Understanding ANIMAL RESEARCH

25 July 2011

Primate research in the UK: a background briefing

As our closest relatives in the animal kingdom, monkeys share some characteristics with humans that are not seen in any other animal. Insights into human disease come from studies on many life-forms from yeasts to nematode worms and from fruit flies to mammals, but some questions about complex processes such as reproduction, ageing and the severe conditions that affect the brain can only be answered though research on non-human primates.

The similarity between primates and humans, which makes primates so important to understanding our bodies and diseases, is also the reason why they must only be used for research which is fully justified. It is also essential to ensure that these intelligent and social animals are looked after well, with good housing and stimulation.

Work which involves animals is a small but important part of biomedical research, and of this work a tiny fraction involves the use of non-human primates. Of the 3.6 million animals used in UK research during 2010, only 0.07% (2,649) were primates.

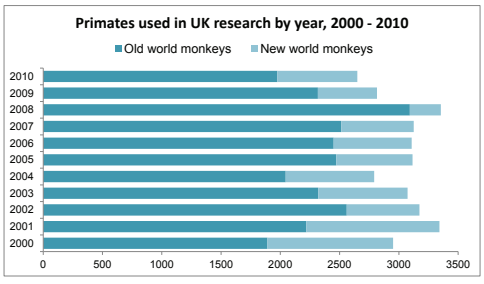
All research involving animals is subject to peer review by funders and ethical review by a local committee. Project licence applications are then reviewed by the Home Office. In addition, research involving primates is reviewed by the NC3Rs to identify and address animal welfare issues.

Types of primates

Primates used in research are divided into Old World monkeys (such as macaques), New World monkeys (such as marmosets) and prosimians (such as tree shrews).

Great apes (such as chimpanzees and gorillas) are the closest animal relatives to humans and have not been used for labaoratory research in the UK for at least 25 years. However, in the studies outlined in *Review of research using non-human primates,* one involved work on captive chimpanzees in the USA and one involved observational studies on wild populations of chimpanzees.

Macaques and marmosets are the most commonly used primates in research, and were used in almost equal numbers in the research reviewed. However, figures for the total numbers of primates used in research show that many more macaques are used than marmosets and other New World primates. Macaques, with human-like immune systems, are more commonly used in toxicity studies and the development of medicines, than primates from the New World. In studies where Old World primates are used, long-tailed (cynomolgous) macaques are now preferred over larger rhesus macaques.



Key research areas involving primates

Projects involving primates are reviewed extensively to ensure that the numbers of animals used are the minimum that will give a meaningful result, and often draw additional data from other models such as humans, computers, cell culture or other animals in related studies.

Neuroscience

Neuroscience produces insights into the function of the human brain and its disease states. Although some characteristics of the human brain are unique, many structures and behaviours are also found in other closely-related species.

The way that neurones grow, develop, and send messages is common to all mammals. In fact, some of these more basic studies can be and are done in rodents and non-vertebrates such as squid. There are, however, advantages to studying the primate brain; its connectivity, size and ageing processes are similar to ours. There are some distinct differences between human and primate brains, for example, the ridges and valleys of the human brain, known as gyri and sulci, are much more pronounced than those of other animals.

Neurological and psychiatric disorders generally involve brain structures that are similar in humans and primates, such as the frontal lobes, so research into such disorders tends to be more dependent on primate studies. Disorders such as depression, schizophrenia, autism and drug addiction are all associated with malfunction of the frontal lobes and their interactions with other parts of the brain. This is also true of head injury, Parkinson's and Huntington's diseases, stroke and some dementias.

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Immunology and infectious disease

Because their immune systems are similar to those of humans, primates are important for studying infectious disease. In *Review of research using non-human primates* most of the studies assessed looked at HIV or malaria, and principally involved macaques, whose immune systems share many characteristics with that of humans.

HIV and AIDS

Initial hopes for the development of a Human Immunodeficiency Virus (HIV) vaccine were dashed when the virus did not cause disease in chimpanzees. However, other primates do have their own species-specific immunodeficiency virus, Simian Immunodeficiency Virus (SIV), and develop an AIDS-like condition when infected with SIV. This is not surprising, as HIV and the SIV have similar genes and properties, both damaging the immune system by attacking T-helper (CD4) white blood cells. There are, however, some important differences. It takes just a few months for SIV infection to progress to simian AIDS as opposed to the many years usually seen in HIV-infected people.

Human studies have shown that most HIV infections occur when the virus crosses mucosal membranes, typically during sex or birth. Further studies, in female non-human-primates, identified the particular cells that are initially infected during heterosexual transmission of the virus. Studying SIV in primates also confirmed that the virus could be transmitted to new-borns through amniotic fluids or breast milk from infected mothers. These discoveries brought opportunities for blocking HIV transmission with medicines, vaccines and other methods such as monoclonal antibodies.

Malaria

Non-human-primates have proved extremely valuable for understanding how malaria infects the body, screening anti-malarial medicines and vaccine development. Malaria is caused by a protozoan parasite that is carried by mosquitoes. Interestingly, although they may harbour the parasite, most primates do not die from malaria. The reason why humans do not resist malaria as other primates do is an important question for researchers to answer. Because primates can harbour infection without becoming seriously ill, they are ideal for research into malarial vaccine and drug development.

Reproductive biology

Most reproductive studies use macaques and marmosets. In the *Review* one study used baboons. Primates are used in this work so that the research is as relevant as possible to the human reproductive system.

Female primates of some species menstruate and undergo menopause in the same way as women. The way that pregnancy is maintained following fertilisation and implantation of the embryo into the uterus is also shared by primates, but not by other mammals.

For example, to understand pregnancy loss researchers have studied pregnancy in primates lacking key hormones alongside studies of normal cultured human uterine tissue. During the first trimester of pregnancy, the production of the hormone progesterone must be switched on and switched off at the right time for the pregnancy to continue. Studies of this process have helped us to understand how the body maintains pregnancy. Another hormone which has been studied in relation to pregnancy loss, prolactin, has an immunoprotective effect when it is found in the womb.

Primate research has been key to the development of treatments for:

- Parkinson's disease: Deep Brain Stimulation
- HIV: anti-retrovirals
- Malaria
- Type 2 diabetes
- Infertility: IVF
- Leukaemia: bone marrow transplants
- Asthma: leukotriene receptor antagonists

Animal welfare and legislation

The use of wild-caught primates is not permitted in the UK without exceptional justification, which is very rarely given. Primates are purchased from captive-bred breeding colonies, and all of the primates covered by *Review of research using non-human primates* were sourced from colonies in the UK, with no need for stressful transportation and quarantine procedures. When primates are used by the contract research industry they are often sourced from overseas, from breeders who meet UK standards for suppliers and are regularly inspected.

Many of the procedures carried out do not necessitate anaesthesia because they are classified as mild, eg taking blood. Indeed, the giving of the anaesthetic and the recovery from it can cause more distress than the procedure itself.

The UK is widely acknowledged to have the strictest regulations of animal-based research in the world and compliance with these regulations is carefully and regularly inspected in all research establishments. The Animals (Scientific Procedures) Act of 1986 requires the individual, the project and the designated place of research to all be separately certified. Suppliers of animals are also strictly regulated. The Home Office carries out multiple unannounced inspections of licensed UK institutions every year.

High resolution images of research animals are available from our online photolibrary at http://www.understanding-animalresearch.org.uk/resources/images_library

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