

Review

Experimenting on LAB Rodents - Ethical Principles

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REZUMAT

Principii etice ale experimentelor pe animale de laborator rozătoare

Știința se bazează pe studii experimentale. Dezvoltarea științelor medicale s-a datorat în principal studiilor experimentale pe animale de laborator. Cercetarea anatomiei și fiziologiei umane s-a realizat încă din antichitate având ca busolă studiul pe animale. Beneficiile cercetării biomedicale pe animale, deși larg acceptate de către oamenii de știință, au ridicat o mare problemă în rândul activiștilor pentru drepturile animalelor. Ea se bazează pe argumente filozofice bine concepute, cum ar fi faptul că oamenii nu au dreptul de a utiliza animale pentru experimente (Singer, 1975; Regan, 1983), cu toate că aceste studii ar putea contribui la dezvoltarea de noi direcții de tratament sau diagnostic în anumite boli. Cu scopul de a obține condiții optime pentru aceste experimente, pentru a reduce durerea și daunele inutile cauzate animalelor, au fost stabilite norme internaționale pentru efectuarea acestor studii, încă din secolul al 20-lea. Cadrul legal românesc cu privire la etica cercetării pe animale, în scop științific, adoptat în 2006, este o preluare a dispozițiilor și legilor Uniunii Europene, adoptate pentru prima dată în 1986, în Strasbourg și modificate până în prezent, pentru a proteja animalele de laborator vertebrate și nevertebrate.

Cuvinte cheie: principii etice, experiment, animal

ABSTRACT

Science is based on experimental studies. Medical science has known progress to the current state, only with lab animals. Human anatomy and physiology research was performed since ancient times along with animal studies. The benefits of animal biomedical research, although widely accepted by scientists, raised a big problem among animal rights activists. It is based on well-conceived philosophical arguments such as that people have no right to use animals for experiments (Singer, 1975; Regan, 1983), although these studies could help to develop new directions for treatment or diagnosis in certain diseases. In order to achieve optimal conditions for these experiments, to reduce pain and unnecessary damage caused to the animals, international rules have been established for conducting such studies, since the late 20th century. Romanian legal frame

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regarding the ethics of animal research for scientific purpose, adopted in 2006, is a takeover from the provisions and laws of the European Union, first adopted in 1986 in Strasbourg and modified until now, to protect vertebrates and invertebrates laboratory animals.

Key words: ethical aspects, experiment, animal

INTRODUCTION

People have reported themselves differently regarding different species of animals and had different reactions about the animal species. The attention paid to them depends on the role held by them in human life, either as pets or as a method of entertainment, either as research subjects.

Some species enjoy privileges as pets (dogs cats, birds, turtles), others are used to satisfy human native instincts as hunting animals.

In scientific purpose, animals were used either because of the similarities with the human species (i.e. monkeys), either because of their ease of use in laboratory experiments.

From an ethical standpoint, the scientist has to clearly structure the experimental objectives so that the results to justify their use, and not human curiosity.

Experimenting on animals was and will remain a basic stone in experimental research, but it's important to justify the use of inferior species for scientific purposes.

Laboratory animal research ethics tried over time to create the principles of experimentation so as to avoid injury or misuse of some animal species and establish purely scientific or medical purposes in which they can be used.

Historical facts

The great discoveries of medicine - such as the rabies vaccine by Louis Pasteur in 1885 - is done by infecting a large number of dogs and rabbits with this disease and getting diphtheria anti-toxin, in 1891, is made by injecting guinea pigs with toxin diphtheria (Post, 2004)

Toxicological testing on animals experienced a growing path in the 19th and the beginning of 20th century, especially in USA, where laws were more superficial.

Different species of animals have been subjected to biomedical research: from sheep infected with anthrax by Louis Pasteur in 1880, the famous

Pavlov's dog in 1890, the dogs used for isolation of insulin in 1922, until the famous Russian dog Laika which became the first animal to orbit the earth.

With the development and the more increasing number of surgical animal experiments for scientific purposes, activists appeared. The first idea appeared in the 1600s, but only as personal opinions of some scientists. (Pence, 1990)

With the advent of humanitarianism, early proponents of animal rights philosophers appear. William Hogarth published the first monograph „The four stages of cruelty”, referring to the barbaric treatment of dogs and cats that are exposed, and Jeremy Bentham argued that the ability of animals to feel pain gives them their right to moral considerations.

In 1875 the first animal welfare organization appears, the Society for Protection of Animals likely to be used for vivisection, founded by Frances Power Cobbe.

In 1892, Henry Salt condemned any form of animal abuse, in his book “Animal Rights”, except for medical experiments

In 1975 Peter Singer published a paper that supports the idea of animal rights, “Animal Liberation”.

To achieve optimal conditions for animal testing laboratory in purely scientific purposes, it was necessary to develop a practical guide. (S.G. Post, 2004)

Research fields

Animal experimentation, animal research or “in vivo” testing include pure research (such as genetics, developmental biology, and behavioral studies) as well as applied research (such as bio-medical research, xenotransplantation, drug testing, and toxicology tests, including cosmetics testing). Animals are also used for education, breeding, and defense research. The practice is regulated to various degrees in different countries.

Scientists prefer the term of „animal experimentation” rather than „vivisection”. (Yarry & Donna, 2005)

The Encyclopaedia Britannica defines "vivisection" as: "Operation on a living animal for experi-

mental rather than healing purposes; more broadly, all experimentation on live animals" (Anon., 2007).

Here, we present some of the scientific branches in which is compulsory to use animals for experimental studies:

1. Research and morphology
 - Embryogenesis and bio-development;
 - Genetics and genetic mutations;
 - Behavioral research (Yamamuro & Yutaka, 2006).
2. Applied Research
 - Genetic changes induced to the animals for studying different genetic diseases (Rosenthal & Brown, 2007);
 - Study of natural evolution of some diseases: Leukemia, HIV, cancer, other infectious diseases;
3. Xeno-transplantation:
 - Organ/tissue transplant;
 - Study of the immune response;
 - Modulation of immune response in reject grafts;
4. Toxicology
 - Testing different substances for therapeutic purposes;
 - Setting LD50 for pharmacologic substances;
 - Testing drugs;
 - Studying pharmacokinetics and pharmacodynamic characteristics of drugs;
 - Testing acute, sub-acute and chronic toxicity;
5. Testing cosmetic products.

Ethical principles

In 1982, International Association for Study of Pain (IASP) formulated a series of requirements for conducting animal studies:

- Studies must demonstrate the usefulness and potential benefits of animal experiments in understanding the mechanisms of acute and chronic pain;
- If possible, the researcher should try painful stimulus on himself, if non-invasive painful stimuli are being used;
- One has to make possible the assessment of pain levels by observing changes in animal behavior than normal;
- Investigator has to make sure that the animal is exposed to minimal intensity stimulus, in order to make possible the experiment;

- Animals who are suffering from chronic pain, have to receive treatment to relieve their suffering;

Studies of pain that occurs in animals paralyzed with neuromuscular blocking substances:

- Must not be conducted in the absence of general anesthesia, and
- The experiment must be as short as possible, in order to allow a reasonable conclusion,
- The number of animals involved in the experiment has to be as small as possible. (Zimmerman, 1983)

European Convention on the protection of animals used for experimental and other scientific purposes (1986, applied in January 1991, adopted by Romania) has passed through a number of legislative changes in 1992, 1993, 1997 and 2003. Its main purpose was to reduce the number of experiments on animals and the number of animals in these investigations.

The main issues presented in the Convention are as following:

- Animal studies can only be performed in researches meant to prevent, diagnose and treat diseases, in the field of forensic investigations in education, the study of physiological mechanisms and environmental protection (art. 2).
- In all proceedings, methods of anesthesia, analgesia or other methods designed to reduce as much as possible the pain and stress experienced by the animal should be applied.
- Exceptions are the cases where pain reduction methods interfere with research results, and when the applied painful stimulus to the animal doesn't produce physiological changes to its natural state (art. 8).

3r's principle

It's a prerequisite principle for achieving an experimental design and it is a starting point in pre-experimental ethics. 3Rs Principle was introduced by Russell and Burch. (Balls, et al., 1995), and it is part of the pre-experimental ethical design meant to create the basis for the experiment itself. the principle is a compulsory filter to achieve a "human" experimental design.

- Reduction - reducing the number of animals involved in the experiment up to

the limit of statistical reliability and elimination of those experiments with doubtful utility or results,

- Replacement - replacing animal testing methods with other physical, chemical or biological methods, being precise and having the advantage of eliminating variability; or replacement of higher animals with inferior vertebrates or invertebrates. Where possible, the scientist must replace in vivo experiments with in vitro ones, or with mathematical models or computer generated models.
- Refinement - procedures must be designed so as to minimize the incidence and severity of injuries caused to the animals, diminishing animal suffering in the benefit of psychosomatic experimental conditions. (Obrink & Rebbinder, 1999) (Festing, 1994). The experimental design has to include methods of painkilling or euthanasia and has to provide a safe a pleasant environment, in order to reduce as much as possible the distress induced to the animals.

European laws

- European Convention for the protection of vertebrate animals used for experimental and other scientific purposes ETS 123/1986: (Anon., 1986; 1991) was one of the first important meetings in which scientists agreed that the experimental research needs ethical principles to protect the animals used in scientific or medical purposes:
 - This Convention applies to any animal used or intended for use in any experimental or other scientific procedure where that procedure may cause pain, suffering, distress or lasting harm. It does not apply to any non-experimental agricultural or clinical veterinary practice.
 - In this Convention, experimental terms were defined as following:
 - “animal”, unless otherwise qualified, means any live non-human vertebrate, including free-living and/or reproducing larval forms, but excluding other foetal or embryonic forms;
 - “intended for use” means bred or kept for the purpose of sale, disposal or use in any experimental or other scientific procedure;

- “procedure” means any experimental or other scientific use of an animal which may cause it pain, suffering, distress or lasting harm, including any course of action intended to, or liable to, result in the birth of an animal in any such conditions, but excluding the least painful methods accepted in modern practice (that is “humane” methods) of killing or marking an animal. A procedure starts when an animal is first prepared for use and ends when no further observations are made for that procedure; the elimination of pain, suffering, distress or lasting harm by the successful use of anesthesia or analgesia or other methods does not place the use of an animal outside the scope of this definition;
- “competent person” means any person who is considered by a Party to be competent in its territory to perform the relevant function described in this Convention;
- “responsible authority” means, in the territory of a given Party, any authority, body or person designated for the relevant purpose;
- “establishment” means any stable or mobile facility, any building, group of buildings or other premises, including a place which is not wholly enclosed or covered;
- “breeding establishment” means any establishment where animals are bred with a view to their use in procedures;
- “supplying establishment” means any establishment, other than a breeding establishment, from which animals are supplied with a view to their use in procedures;
- “user establishment” means any establishment where animals are used in procedures;
- “human method of killing” means the killing of an animal with a minimum of physical and mental suffering appropriate to the species.

Other important directives which come in help regarding experiments on lab animals are:

- Decision 90/67 / EEC
- Directive 2003/65 / EC
- The revised accommodation and care of animals used for experimental and other

scientific purposes ETS 123rev. / 2006

- Directive 2010/63 / EU

Romanian laws

In Romania, the ethical aspect of experimental animal studies was not entirely foreseen until after the year 2000, but now we are trying to standardize the experiments according to the European laws. The Romanian government approved the following laws:

- Law 305 of 12/07/2006 ratifying the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes adopted in Strasbourg on the 18th of March 1986, and the Protocol amending the European Convention for the protection of vertebrate animals for use in experiments and other scientific Strasbourg, 22 June 1998, signed by Romania on the 15th of February 2006.
- Order No 84 of 30 August 2005 of ANSVSA approving the sanitary veterinary regulation on creating a consultative committee for protection of animals used for experimental and other scientific purposes.
- Law no. 43 of April the 11th 2014 on the protection of animals used for scientific purposes. (Decun & Bodnariu, 2009)

CONCLUSIONS

Controversies on animal studies continue. Discussions continue to be polarized in two directions: restricting research conducted on animals and medical benefits imposed by this research.

Unfortunately, only a few of the members of the ethics committees for animal experiments in different research institutions possess knowledge about ethical principles. This puts the researcher in a position to thoroughly explain what he intends to do in terms of surgical technique, anaesthesia for each animal. This method makes the research to become untenable. (Astarastoe & Trif, 1998)

Emphasis is currently put on "the principle of the three R's": reducing the number of animals used for

experiments, redefinition of research procedures in order to relieve pain in laboratory animals and replacement animal models with alternative methods such as tissue cultures or mathematical models.

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