving Animals,* which seeks to clarify the debate and aims to help people analyze the scientific and ethical issues. The Report is the outcome of 2 years of deliberations by a Working Party that I chaired, composed of academic and industry scientists, philosophers, members of animal protection groups, and one lawyer.[2] To inform their discus-

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[1]See the Council's website (www.nuffieldbioethics.org) for additional information.

[2]The members of the Working Party include the following: Baroness Perry of Southwark (Chairman), House of Lords Science and Technology Select Committee and Pro-Chancellor of the University of Surrey; Professor Kenneth Boyd, Professor of Medical Ethics, University of Edinburgh; Professor Allan Bradley FRS, Director, The Wellcome Trust Sanger Centre, Cambridge; Professor Steve Brown, Director, MRC Mammalian Genetics Unit, MRC Mouse Genome Centre, Medical Research Council, Harwell; Professor Grahame Bulfield, Vice-Principal and Head of College of Science and Engineering, University of Edinburgh; Professor R. D. Combes, Scientific Director, Fund for the Replacement of Animals in Medical Experiments (FRAME); Dr. Maggy Jennings, Head of Research Animals Department, Royal Society for the Prevention of Cruelty to Animals; Professor Barry Keverne, Director of Sub-Department of Animal Behaviour, Department of Zoology, University of Cambridge; Dr. Mark Matfield, Executive Director, The Research Defence Society; Dr. Judy MacArthur Clark, Chair, Farm Animal Welfare Council; Professor Ian McConnell, Professor of Veterinary Science, Centre for Veterinary Science, Department of Clinical Veterinary Medicine, University of Cambridge; Dr. Timothy H Morris, Head of Comparative Medicine and Investigator Support, Laboratory Animal Science (LAS) UK, GlaxoSmithKline; Professor Martin Raff FRS, MRC Laboratory for Molecular Cell Biology, University College London and member of the Nuffield Council; Mr. Nick Ross, Broadcaster and member of the Nuffield Council; Dr. Lewis Smith, Syngenta CTL; Professor John Spencer, Professor of Law, Selwyn College, University of Cambridge; Ms. Michelle Thew, Chief Executive Officer,

sions, the Working Party sought advice from a wide range of experts and held a public consultation for 3 months.

UK regulation on animal research is often cited as the strictest in the world. The Animals (Scientific Procedures) Act 1986[3] requires researchers to obtain several types of licenses from the government before any animal can be used in harmful procedures. Before a license is granted, researchers must carry out a "cost-benefit assessment" to ascertain whether the likely benefits of the research (e.g., in terms of knowledge gained) outweigh the costs to the animals (possible pain, suffering, or distress). Government inspectors ascertain that research facilities are adhering to regulations and guidelines. The Act also requires researchers to demonstrate that refinement, reduction, and replacement (the 3Rs[4]; Russell and Burch 1959) have been implemented as far as possible before a license is granted. In 2004, the UK government established a National Centre for the 3Rs (NC3Rs), which funds 3Rs-related research, develops a range of resources, and organizes workshops to disseminate and advance information.[5]

Assessing Pain, Distress, and Suffering in Animals

The impact of research on animals and their welfare depends on the nature of the experiments. However, many factors other than the experiment itself can have an effect, including conditions during breeding, transport, housing, handling, and restraint. Although it is impossible to get "inside the mind" of an animal, we can make meaningful "approximations" in assessing the pain and suffering they may experience. Observations of animal behavior and evaluation of signs of distress (e.g., increased levels of specific hormones or weight loss) combined with an awareness of species-specific needs and a critical use of empathy can lead to useful assessments of animals' well-being.

Using genetically modified (GM[4]) animals in research may raise particular problems in assessing welfare. The implications of introducing and deleting specific genes cannot usually be predicted, and the effects on welfare can be difficult to detect and measure. One report suggested that 10% of GM animals experienced harmful effects. Another found that 21% experienced minor discomfort, 15% experienced severe discomfort, and 30% had an increased risk of death and disease.[6] Another concern is that most methods of producing GM animals are inefficient, and large numbers of animals are required to produce individual strains.

Does Animal Research Lead to Valid Results?

Although the focus of the Report was on the ethical issues raised by animal research, scientific questions also needed to be considered. Indeed, if it were the case that harmful animal research provided no useful knowledge or application, it would be difficult to justify it morally.

There is disagreement about whether research involving animals is useful for studying human disease and for toxicity testing. Some claim that because of biological differences between humans and animals, results from animal studies cannot be applied reliably to humans. Cases of medical research involving animals where progress has been difficult, such as cancer and HIV/AIDS research, are used to support this view. Adverse drug reactions (ADRs[4]) are also seen by some as evidence that animal research cannot always predict the effects of drugs and medicines on humans. However, such claims need to be treated with some caution. ADRs have a number of causes. Many are avoidable, for example, where they arise from prescription errors or from interactions between different medicines taken simultaneously. In 2004, researchers conducting the largest prospective analysis in the United Kingdom of ADRs as a cause of admission to hospital found that more than 70% were avoidable and could have been predicted by taking into account pharmacological properties of the medicines involved.[7] Phases I–II of human clinical trials in the development of a medicine include up to 5,000 patients to monitor efficacy and safety. If severe ADRs occur during these trials, the development of the medicine is not usually taken further. However, ADRs may occur at very low statistical frequencies (e.g., 1 in 10,000) and hence may not be revealed at this stage. Thus, in making inferences about the occurrence of ADRs, and the role that animal research plays, it is unknot helpful to generalize. ADRs can occur for a number of reasons and could, in principle, also be caused by a medicine that, hypothetically, had been developed without the use of animals.

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[3]Home Office Animal (Scientific Procedures) Act 1986. Available online (http://www.archive.official-documents.co.uk/document/hoc/321/321-xa.htm).

[4]Abbreviations used in this article: 3Rs, refinement, reduction, and replacement; ADR, adverse drug reaction; GM, genetically modified.

[5]See the NC3Rs website (www.nc3rs.org.uk) for further information.

[6]Reported in BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on Refinement (2003) Sixth Report: Refinement and reduction in production of genetically modified mice Lab Anim 37:3, Supplement S1–49, available online (http://www.ingentaconnect.com/content/rsm/lab). Accessed April 21, 2005; Thon R, Lassen J, Kornerup Hansen A, Jegstrup IM, Ritskes-Hoitinga M. 2002. Welfare evaluation of genetically modified mice—An inventory study of reports to the Danish Animal Experiments Inspectorate. Scand J Lab Anim Sci 29.

[7]Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, Farrar K, Park BK, Breckenridge AM. 2004. Adverse drug reactions as cause of admission to hospital: Prospective analysis of 18,820 patients. BMJ 329:15–19.

Most of those who argue that animals can provide scientifically valid "models" for humans do not contend that every use of animals yields immediately useful results, nor that the use of animals is always the most suitable approach. However, they firmly refute the claim that cases in which animal experiments can be regarded as flawed are sufficiently widespread and indicative of a common, underlying difficulty such that the concept of animal research as a whole is flawed. The Working Party examined arguments about the implications of the evolutionary relatedness of humans with other animals. It concluded that continuities in the form of behavioral, anatomical, physiological, neurological, biochemical, and pharmacological similarities provide sufficient grounds for the hypothesis that animals can be useful models to study specific aspects of biological processes in humans, and to examine the effects of therapeutic and other interventions. A wide spectrum of different kinds of biomedical research activity is described in the Report, between them employing a variety of different kinds of animal model to address a range of different objectives. They included basic physiological studies (Chapter 5), more applied work on human diseases and genetic disorders (Chapters 6 and 7), pharmaceutical discovery and development (Chapter 8), and toxicity testing (Chapter 9). The examples show that research and testing involving both genetically normal and GM animals has proved relevant to humans and, in combination with other methods such as in vitro and clinical studies, has contributed significantly to biomedical understanding. The cases presented show that there are numerous instances in which extrapolations from animal studies can be made in a meaningful way, provided that the animals involved are sufficiently similar to humans in relevant aspects of the biological phenomenon or disease being studied.

The Working Party concluded that in principle, animals can be useful models for studying specific aspects of human biology, and the effects of chemicals and medicines in humans. However, each type of research or testing must be judged on its own merits on a case-by-case basis. The Working Party recommended that the predictability and transferability of research involving animals should be evaluated more fully. In response to public concerns, priority should be given to reviewing the transferability of research that causes substantial pain and suffering to animals, and research that involves primates. A positive development in this area has been the establishment by four UK medical organizations of a working group to study the scientific basis for using primates in research and the available alternatives. At the time of writing, the group was due to report its findings in autumn 2006.[8]

Is It Morally Acceptable to Cause Pain and Suffering to Animals?

The Working Party considered commonly encountered ethical questions and arguments to clarify the debate, identify agreement, and understand what lies behind remaining disagreement on whether research on animals is morally justified. The question of defining the moral status of humans and animals often arises in the debate on animal research. Are humans morally more important than all animals? Is there a sliding scale with humans at the top and the simplest animals at the bottom? Or are humans and animals morally equal? The Working Party suggested that the proper moral treatment of a being depends on the characteristics it possesses, rather than simply on the species to which it belongs. It identified five morally relevant features:

- Sentience (the capacity to feel pleasure and pain);
- Higher cognitive capacities (e.g., the ability to use language and learn complicated tasks such as making and using tools);
- The capacity to flourish (the ability to satisfy species-specific needs);
- Sociability (being a member of a community); and
- Possession of a life (attributing value to life itself).

What weight should be given to each of these morally relevant features in considering whether or not research is acceptable? Are they factors to be weighed against human benefit? Should they be understood as absolute limits? For example, should any use be prohibited for animals that are capable of suffering, or only for those that have higher cognitive capacities? Many people seem to support a "hybrid" approach. This approach involves a combination of establishing definite limits (e.g., "animals with higher cognitive capacities, such as orangutans, should never be used in research") and weighing the costs and benefits of a particular action (e.g., "research that causes minimum pain to a mouse is acceptable if it ascertains the safety of a chemical"). This approach can also be found in the UK Animals (Scientific Procedures) Act 1986.[9]

The ethical debate comes down to disagreement on two questions: (1) What are the absolute limits?, and (2) How do we weigh the different morally relevant factors within the permitted limits? To provide answers, we need to consider at least five further related questions:

- What are the goals of research?
- What is the probability of success?
- Which animals are to be used?

[8]Academy of Medical Sciences/Medical Research Council/Royal Society/Wellcome Trust study into the use of non-human primates (NHP) in research. Available online (www.nhpstudy.com).

[9]Home Office Animal (Scientific Procedures) Act 1986. Available online (http://www.archive.official-documents.co.uk/document/hoc/321/321-xa.htm).

- What effect will there be on the animals used in the experiment?
- Are there any alternatives?

After considering these questions, members of the Working Party could not agree on a single ethical position that reflects the range of views that exists in society. Instead, it presented an outline of the following four possible ethical positions, which represent points on a continuum:

1. Valuable animal research requires no further ethical justification (no member of the Working Party took this position).
2. Animal research is morally acceptable if the costs (e.g., the pain and suffering experienced by the animal) are outweighed by the benefits (e.g., the knowledge gained from the research), but every reasonable step must be taken to reduce the costs to animals.
3. Animal research poses a moral dilemma. Whatever you decide, you will act wrongly, either by neglecting human health and welfare or by harming animals.
4. There is no moral justification for any harmful research on animals that is not to their benefit.

Can We Ever Agree on Research Involving Animals?

Despite the wide range of views that exists among members of the Working Party, the Report presents a "Consensus Statement" that identifies agreement on several important issues. For example, members of the Working Party agreed that historically, animals have been used in a wide range of scientific research activities that have provided many benefits to society. They also agreed that a world in which the important benefits of such research could be achieved without causing pain and suffering to animals must be the ultimate goal.

All members of the Working Party acknowledged that as in other areas of ethically contentious issues such as abortion or euthanasia, any society needs to settle on a single policy for practical purposes. Steps therefore need to be taken to reduce as far as possible existing disagreement, and the Working Party sought to make unambiguous recommendations in specific areas in order to accomplish this task.[10] The recommendations focus on promoting the 3Rs and improving the quality of the debate, and are outlined in more detail below.

[10]Several recommendations aim to improve the conditions under which animals are used. All members of the Working Party endorsed them, but the endorsement should not be taken to imply the acquiescence to animal experimentation of those members who fundamentally oppose it. Some members would have preferred the recommendations to have gone further in specific areas, but they nevertheless did accept them as steps in the right direction.

The Working Party concluded that the concept of the 3Rs and the hybrid moral position (some absolute limits, some weighing of the costs and benefits) could be accepted, or at least tolerated, by most members of society. By fine tuning the approach to animal research—relaxing some restrictions and introducing others—more people may be able to endorse the regulations than has been the case so far. Not everyone will be able to fully support the 3Rs and the hybrid moral position, but they may be able to tolerate it as a compromise while continuing to campaign for changes in policy.

Improving the Debate

If this approach is to count as a fair process, all involved need access to relevant information about research involving animals in order to judge whether it is justifiable. In addition, the discussion must be conducted in a fair and informed manner, to permit all reasonable participants to present their case. Finally, there must be a genuine possibility for policies to be readjusted. Forcing research out of the country through the use of violence and intimidation is no solution to the complex issues raised by the research. The Working Party agreed that the threat and use of violence and intimidation by a small group of activists to pursue the case against research on animals is morally unjustified.

The Working Party made several recommendations on how the availability of information on research involving animals could be improved. For example, it suggested that researchers should be more open to two-way dialogue to improve and sustain public trust. It also proposed that annual statistics on animal research produced by the UK government should be revised to reflect how many animals of a particular species experience pain and suffering during experiments, to what degree, and for how long. The presentation of the information was improved in this year's publication of statistics (Home Office 2006), but further changes are needed to fulfill the Working Party's recommendation. These changes may in fact become mandates under European legislation in the future: the European Commission consulted in the summer of 2006 on revisions to its Directive for the protection of animals used in experiments. Depending on the outcome, the revisions may require improvement in the quality and usability of the annual statistics produced in all member countries.

The 3Rs

The Working Party concluded that practical advances in scientific methods can make a considerable contribution to the reduction of disagreement on research involving animals. For this reason, the importance of the 3Rs, and especially the need to find replacements, cannot be overstated. There is a moral imperative to develop new alternative methods where gaps exist and to use currently available

alternatives. To improve the application of the 3Rs, the Working Party made a number of recommendations, including the following:

- A thorough analysis of the scientific barriers to replacements should be undertaken by the relevant government department.
- Scientific publications should include more information on how the 3Rs have been applied in the work described.
- Funding bodies should support applications for research that aims to find solutions for implementing the 3Rs in challenging areas.
- Harmonization of test guidelines, so that a single study design is acceptable to regulatory authorities in many countries, is a very valuable way of reducing the use of animals in safety testing. The United Kingdom should make it a priority to identify areas in which harmonization is difficult.
- The government and the scientific community should engage more in a systematic and visible (to ensure accountability) search for methods involving the 3Rs in toxicology.

Many varied opinions were expressed throughout the course of the Working Party. A respect for beliefs different from one's own enabled members of the group to agree on the Consensus Statement and to present recommendations, in particular in relation to the 3Rs and to improving the quality of the debate. While it was not possible to attribute to all members of the group the recommendations presented on any one issue, all members do accept that the recommendations are valid contributions to the debate. Members believe that this approach should contribute to fair and balanced discussions among individuals and should aid decision making by those in government or other official and regulatory bodies, both in the United Kingdom and abroad. In particular, it is crucial to avoid polarization of the debate if the true complexity of the issues is to be acknowledged and if the debate is to move forward.

References

Home Office. 2006. Statistics of Scientific Procedures on Living Animals Great Britain 2005. Norwich, UK: Stationary Office. Available online (http://www.homeoffice.gov.uk/rds/pdfs06/spanimals05.pdf).

Nuffield Council on Bioethics. 2005. The Ethics of Research Involving Animals. London, UK: Nuffield Council on Bioethics. Available online (www.nuffieldbioethics.org/go/ourwork/animalresearch/introduction).

Russell WMS, Burch RL 1959. The Principles of Humane Experimental Technique. London: Methuen & Co. LTD. [Reissued: 1992, Universities Federation for Animal Welfare, Herts, England.] Available online (http://altweb.jhsph.edu/publications/humane_exp/het-toc.htm).