

# BioFokus Spezial

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## Non human primates as models in research – The view of scientists



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# From animal physiology to human health

## Between medical challenges, ethical and legal obligations, and unobjective criticism: why animal studies in basic biomedical research are indispensable

Gerhard Heldmaier and Stefan Treue

The daily reports during the past months on the suffering of Ebola patients and their relatives demonstrate just how helpless science, medicine and politics are in the face of this epidemic: vaccines are tested but are as yet unavailable; specific Ebola drugs to treat acute patients do not exist. They do not exist because we lack basic knowledge. We don't know how these viruses penetrate cells, how they annihilate and outmanoeuvre our body's own defences, or which treatment can be employed to destroy them. Entirely new paths of treatment must possibly be found. A treatment involving fragments of genetic material (siRNA) recently successfully cured Rhesus monkeys infected with the related Marburg virus. However, many additional studies on animals and ultimately also on people are required before a successful treatment becomes available.

Medicine is further advanced when it comes to supporting those people suffering from Parkinson's Disease. Deep brain stimulation enables thousands of patients to avoid the movement disorders that are characteristic of this disease. In this treatment, patients are implanted with an electrode deep in the brain, used to stimulate the regions that in Parkinson's have lost their capacity to function normally. This treatment helps to establish a previously unrivalled quality of life for those affected. In this case too, it was basic biomedical research, including studies and a series of tests on monkeys, that laid the foundations for this treatment.

These two current medical challenges demonstrate that research on animals is necessary – and why. Whenever research focuses on functions in the intact organism, studies on animals are necessary, for example in infectious biology, cardio-vascular research, endocrinology and the neurosciences. Overall, research on animals plays only a minor role in the biosciences, numerically speaking. Instead, cell or tissue cultures are ordinarily used to discover information about biochemical processes, signal transfer or gene expression. But animal research has a key function, in that it is the only way to elucidate the significance of these details for the body as a whole.

Animal research is unavoidable and essential for understanding the foundations of life and to achieve advances in medicine. We impair or destroy life in order to learn more about it – a classic ethical dilemma. This dilemma is heightened by the fact that research also has an ethical responsibility towards people to improve medical care with new findings.

This ethical area of conflict is a big hurdle for all those working with animals in science. Nobody performs animal studies without reason. It is a prerequisite to first have a profound scientific question that promises a significant amount of information to be gained, and that can only be answered through research on animals. Of course, the relevant training and professional experience must also guarantee that the animals come under as little strain as possible. These are essential conditions for the success of a research project, and adhering to them is therefore also in the researcher's own interest.

The 3 Rs – “Reduce, Refine, Replace” – formulated by Russell and Burch in their book “The Principles of Human Experimental Technique” in 1959, now form the guiding ethical principle of research around the world. They oblige researchers to reduce the number of animal experiments to the minimum necessary to answer a scientific question, to refine research methods to minimize the animals' strain, and to use replacement methods for research on animals whenever possible.

Added to the ethical dimension is the legal question – over the last few decades, animal protection laws in Germany have been tightened several times. Among the laws now in force across Europe, there is an official approval process in which representatives from animal protection associations also participate. Experiments can only be approved when there are no alternative methods, and when they serve important goals. If approved, protocol must be followed to the letter regarding the animals used. Veterinary inspection officers and animal welfare officers monitor the animals' keeping, the ongoing projects and make sure that protocol is followed. When the project is concluded, a final report must be submitted to the

approval authority. There is no other branch of research with this level of bureaucratic effort and such a dense control network.

Yet despite the central importance of animal research for medical and scientific progress, and despite all the high ethical (self-)obligations and legal requirements, studies on animals are often critically viewed or even categorically opposed. False claims are sometimes made to argue against any possible necessity or value of animal research; scientists are defamed and threatened.

One of the most common arguments against animal research is the claim that it is unnecessary because animal-free replacement methods are available. This is simply incorrect because studies in animals are only permissible when there are no replacement methods. Replacement methods using cell cultures, for example, are continually being improved and re-developed. There has recently been success combining several cell types and generating spatial structures resembling tissue. Replacement methods, however, have system-based limits, as these artificially cultivated cells and tissues cannot completely reproduce conditions in the intact animal. Therefore, the findings gained from these artificial systems must ultimately be verified in the intact organism.

Another frequent argument against animal research is the alleged impossibility of transferring findings obtained from animals to humans. Of course, there is no one-to-one transferability from animals to humans – humans are not mice. Due to the similarity of cell and organ function in mammals, however, it is to be expected that it is fundamentally possible to transfer the principles to humans. Nevertheless, careful consideration and an in-depth knowledge of comparative physiology are required before drawing conclusions for humans from the results of studies on animals.

In the discussion about transferability, it is often suggested that the apparently ethically superior applied research can be separated from the allegedly senseless and therefore indefensible basic research. Ultimately, however, the latter is the driving motor for innovation and a prerequisite for all applications. New knowledge about Nature opens up new paths to us – to help us make better use of the natural resources at our disposal and to improve the medical care of humans and animals. Basic research and applied research are therefore inseparable, and subject to the same ethical challenges.

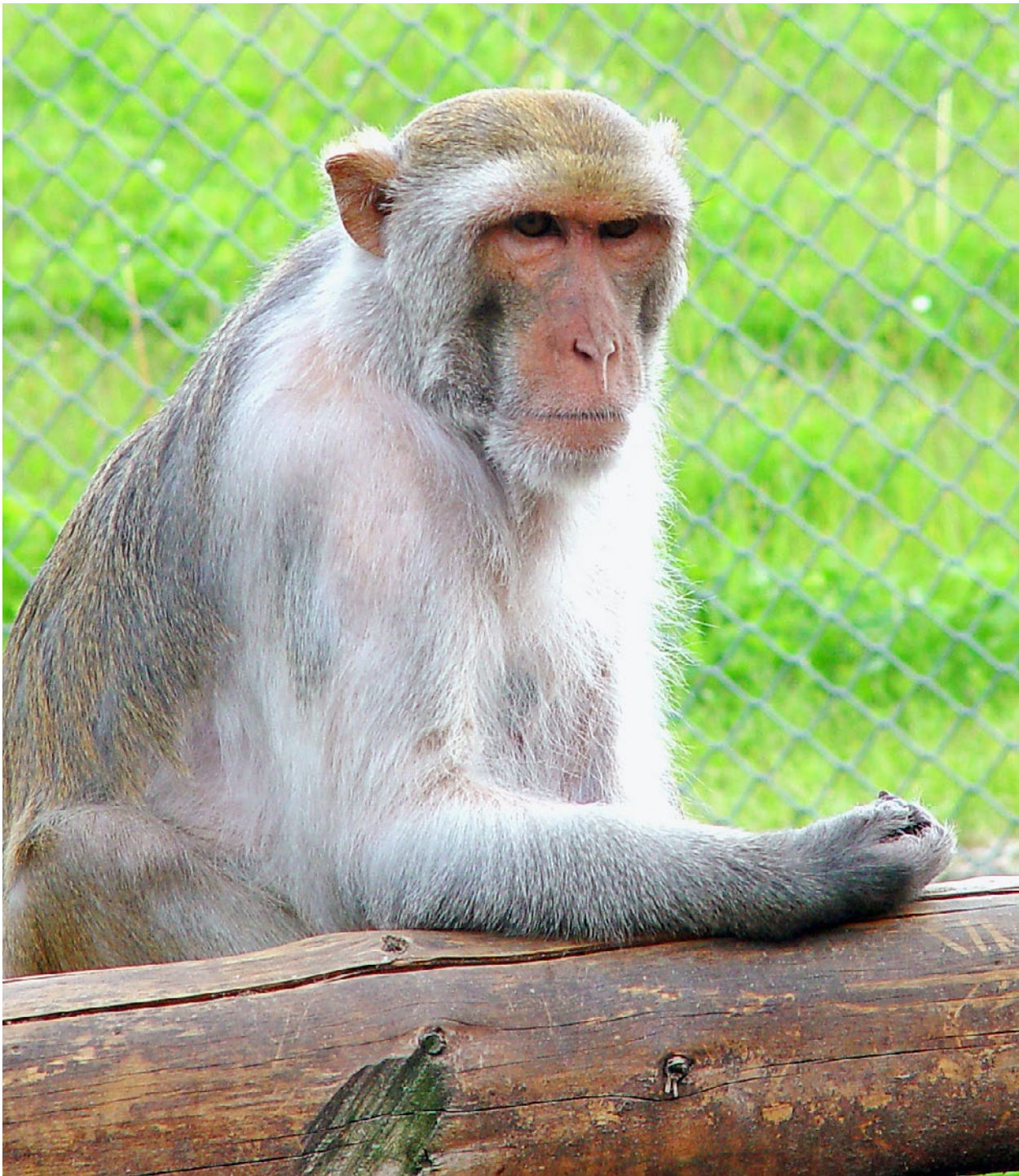
A final argument from opponents to research on animals is that far too many animals are used in experiments. In fact, at present around three million

animals per year are used for scientific purposes in Germany. Contrary to what is often suggested, the proportion of primates is extremely small. Despite the great scientific significance of research on monkeys, they make up only 0.05% of all laboratory animals. Almost three-quarters of the animals used are mice (73 per cent), followed by rats (14 per cent). Half of these animals are used for studies, i.e. the animals are treated, for example, with new drugs and the effect is monitored over days or weeks. The rest are euthanized without undergoing prior procedures in order to obtain tissue for research and to apply replacement methods.

At first glance, three million is a shockingly high figure. According to statistics from the Federal Ministry of Agriculture, however, a total of 760 million animals are used at the same time, mostly for our food. This high figure for annual animal consumption in Germany shows that using animals is accepted in our society. We do not only use them for food; we also kill them as pests, we hunt, we fish, we destroy habitats for agriculture, roads and settlements, we keep them as pets and we use them in research. The number of animals used in research amounts to 0.4 per cent of the officially recorded animal consumption. Is that excessive or reasonable for obtaining scientific knowledge and improving our medical care? There is no catch-all answer for this. Each person must decide for themselves whether they accept this situation or not, and if not, then at least think about it the next time they visit the doctor.

In any case, the number of animals used in research will continue to rise in future despite all efforts to find replacement methods – and despite all criticism. Our improved understanding of the similarities and differences between animals and people and the rapidly progressing development of genetically engineered methods enable us to gain new insights into the foundations of life processes and diseases. This gives us hope for new and better diagnoses and treatments; personalised medicine is a buzzword here, that is, treatments tailored especially to a particular patient.

In this context, scientists, their associations and the pharmaceutical industry must educate the public much more openly and clearly about the questions, methods and results of this type of research. Indeed, numerous reports have been published on the importance of animal research and many researchers studying animals have, over the past few years, arranged open-house days at their institutes or spoken about animal research at events. These sources of information meet with great interest from the public, but reach too few people. The majority of



*Rhesus monkey, German Primate Center, Kurt Fahrner*

researchers have been somewhat reticent in the past, either from a fear of hostility or because they have underestimated the importance of informing the public. In view of the social significance of the topic, this reticence needs to end.

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