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Articoli

Ethics and Animal Experimentation. The Relevance of Beauchamp and DeGrazia's *Principles*

Etica e sperimentazione animale. La rilevanza dei Principi *di Beauchamp e DeGrazia*

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ABSTRACT

In a perspective that assigns non-human sentient beings an important moral status, animal experimentation appears justified only when it is a necessary and sufficient condition to preserve our health, namely when it is the only means to achieve this goal (at least in principle the greater cognitive, emotional and social complexity of human beings would seem to justify a preference for them over less mentally complex individuals in dilemmatic situations). My paper examines Beauchamp and DeGrazia's recent book on Principles of Animal Research Ethics, which, by developing and integrating the old conception of the Three R's, helps us to identify the specific moral rules that must govern scientific research involving animals.

ABSTRACT

In una prospettiva che assegna agli esseri senzienti non umani un importante status morale, la sperimentazione animale appare giustificata solo quando è condizione necessaria e sufficiente per ottenere risultati rilevanti per la nostra salute, ossia quando è l'unico mezzo per conseguire questo scopo (la maggiore complessità mentale degli esseri umani può infatti giustificare il fatto di dare loro la precedenza rispetto a esseri meno complessi sul piano cognitivo, emotivo e sociale in situazioni di dilemma). A tal proposito il paper analizza il recente libro di Beauchamp e DeGrazia, Principles of Animal Research Ethics, il quale, sviluppando e integrando la filosofia delle Tre R, ci aiuta ad articolare le specifiche regole morali che devono governare la gestione degli animali nella ricerca scientifica.

KEYWORDS

Animal experimentation
Sperimentazione animale

Moral status
Status morale

Moral principles
Principi morali

3 Rs philosophy
Filosofia delle 3 R

Social benefits
Benefici sociali

Animal welfare
Benessere animale

1. INTRODUCTION

In the last years I have argued in support of the thesis that sentient animals have a significant moral status, namely they have an intrinsic relevance and we have a direct obligation not to make them suffer and not to kill them (Allegri 2015, Allegri 2018). This attribution makes problematic a non-vegetarian or almost vegetarian diet and other uses of animals (for example in zoos, circuses, etc.). However, there is one area in which the reasons of animals defenders are challenged in a stronger way and that is the field of experimentation. In this paper I intend to briefly discuss such a thorny topic in the light of the very recent volume by Beauchamp and DeGrazia, *Principles of Animal Research Ethics*. My aim is not so much to present particularly original conclusions, but to point out the importance of this book in the context of a conception that considers animal testing as acceptable only when it is a necessary and sufficient condition to achieve results relevant to human health.

2. ETHICS AND ANIMAL EXPERIMENTATION: THE SEARCH OF A POINT OF EQUILIBRIUM

According to Hal Herzog the arguments in favour of research are stronger than those supporting any other use of animals (Herzog 2010, 234). It may be so, but every year in the world many million animals die in laboratories (mainly mice and rats, by far the most used in research, both for their fertility and for their rapid generation times) (Herzog 2010, 214). If we accept the thesis that even sentient beings of other species suffer harm from pain and death induced in advance, this numbers can hardly be morally justified. Especially if with the research that determines them are not at stake vital interests of the human being.

This is the case with all experiments for commercial purposes (but also military and psychological experiments to which Singer turned his attention in *Animal Liberation*; see Singer 1990). The economic and scientific interests of man cannot take priority over the lives of other animals. These assumptions have become now widely dominant and have led to practical consequences of considerable importance. From March 11, 2013 in Europe came into effect a total ban on animal testing of cosmetic ingredients or si-

milar, such as lipsticks, rimmell, toothpastes, deodorants, sunscreens etc. A ban extended to imports from non-European countries of cosmetics tested on animals. It seems to me a result of great civilization, that I hope will be a point of reference for other countries that instead continue to "test" such products on the skin of sentient beings.

More problematic for animal rights defenders is the theme of medical-pharmaceutical experimentation. But even in this area it seems to me entirely plausible to make a distinction immediately. It is one thing to consider morally justified to harm or sacrifice the life of animals for fundamental human interests (for example discovering the vaccine against a serious disease that causes the death of humans); another is to consider it justified for less urgent human interests. I would therefore say that it is not enough that it is medical-pharmacological and non-commercial research to justify the use of animals. It is necessary that vital human interests are at stake. And the moral legitimacy of experimentation remains excluded if there are other means to safeguard human life equally (at the same level). Namely, experimentation on animals should not only be *a* means to achieve results relevant to human health, but *the only means* to achieve this goal. In other words, experimentation must not only be a *sufficient* condition, but also a *necessary* condition to preserve our health. In such an eventuality it is more difficult to deny moral justification to research with animals. From this point of view, an *a priori* absolute closure does not appear convincing, because at least in principle the greater cognitive, emotional and social complexity of typical human beings would seem to justify a preference for them over less mentally complex individuals in dilemmatic situations.[1]

But, although expressing in absolute terms the prohibition on the use of animals for research purposes seems excessive, a strong *prima facie* ban remains against animal testing. It is not a permissible *act qua talis*. On the contrary, it is in itself impermissible, and it would be desirable never to do so. It can be justified, I repeat, only if it is a necessary and sufficient condition to save human lives. But does it satisfy both of these two clauses?

In this regard we are far from reaching an unanimous opinion. The data are conflicting, as are the opinions of the scientific community.[2] Already on the parameter "sufficiency" legitimate doubts arise. On several sides there is a tendency to diminish the relevance of the use of animals for the improvement of our health conditions. For example, organizations such as the *Physicians Committee for Responsible Medicine* and the *National Anti-Vivisection Society* argue that many advances in our health are actually the result of a marked improvement of the hygienic-sanitary conditions and food, to which we owe, even before the introduction of vaccines, the large decrease in infant mortality (Herzog 2010, 214-217). In addition, many scholars point out the difficulty of applying the results obtained on mice to humans, highlighting their failures. Between the two species there are undoubtedly biological similarities (we have more or less the same number of genes, about twenty-two thousand, we share the same basic metabolic processes etc.), but also huge differences (our brain weighs a thousand and five hundred times theirs; our metabolism is seven times slower than theirs; our evolutionary history has been divided from their sixty million years ago, at the time of the dinosaurs, when we have the last common ancestor) (Herzog 2010, 216-218). For example, mice do not seem to be appropriate experimental models for human immune system deficits. While rodent immune disorders can be cured with dozens of therapies, very few of these can bear positive fruit in humans (Davies 2008). Even greater problems are found in neurology, where an emblematic case is that of amyotrophic lateral sclerosis (ALS), a pathology that is currently incurable. It has been found that several drugs (at least a dozen) that had given good results on mice with ALS, prolonging their lives, have proved completely ineffective when applied to humans. An even worse performance was provided by a drug that proved to be valid in several tests on mice and that instead aggravated the conditions of human patients (Schnabel 2008).

From the opposite side, however, it is argued that, despite the importance of factors such as the improvement of hygienic-sanitary conditions and the problems of the transition from animals to humans, most of the progress in contemporary medicine is due to animal experimentation. Without it, we would not have vaccines (which also protect the animals themselves from rabies, distemper, etc.), antibiotics, transplants. Than-

ks to experimentation on mice, we have achieved epochal results in immunology, cancer research, cardiovascular diseases, etc., discoveries marked by the award of many Nobel Prizes. From studies on these animals we have learned the vast majority of things we know about the functioning of mammalian genes (Roberts, Threadgill 2005). With regard to the difficulty of transferring to humans the data obtained from research on other sentient beings, the defenders of animal experimentation observe that it is not so much the extrapolation from a single animal species to humans that counts, but rather the possibility of a series of observations in many animal species that allows us to build a catalogue of knowledge useful to understand if we should conduct an experiment on humans and, if so, what are the possible toxic and therapeutic effects to take into account.

But even if we admit this and accept that fundamental scientific results have been achieved through animal testing, the problem is whether there are alternative methods today that can enable us to achieve similar progress in research. By asking ourselves this question we move from the topic of animal testing as a sufficient condition to the topic of animal testing as a necessary condition.

Alternative methods are now available and consist mainly of two strategies. The new frontier are the human tissues reproduced *in vitro*, with which one can verify the effects of drugs on metabolism and test the effectiveness of vaccines. Next to the *in vitro* methods is the way of so-called experimentation *in silico*, namely the use of software capable to predict statistically the mode of action and the possible toxicity of a chemical substance by comparison with structurally related compounds of which we already know the outcome.

But the scientific community is in deep disagreement on the thesis that already now (and perhaps even in the future, at least in the near future) alternative methods can entirely be substitutive of the traditional methods that use animals. The utilization of alternative methods is seen by some more as complementary (integrative) rather than substitutive of the usual research. Many scholars in fact point out that methods such as *in vitro* cultures or computer simulations are not able to reconstruct the complexity of an entire organism, whose individual components are not compartmentalized, but interact with each other.[3]

But even accepting this perspective, and therefore admitting that sometimes animal testing is both a necessary and a sufficient condition to preserve our health, i.e. it is the only means of achieving this objective, it is necessary to indicate appropriate moral principles to regulate research in accordance with the thesis that recognizes non-human sentient beings an important moral status. Until now the point of reference for those who on the one hand cared about the fate of animals on the other the needs of scientific research has been the so-called philosophy of the Three Rs (*Replacement, Reduction, Refinement*), an approach formulated at the end of the fifties of the twentieth century by William Russell (a zoologist and psychologist) and Rex Burch (a microbiologist). According to these two thinkers is to adopt a research model, which, while justifying the use of sentient beings, points 1) to replace, when possible, the animals used in experimentation with alternative methodologies and, when it is not possible, to use animals with the lowest degree of neurological development); 2) to reduce the number of animals to the minimum required to obtain scientifically sound data; 3) to refine (i.e. to improve) the procedures in order to minimize the harm and suffering for the animals (Russell, Burch, 1959).

But recent times have brought us an important novelty in this respect. Infact, Beauchamp and DeGrazia's new book, *Principles of Animal Research Ethics*, aims to develop (and, where necessary, correct and supplement) the model that for many years has served as a guide for the ethics of animal experimentation (often considered insufficiently responsive to the moral status of animals by animal rights defenders).[4] It is a text worthy of the utmost attention, written by two of the greatest bioethicists in the world. Beauchamp is the author, along with James Childress, of the most famous handbook of biomedical ethics, *Principles of Biomedical Ethics* (see Beauchamp and Childress 2013). David DeGrazia is one of the leading experts in animal ethics (in addition to numerous articles, see DeGrazia 1996 and DeGrazia 2002). But his contributions are essential in many other sectors of bioethics (see, for example, DeGrazia 2005, DeGrazia 2012). Their volume is accompanied by a critical commentary of important scholars (Larry Carbone, Frans

de Waal, Rebecca Dresser, Joseph Garner, Brian Hare, Margaret Landi, and Julian Savulescu), covering the following areas: biomedical research, veterinary medicine, biology, zoology, comparative psychology, primatology, law, bioethics, philosophy.

3. THE IMPORTANCE OF BEAUCHAMP AND DEGRAZIA'S PRINCIPLES

The objective of Beauchamp and DeGrazia's book is not to replace the model of Russell and Burch «but to add complementary content for animal research ethics that the 3 Rs framework fails to provide» (Beauchamp and DeGrazia 2019, 3). Beauchamp and DeGrazia identify significant gaps in the content of the Three Rs conception of animal research ethics. According to them, «Russell and Burch's principles neglect several important aspects of animal welfare as well as some important considerations pertaining to the human social benefits that justify animal research» (Beauchamp and DeGrazia 2019, 3).

First of all, the Three Rs approach lacks a general ethical perspective, indicating the principles and values that should guide the use of animals in research (Beauchamp and DeGrazia 2019, 3; 2020, IX). Secondly, Russell and Burch's view considers the welfare of animals only in scientific research procedures, when instead it is important to put attention to all relevant aspects of life of animals used in experimentation and therefore also to their well-being outside their use in scientific procedure (for example their welfare in transportation, housing, food, and companionship) (Beauchamp and DeGrazia 2019, 3; 2020, IX, 4, 22). Moreover they set no limits on the duration and severity of damage suffered by animals (Beauchamp and DeGrazia 2020, 22). Finally the Three Rs model «is silent regarding which scientific objectives are worth pursuing in light of their scientific and social importance, their likely costs or risks to human beings, and the expected harms to animal subjects» (Beauchamp and DeGrazia 2020, 22; see also IX, 4; see also 2019, 3).
Beauchamp and DeGrazia aim to fill these three gaps. And they do it with a model based on three fundamental moral norms and two core values, in their opinion able to bring together open-minded representatives of the animal research and defenders of the moral status of animals. The three fundamental moral standards are the following:

«(1) sentient animals have moral status and therefore are not merely tools of research;[5] (2) the only possible justification for (non-therapeutically) harming animal with moral status, including animal research subjects, is the prospect of substantial and otherwise unattainable social benefits; and (3) any permissible harming of animals in research is limited by considerations of animal welfare.» (Beauchamp and DeGrazia 2020, 2-3).

The two core values are *social benefit* and *animal welfare*. On the basis of this small set of moral norms and core values, they present a framework of six moral principles containing three principles of social benefit (The Principle of No Alternative Method, The Principle of Expected Net Benefit, The Principle of Sufficient Value to Justify Harm) and three principles of animal welfare (The Principle of No Unnecessary Harm, The Principle of Basic Needs, The Principle of Upper Limits to Harms). Let's see them in more detail.

1) *The Principle of No Alternative Method* asserts that the use of sentient animals in testing is morally legitimate only if the social and scientific benefits obtained through animals are not achievable through methods that do not use animals. «If, for example, methods that use human tissues, cell cultures, or computer models are sufficient, sentient animals must not be used» (Beauchamp and DeGrazia 2020, 7). This principle expresses the same requirement advanced by the first of the 3 Rs, namely replacement.

2) *The Principle of Expected Net Benefit*, for which, once the first principle is satisfied, we must ask ourselves if the benefits of a research project outweighs its costs. This second principle asserts that a necessary condition for the use of animals in a research project is that it offers an expectation of net benefit for human society, i. e. the perspective of social benefit have to exceed foreseeable costs and risk for humans. Otherwise, «inadequate grounds exist to support a claim that the research is justified and worth pursuing even from a standpoint that considers only human interests – that is, a standpoint that does not take account of the interests of animal subjects» (Beauchamp and DeGrazia 2020, 9).

3) *The Principle of Sufficient Value to Justify Harm* points out that if a research project overcomes the constraints of the first two principles, then it «offers the prospect of a net benefit to human society (as required by the second principle) that is not feasibly available in any other way because there is "no alternative method" (as required by the first principle)» (Beauchamp and DeGrazia 2019, 5). At this point, however, animal welfare comes into play. We must ask ourselves if the perspective of benefit of the research are such to outweigh the harms suffered by the animals used. This principle consents the research only if the answer is positive. In detail, it asserts that «the prospect of a net benefit for human society from a research study must be sufficiently valuable to justify expected harms to animal subjects» (Beauchamp and DeGrazia 2019, 5). The difficult question to be answered is "what counts as sufficiently valuable?". And the answer depends also on the degree of moral status that we must attribute to animals. In this respect the authors assert that «Our framework rests on the assumption that animals have a significant level of moral status or inherent moral importance, but that assumption leaves open exactly how much and which levels of protection are justified» (Beauchamp and DeGrazia 2019, 5). This makes it problematic in some cases the application of the principle. About it Beauchamp and DeGrazia state that «the only sensible procedure to get an answer to this question is to leave it open for debate in review committee meetings and comparable deliberative settings» (Beauchamp and DeGrazia 2019, 5).

4) *The Principle of No Unnecessary Harm*, for which «animal subjects must not be harmed unless a particular harm is necessary for and morally justified by scientific purposes» (Beauchamp and DeGrazia 2019, 5). This principle is similar to the third of the 3 Rs, namely refinement, but Beauchamp and DeGrazia make their principle wider, because it is not limited to scientific procedures. Beyond that, it requires, in addition, the minimization of harms associated with the feeding, housing, and transport of animals.

5) *The Principle of Basic Needs* is an integration of the previous principle. For this principle in the research activity it is necessary to satisfy the basic needs of the animals used. By "basic needs" Beauchamp and DeGrazia mean the general living conditions of animals that are relevant for a good quality of life. They include, for instance, nutritious food and clean water, freedom of movement with adequate space etc. This principle fill a gap of the 3 Rs framework in which «lacks any explicit statement of a general expectation to meet animal subjects' basic needs» (Beauchamp e DeGrazia 2019, 6).

6) *The Principle of Upper Limits to Harms* states that it is necessary to establish a limit on the harm that may be imposed on animals in the experimental procedures. This principle for the authors represents an additional advantage over the three R framework, which provides no limit to the permissible harm. But Beauchamp and DeGrazia assert that the Principle of Upper Limits to Harms can admit some exceptions. They acknowledge that extraordinary circumstances (which occur rarely) may sometimes justify overriding it (social interests of great importance, public health emergencies «such as a highly lethal epidemic for which no effective vaccine or treatment exists», Beauchamp and DeGrazia 2019, 6).

4. CONCLUSIONS

The contribution offered by these principles of Beauchamp and DeGrazia is undoubtedly remarkable. So far «no code or regulatory scheme presents of framework of general principles of animal research ethics together with an analysis of the principles' meaning and moral requirements» (Beauchamp and DeGrazia 2020, IX). I think we can agree with Savulescu who says that «The six principles of Beauchamp and DeGrazia […] are arguably the most constructive step forward in the ethics of animal experimentation in the past fifty years» (Beauchamp and DeGrazia 2020, 127).

However, as Beauchamp e DeGrazia admit, much of this rules are already presents in codes, laws and regulations of the most advanced countries, even if they have not had a sufficient philosophical elaboration. In particular, we find them in European legislation. For example, if with regard to principle 6, the authors note that no limit on permissible harm to animals is foreseen by «US government principles and, as far as we know, every other code guiding publicly funded animal research in the United States» (Beauchamp and DeGrazia 2019, 6). They themselves recognize that this limit is instead provided for by European

Union legislation (Beauchamp and DeGrazia 2019, 6). Such limit is present in the Directive 2010/63/EU on the Protection of Animals Used for Scientific Purposes, Preamble 23:

«From an ethical standpoint, there should be an upper limit of pain, suffering and distress above which animals should not be subjected in scientific procedures. To that end, the performance of procedures that result in severe pain, suffering, or distress [that] is likely to be long-lasting and cannot be ameliorated, should be prohibited[6].»

Beauchamp and DeGrazia's moral assumptions (as the philosophy of the Three Rs), find important confirmations also in the Italian legislation. Already the legislative decree 116 of 1992 stipulated that «The experiments should be carried out so as to avoid unnecessary distress and suffering or pain to animals» (Art. 6). And above all that «experiments […] can only be performed when, for obtaining the result sought, it is not possible to use other scientifically valid methods, reasonably and practically applicable, not entailing the use of animals» (Art. 4). This law has been strengthened by Legislative Decree 26 of March 4, 2014, called to implement the EU Directive 63/2010. Paragraph 2 of art. 1 of the new Decree reproduces, with slight modifications, the aforementioned art. 4 of the Decree of 1992[7]. Paragraph 3 specifies the range of application of the decree. And the reference is precisely to those animals, indicated by Beauchamp and Childress, on whose sentience there are less doubts: vertebrates and cephalopods. Art. 13 reiterates the contents of Art. 1 paragraph 2, specifying that if the use of animals is inevitable, it is necessary to follow the procedures that require the least number of them and "use animals with the least ability to feel pain". In addition, we must try to avoid the death of the animal as the point of arrival of the experiment, but if this is not possible, a death without suffering must be guaranteed. Finally, it should be noted that each Italian university or research centre has set up an ethical committee for animal experimentation (before CESA, now OPBA), whose task is to verify that projects involving the use of animals are ethically justifiable, verifying whether there are no alternative procedures for achieving the same results. Or, in the alternative, prescribing the use of as few animals as possible and with the lowest brain level. Only under these conditions projects should be approved. Furthermore, OPBA must check the enclosures and ensure the welfare of the animals staying there.

We are therefore faced with encouraging laws and regulations, which confirm the principles of Beauchamp and DeGrazia and go in the right direction. Waiting for the day when we could do without animals in research altogether.

NOTE

1. I deepened this point in Allegri (2015) to which I refer.

2. For a defence of animal experimentation, see for example Morrison (2009). For critical voices, see Pound et al. (2004); Giles (2006).

3. For example, «it is not possible to reproduce artificially, *in vitro* or *in silico* and in order to control the variables involved, the complex process of tumor proliferation or metastases. Just as one could not reproduce in a cell culture a myocardial infarction. Or diabetes, Parkinson's, etc. These are organ diseases to which contribute different cells and biochemical processes that can only be studied in an animal» (Corbellini and Dejana 17 novembre 2013, 33). More broadly, see Corbellini and Lalli (2016).

4. The theses of the book are anticipated in Beauchamp and DeGrazia 2019, a paper to which I will make extensive reference.

5. The range of sentient animals includes all (or almost all) vertebrates and cephalopods, thesis that is prevalent in the writings of DeGrazia (see, for example, DeGrazia 1996).

6. About Directive 2010/63/EU now see Pavone 2020.

7. «It allowed the use of animals for scientific or educational purposes only when, for obtaining the result sought, it is not possible to use another method or testing strategy scientifically valid, reasonably and practically applicable, not entailing the use of living animals».

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