Bioethics
A Coursebook

Compost Collective

https://www.openbookpublishers.com

ISBN Paperback: 978-1-80511-510-6
ISBN Hardback: 978-1-80511-511-3
ISBN PDF: 978-1-80511-512-0
ISBN HTML: 978-1-80511-514-4
ISBN EPUB: 978-1-80511-513-7

DOI: 10.11647/OBP.0449

Cover image by Bartaku Vandeput.
Cover design by Jeevanjot Kaur Nagpal

5. Animal Ethics and Animal Experimentation

Animal ethics

Discussion: Do you think it is permissible to eat other-than-human animals? What arguments for and against eating animals can you come up with?

Humans and other-than-humans

What are our duties and rights towards other-than-human animals? Should we eat them? Should we use them in animal experiments? Discussions around these topics often lead to heated debates. The way we view animals, whether it relates to their place in our lives or the cultural context we find ourselves in, influences our perspectives on practices such as consuming meat. We differentiate between animals that we classify as food and those we classify as companions. Why do we draw such distinctions? Is it even acceptable to draw moral distinctions between humans and other-than-human animals? Often, discussions surrounding animal experiments or meat eating resort to lifeboat scenarios. In such scenarios, people are asked to weigh the lives of a human vs an other-than-human animal. In the lifeboat case, it is then assumed that, of course, if there is only a place for three in a lifeboat, and there are three humans and a dog, the dog will have to go. However, such oversimplified scenarios fail to encompass the complexities of real ethical considerations. Indeed, because many intuit that the dog would have to go, it is automatically extrapolated that it is acceptable to eat meat or to engage in animal experimentation. However, we tend to forget that the lifeboat is an exceptional situation, one that is probably never going to happen. In fact, it has nothing to do with the complexities of the real-life ethics of animal experimentation or meat eating.

Before we delve into ethical questions regarding animals, more specifically animal experimentation, it is interesting to look at how views on human relations with other-than-human animals have evolved historically. What follows focuses on Western philosophy. However, we must not forget that much can be gained through engaging

 https://doi.org/10.11647/OBP.0449.05

with other-than-Western approaches that have not taken the supremacy of humankind at face value.

In *On the Soul*, Aristotle (1984) describes the existence of different types of souls, each associated with specific properties and functions. According to Aristotle, plants possess the vegetative soul, which allows them to grow, reproduce, and nourish themselves. Animals, in addition to the vegetative soul, possess a sensitive soul, enabling them to perceive their surroundings, experience sensations, and engage in basic forms of cognition. Humans, according to Aristotle, possess vegetative and sensitive souls as well, but what sets them apart is the rational soul. This rational soul endows humans with the unique ability to engage in higher-order thinking and reason and possess intellectual capacities, distinguishing them as the pinnacle of the natural world. At the same time, there is a continuum from plant to human being. In Christian thinking in medieval times, this idea that humans are above plants and other-than-humans took over. At the same time, there was also the idea of God, who is above humans. Indeed, human beings are created in God's image, but at the same time, they share lower functions with other-than-human animals. What we should aspire to, however, is to be more like God and less like our animal brethren. Animals, moreover, are created to serve human beings. This is the idea of *separation*. We must strive to be more god-like, and too much engagement with animals is frowned upon or even morally suspect. This idea still survives in the modern day. Expending lavish amounts of money or love on one's companion animals is often seen as untoward, as if this is somehow misguided.

In early modern philosophy, René Descartes firmly separated animals and humans (1972). What we have in common with them is our body, which is machine-like, an automaton. Only human beings have souls and can feel and think. This is the origin of modern animal experimentation. As animals have the same 'machinery' as human beings, but no soul, they can be cut open and experimented on at will. At the same time, it is rumoured that Descartes had a dog, Monsieur Gnat, that he doted on. This is a fine example to demonstrate that even if we are rationally convinced that animals are mere automata, this conviction is overruled by the relation we have with them.

Charles Darwin put human beings right back in the continuum of the tree of life (1871). We are animals, we have animals as ancestors. This does not automatically mean that human beings fall from their pedestal. Some people would argue that human beings are at the top of the tree of life, that they are the acme of evolution. Human beings are the most evolved, the most superior. Others argue that there is no such hierarchy in evolution. We are animals amongst other animals.

Animal ethics

What rights and duties do we have towardsother-than-human animals? What rights do they have? To answer these questions, we can look back at the moral theories we saw in Chapter 2. Jeremy Bentham, one of the arch-fathers of utilitarianism, had a

hedonistic view of what is good. For him, what is good is pleasure, and what is bad is suffering. This means that for him, all creatures that can suffer count, and should be included in moral reflection.

> The day may come, when the rest of the animal creation may acquire those rights which never could have been withholden from them but by the hand of tyranny. The French have already discovered that the blackness of skin is no reason why a human being should be abandoned without redress to the caprice of a tormentor. It may come one day to be recognized, that the number of legs, the villosity of the skin, or the termination of the os sacrum, are reasons equally insufficient for abandoning a sensitive being to the same fate. What else is it that should trace the insuperable line? Is it the faculty of reason, or perhaps, the faculty for discourse? [...] the question is not, Can they reason? nor, Can they talk? but, Can they suffer? Why should the law refuse its protection to any sensitive being? [...] The time will come when humanity will extend its mantle over everything which breathes. (Bentham, 1789, chapter 17)

Peter Singer, a contemporary ethicist, has taken up Bentham's idea in his seminal work *Animal Liberation* (*Singer, 2002*), as we have seen in the chapter on environmental ethics. He is often associated with animal rights, but in fact, rights are deontological concepts. They are somewhat inalienable. In a utilitarian approach, interests can be weighed against one another. And here lies the difficulty. How do we weigh the suffering of a more-than-human animal against the joy or the suffering of a human being? Which animals can suffer? How can we know that for sure? This is called *'the problem of other minds'*. How do you know that others suffer or do not suffer as much as us? In animal experimentation, it is often assumed that we need more knowledge, hence more experiments, to find out whether certain animals can experience pain. But maybe it is better to assume that animals can suffer.

Different ethical approaches yield contrasting perspectives on the treatment of animals. When adopting a deontological approach instead of utilitarianism, discussions revolve around rights, duties, and personhood. Immanuel Kant, whom you might remember from our discussion on deontology, regarded rationality as the defining characteristic of being deserving of respect. Consequently, animals lacking rationality were considered mere means rather than beings to be given intrinsic value. However, proponents of the animal rights movement, such as Tom Regan (Regan, 2004), propose viewing animals as 'subjects of a life'. Although animals may lack rationality, they possess futures, life goals, and interests in survival—traits that warrant respect, duties, and rights. This perspective diverges from utilitarianism, as it emphasizes inherent entitlements rather than outcomes, regarding animals as inherently valuable.

There are individuals who challenge the assertion of animal rights and argue from a contractarian standpoint. Contractarians suggest that morality is founded on a social contract, wherein individuals agree to abide by certain rules. According to this perspective, animals do not belong to the moral community since they are not part of this contractual agreement. Only beings who willingly enter into the contract are

considered moral beings and possess rights. Consequently, animals are excluded from these rights. However, contractarian approaches face criticism due to the 'argument from marginal cases'. This argument states that there is no morally relevant property to distinguish all humans from all other-than-human animals, so marginal cases (newborns, people in a persistent vegetative state, etc.) and animals should be treated alike. If you argue that it is acceptable to experiment on animals because they lack a certain characteristic, such as rationality, you run into a problem because many humans might also lack this characteristic. Philosopher R. G. Frey suggests that while there may be important differences between typical adults and animals, the ethical justification for conducting research on certain humans, such as those in a vegetative state, might be even stronger than for research on other-than-human animals, if we consider having higher cognitive capacities as morally relevant (1988). Hence, if research on such humans is deemed immoral, there is no morally justified basis for conducting research on sentient creatures who meet or exceed the conditions that protect the marginal cases. Although this argument might be considered ableist, it does show that it is nigh impossible to find arguments to include all human beings in the moral realm and exclude all non-humans.

Others have argued that there is a characteristic that binds all human beings and separates them from other-than-human beings, and that is the fact that they belong to the human species. Hence, there is a symbolic value assigned to human species membership that needs no further proof. For many ethicists, however, this is a form of speciesism. Speciesism is the (unwarranted) assignment of different values, rights, or special considerations to individuals based on their species membership, without further motivation. The term was first used by Richard Ryder of the Oxford Group in 1970, and popularized by Peter Singer (1975). Speciesism is analogous to sexism and racism. These authors all challenge the notion that arbitrary factors such as species, sex, or race should determine an individual's moral status or entitlement to equal consideration and respect.

Thinking about topics such as meat eating and animal experimentation is difficult. It is hard to defend our current practice of using animals as means to our ends based on their rationality or lack of self-consciousness. Every week, new findings regarding the intricate lives of animals are published. In the words of Mary Midgley, animals matter. In her book *Animals and Why They Matter* (*2007*), Midgley argues against lifeboat arguments that vet the lives of humans vs against those of other-than-humans. She says that there is no homogenous group of 'animals', but each species must be considered separately. Moreover, it is important to recognize that we have relationships with certain animals and not with others. Generalized moral theories and principles will only take us so far in thinking about what we owe them.

Animal experimentation

Introduction

Other-than-human animals are being used in scientific contexts for various purposes, including fundamental research, testing, education and training, the creation and maintenance of genetically altered animal models, and the use of organs or tissues. Under European law, an animal experiment or 'procedure' has been defined as "any use, invasive or non-invasive, of an animal for experimental or other scientific purposes, with known or unknown outcome, or educational purposes, which may cause the animal a level of pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice" (Directive 2010/63/EU, Art. 3, L277/39). In 2021, out of all animals used in animal experiments in the EU and Norway, more than 96% were rodents, fish, birds, and rabbits. 40.9% of animals were used for basic research, 31.2% for translational and applied research, and 22.5% for regulatory use and routine production (ALURES database). Directive 2010/63/EU is only applicable to live animals; the killing of animals solely for the use of their organs or tissues is not considered and, thus, not recorded as an animal experiment.

Inflammatory bowel disease (IBD) refers to conditions characterized by chronic inflammation of the gastrointestinal tract. In the long term, patients with IBD are at risk of developing colorectal cancer. A researcher is interested in the molecular mechanisms behind this development, from chronic inflammation to cancer, and suspects a specific protein X to be involved. If this is true, protein X could be a potential target for therapeutic interventions. To test this hypothesis of protein X's involvement, the researcher will use a genetically altered mouse model where the gene for protein X is deleted. For a period of twelve weeks, twenty genetically altered mice and a control group of twenty mice without genetic alterations will be subjected to a toxic substance that induces gut inflammation followed by colorectal tumour formation. The mice experience increasing discomfort and pain (diarrhea, bloody stool, etc.) over the course of the treatment. After the treatment, the mice will be euthanized and their colons will be dissected to evaluate tumour formations.

- Do you think the researcher can use these mice to test their hypothesis? Why do you think this?
- Would your opinion change if the researcher used worms, chickens, or pigs for the experiment?
- Does the purpose of the research matter?
- Would you set any conditions for the research to be allowed?

- Would your initial opinion change if you knew that the experiment did not lead to any conclusive results in the end?

Two questions on animal experimentation

Animal experimentation has been the subject of many debates. Questions and criticisms can generally be divided into two topics: (1) the scientific utility and validity of animal use, and (2) the ethical permissibility of animal use. The first topic concerns the question of whether the scientific use of other-than-human animals leads to valid, useful, and relevant results. The second debated question is whether it is permissible for humans to subject other-than-human animals to pain, suffering, and death to achieve these results. Of course, the question of moral justification is also related to the question of scientific justification. If the use of animals in research does not result in any useful knowledge that could not be gained through other approaches, it will be harder to morally justify harm caused to them . However, even if animal experimentation can be justified scientifically, the question of ethical justification still remains.

The scientific utility and validity of animal experiments

The general scientific rationale for using other-than-human animals in research and testing is based on the need to advance scientific knowledge, from which humans and other animals can benefit. Animal models are considered valuable in research on disease mechanisms, the development of therapeutic interventions, and testing the safety and toxicity of various substances or interventions. The use of other-than-human animal models is generally based on their anatomical and physiological similarities to humans. Mammals, in particular, are seen as informative models for human anatomy and (patho)physiology because of their close evolutionary distance from humans. Human diseases—such as infectious diseases, cancer, and epilepsy—also affect other-than-human animals, so studying disease mechanisms in those animals might be informative for the medical knowledge of humans. The mouse models for studying rheumatoid arthritis (McNamee et al., 2015) and the rhesus monkey model for polio vaccine development (Curtis, 2004) are some examples of successful animal models for human disease. Although alternatives are being developed, animal models are generally still deemed necessary for the investigation and evaluation of system- and organism-level physiological functions and interactions in biomedical research.

However, some critics of animal experimentation question the scientific utility and validity of (some) animal disease models and, specifically, the transferability of results from the other-than-human animal model to humans. Indeed, despite biological similarities, interspecies differences may hinder the extrapolation of results from animal studies to the human context. Critics often refer to the fact that more than

90% of drug candidates identified in preclinical studies (including animal studies) have failed in clinical trials (Dowden and Munro, 2019). For example, HIV vaccines that seemed effective in chimpanzees have failed in subsequent human clinical trials, and no animal HIV model has been able to capture all features of human HIV-1 infection (Hatziioannou and Evans, 2012; Policicchio et al., 2016). In addition to the risk of incorrectly identifying drug candidates for human diseases, potential drugs or interventions for humans may be disregarded due to their failure in animal models.

Based on these criticisms of the scientific utility or validity of other-than-human animal models, some opponents of animal experimentation argue that all animal models are not sufficiently useful and should be replaced with other approaches, such as cell or tissue cultures, post-mortem research on humans, and computer simulations, which are deemed more reliable for research on human conditions. However, not all critics of the scientific validity of animal studies take such an *abolitionist* stance. Some do not deny that animal models may be useful in some cases, but assert that the predicative value of animal models is overstated and that other approaches may be more reliable for obtaining results relevant to humans. Others acknowledge that animal models may not always offer the most suitable approach, but argue that other modelling approaches—such as *in vitro* human cell or tissue models—also have limited transferability and predictive value. They argue that, although critical reflection is needed, animal research can still be scientifically valid or even necessary for research or testing.

In response to the debate, the Nuffield Council on Bioethics has issued the following conclusion on the scientific validity of animal and research testing:

> We concluded that continuities in the form of behavioural, 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. […] 'the scientific validity of animal experiments is a condition capable of being fulfilled, but has to be judged case by case and subjected to detailed critical evaluation'. (Nuffield Council of Bioethics, 2005, p. 178)

In this conclusion, the Council affirms that animal experiments can be scientifically valid, while also acknowledging the limits of animal models of human disease and pointing to the need to carry out a critical evaluation of the study design and decide on the validity of an animal model on a case-by-case basis.

The ethical permissibility of animal experiments

The second big question in the debate on animal experimentation concerns the morality of humans using other-than-human animals for research, and, in particular, the permissibility of subjecting the animals to pain, suffering, and death for research. Various arguments for and against have been posed. Disagreements often come down

to two aspects: (1) the moral status of humans and other-than-human animals, and (2) the reasoning and conclusion on the acceptability of animal research. However, there are also other points of debate, such as the extent of suffering other-than-human animals experience and whether or not we have a duty to alleviate and/or prevent it.

The moral status of humans and other-than-human animals

Assessments of the morality of humans using animals for research and testing often begin by considering the moral status of other-than-human animals: do other-than-human animals have moral status or moral importance, and how does it relate to the moral status of humans? Generally, there are three positions on this debate: (1) the clear-line view, (2) the moral equality view, and (3) the moral sliding scale view.

According to the clear-line view, there is a categorical moral division between humans and other-than-human animals. This view is based on the assumption that there is some morally relevant, specific property that is unique to or possessed by humans and that all other-than-human animals lack. This specific property is then considered vital for clearly assigning higher moral importance to humans.

The moral equality view posits no such categorical moral distinction between humans and all (or some) other-than-human animals. It claims that biological species classifications, as such, are insufficient for delineating humans as having higher moral importance than all other-than-human animals. As a result, some proponents of this view (e.g. Richard Ryder, Peter Singer) consider it 'speciesist' to assign higher moral importance to humans on the basis of species membership. Drawing analogies with sexism and racism, the concept of speciesism is characterized by an unjustified bias in favour of the interests of one's own species. According to this view of moral equality, humans and (some) other animals should be considered moral equals.

In between these two extremes, the moral sliding scale view argues against the clear dividing line for moral importance between humans and all other-than-human animals, opting for a scale ranking moral importance. According to this view, one or more specific features can be used to decide on a hierarchy of moral importance with, for example, humans at the top, followed by primates, rodents, zebrafish, fruit flies, and single-cell organisms. The morally relevant properties can be biological—e.g. the scale of neurological complexity—or not biological—e.g. 'capacity to flourish', which we have already discussed in the chapter on environmental justice. Other examples of morally relevant properties can also be found in the chapter on environmental ethics.

It should be noted that these views on the moral status of animals do not give straightforward answers to the question of whether it is ethically permissible to experiment on animals. For some, ascribing lower moral status to animals would justify all animal experimentation (an 'anything goes' view), while for others, the higher moral status of humans includes a moral duty of stewardship, care, or compassion to 'lesser' beings. This challenge of stewardship is also relevant for the moral sliding scale view. Additionally, the acceptability of animal research may not solely depend

on the specific characteristics of the animals used, but also on the experiment's welfare implications for the animals. The moral equality view also does not necessarily defend or oppose animal experimentation.

In relation to the different views on the moral status of humans and animals, we can ask what features of humans and animals could be relevant to the assignment of moral status and subsequent constraints on how animals or humans can be treated or used. Various morally relevant features have been proposed, among which sentience, higher cognitive capacities, capacity to flourish, sociability, and possession of life have been the most popular. These features have been used in defence of different views on the moral status of humans and other-than-human animals, either as a single overriding criterion or as part of a combination of criteria for deciding position on a moral hierarchy. In subsequent discussions on the acceptability of animal research, different weights are assigned to these morally relevant features—some of them are regarded as absolutely sufficient to constrain the use of an animal in research, whilst some must be balanced with other factors.

There are multiple approaches to the ethical consideration of animal use for research, which partly depend on the moral theories followed. The approaches are generally based on different views on morally relevant features and their normative consequences. Ethical considerations on animal experimentation are usually similar to or an extension of approaches to animal ethics in general (see earlier). Here we briefly consider consequentialist, deontologist, and hybrid approaches.

Consequentialist approaches

Consequentialist approaches involve weighing up consequences to determine the acceptability of an action. A consequentialist evaluation of a specific animal experiment may require the consideration of three questions. First, there is the question of how the goals of the research are valued. This question often comes down to evaluating the benefits of the specific research goal. It is also important to consider for whom those benefits apply and how speculative the gains might be. One issue with this approach is the difficulty in predicting the value of a certain type of research beforehand, especially in the case of basic research. There is some disagreement on whether only immediate benefits should be considered or whether there is also intrinsic value in contributing to the overall sum of scientific knowledge. Second, there is the question about *the degree of harm experienced by the animals.* This depends on the number of animals used, and their capacity to experience pain, suffering, distress, or other harms from being subjected to the experiment. It might also be relevant to consider harm experienced during breeding, transport, housing, and handling. However, the degree of harm experienced by animals is also difficult to assess and doing so requires approximations and definitions of harm. For example, there is some debate on whether prematurely ending an animal's life, even if it does not suffer any pain or distress from the action, should be considered as harm to the animal or not. Finally,

consequentialists may question whether a *better balance between the costs and benefits* is possible. Consequentialism requires an optimization of the overall consequences. Each research project should investigate whether other approaches would produce a better balance between overall benefits and costs. Are there, for example, non-animal alternatives available to achieve the valuable research goal, for which the degree of harm would be significantly reduced? Additionally, if no non-animal alternatives are available, a better balance could be achieved by reducing the number of animals used and/or refining the severity of procedures in order to reduce the harm experienced.

One of the main difficulties of consequentialist approaches is determining whether benefits outweigh costs. Even if the benefits and costs of a certain type of research can be reasonably identified, the direct comparison of benefits and costs often proves quite difficult. What degree of animal suffering would be too much in relation to the predicted benefits of the research? Is it more important to minimize suffering or maximize benefits? How do we integrate the degree of uncertainty for envisioned consequences in this calculation? Is there a difference in moral weight between causing suffering to animals and alleviating suffering for humans? This balance also depends on the assumed view on the moral status of humans and other-than-human animals.

In *Animal Liberation* (2002), Peter Singer follows a consequentialist approach to the ethical permissibility of animal experimentation. He starts from a view of moral equality view in the sense that he does not consider species as a relevant moral factor for distinguishing between the moral status of humans and other-than-human animals. Moreover, he regards all beings capable of suffering as worthy of equal consideration of their interests. Thus, in the context of animal experiments, the interests of the other-than-human animals should also be taken into consideration for the overall cost-benefit evaluation. His position does not *de facto* reject all animal research, but it requires scientists to clearly demonstrate the benefits of the research in comparison to the suffering inflicted on the animals, as well as evaluation by a board including scientists and members of the animal welfare community.

Deontology

As mentioned earlier, deontological approaches to animal ethics are generally based on rights, duties, and personhood.

Immanuel Kant (1963) found that, in contrast to humans, all other-than-human animals lack rationality, which he considers a vital property for the assignment of moral status (*clear line view*). In a Kantian view, rationality is required in order to have inherent value, and to be deserving of respect or rights. Following this deontologist view in the strictest sense, we would have no moral obligations towards animals, meaning they can be used as mere means to an end, although Immanuel Kant himself admitted that we should not be unnecessarily cruel to animals. This 'anything goes' position would allow all other-than-human animals to be used for research, regardless of the benefits of the research provided it does not violate the rights of any humans.

The animal rights movement finds no categorical distinction between humans and (some) species of other-than-human animals (*moral equality view*), and, in contrast to Singer, argue from that position in deontological terms. Tom Regan (2004) focuses on the inherent rights of animals instead of considering their interests and suffering. He suggests that, just like humans, animals have inherent value as 'subjects of a life'. Hence, his conclusion is also based on deontological reasoning, although he draws a different conclusion than Kant's because his view on animals is different. Animals have rights because of their inherent value as 'subjects of a life' and thus need to be treated with respect, not as mere means to an end. As a result, Regan holds an abolitionist view on animal use in science. Every form of animal research—regardless of its potential benefits for humans or other animals—would violate the animal's rights, so we have a duty not to use animals for science.

Hybrid approach

The most common approach to ethics in animal experimentation is a hybrid approach based on the sliding scale of moral status. An animal's position on the scale depends on a number of defined morally relevant features, which impose limitations on how the animal may be treated for research. The morally relevant features include sentience (the capacity to feel pain and pleasure), higher cognitive capacities (self-consciousness, rational will, communication, tool use, having moral systems, etc.), the capacity to flourish (have interests/needs met) in a specific environment, sociability (relations with humans and other animals), and possession of life. Based on the possession of some morally relevant features, some animals are ruled out completely from use in research. The use of chimpanzees, for example, is generally prohibited because they possess higher cognitive capacities. Within those very strict limits, the hybrid approach allows costs and benefits to be weighed up to evaluate the use of animals. For example, using mice to test the safety of an important, frequently used chemical may be permitted if the test inflicts minimal pain on the mice.

So, among proponents of the hybrid approach, the ethical debate on animal experimentation boils down to disagreements on two questions: (1) 'what are the absolute limits?', and (2) 'how should morally relevant factors be weighed within the permitted limits?"

When ethically evaluating the use of a particular animal for research, the following questions at least should be considered:

1. *What are the goals of the research*? Are these immediate goals (e.g. translational research) or long-term (basic research)? Are the goals of the research valuable to pursue? What are the potential benefits of the research? Who would benefit?
2. *What is the probability of successfully achieving the benefits?* What is the probability of achieving the goals of the research? How likely are the

predicted benefits? Predictions can be made based on earlier experiments, literature, or similar research.

3. *Which animals are to be used?* Which animals would be most suitable to answer the research questions? The choice of animal model can be based on genetic, physiological, or structural similarity to humans, specific characteristics that facilitate research, the researcher's expertise, etc. These considerations are important to ensure the scientific validity of the animal use. Is the most suitable animal 'prohibited' from use for (this type of) research? If so, would another animal model be appropriate for the research?
4. *What is the effect of the research on the animals?* Do the research procedures cause harm or distress to the animals, and what is the severity of the harm/distress? What is the effect of breeding, housing, transportation, and handling for the research? Is the harm or distress experienced throughout the entire experiment or only at a specific time point?
5. Are there any alternatives? Is it possible to replace the animal model with a cell or tissue model, computer model, etc.? Would a 'lower' animal also be appropriate for answering the research questions? Would another animal experience less harm from the research environment? Would another experimental approach require fewer animals, or reduce the harm or distress experienced by the animals?

Most European legislation follows the hybrid approach to the ethical permissibility of animal research. Directive 2010/63/EU sets an absolute limitation on scientific animal use by prohibiting the use of great apes in procedures (for the EU definition of 'procedure', see introduction). Additionally, some research goals are also restricted, with an EU-wide ban on testing finished cosmetic products on animals (Regulation (EC) N° 1223/2009), and a Belgian ban on animal research for the development of tobacco products (Royal Decree of 28 October 2008).

Outside of those limitations, EU (and Belgian) legislation focuses on balancing the costs and benefits of animal use by stipulating replacement, reduction, and refinement (the three Rs). The three Rs were first published in *The Principles of Humane Experimental Technique* by Russel and Birch (1959) as an approach to improve the treatment of animals in research, as well as the quality of animal studies. In current practice, the three Rs should be used to minimize animal use as well as the potential harm, pain, or distress experienced by animals in scientific research.

- *Replacement*: The substitution of live, conscious higher animals with insentient material (e.g. cell or tissue cultures, in-silico models).
- *Reduction*: The reduction in number of animals used to obtain information of a given quantity and precision. This often requires statistical power analyses to determine the minimum number of animals required to gain sufficiently significant results.

- *Refinement*: Any decrease in the incidence or severity of inhumane procedures. This also includes using enrichment approaches to decrease stress or harm experienced by the animals during experimental procedures, breeding, housing, transport, and handling. Examples of enrichment approaches include providing nesting materials in mice cages (Olsson and Dahlborn, 2002), or tickling lab rats at regular intervals (Cloutier et al., 2015).

To promote replacement, reduction, and refinement in scientific animal use, the European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM) has been set up. This laboratory is tasked with validating methods that reduce, refine, or replace the use of animals for safety testing and efficacy/potency testing of chemicals, biologicals, and vaccines.

Discussion: Can you think of situations or types of experiments which would be difficult to evaluate based on the hybrid approach and 3Rs? Think of conflicts between interests, concepts, principles, etc.

Numerous criticisms and remarks have been made on the current hybrid approach to ethically evaluating scientific animal use. Some criticisms, such as those from the animal rights movement, stem from differing moral theories followed and differing views on the moral status of animals. Other criticisms do not necessarily disagree in those regards but do point out some weaknesses or conflicts within this current approach.

In some cases, there are conflicts between the reduction and refinement requirements of the three Rs. To reduce the required sample size for sufficient statistical power, variability in measurements has to be reduced. However, reducing response variability may require experimental methodologies which cause more pain and distress to the animals. Is it better to use fewer animals but cause more severe harm to those animals, or to use more animals but subject them to less severe harm? The hybrid approach does not provide straightforward answers to these conflicts.

Some critics point to the difficulty and arbitrariness of comparing and weighing morally relevant factors on which distinctions between different species are made in the hierarchy of moral importance. Why do the higher cognitive capabilities of great apes justify a ban on their use in research, but not the sociability of beagles? Why are the restrictions set out by Directive 2010/63/EU applicable to the use of vertebrate animals and cephalopods, but not other invertebrates (*C. elegans*, fruit flies, etc.)?

Lastly, the 'humane killing' of animals to use their tissues and organs in research does not fall under the definition of 'procedure' or 'animal experiment' in European law. As a result, prematurely ending the life of an animal is considered insufficient harm to require the same restrictions as other harms such as pain or stress.

Conclusion

Arguments on the ethical acceptability of humans eating, using, or experimenting on other-than-human animals take various forms. In this chapter, we introduce animal ethics and begin to show the range of approaches to animal experimentation ethics. We highlight two ways in which arguments on the ethical permissibility of animal experimentation can differ: namely, the moral status of other-than-human animals and the moral theories on which the argumentation is built. Along these dimensions, we provide students and researchers with a brief overview of some arguments for and against animal experimentation. Finally, we also lay out the hybrid approach to animal experimentation ethics, which underpins current evaluation policies and EU regulation on the ethical acceptability of animal studies.

Bibliography

"28 OKTOBER 2008. - Koninklijk besluit tot wijziging van het koninklijk besluit van 30 november 2001 houdende verbod op sommige dierproeven voor wat betreft de uitvoering van dierproeven voor de ontwikkeling van tabaksproducten". https://etaamb.openjustice.be/nl/koninklijk-besluit-van-28-oktober-2008_n2008024478.html

Aristotle. *De Anima* (On the Soul). Translated by J. A. Smith, in The Complete Works of Aristotle, edited by Jonathan Barnes. Vol. I. Princeton: Princeton University Press, 1984.

Beauchamp, Tom L., and R. G. Frey, eds. 2011. *The Oxford Handbook of Animal Ethics*. Oxford Handbooks. Oxford: Oxford University Press.

Bentham, J. 1789. *An Introduction to the Principles of Morals and Legislation*. London: T. Payne.

Cloutier, Sylvie, Chelsea Baker, Kim Wahl, Jaak Panksepp, and Ruth C. Newberry. 2013. "Playful Handling as Social Enrichment for Individually- and Group-Housed Laboratory Rats". *Applied Animal Behaviour Science, Special Issue: Laboratory Animal Behaviour and Welfare* 143 (2): 85–95. https://doi.org/10.1016/j.applanim.2012.10.006

Curtis, Tom. 2004. "Monkeys, Viruses, and Vaccines". *The Lancet* 364 (9432): 407–8. https://doi.org/10.1016/S0140-6736(04)16746-9

Darwin, Charles. 1871. *The Descent of Man, and Selection in Relation to Sex*. 1st edition. London: John Murray.

Descartes, René. 1972. *Treatise on Man*. Translated by Thomas Steele Hall. Cambridge: Harvard University Press.

Dowden, Helen, and Jamie Munro. 2019. "Trends in Clinical Success Rates and Therapeutic Focus". *Nature Reviews Drug Discovery* 18 (7): 495–96. https://doi.org/10.1038/d41573-019-00074-z

European Commission. n.d. "ALURES - ANIMAL USE REPORTING - EU SYSTEM". Accessed 11 July 2024. https://webgate.ec.europa.eu/envdataportal/content/alures/section1_number-of-animals.html

—— 2009. "Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on Cosmetic Products". November. https://health.ec.europa.eu/system/files/2016-11/cosmetic_1223_2009_regulation_en_0.pdf.

—— 2010. "Directive 2010/63/EU of the European Parliament and of the council of 22 September 2010 and of the council of 22 September 2010 on the protection of animals used for scientific purposes". http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:276:0033:0079:eN:PDF.

Frey, R. G. 1988. "Moral Standing, The Value of Lives, and Speciesism". *Between the Species* 4 (3): 191–201. https://doi.org/10.15368/bts.1988v4n3.8

Hatziioannou, Theodora, and David T. Evans. 2012. "Animal Models for HIV/AIDS Research". *Nature Reviews Microbiology* 10 (12): 852–67. https://doi.org/10.1038/nrmicro2911

Kant, Immanuel. 1963. *Lectures on Ethics*. Translated by Louis Infield. New York: Harper & Row.

McNamee, Kay, Richard Williams, and Michael Seed. 2015. "Animal Models of Rheumatoid Arthritis: How Informative Are They?". *European Journal of Pharmacology* 759: 278–86. https://doi.org/10.1016/j.ejphar.2015.03.047

Midgley, Mary. 2007. *Animals and Why They Matter*. Athens: University of Georgia Press. https://ugapress.org/book/9780820320410/animals-and-why-they-matter

Olsson, I. Anna S., and Kristina Dahlborn. 2002. "Improving Housing Conditions for Laboratory Mice: A Review of 'Environmental Enrichment'". *Laboratory Animals* 36 (3): 243–70. https://doi.org/10.1258/002367702320162379

Policicchio, Benjamin B., Ivona Pandrea, and Cristian Apetrei. 2016. "Animal Models for HIV Cure Research". *Frontiers in Immunology* 7: 12. https://doi.org/10.3389/fimmu.2016.00012

Regan, Tom. 2004. *The Case for Animal Rights*. 2nd edition. Berkely: University of California Press.

Reza Khorramizadeh, M., and Farshid Saadat. 2020. "Animal Models for Human Disease". *Animal Biotechnology*, 153–71. https://doi.org/10.1016/B978-0-12-811710-1.00008-2

Russell, William Moy Stratton, Rex Leonard Burch, and Charles Westley Hume. 1959. *The Principles of Humane Experimental Technique*. Vol. CCXXXVIII. London: Methuen.

Singer, Peter. 2002. *Animal Liberation*. 2nd edition. New York: Ecco.

"The Ethics of Research Involving Animals". 2005. London: Nuffield Council on Bioethics. https://www.nuffieldbioethics.org/publications/animal-research

"The Internet Classics Archive | On the Soul by Aristotle". n.d. Accessed 11 July 2024. http://classics.mit.edu/Aristotle/soul.html

Van Norman, Gail A. 2019. "Limitations of Animal Studies for Predicting Toxicity in Clinical Trials". *JACC: Basic to Translational Science* 4 (7): 845–54. https://doi.org/10.1016/j.jacbts.2019.10.008