The Moral Standing of Non-human Primates: Why They Merit Special Consideration

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Summary — Scientific experiments with non-human primates are viewed very controversially. Those who use non-human primates for scientific purposes contend that the results will be of great benefit to humans. They say that the distress to the animals is minimal and that, therefore, their experiments are ethically acceptable. On the other hand, there are those who oppose non-human primate experiments altogether, due to the close relationship between these animals and humans. In a literature study on non-human primate experiments in fundamental brain research, the outcome of research projects performed over the period of a decade was evaluated retrospectively. Objective criteria were applied both for determining the cost (internationally published distress scores, taking into account distress due to procurement, transportation and housing) and the benefit (evaluating publications that arose from the experiments, citation scores and so forth). Taking the example of electrophysiological recordings in the brain of the awake macaque, this balancing ended up very different from that proposed by the scientists, and did not support the conclusion that the experiments had been ethically acceptable.

Key words: *balancing of distress/benefit, distress scores, ethical acceptability, fundamental research, non-human primates.*

Introduction

In the European Union, every year approximately 10,000 non-human primates are being used for experimental and other scientific purposes. The species most frequently used are macaques, such as rhesus monkeys and long-tailed macaques, but marmosets, vervets, squirrel monkeys, baboons and chimpanzees are also used. The more that is learned about non-human primates, humankind's closest relatives in the animal kingdom, the more it becomes evident that the differences between humans and the non-human primates are only small. True qualitative differences do not exist at all. Non-human primates are highly sentient animals with a high degree of consciousness.

Non-human primates are being used in basic research when severe and incurable human diseases such as Parkinson's disease, Alzheimer's disease, and schizophrenia and other psychiatric diseases are investigated. Infectious diseases are also studied with these animals, e.g. infections with HIV or hepatitis A and C, and also, recently, BSE. Other areas of basic research in which non-human primates are being used are the fields of neurophysiology, especially brain research, and reproductive physiology. Non-human primates are also being used in applied research for the development and testing of pharmacological products and vaccines.

Those who are in favour of using non-human primates in research argue that these animal species are especially well-suited for the tests because of their similarity to humans, and, therefore, the results of the experiments can better be extrapolated to the situation in humans. On the other hand, scientists who oppose the use of non-human primates argue that it is exactly the similarity between humans and the non-human primates that leads to the inevitable conclusion that procedures that would be unethical if performed on humans, for the same reasons, should not be performed on non-human primates.

Principles for Ethical Evaluation

The German *Animal Welfare Act* (1) requests an ethical evaluation of the acceptability of animal experiments on a case by case level. Article 7/3 states:

Animal experiments are only permitted if the expected pain, distress or damage to the experimental animal is ethically acceptable in relation to the purpose of the experiment.

Such an ethical balancing is requested as part of the German licensing system, which is mandatory for experiments performed in the area of fundamental research. It is also relevant in the notification system, which covers tests that are required for legal purposes; e.g. for the safety testing of drugs or chemicals. However, there is no official guidance on how to determine distress to the animals or benefit from the experiments.

Therefore, it is unclear whether the principles of Article 7/3 of the German *Animal Welfare Act* have actually been met when experiments are performed. In pursuance of this question, Rusche & Apel (2) have analysed if the scientists' balancing of the expected distress and benefit of experiments can be confirmed retrospectively. In this study, all experiments from the area of fundamental brain research were evaluated that had been performed during a ten year period by scientists who currently work at the University of Bremen. The material gathered was mainly publications by the scientists in scientific journals. This information was supplemented by quotations from interviews that the scientists gave in the media. Licence applications are confidential in Germany, so could not be used. In the following section, the outcome of this study is presented.

Aspects to be considered in evaluating the distress to non-human primates

For a comprehensive evaluation of the distress inflicted upon laboratory animals, all aspects of the life of the animals that give rise to concern must be taken into account (3). These include distress due to acquisition, due to accommodation and due to the experimental procedure itself.

With regard to the acquisition of non-human primates, it must be kept in mind that wild-caught primates continue to be used for experimental purposes. These animals are not accustomed to living in laboratories and suffer from increased distress due to the profound change in living conditions after their capture. Additionally, they must endure a long and stressful voyage to their countries of destination, mainly under very confined conditions. Frequent casualties that occur both during capturing and during transport increase the cost of wild-capturing non-human primates. However, purpose breeding of non-human primates also gives reason for concern, since breeding colonies are regularly replenished by wild-caught animals. Many breeding establishments are located in the countries of origin. Often, they house the animals under very poor conditions. Here, again, distress and loss of animals due to long transportation must be considered when determining the cost of an experiment conducted with these animals (4).

It is difficult, if not impossible, to house non-human primates in laboratories in a manner that can adequately fulfil their basic ethological and physiological needs. Non-human primates are highly social, intelligent, active animals that require social contacts in stable, harmonious groups and a complex, challenging environment that provides meaningful activity. In many instances, the housing conditions alone pose considerable distress to these highly active animals (5).

Last, but not least, distress caused by the experimental procedure must be evaluated on a case by case basis, including all parts of the procedural protocol, in order to achieve an objective scoring. Different institutions have published a number of distress catalogues (6, 7). Even though specific procedures might be classified differently in different distress scores, their use helps to set the distress evaluation in an objective frame.

Aspects to be considered in evaluating the scientific benefit of non-human primate experiments

There are no official criteria for the determination of the benefit of an experiment. In addition, few publications exist on this subject. In the following section, the concept of the ethical balancing of animal experiments published by Scharmann & Teutsch (8) will be presented, as this article is one of the very few in which an attempt has been made to define objective criteria on how to determine the benefit of an experiment. The authors start out by stating that:

[It] *is to be asked, if experiments in basic research that involve moderate to severe distress are ethically acceptable. . . . Such experiments* [are] *only acceptable if they are of an outstanding and important benefit to humans. If such a benefit is not foreseeable in basic research, for ethical reasons only experiments that involve minor distress to the animals should be permissible.*

For Scharmann & Teutsch, the scientific value of an experiment relates to the benefit of the test results to humans. Their balancing is based upon the question of, "how soon and how likely the benefit is expected to become available". If the outcome of the experiment and time necessary to come to the expected benefit are not determinable, the scientific benefit is considered to be low. If there are chances that the benefit will become available within a decade, the benefit is considered to be medium. And finally, if there are good chances to come to relevant results within five years, the expected benefit is considered to be high.

Ethical evaluation of electrophysiological recordings in the brain of awake macaques

The experiments encompassing electrophysiological recordings in the brain of awake macaques (9, 10) begin with a training phase, in which the non-human primates have to learn to master certain tasks. This entails the animals being deprived of water in order to make them willing to cooperate.

As a reward for particular responses, they are then given small quantities of fluids. The training phase is followed by an operative intervention under anaesthesia in which the roof of the skull is opened in order to implant inlet tubes so that electrodes can be introduced to specific regions of the brain. During the actual experiment, the non-human primates are strapped in so-called "primate chairs", with their heads screwed into position so that they cannot move them. During the entire testing phase, the animals are again deprived of water. In the experiment, which can often continue for hours, certain responses are rewarded, e.g. with drops of fruit juice. Only on days when no trials are taking place do the animals have access to additional fluids — but again, this is restricted. Once a series of trials has been completed, the animals are either killed and their brain is subjected to a histological examination or they are used for a new series of trials.

In the scientific publications evaluated, no comments were found on the distress to the animals due to the methods performed. When scientists are asked in public how much distress the animals they use are likely to endure, they neither take into consideration distress caused by the acquisition of the animals nor the suffering caused by the housing conditions. Scientists contend that electrophysiological recordings in the brain of the awake macaque cause minor discomfort to the animals.[1] It is argued that introducing electrodes into the brain is not painful to the animals and that their willingness to cooperate during the recordings shows that their well-being is not being impaired. However, a critical evaluation of this estimation reveals that the scientists are underestimating the distress of specific parts of the experimental protocol, as well as omitting other parts.

Even if the animal does not suffer any pain as a consequence of the electrodes being introduced, there are a number of other reasons for classifying such experiments as distressful to the animal. The operative intervention in itself is a source of stress to the animal. First of all, the animal is torn away from its peer group. The anaesthetic itself is both a physical and a psychological stressor. Aftereffects of the intervention, such as possible inflammations around the electrode connector, must also be viewed as a source of discomfort to the animal. The animal has to be kept in isolation for at least the duration of the healing process, if not for the entire duration of the experiment, in order to prevent the implanted device from being damaged by other members of the group. This isolation must likewise be regarded as stressful to macaques, which are very sociable animals. In the distress score of the Scientists Center for Animal Welfare (Bethesda, MD, USA [7]), surgical interventions for the implantation of electrodes would be classified in Category C (of five categories) covering "experiments that involve some significant but unavoidable stress or pain (of short-duration) to vertebrate animal species".

In this distress score, water deprivation of longer duration has to be classified as highly stressful (Category D "experiments that involve significant but unavoidable stress or pain to vertebrate animal species") to the animals, as does the use of the so-called primate chair and the fastening of the head (7). Hampson *et al.* also consider such measures to cause great suffering and anxiety (11). A cooperation that is obtained through depriving the animal of water and strapping it in the primate chair must rather be viewed in terms of the resignation of an animal confronted with a situation from which there is no escape.

Finally, when assessing the degree of stress caused to the animal, it should not be forgotten that most of the non-human primates are killed once the experiment is over in order that a histological examination can be carried out on their brains. However, in distress scores, death is not considered as a relevant issue, provided that the animals are killed humanely.

With regard to the estimation of the expected benefit from the results of electrophysiological recordings, scientists publicly contend anything up to assertions that such experiments will cure schizophrenia, and Alzheimer's and Parkinson's diseases.[2]

[1]*In an interview published in the daily newspaper* taz Bremen*, on April 28th, 1997, the neurophysiologist conducting the electrophysiological recordings stated: "For the animals themselves the experiment does not involve any distress that would be more strenuous than life in the wilderness. Realistically seen, macaques do not really have a smooth life in their natural habitat. They live in groups, in which fights and injuries occur. Monkeys also fall from trees more frequently than one would imagine. There's probably not an older monkey that wouldn't have already survived a fracture or a major injury. Thus, contrary to the romantic illusions that many of us have due to the pretty animal videos, life in the wilderness is far from being a bed of roses". (Translation by U.G.S.)*

[2]*A scientist of the Bremen Brain Research Institute stated in a radio interview (printed in:* Documentation of the 9th Bremen University Talk, What can we learn from brain research, *1997): "Basic research that my colleagues and I are working on is taking different directions. First of all, of course, clinical neurology, psychiatry. There one strives to understand what are the causes for severe brain damages and mental diseases. In this context you have to keep in mind that these mental diseases are amongst the worst and that up to 10% of our society suffer from such diseases, for example schizophrenia, severe depressions, Alzheimer's, Parkinson's, these are horrible diseases. The perspective, to become able to treat these well one day and even cure them is tremendous. In fact, this legitimates everything". (Translation by U.G.S.)*

The respective publications reveal that the results obtained with the electrophysiological recordings cover information on how groups of nerve cells respond when the animal reacts to certain visual stimuli. The question of how specific nerve cells of non-human primates respond under specified conditions can indeed be clarified through such experiments. However, it is questionable whether the experiments could have any relevance for understanding severe neurological disorders in humans. Making use of the Science Citation Index (Thomson ISI®, Philadelphia, PA, USA), an assessment was made of which other scientists quoted the publications on electrophysiological recordings in their own publications. The results of these experiments were mainly quoted in publications that also covered topics from fundamental brain research. There was no evidence that the results of the experiments contributed to the cure or even the understanding of any neurological disorders. Thus, one cannot help suspecting that, if scientists refer to diseases such as schizophrenia, Alzheimer's disease or Parkinson's disease, when arguing for their research projects, these are not objective arguments. They are likely to be used because the public is scared of these diseases on the grounds that people will be more inclined to accept experiments that they would otherwise regard as unacceptable, if they believe that these experiments can make a contribution to lightening their fear. In the advertising sector, playing on fear is viewed as one of the shabbiest methods of persuasion and is banned.

From these discussions, it becomes apparent that the ethical balancing of the acceptability of electrophysiological recordings in the brain of awake macaques will end up very differently according to the estimations of distress and benefit performed by the scientists or performed according to objective criteria. Whereas the estimation of the scientist that the distress is minor and the benefit major leads to the conclusion that the experiments are ethically acceptable, this balancing cannot be confirmed by an objective scoring. When applying the distress categories of published distress scores, the experiments have to be considered as highly distressful, whereas a concrete medical benefit from the results of the experiments cannot be foreseen. According to this classification, the experiments are not ethically acceptable. The finding that there is a discrepancy between the ethical balancing by the scientists and ethical balancing based upon objective criteria is confirmed by similar retrospective studies that evaluate the cost of and benefit from scientific procedures with animals (3, 12).

Conclusion

From the point of view of animal welfare, non-human primates merit special consideration, primarily because of their close relationship to humans. This similarity leads to special ethical problems when causing the animals distress due to acquisition and housing, and due to the experimental protocols. Additionally, a scientific evaluation of experimental results gained through research with non-human primates shows that non-human primate "models" are not the golden key to scientific answers on difficult questions.

Instead of continuing to perform experiments with non-human primates, there should be a critical evaluation of the true cost and benefit of these procedures. Conducting research on brain physiology with non-human primate experiments must be considered as an outdated approach, as modern, non-invasive procedures that can be directly applied to humans now exist for investigating neurological processes in the brain. With such non-invasive procedures, scientists can study how groups of nerve cells respond when human volunteers react to visual stimuli. The use of these methods increases the value of the results of the respective research, since problems of whether they can be transferred from one species to another do not arise. Thus, discontinuing electrophysiological recordings in the brain of the awake macaque and concentrating, instead, on new methods, might lead more quickly and more efficiently to the scientific answers being sought.

In an article discussing the ethical acceptability of surgical procedures in the brains of living non-human primates, Flury offers four hypotheses (13). These hypotheses summarise the essence of the ethical conflict with regard to the use of non-human primates for scientific purposes:

1. *All natural characteristics inherent to humans that would ensure them a moral status are also present in primates.*

2. *If the brain of these animals differs from the human brain to an extent that operations in living animals become legitimate, the scientific value of these programs is questionable. If however the differences are only small, the scientific value is evident but the procedures are not acceptable.*

3. *Only to a very limited extent are humans willing to accept restrictions of their quality of life for the purpose of possibly saving human lives. Therefore it is unacceptable to request the greatest sacrifice imaginable from animals for this same purpose.*

4. *The value of basic research cannot outdo all other moral factors.*

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