

The Use of Nonhuman Animals in Biomedical Research

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Abstract: Opposition to the use of animals in biomedical research rests on diverse scientific and ethical arguments. Here I offer a response to key objections and argue that the responsible use of animals in biomedical research with the goal of advancing medical knowledge, science and human health, is scientifically and morally justified. My views are unlikely to be shared uniformly across the scientific community. Thus, I hope this personal perspective persuades other scientists, public health officials, scientific organizations and our academic leadership to join the debate and invites opponents of animal research to create an atmosphere where civil discourse can take place, free of threats and intimidation. The public deserves an open and honest debate on this important topic.

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Scientists have a duty to talk to the public.¹ Why? Because social policies need to be decided on the basis of rational grounds and facts. These include important issues ranging from climate change, to the goals of the space program, to the protection of endangered species, to the use of embryonic stem cells or animals in biomedical research. Both the public and policy makers need to understand not only the scientific justification for our work but also, in some cases, why we deem our studies to be morally justifiable.

The time is ripe for a more open, public and honest debate about the role of scientific experimentation in animals. What follows are some of my thoughts on this topic. I hope this perspective encourages other scientists to join the discussion and prompts opponents of animal research to create an atmosphere where civil discourse can take place, free of the threats, harassment and intimidation that are increasingly directed at biomedical scientists and their families.^{2,3}

Criticism to the use of animals in biomedical research rests on varied scientific and ethical arguments. The discussion below is necessarily incomplete but represents an initial effort to answer some key objections. We start by addressing the opposition's claims regarding the validity of the scientific work to human health and then turn our attention to ethical issues.

ARGUMENTS AGAINST THE USE OF ANIMALS IN SCIENTIFIC RESEARCH

Let us first consider some common criticisms directed at the scientific basis for animal research.

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CLAIM: HUMANS DO NOT BENEFIT FROM ANIMAL RESEARCH

One extreme view holds that information gathered from animal research cannot, even in principle, be used to improve human health. It is often accompanied by catchy slogans such as “If society funds mouse models of cancer, we will find more cures for cancer in mice.”⁴ It is argued that the physiology of animals and humans are too different to allow results from animal research to be extrapolated to humans.⁵

Such a blanket statement is falsified by numerous cases where experimentation on animals has demonstrably contributed to medical breakthroughs. The experiments on cardiovascular and pulmonary function in animals that began with Harvey and continued with the Oxford physiologists⁶ established the understanding of what the heart and lungs do and how they do it, on which the modern practice of internal medicine rests. Modern medical practice is inconceivable in the absence of the insights gained from these experiments. Anti-coagulants were first isolated in dogs; insulin was discovered in dogs and purified in rabbits; lung surfactants were first extracted and studied in dogs; rabbits were used in the development of *in vitro* fertilization; mice in the development of efficient breast cancer drugs and so on.

For the sake of completeness, it must be noted that the other extreme—the notion that all medical advances are a result of animal research—is false as well. Important medical advances, such as sanitation and the discovery of aspirin, were conducted without the use of animals.

CLAIM: ANIMAL RESEARCH HAS A VERY LOW SUCCESS RATE

Here the claim is not that animal research has never produced benefits, but it has done so with a very low success rate, which in the minds of our opponents is enough to deem the work unacceptable.^{5,7} But what does very low mean exactly? Is the term meant to be interpreted in absolute or relative terms? If the comparison is relative, then very low relative to what?

Absolute Interpretation

If one is to interpret the success rate as an absolute figure, then the assertion does little more than restate what is an inherent property of the scientific method.⁸ Scientific research involves a continuous cycle of 3 phases: postulating a theory that can account for the existing data, generating novel predictions from the theory and testing them experimentally. While searching for answers to difficult problems (such as developing a cure for cancer), it is expected for many paths to lead to dead ends. This is a feature of science, not a bug. The scientific method allows us to rule out hypotheses proven wrong by data and systematically narrow down the list of possible explanations until we converge on an answer. History has shown, time and again, that such a strategy works, producing advances in everything from mathematics and physics, to life sciences and medicine. Incorrect hypotheses and negative findings are integral, fundamental and inseparable components of the scientific method.

Grasping the principles of the scientific method is not difficult. Accepting its consequences in the field of animal is hard. The implication is one we would naturally resist: animals, if used in scientific studies, will sometimes be used in experiments that do not yield immediate, tangible benefits.

We must understand and accept the fact that science does not provide recipes. There is no recipe that can ensure a particular type of work that will lead to a unified theory of physics. There is no line of research guaranteed to yield a proof or a rejection of a mathematical conjecture. There is no recipe that can ensure a particular type of work, whether using humans or animals, will lead to cures for cancer, paralysis or autism. Anyone claiming to know with certainty where the answers are to be found, or where they are not to be found, is simply not credible.

Relative Interpretation

An alternative interpretation is that the success rate of animal research should be interpreted as relative to a baseline. The critics are vague about what this baseline is, but the implication seems to be the success rate one would achieve solely by human-based medical research.⁷

This claim can be verified because there is plenty of scientific research performed with human subjects alone, from cancer to Alzheimer's and Parkinson's disease. If there was an obvious advantage for such work in yielding new cures and therapies, we would certainly know by now. To the best of my knowledge, there are no data to support this view.

One may also interpret the baseline success rate as the one we all wish it could be. Patients and families that anxiously await new developments to treat their loved ones surely must feel the rate at which new therapies are generated is low. So does everyone else, including the physicians who care for the patients and the scientists who do their best to develop new cures and therapies as fast as they possibly can. We all wish that effective treatments could be developed faster. In the absence of a viable alternative, this lament is hardly an argument against the use of animals in medical research.

Finally, and perhaps most surprising, it has been stated that the success rate of animal research is comparable to that of astrology.⁹ Our discoveries, we are told, are mere chance events that are not causally related to our investigations. The origin of the claim rests on anecdotes describing serendipitous discoveries in science. Yet, as Louis Pasteur commented, "Chance favors the prepared mind." What he meant, of course, is that an accidental observation will generate a finding only in the mind of someone who has been thinking about the problems for some time, and who is a keen observer.

CLAIM: RESEARCHERS MUST PROVE ANIMALS ARE NECESSARY FOR THEIR WORK

Faced with irrefutable causal links between animal studies and medical breakthroughs, opponents of animal research typically respond with a claim and a demand of their own.

The claim is that such research represents work performed decades ago.^{5,7} On one hand, they accept that we have learned much about the respiratory, circulatory and digestive systems from animals that has been relevant for human health. On the other, they contend that the problems we face today are more complex and subtle. There is little or nothing left to be understood about basic biological function from animals that is relevant to human conditions. In other words, the entire field of animal research is declared to be exhausted of fundamental results.

Any scientist will be perplexed and baffled by such statements. Surely, the claims must come from those with a poor appreciation of the time scales involved in bringing basic research results to the clinic. Indeed, it can take many years, even decades. For example, consider the development of electrocardiography, which relied on classic studies on bioelectricity in the 18th century by Galvani and Volta, with the first measurements of electrocardiograms in humans near the beginning of the 20th century.¹⁰

Second, only someone lacking in scientific humility can declare an entire field to be depleted of fundamental results. Can we imagine a similar claim made about mathematics or physics? After all, one may argue, these are areas of research that are more than 2000 years old! What else could be left to discover? But our critics do not claim these fields to be depleted of results. Oddly enough, their claims are restricted just to those areas of scientific inquiry that involve the use of animals.

One can simply point to some recent examples to prove the claim false. Consider the development of Herceptin to fight breast cancer,¹¹⁻¹³ antivascular endothelial growth factor (VEGF) therapy for retinal vascular disorders¹⁴⁻¹⁶ or RNAi drug delivery.¹⁷⁻²¹ All these represent recent breakthroughs that were obtained by the scientific use of animals (including worms, mice and monkeys) in just the last 2 decades.

What about their demand? Our critics insist that if scientists are to claim that animals are necessary for their research, that a proof be provided showing there was no other way of obtaining the results that circumvented animal use.

What do scientists mean when they say animals are necessary in their work? In most cases, I submit the meaning is that animals are necessary in the sense that the data they seek requires the use of invasive methods, which we would not apply in humans because of the high risks involved and the resulting ethical concerns. Furthermore, it means that a reasonable effort was made to identify potential alternatives in which the data could have been collected without the use of animals. Thus, the necessity is partly an ethical one, not a scientific one. There is nothing in the science per se that would invalidate the use of invasive methods in human subjects. For example, cancerous tumors can certainly be grown in humans as they are in mice, but we do not consider the practice morally acceptable. In other cases, there are clear practical reasons for the selection of animal species. In many genetic studies, one needs to work with organisms that have short generational times, like fruit flies. In studying development, the ability to observe deep tissue *in vivo*, such as in transparent zebrafish eggs, offers a tremendous practical advantage. Finally, animals allow scientists to control many external factors that might otherwise affect the outcome of experiments, such as diet, temperature, humidity and genetic composition, in ways that are not possible in humans.

In contrast, our critics often adopt a stricter interpretation of necessity, arguing that scientists are claiming that animal research is the only possible way to obtain the data they need, and they demand proof to this effect. In the words of Greek²²:

"[. . .] the claimant must essentially prove a negative; that the discovery could not have been made any other way. Although difficult, this can be done and indeed must be done for the claimant to say the discovery was dependent on animal use."

This is an unreasonable demand based on a straw-man argument. First, as noted above, this is not what scientists mean. Second, there are infinite possibilities that must be considered for one to prove that no other method could have

generated the same result without the use of animals. Proving the positive, in contrast, should be simpler. Those with the absolute conviction that animals are unnecessary in biomedical research could prove their point by simply showing there is another way. Such a demonstration would be a tremendous contribution to society. Finally, as remarked by an anonymous reviewer, once a mountain has been reached, it is sometimes possible to look back down and find an alternate path that would have been easier or that might have avoided some segment. However, this does not mean one could have located that alternate path during the initial climb.

CLAIM: ANIMAL MODELS ARE NOT PREDICTIVE OF HUMAN RESPONSES

This claim is a centerpiece of many arguments. It effectively states that it is impossible to model human disease in animals because any treatments we develop in animals will not translate to humans. Prediction is no doubt a goal of scientific work and some, but not all, of animal research aims at modeling disease in human subjects.

Predictions are the fruits of theories that can be tested experimentally. If the prediction is false so is the theory, and a new one must be generated based on prior knowledge and the specific way in which the data falsified the theory. Interestingly, those that claim animal models are not predictive of human response take some literary license in restating the above along the following lines^{5,7}:

Predictions, generated from hypotheses, are not always correct. But if a modality or test or method is said to be predictive then it should get the right answer a very high percentage of the time [...]

If a modality consistently fails to make accurate predictions then the modality cannot be said to be predictive simply because it occasionally forecasts a correct answer. The above separates the scientific use of the word predict from the layperson's use of the word, which more closely resembles the words forecast, guess, conjecture, project and so forth. [...]

Many philosophers of science think a theory (and we add, a modality) could be confirmed or denied by testing the predictions it made.

This language delicately nudges the reader to equate different concepts, namely theory, hypothesis, modality and method. In this deceptively innocuous equation, resulting from either an honest misunderstanding or mischievous intent, lies the foundation to a seriously flawed argument.

For example, the statement:

"... if a modality or test or method is said to be predictive then it should get the right answer a very high percentage of the time."

is not accurate. It is theories that generate predictions, not modalities or methods.

Consider the domain of physics. Here, physicists put forward mathematical theories of some natural phenomenon which, in turn, generate predictions. These predictions can be experimentally tested. If a prediction is falsified, so is the theory. When this occurs, scientists seek to understand how the data depart from the prediction and use prior knowledge and intuition to develop a new working hypothesis, which is embedded in a new theory. Mathematics is the language of physics—its methodology. Obviously, by using mathematical language, one can create many different theories. The overwhelming majority of them will be false. Science is difficult because most of the time our ideas turn out to be wrong.

The point is that one's ability to conjure up vast numbers of incorrect theories does not invalidate mathematics as a method in the physical sciences. Mathematics can in fact be used to arrive at accurate descriptions of how matter behaves. It makes no sense to describe this state of affairs by stating that mathematics (the modality) gets it right occasionally. Mathematics does not generate theories—people do.

A similar situation arises in the domain of biomedical research. Researchers create models of disease in animals by trying to replicate what they believe are the essential components at play. These animal models can then be used to generate predictions for therapeutic interventions, which can then be tested in human clinical trials. If a prediction is falsified, so is the animal model of disease. Let me repeat, it is the specific animal model that is falsified. When this happens, scientists seek to understand how the data depart from the prediction, what other factors were ignored that might play a role and use prior knowledge and intuition to develop a better, improved model. In the course of developing and refining such a model, scientists will go through many such cycles. A model is expected to be valid once it captures all the key ingredients of the human condition.

The fact that one can postulate inaccurate animal models of human disease does not invalidate the whole methodology of animal research, it merely shows the work is difficult. But animal models can in fact be successful. It is a mistake to conclude that animal models get it right occasionally. The scientific question is not whether animals can be used to generate inaccurate models of human disease but whether they can be used to generate faithful ones. The answer is yes they can.

It is also worth noting that a theory can often capture partial patterns in the data. Thus, even though we might know a theory to be strictly incorrect, it can still be used to our benefit until refinements are developed. Consider the standard calculation of an object falling in a gravitational field based on Newton's laws of motion. The resulting model is only approximate and can be substantially improved by incorporating drag forces resulting from air resistance and how they depend on the shape of the object. And yet, for many purposes, the original model, although strictly incorrect, is sufficient to make reasonable predictions in many circumstances.

Similarly, some animal models may be strictly incorrect in that they do not capture all the behavior in the human condition, and improvements are clearly needed. However, they have predictive value, which make them utilizable until these refinements are worked out. One such example is the question of determining the first dose of potential new medicines to human subjects.²³

The conditions for honest debate are eroded when critics cherry pick animal models that have poor predictive power, deliberately cite scientists who acknowledge these limitations out of context, completely ignore their explanations of what have they have learned from the results, disregard their ideas as to how the models can be improved and package such examples as proof that animal research is not predictive of human responses.⁵ Such mischaracterization of scientific research must be forcefully rejected.

CLAIM: BASIC RESEARCH IS KNOWLEDGE FOR KNOWLEDGE'S SAKE

Animal models of disease are only 1 way in which animals are used in science. A substantial amount of research is aimed at understanding the basic biological processes of life

and disease, so-called basic research. The function of cells, how they communicate, how they develop, how they age and how they die are all part of the foundations of biological science.

Some have characterized this research as “knowledge for knowledge’s sake”, the benefits of which, we are told, are so unlikely to materialize that one cannot possibly justify the use of animals in this type of work.⁷ However, it is precisely such basic knowledge, from the abstract geometric theorems of ancient Greece, to the physical models of atoms and subatomic particles, to the inner workings of cells and organs that are responsible for our greatest scientific advancements. The mission of the National Institutes of Health (NIH) recognizes this fact in its opening statement,

NIH’s mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life and reduce the burdens of illness and disability.

Implicit in this declaration is the acknowledgment that it is basic knowledge that drives advancements in our health and well being. Translational or applied research would not exist without basic knowledge as the raw material. Nevertheless, scientists engaged in basic research are continuously challenged to explain the value of their work. Approximately 35 years ago, the National Science Foundation was asked by the House Committee on Appropriations exactly this question²⁴: “Why does the foundation persist in supporting research whose results have no apparent value to the American people?” The request prompted not only a response from National Science Foundation but also the compilation of an entire volume describing the multiple ways in which basic research has led to technological and medical advancement.²⁵ In its introduction, Isaac Asimov presented an eloquent defense of basic research and concluded²⁵:

[...] And now we stand in the closing decades of the twentieth century, with science advancing as never before in all sorts of odd, and sometimes apparently useless, ways. We’ve discovered quasars and pulsars in the distant heavens. Of what use are they to the average man? Astronauts have brought back rocks from the moon at great expense. So what? Scientists discover new compounds, develop new theories, work out new mathematical complexities. What for? What’s in it for you?

No one knows what’s in it for you right now, any more than Plato knew in his time, or Faraday knew, or Edison knew, or Einstein knew. But you will know if you live long enough; if not, your children or grandchildren will know. [...]

In fact, unless we continue with science and gather knowledge, whether or not it seems useful on the spot, we will be buried under our problems and find no way out. Today’s science is tomorrow’s solution – and tomorrow’s problems too – and, most of all, it is mankind’s greatest adventure, now and forever.

Today’s science is tomorrow’s solution. Even though we might not be able to benefit directly from the basic research of today, we owe it to our children and our grandchildren to develop the knowledge that they will need to build a better future for their generation and those to come. Basic knowledge about life processes is part of this endeavor.

CLAIM: ALTERNATIVES TO ANIMAL RESEARCH ALREADY EXIST

To the scientist, this claim is perhaps the most infuriating of all, because it not only pertains to the scientific work, but it represents an attack on our ethical conduct. Scientists are effectively accused of engaging in animal research even though

alternatives are supposedly available. The Humane Society of the United States web site states²⁶:

If animal experimentation was the hallmark of twentieth century biomedical research, sophisticated nonanimal methods are likely to characterize twenty-first century research. Many humane state-of-the-art alternatives to animal experiments have already been shown to be effective in advancing medical progress, cutting research costs and eliminating animal suffering.

We are told, for example, that today’s computer simulations are advanced and detailed enough to be able to replace animals in many studies and that functional magnetic resonance imaging can be used to replace all our electrophysiologic studies of brain function in animals. This is utter nonsense. It is scientists who have developed these techniques, not the opponents of animal research. What reasons would we have to reject our own methods? Do the critics truly believe scientists engage in animal research despite the existence of viable alternatives? Apparently so. Greek²⁷ defends this notion by citing Upton Sinclair: “It is difficult to get a man to understand something when his salary depends upon his not understanding it.” Other animal activists appear to believe in a vast conspiracy network that includes the NIH, the Center for Disease Control, the US Department of Agriculture and many scientific professional organizations, all of which work together to promote the practice of animal research for mere financial gain. Needless to say, such theories do not stand scrutiny.

Once again, these are shameful attacks that detract from honest debate. The methods suggested are already being used in conjunction with animal research but are incapable of replacing the studies that require access to cellular and molecular processes. Every single scientist I know will support and embrace the use of alternatives if and when they become available. None of them derives any pleasure in harming animals. It should also be noted that our funding agencies require each study submitted for consideration to justify the use of animals and species in each case and to clearly explain all the alternatives that have been considered and ruled out.

ETHICS OF ANIMAL RESEARCH

Even if we grant that biomedical research using animals advances human/animal health and well being, one can still ask whether the work is ethically permissible. Moral philosophers bring important issues to the table that cannot be dismissed easily.^{28–36} I believe that scientists ought to familiarize themselves with the arguments, understand that there are some complex moral questions being raised and confront the ethical arguments directly.

It is useful to start by noting some points of agreement. I accept that history shows moral boundaries to be dynamic. One example suffices to make the point: at one time, society recognized slavery as morally acceptable, it is no longer so. Thus, animal research can neither be defended exclusively on the grounds that the work, today, is legal, well regulated, includes work aimed at replacing, refining and reducing the use of animals and is supervised by a multi-tiered oversight system, nor can it be justified exclusively based on public support. The justification of animal research requires an ethical argument as its core.

THE MORAL STATUS OF ANIMALS

Rights, properly defined, are claims (or potential claims) to be exercised against another within a community of moral

agents.³⁷ Animals cannot have rights because they are not able to participate as autonomous rational agents in our moral community. You cannot bring a claim to a dog that attacked you. The dog cannot recognize your interests. This, however, does not preclude animals from having moral status.³⁸ A living being is said to have moral status if we are morally obliged to give weight to their interests independent of their utility to us. Both animals and humans may be considered to have interests in their well being, freedom and life and thus to have moral status.

What is the moral status of nonhuman animals? On one end of the spectrum, we find those that may think that animals have no moral status at all and that we can do with animals as we please. On the other end of the spectrum, we find those who think that the moral status of sentient animals is equal to that of humans.³³ My position lies in-between these extreme viewpoints. I believe moral status to be graded according to the cognitive capabilities of each living being. Unfortunately, the first hurdle faced by anyone sharing this view is that some theorists would reject moral status as possible accepting degrees.³⁶

Elizabeth Harman is clear on this point³⁹:

We have no reason to posit such degrees of moral status, so we can conclude that moral status is not a matter of degree but is rather on/off: a being has moral status or lacks it.

Francione agrees³³:

We have two choices – and only two – when it comes to the moral status of animals.

And Regan³⁰ writes similarly in terms of the inherent value of animals:

Two options present themselves concerning the possession by moral agents of inherent value. First, moral agents might be viewed as having this value to varying degrees, so that some may have more of it than others. Second, moral agents might be viewed as having this value equally. The latter view is rationally preferable. [...] We must reject the view that moral agents have inherent value in varying degrees. All moral agents are equal in inherent value, if moral agents have inherent value.

REJECTING THE EXTREMES OF THE SPECTRUM

The extreme views have the virtue that are simple to understand and apply; the problem is that they are wrong. Most of us readily reject the Cartesian view that animals as mere things based on multiple scientific evidence, starting with the work of Darwin. I will therefore concentrate my effort into explaining my reasons for ruling out the other extreme—the animal rights view.

Animal rights theories posit that once a living being satisfies some basic characteristics (such as exhibiting a minimum level of sentience³³ or passing the subject-of-life criterion³⁰), they attain the same moral status as that of a normal human. Such all-or-none theories of moral status admit a moral universe with 2 possible equivalence classes, one that includes rocks and a second one that includes normal humans.

Is this so? What would be the moral status of single-cell organisms, plankton, worms, coral reefs, mice, cats, monkeys and great apes? Do we accept that in each case we must equate their moral status to that of a rock or a human? My moral intuition rejects such conclusion and, along with it, the notion of all-or-none moral status.

I submit it would be morally permissible to save my child and not a mouse in a burning house scenario. Curiously, this intuition is shared by my opponents,^{30,33} although they fail to recognize the implications. Francione³³ justifies his decision by explaining that, “I better understand what is at stake for the human than I do for the dog. But this is a matter of my own cognitive limitation and how it plays out in these extreme circumstances [...]”

It is important to recognize that his decision to consistently select a human over the animal in these circumstances cannot be derived from an application of animal rights theory. Instead, the theory directs us to flip a fair coin among 2 living beings with equal moral status to decide who should be saved. The justification offered, based on our cognitive limitation in understanding animal minds, ceases to be one at the same instant we recognize it as one. Clearly, we are free to overcome our limitations by doing what is right according to the theory: rendering a fair, random decision between 2 living beings of equal moral status. And yet, neither Francione nor Regan seems ready to act in such a way.

Further, Francione³³ clarifies that, “my decision to favor the human does not mean I am morally justified in using dogs in experiments or otherwise treating dogs exclusively as means to my ends.” This is a straw man. The point is that his refusal to act according to the theory cannot be justified in any other way but one: the theory is wrong and must be rejected. In rejecting the animal rights theory, I am not subscribing to the notion that animals are things and we should be able to do with them as we please. I reject such attempt at robbing others of the possibility to argue for moral theories based on graded moral status of living beings.

The validity of all-or-none moral status has been questioned before, and indeed, the moral philosophy literature is much more complex than the animal right activist in the street seems to know or acknowledge.^{38,40,41} In particular, the notion of a graded moral status (defined as the degree a being’s interests are protected vis-a-vis other beings) has been defended as a reasonable, alternative possibility.⁴¹ One such example is the sliding scale model, where the moral weight of someone’s interests depends on the individual degree of cognitive, affective and social complexity.⁴¹ In this model, scientific facts about animal cognition and how we interpret the minds of animals are key in deciding how we weigh their interests. And it is what we know about the minds of animals that must primarily guide our ethical judgments, which is not just how we feel about them.⁴² Ethical boundaries may shift as we learn more about animal minds but, given our current knowledge, there is good reason to grant humans the highest moral status followed by great apes, dolphins, monkeys, higher mammals, rodents, insects and so on. The sliding scale model is fully compatible with the views of many scientists and certainly with the NIH guidelines, which requires the use of the simplest organism that can provide the scientific data without compromising the validity of the study.

It should be emphasized that once the 2 extreme positions on moral status are rejected, all the theoretical frameworks that remain standing can be reasonably characterized as animal welfarism of various degrees, and importantly, all of them would allow for animal experimentation to some extent.

EQUAL CONSIDERATION OF EQUAL INTERESTS

The principle of equal consideration calls for giving equal weight to relevantly similar interests. Utilitarian³⁵ and animal rights³⁰ theories are both based on the principle of equal

consideration and constitute the central theories used to challenge scientific work with animals. Is equal consideration violated in biomedical research that use animals?

Clearly, in animal research, the ultimate cost to animals is the loss of life. Many philosophers agree, however, that the interests of (normal) humans and animals in life are not relevantly similar.^{41,43,44}

Human life is the execution of an aspiration—a life's plan. Human life is a process that cannot be reduced to mere living by satisfying our immediate biological needs.⁴³ Humans are not content with living, they need to live well and realize their ambitions. Among these ambitions is the need to transcend our biological lives in some shape or form, by contributing to science, arts and society, in ways that improve the well being of living beings in our planet. When these needs are denied, and despite having all their biological needs met, humans can willfully terminate their own life.

Interests in life are not relevantly similar among humans and animals—the same things are not at stake. In recognition of this fact, many philosophers who would agree that, when faced with a choice between the life of a mouse or a human in a burning house scenario, we might be well justified in choosing the human. The moral status of the mouse is not equal to that of the human. Below, I suggest scientists are making a similar choice when they decide to engage in animal research. Not in an abstract or hypothetical scenario, but a rather concrete one where lives are at stake.

HUMAN ABILITY TO CHALLENGE NATURE AND SUFFERING IS UNIQUE

Humans can transcend their biological lives in ways that other animals cannot. Relevant to this discussion is the fact that humans are unique in their ability to study and understand nature, including the basic biological principles underlying life and disease processes. We have the unique ability to store and accumulate vast amounts of knowledge in perpetual form, securing benefits to all future generations, challenge nature by means of technological might and, in short, improve well being of all living creatures on the face of the planet.

Our abilities also carry a moral burden, as we often find ourselves having to make difficult decisions concerning that trade off human and animal life. As a concrete example, consider a patient with severe aortic stenosis, which has a mortality rate of approximately 75% 5 years after diagnosis. The patient's life can be saved by replacing the valve in his heart with one from a pig. Is it morally permissible to carry out such a procedure? In some respects, we are facing a burning house scenario: it is either a pig or a human. Those that consider the moral status of the pig equal to that of the patient must effectively condemn the patient to death for the same reasons we would not take the heart valve of another human as a replacement.

Another example comes from recent advances in neonatal care. The rate of premature birth has increased by 36% since the 1980s. Most babies born before 37 weeks of pregnancy are premature and are at risk of complications. In the United States alone, approximately 13% of babies are born prematurely and will spend the first few days of their life in the neonatal intensive care unit. Among babies born before the 34th week, 23,000 of them each year will suffer from respiratory distress syndrome. These babies lack a protein in their lungs (called surfactants) that keep the air sacs in the lungs from collapsing. If left untreated, these babies would die.

Surfactants were discovered, and their chemical composition was analyzed by experimentation in dogs.⁴⁵ The fruits of this research were translated into the treatments using surfactants in the 1990s, which reduced the death of babies from respiratory distress syndrome by approximately 50%. In other words, slightly more than 10,000 babies are saved every year, in the United States alone as a result of surfactant replacement therapy.⁴⁶ This amounts to more than 1 baby per hour. The use of the dogs in research produced these enormous benefits that are realized each hour when a proud mother goes back home carrying her newborn baby instead of doing so empty handed. Those that consider the moral status of dogs equal to that of human babies must have declared such research unethical.

When scientists are confronted with the incredible suffering caused by disease on one hand and faced with our proven ability to challenge such maladies on the other, we feel a moral imperative to act. True; under normal circumstances, nobody would want to inflict unnecessary harm to animals. But to the patients and their families, these are no normal circumstances; the scientist, in some cases, cannot see any other way to help them but to experiment in animals. Such is our plight, which was recognized in the words of Charles Darwin⁴⁷ when he wrote to the London Times:

[...] I know that physiology cannot possibly progress except by means of experimenting on live animals, and I feel the deepest conviction that he who retards the progress of physiology commits a crime against mankind.

UTILITARIAN CONSIDERATIONS

What is the likelihood any 1 experiment will advance our knowledge and produce important benefits? Given our preceding discussion of the scientific method, it is clear there is a problem with deciding the moral worth of scientific work based on its consequence, because that the outcome is initially unknown.

Singer, for example, justified the use of monkeys in the development of a therapy for Parkinson's disease in a recent encounter with neuroscientist Tipu Aziz, who was explaining to Singer that⁴⁸:

To date 40,000 people have been made better with this [Parkinson's therapy], and worldwide at the time I would guess only 100 monkeys were used at a few laboratories.

To which, Singer replied:

Well, I think if you put a case like that, clearly I would have to agree that was a justifiable experiment. I do not think you should reproach yourself for doing it, provided—I take it you are the expert in this, not me—that there was no other way of discovering this knowledge. I could see that as justifiable research.

The problem is that this is a *post hoc* justification. There was, of course, no way for anyone to know the experiments would yield such important benefits. One must ask how a utilitarian would respond had he/she been asked to approve the experiments before they were conducted.

Individual experiments cannot be justified based on utilitarian considerations unless we allow for some probabilistic calculus of cost/benefits. This is, as a matter of fact, the task performed by the Center for Scientific Review at the NIH, where a panel of experts evaluate and recommend scientific proposals so that our society can fund the most promising research as judged by our best scientific minds. This system is

the one that has allowed the development of cutting-edge drugs and cures for conditions that would have surely killed our parents and grandparents.

The relevant question for the utilitarian is, has animal research so far, as a field, produced sufficiently important benefits as to be justified? I honestly believe that any person with basic knowledge of medical history must answer this question in the affirmative. Recall what medical science was merely a couple of generations ago: a visit to a physician might have resulted in a recommendation to induce vomiting, diarrhea or, more commonly, bleeding. Diphtheria, mumps, measles and polio were common and untreatable. Life expectancy in the United States was less than 50 years; it is now close to 80 years. Animal research was an integral part of these past achievements. Our generation benefits from treatments and medicines that our parents and grandparents only dreamt about. Moreover, our children, grandchildren and all future generations will benefit as well. Thus, any utilitarian calculation of the benefits will show that they are not merely astronomical, but infinite. Harms, of course, must also be counted, including the life of the animals used and any negative outcomes that might be attributed, in part, to the use of animals in research. When the costs and benefits are tallied, I believe we must agree animal research has been justified. It is doubtful this picture and our assessment of the work will change substantially in the near future.

WHAT ABOUT MARGINAL CASES?

We are often challenged to spell out the criteria that makes some experiments justified in some animals but not in some humans that might have comparable interests. These criteria, we are explained, must be evaluated for each individual subject^{30,35,37,49} (so-called moral individualism⁵⁰). No matter what criteria are selected, it is likely we will find some humans (the senile, the severely mentally impaired or the minimally conscious patient) who would qualify for invasive research. We are then asked to be logically consistent and accept that we should also be experimenting in these human patients along with the animals.

First, I note that no matter what criteria are selected, the moral status of a rock, a dead cat, or human remains should all equal to each other (they are all inanimate objects with no interests of their own). Although nobody will object to a child playfully kicking a rock, most will not feel comfortable with him kicking a dead cat for his or her amusement or using human remains in an art project for school. Clearly, there are relational properties that come into play about how to judge the moral status of deceased organisms or inanimate objects. We believe that we owe dignity to the deceased cat and human in ways that do not apply to the rock. Conversely, special relations call for some inanimate objects to have moral status because of their importance to humans, such as the Church of the Nativity, the Western Wall or the Black Stone in Mecca. Damaging such inanimate objects would certainly cause much human suffering, and consequently, these objects have higher moral status than others. As I discuss below, such relational properties might be integral to the definition of human kind as well.⁵¹

Second, if we insist on moral judgments being based on properties at the individual level alone, the resulting theory is not really practical. Moral individualism is a necessary condition to pose the marginal case scenario. But are we ready to evaluate every single individual we encounter in life to decide on his or her moral status? Are we to assess the child

now crossing the street? And the dog walking along? And the squirrel that just rushed in front of our moving car? Consistency demands that we do, but applicability demands that we do not. A consistent moral theory that cannot be practiced has little value.

Instead, our daily behavior is aided by organizing the world into different categories (or kinds) of living beings and our assessment of their interests and moral status.³⁷ Our brain's ability to quickly recognize species membership makes such a kind a rather natural choice. This enables us to immediately recognize the interests of the squirrel running in front of our car and avoid running it over (there is really no need to assess the individual interests and moral status of this one particular squirrel). Thus, we must understand that interests of living beings can be assessed in most cases based on the normal life of its species.⁵¹

HUMAN RELATIONSHIPS ARE UNIQUE: THE HUMAN FAMILY

I happen to be writing this article as the world anxiously awaits the rescuing of 33 miners trapped in Chile. They have been entombed underground for 70 days, under 700 m of hard rock, in damped and hot conditions, in nearly complete darkness and physically and psychologically weakened. An estimated 1 billion people have been following the fate of a truly insignificant number of individuals. Thousands across many countries have mobilized to make the rescue possible. The economic cost of the operation is unknown, likely exorbitant, and appropriately irrelevant.

As miners start coming out of a small duct, the spectacle is surreal. Earth appears to be giving birth anew to those that a couple of months ago were presumed dead. Across the planet, people wipe tears of joy and celebrate the unique value of human life. We feel good because, for once, we acted according to what we think is the proper moral status of human life—the gold, machinery and financial cost is insignificant compared with the life of the miners. It is in these extreme circumstances that the human race is at once redeemed and when John Donne's words acquire extra meaning:

No man is an Island, entire of itself; every man is a piece of the Continent, a part of the main; [...] any man's death diminishes me, because I am involved in Mankind; And therefore never send to know for whom the bell tolls; It tolls for thee.

It is here, then, that we realize that any moral theory that includes relational characteristics among human beings sets human (kind) apart in a unique way. And this argument has been articulated previously. It is accepted that we might be morally justified in giving one's immediate family higher moral status because of our special relations. Kittay⁵² has argued that species membership can be considered an extension of such family and community membership concepts, agreeing with the notion that, "As humans, we are indeed a family."

ASSUMING RESPONSIBILITY AND STEWARDSHIP

Feelings of embarrassment and guilt are understandable responses to any emergent recognition of the unique moral status of human life. Embarrassment because innumerable animals, even entire species, have been wronged by our disregard for animal life and the environment. Guilt because we abhor discrimination, which makes us prone to misconstrue factual statements about evolutionary biology and interpret any

implication of unequal moral status as an expression of human arrogance, bias and prejudice.

However, no amount of denial, guilt or embarrassment can erase or blur our differences. Declaring equality is not a remedy. To the contrary, a responsible and sensible sharing of the planet among all its inhabitants will result the sooner we acknowledge our differences. Accepting that evolution has put us in a place to be the stewards of our planet, its environment and all living creatures within it, carries a tremendous responsibility that we must accept and face.

CONCLUSION

The contributions of animal research to medical science and human health are undeniable. Scientific expertise, consensus and facts on the use of animal research must be weighed accordingly to have an honest, public discussion. When the majority of scientists see the work as scientifically justified, and so do the many professional medical and scientific organizations, the expert views cannot be simply dismissed based on wild claims of ulterior motives, self-interest and conspiracy theories.

Why is the use of animals in scientific experimentation morally permissible? In my view, it is because the moral status of animals is not equal to that of humans and because opting out of the research condemns our patients (both animal and human) to suffer and die of disease. Stopping the research would be, as Darwin correctly judged, a crime against humanity. I have come to appreciate the compassion animal activists have toward animals. Paradoxically, this compassion does not seem to extend to human patients. Hopefully, animal activists will come to accept that our work is driven similarly by an honest attempt at advancing knowledge and alleviating suffering and disease in the world.

I reject moral theories that posit all-or-none moral status for all living organisms. I identified the existence of moral theories that admit degrees of moral status, which are compatible with the practice and regulations of animal research (such as the sliding scale model). Thus, the responsible, regulated animal research with the goal of advancing medical knowledge and human health can be morally justified by a spectrum of existing theories.

The public must know that all those participating in animal research recognize our moral obligations to the welfare of the animals, to reduce the number used and the amount of suffering involved, and the need to develop alternative methods. Such recognition is embedded in our regulations (the Animal Welfare Act and NIH guidelines) and in specific federal programs that are designed to fund the search for alternatives to animal research. No doubt regulations and compliance systems can continuously be improved. Our society could also benefit by holding regular discussions about the science of animal cognition, and how such data could be used to promote animal welfare and provide guidelines as to the type of experimentation we deem permissible in different species.

Scientists have regularly spoken up in defense of animal research.^{2,10,53,54} I now add my voice and encourage other scientists to share their opinions on this important topic. I trust that funding agencies and our public health officials will also find their participation in public dialog pertinent. The same applies to the many private medical foundations and patient groups that support the responsible use of animals in biomedical research. At stake is nothing short of the future health of the nation and our children.

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